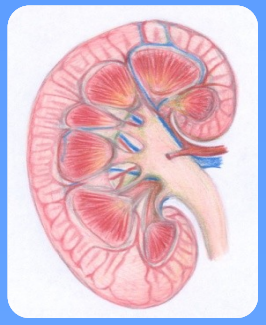
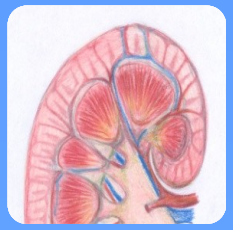
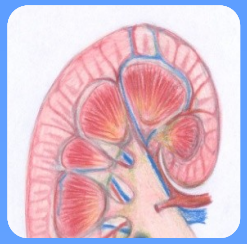


Nephrotic/Nephritic Syndrome 211



Pathology of Nephrotic/Nephritic Syndrome

Hala Kfoury Kassouf MD, KSUF, RCPA, EBP
Assistant Professor of pathology
Consultant Pathologist
King Saud University
King Khaled University Hospital

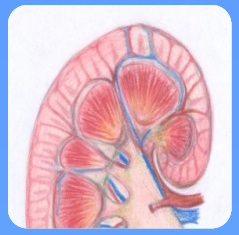


Kidney – functional anatomy compartments:

1. Tubular
2. Glomerular
3. Interstitial
4. Vascular

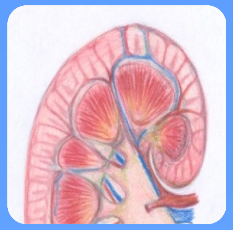
Glomerular diseases

- clinical manifestations



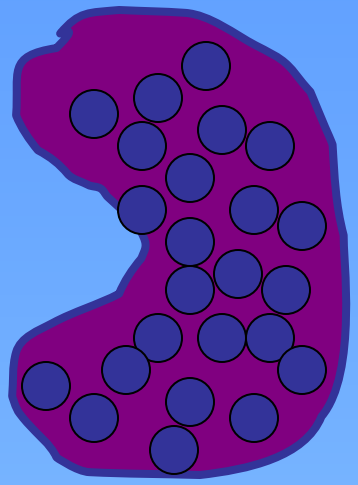
The "glomerular" syndromes

Acute nephritic syndrome	Hematuria, azotemia, variable proteinuria, oliguria, edema, and hypertension
Rapidly progressive GN	Acute nephritis, proteinuria, and acute renal failure
Nephrotic syndrome	>3.5 gm proteinuria, hypoalbuminemia, hyperlipidemia, lipiduria
Chronic renal failure	Azotemia → uremia progressing over years
Asymptomatic hematuria or proteinuria	Glomerular hematuria; subnephrotic proteinuria



Pathology of the kidney

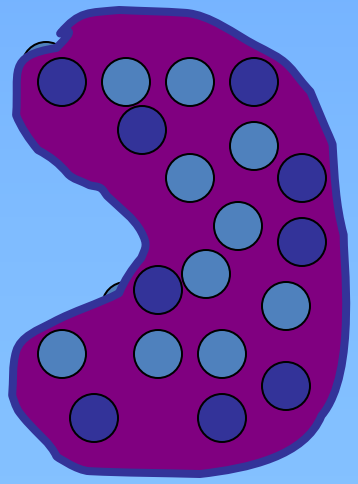
Glomerular diseases



Diffuse :

all glomeruli

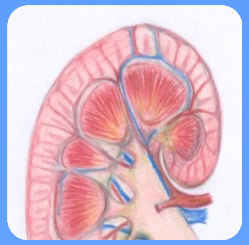
Global



Focal:

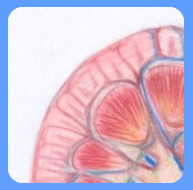
some glomeruli

Segmental



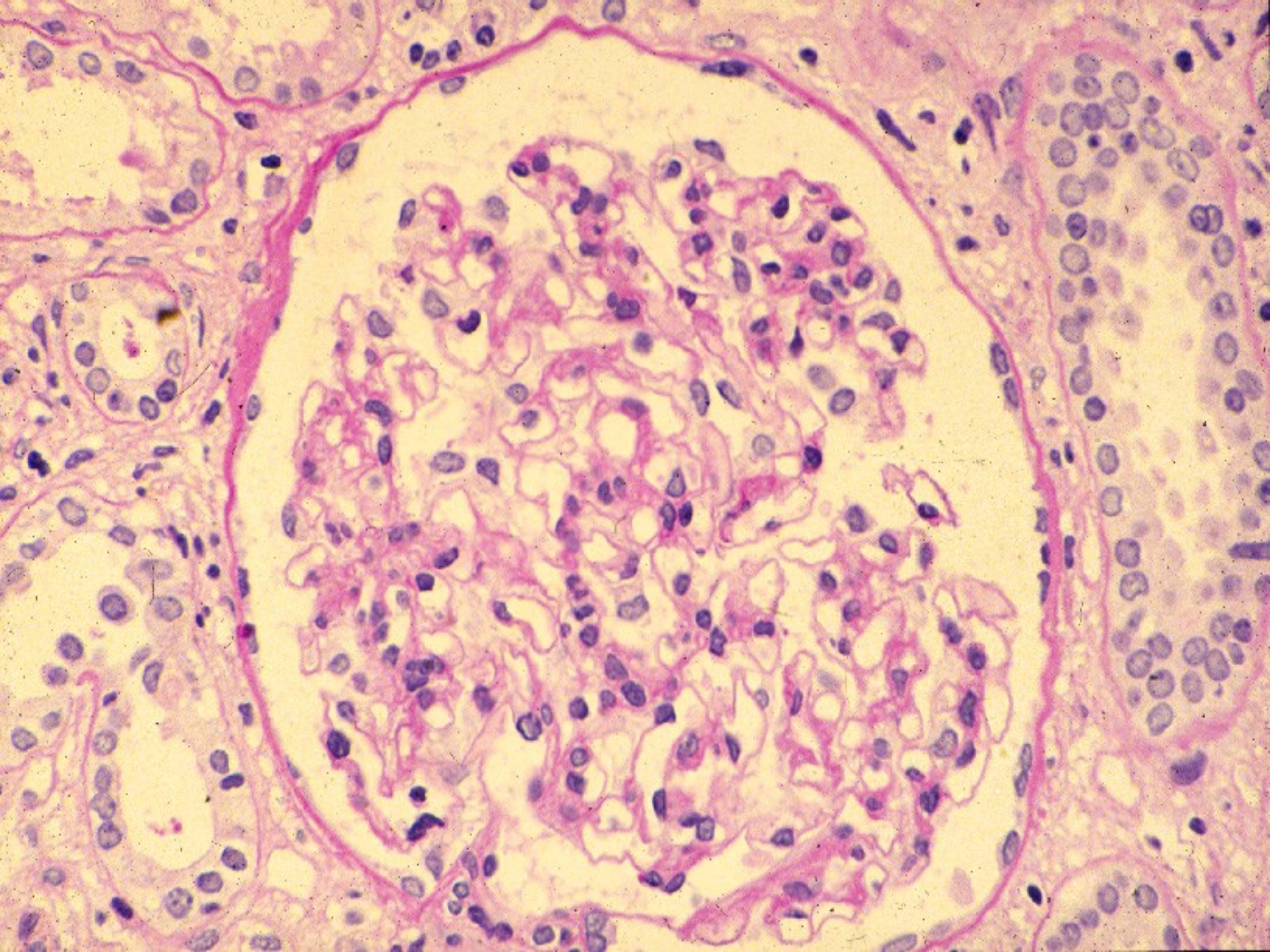
Renal biopsy

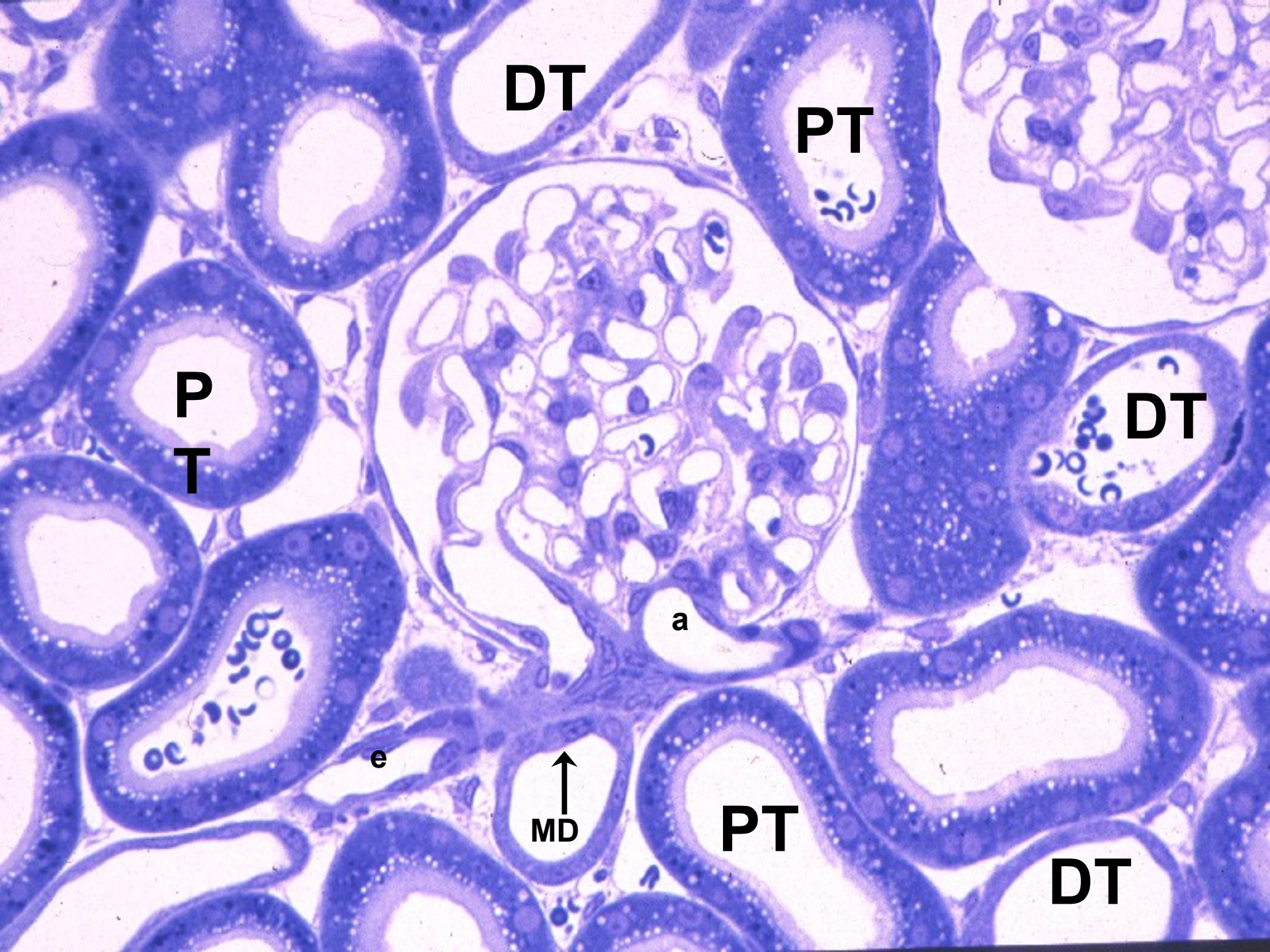
- Different steps are required for a proper diagnosis .
- Adequacy of the biopsy: role of the pathologist .
- What are the different ancillary studies required ?



Percutaneous kidney biopsy specimen

Selected and submitted to:

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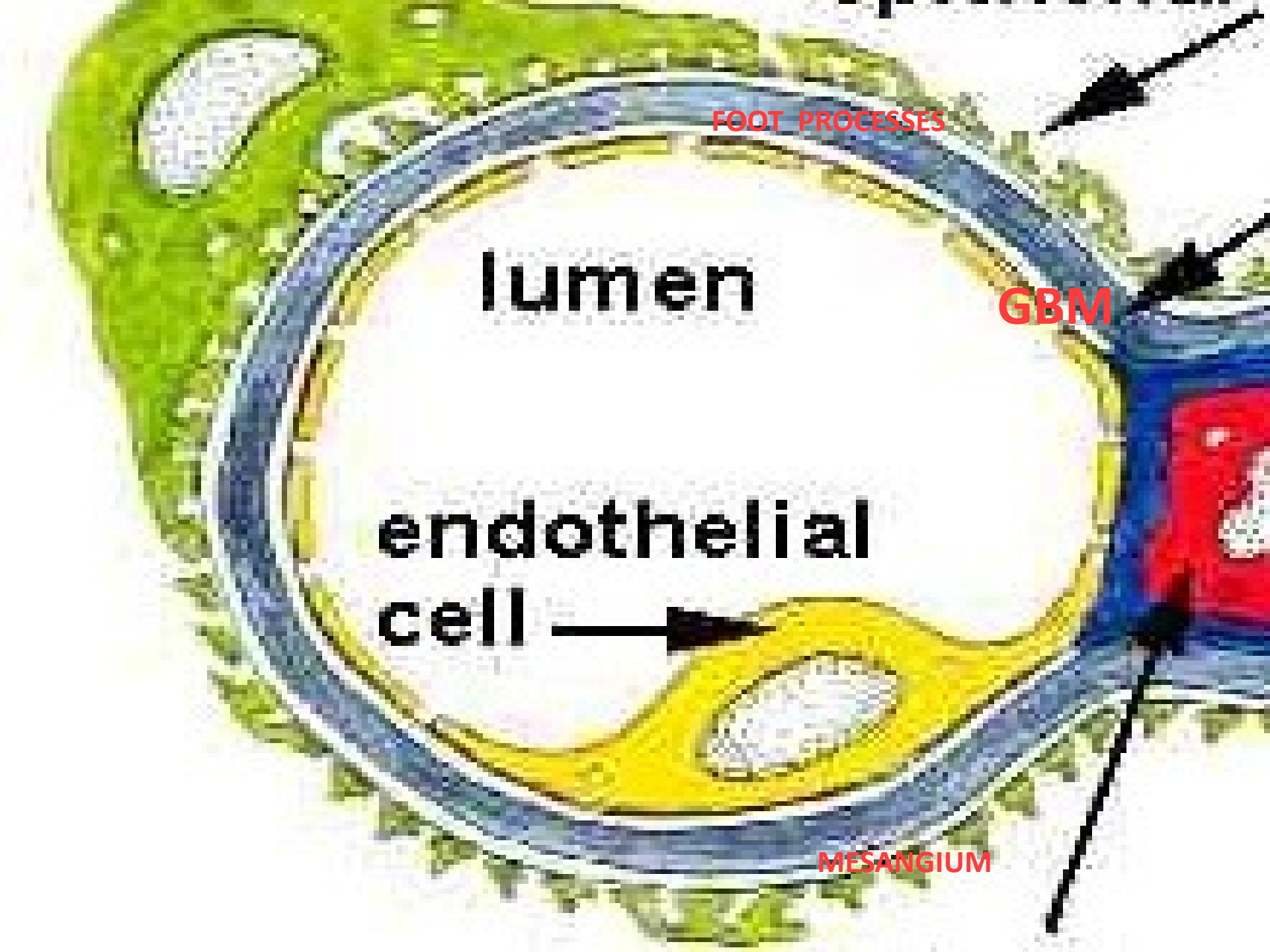
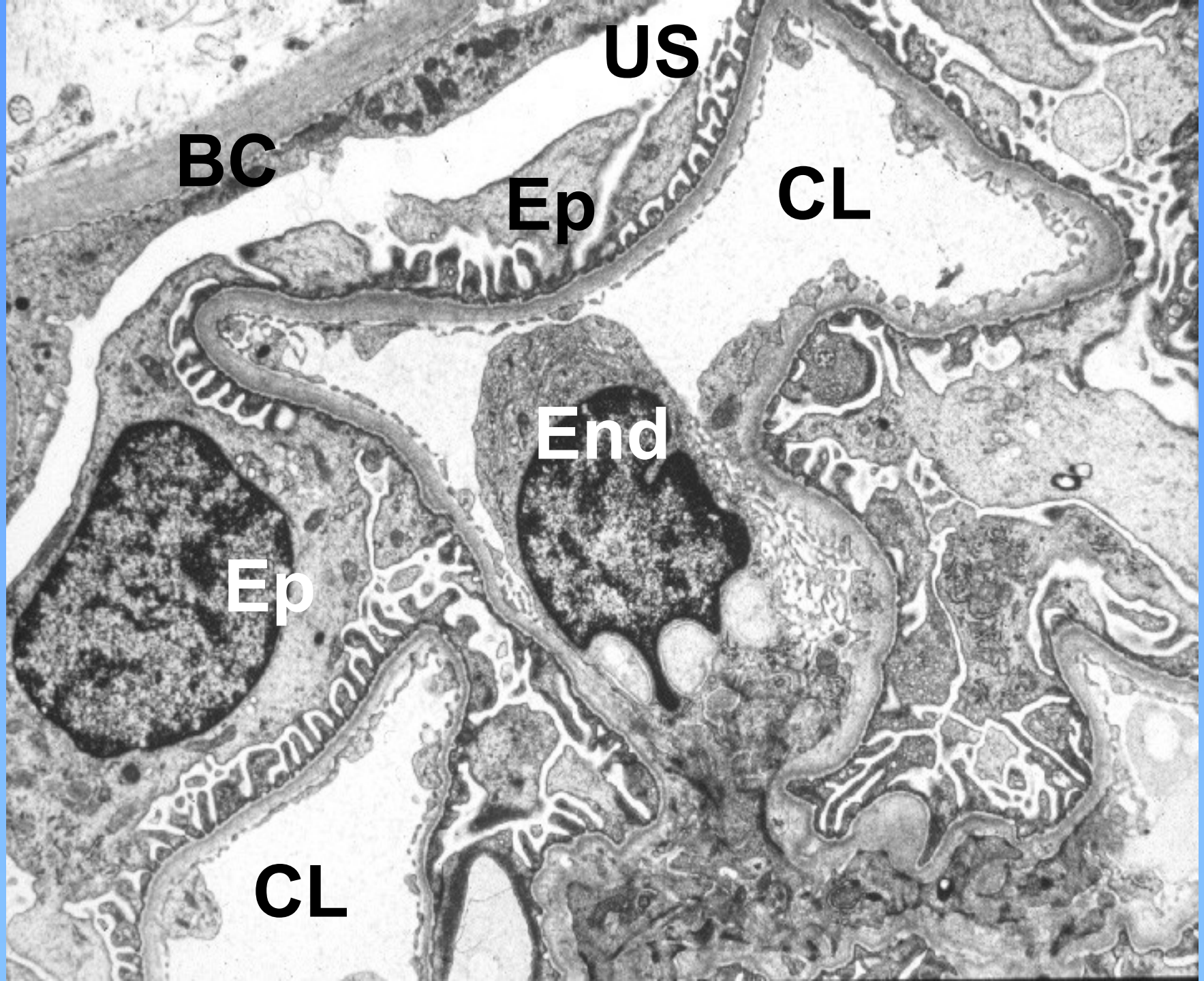

FOOT PROCESSES
lumen
GBM
endothelial cell
MESANGIUM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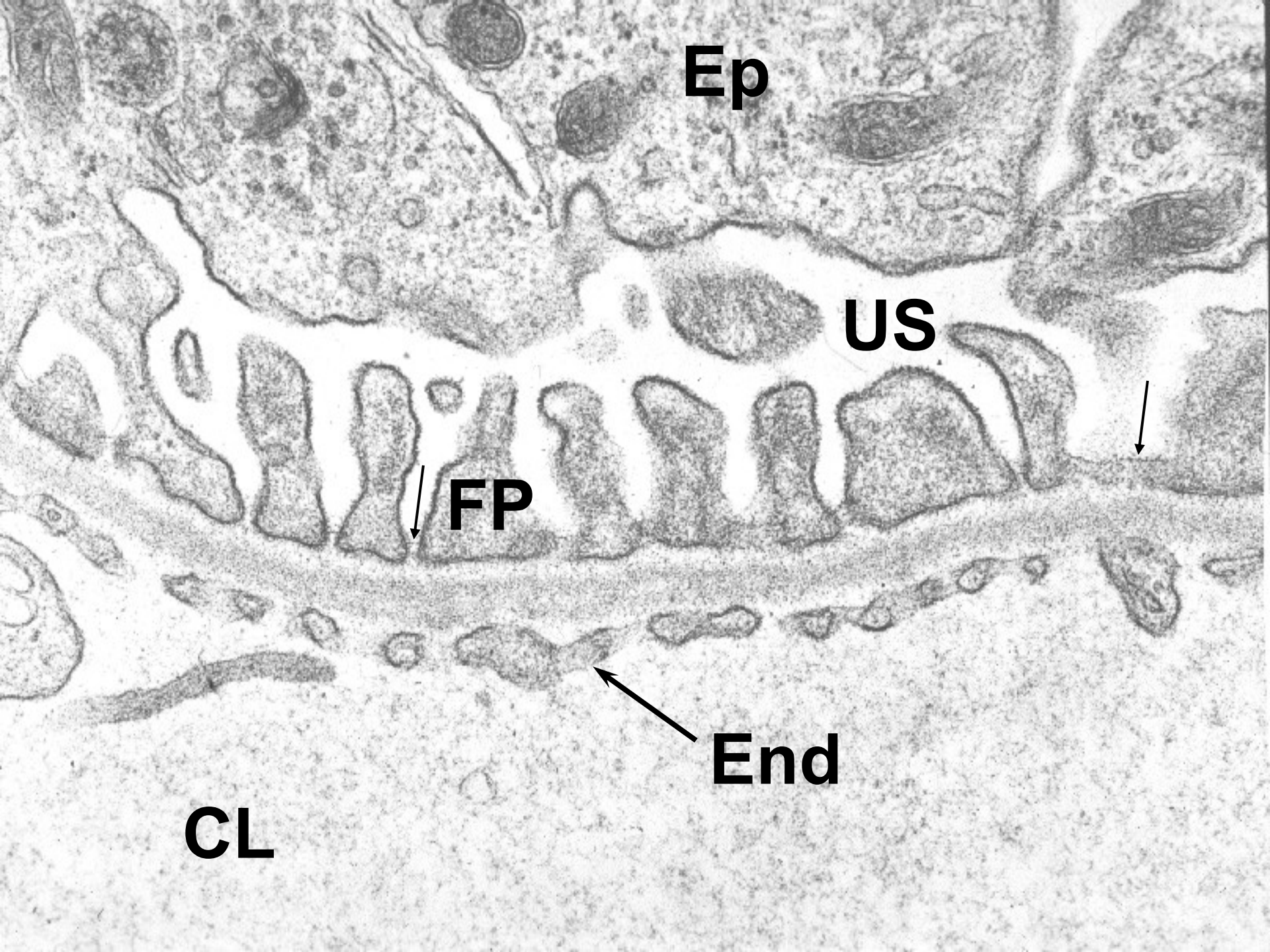
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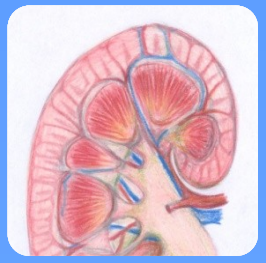
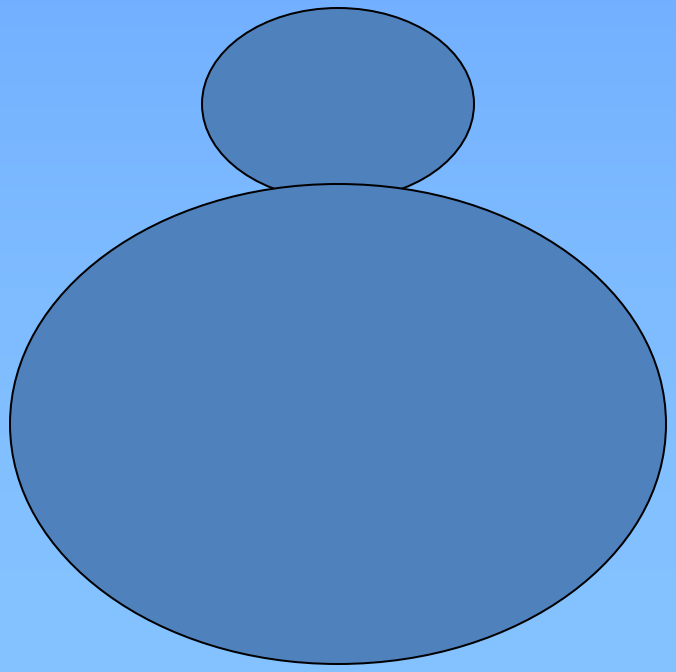
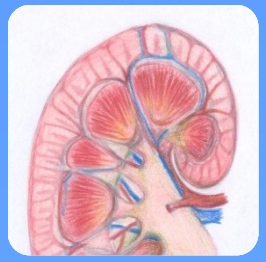


Renal tutorial

The nephrotic syndrome:

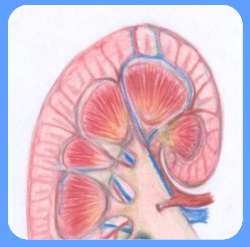
Proteinuria: (> 3.5g/24 h)
Hypoalbuminemia.
Hyperlipidemia
Edema





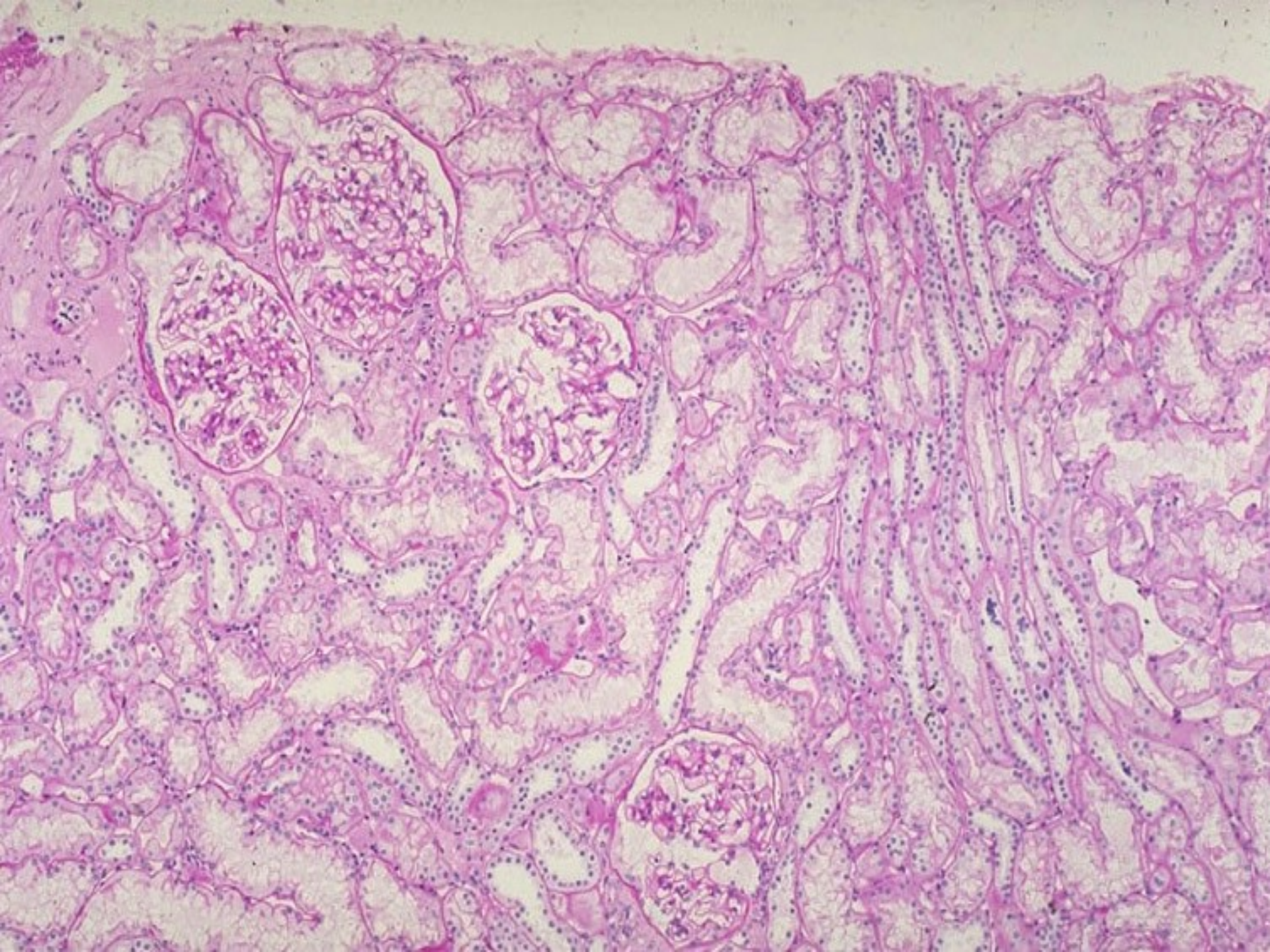
Renal biopsy

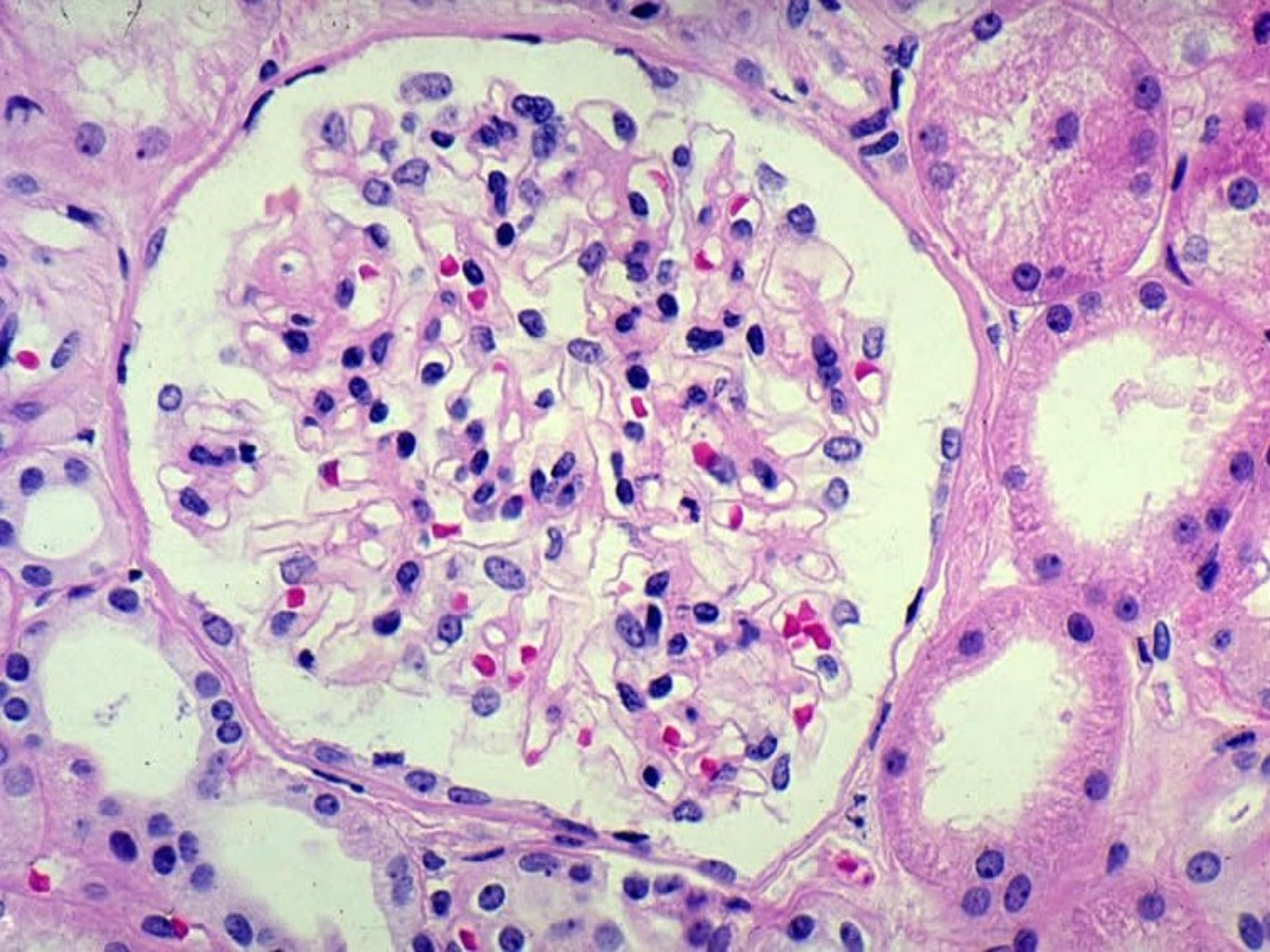
The structural abnormality shared by all the nephrotic conditions with heavy proteinuria is the simplification or fusion of the cell foot processes.

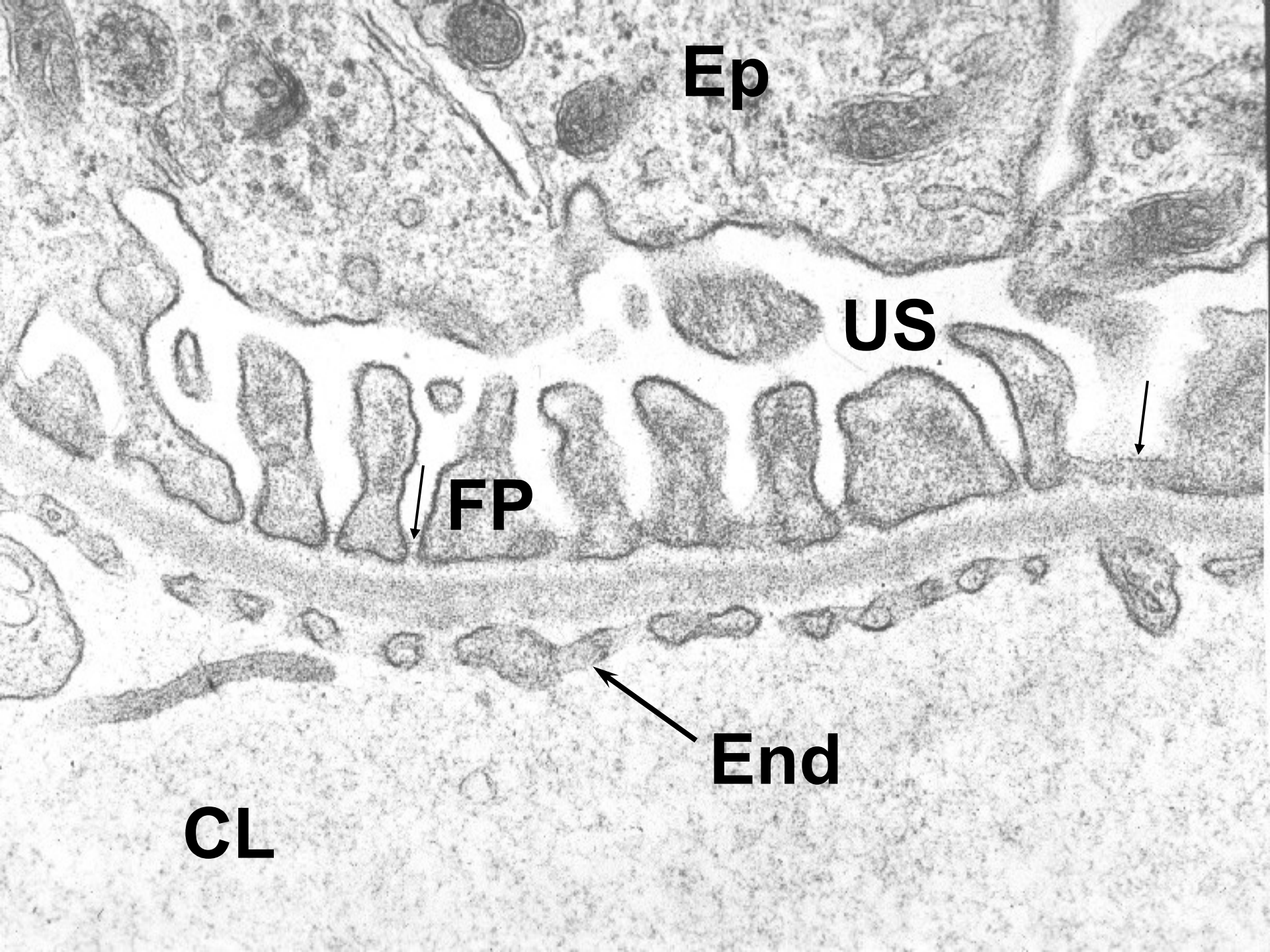


MINIMAL CHANGE DISEASE

DIFFUSE EPITHELIAL CELL DISEASE



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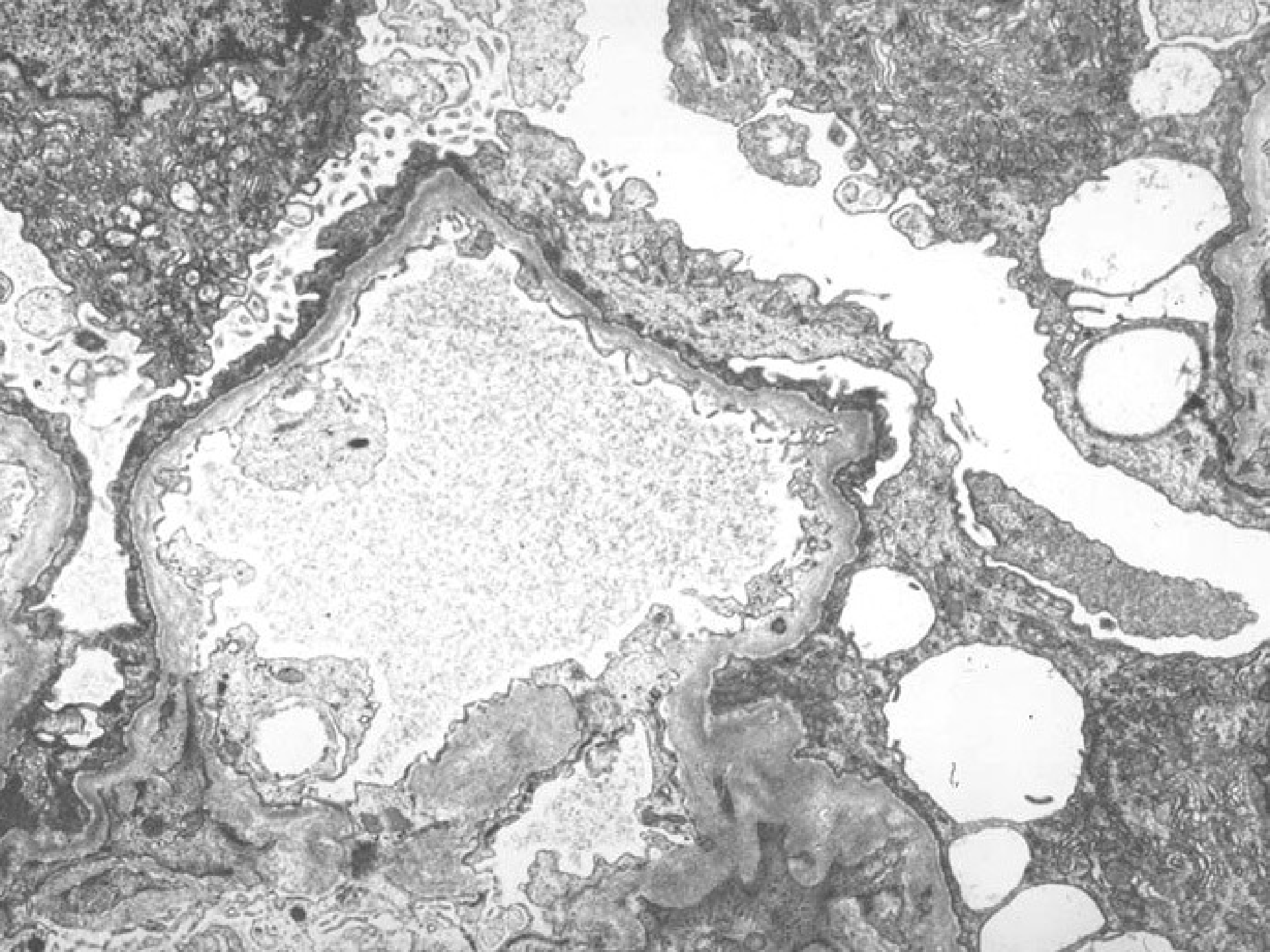
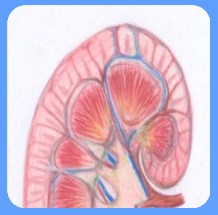
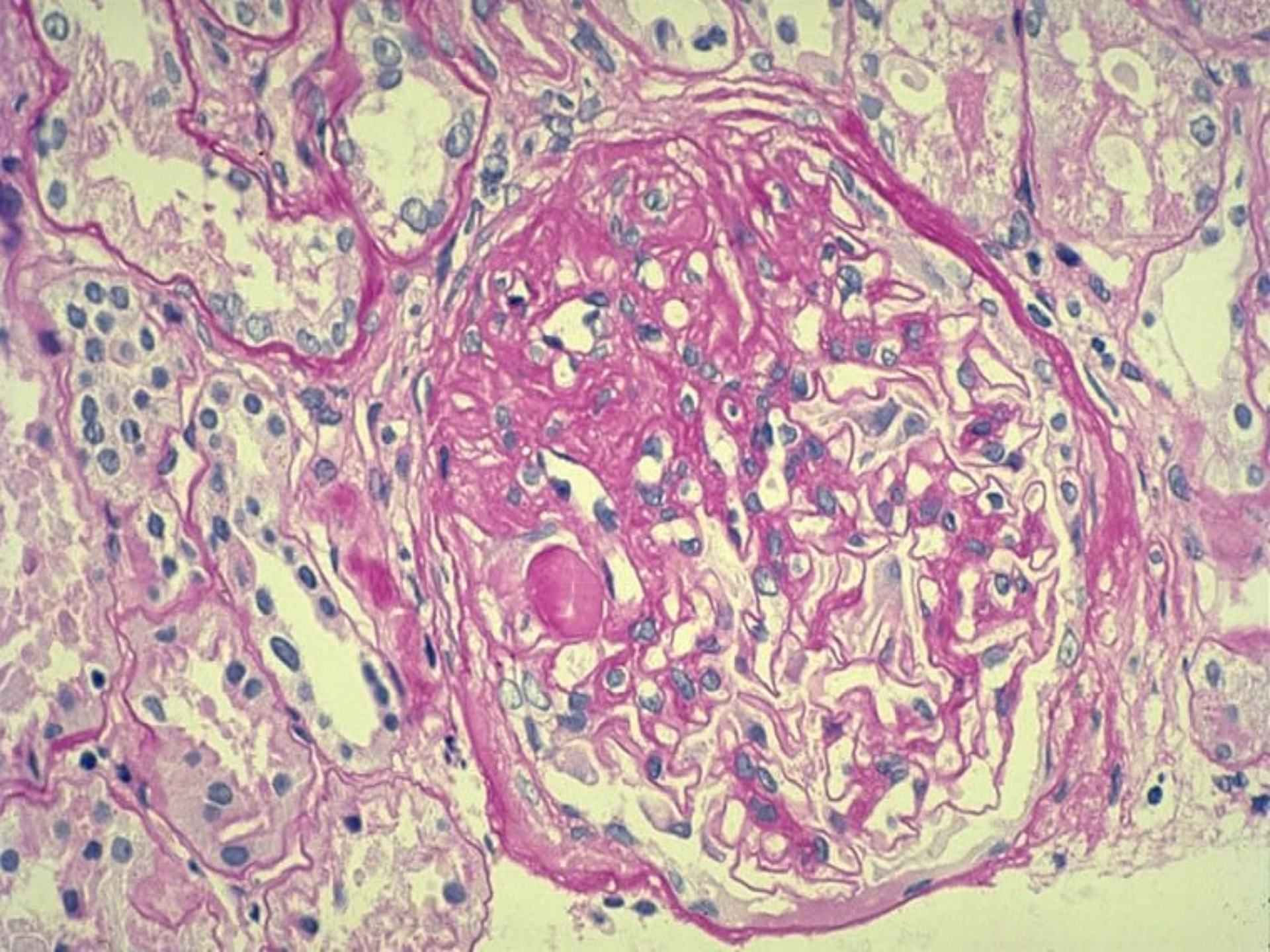
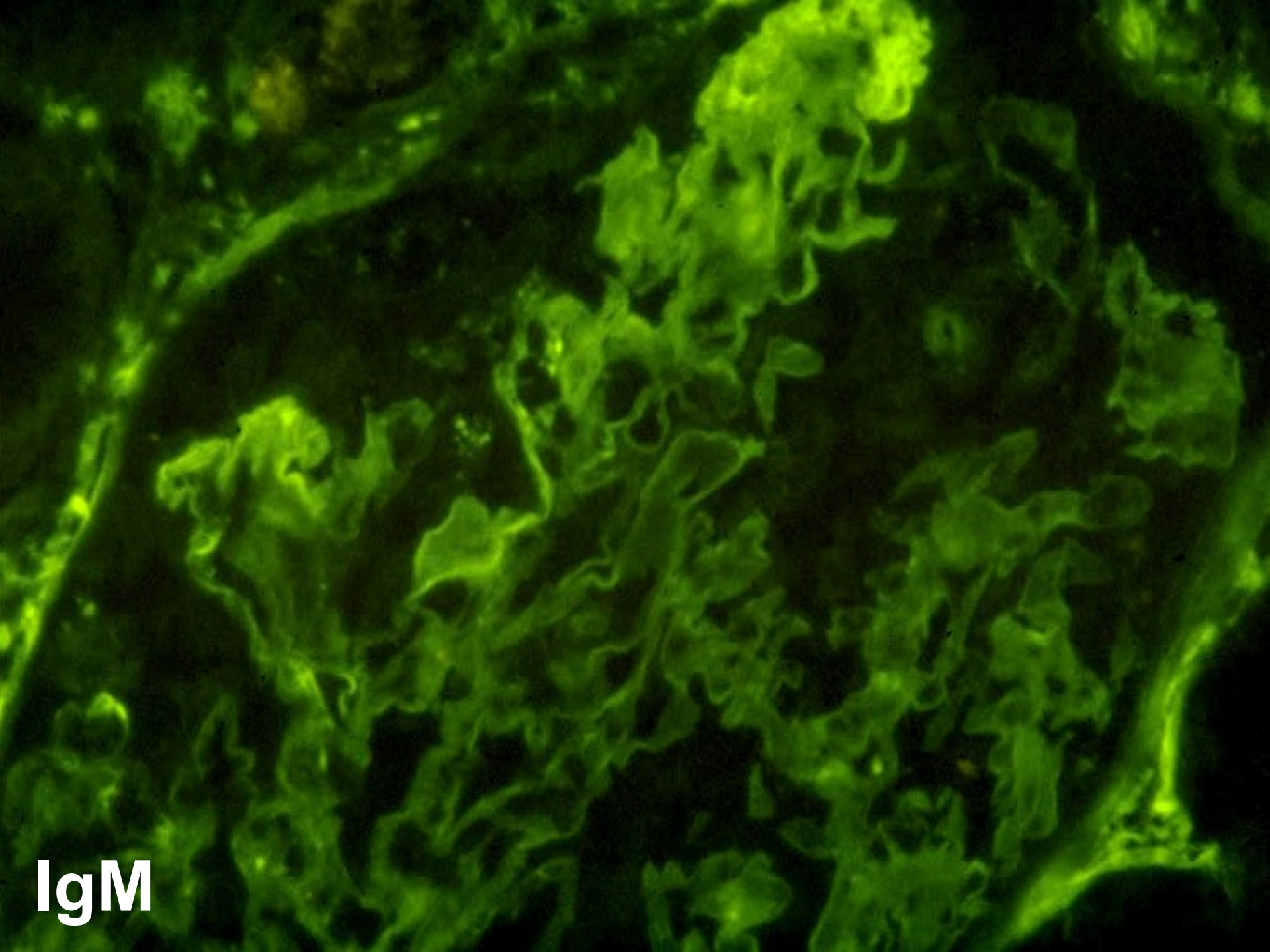


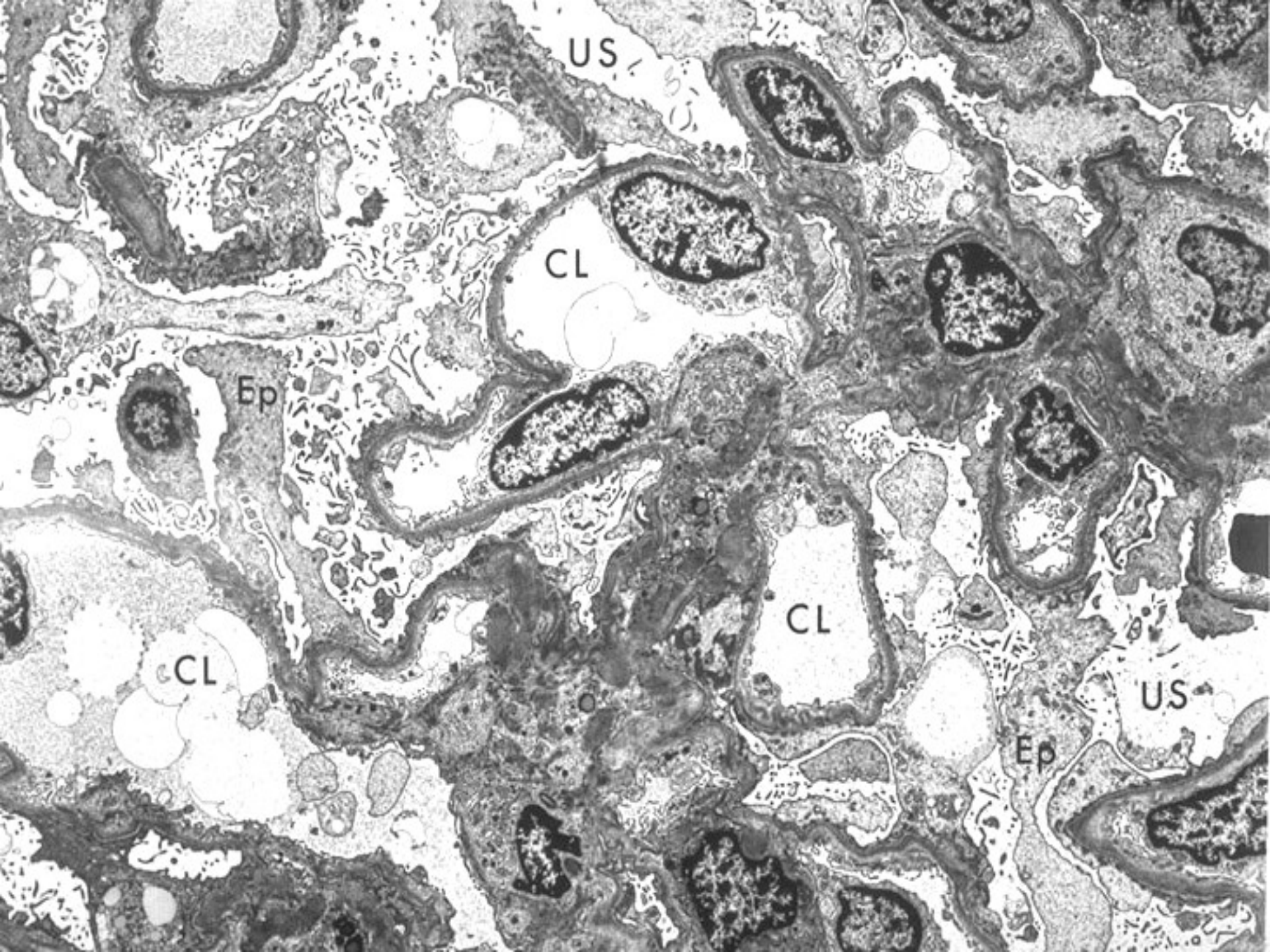


FSGS

Focal and segmental glomerulosclerosis




IgM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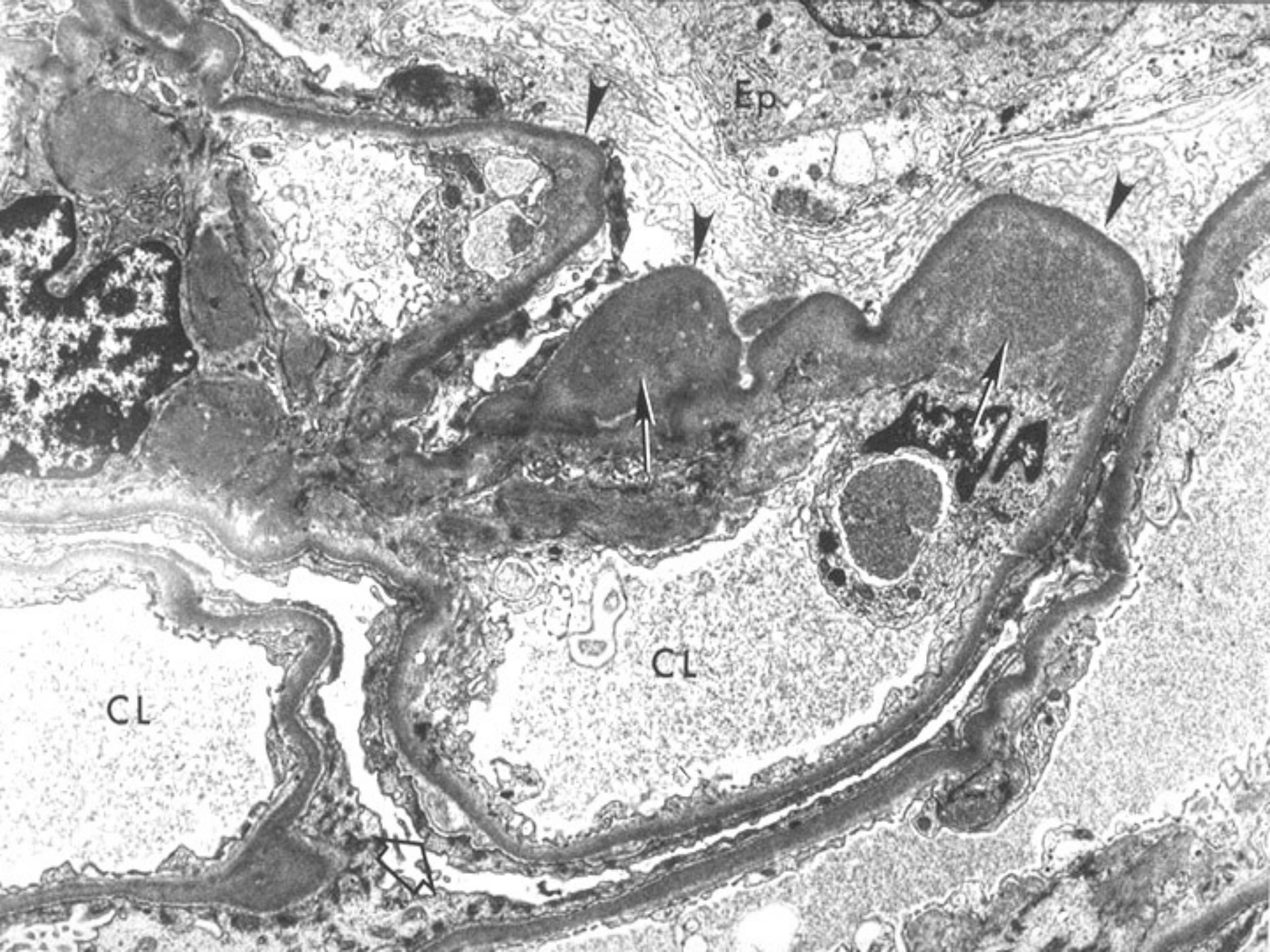
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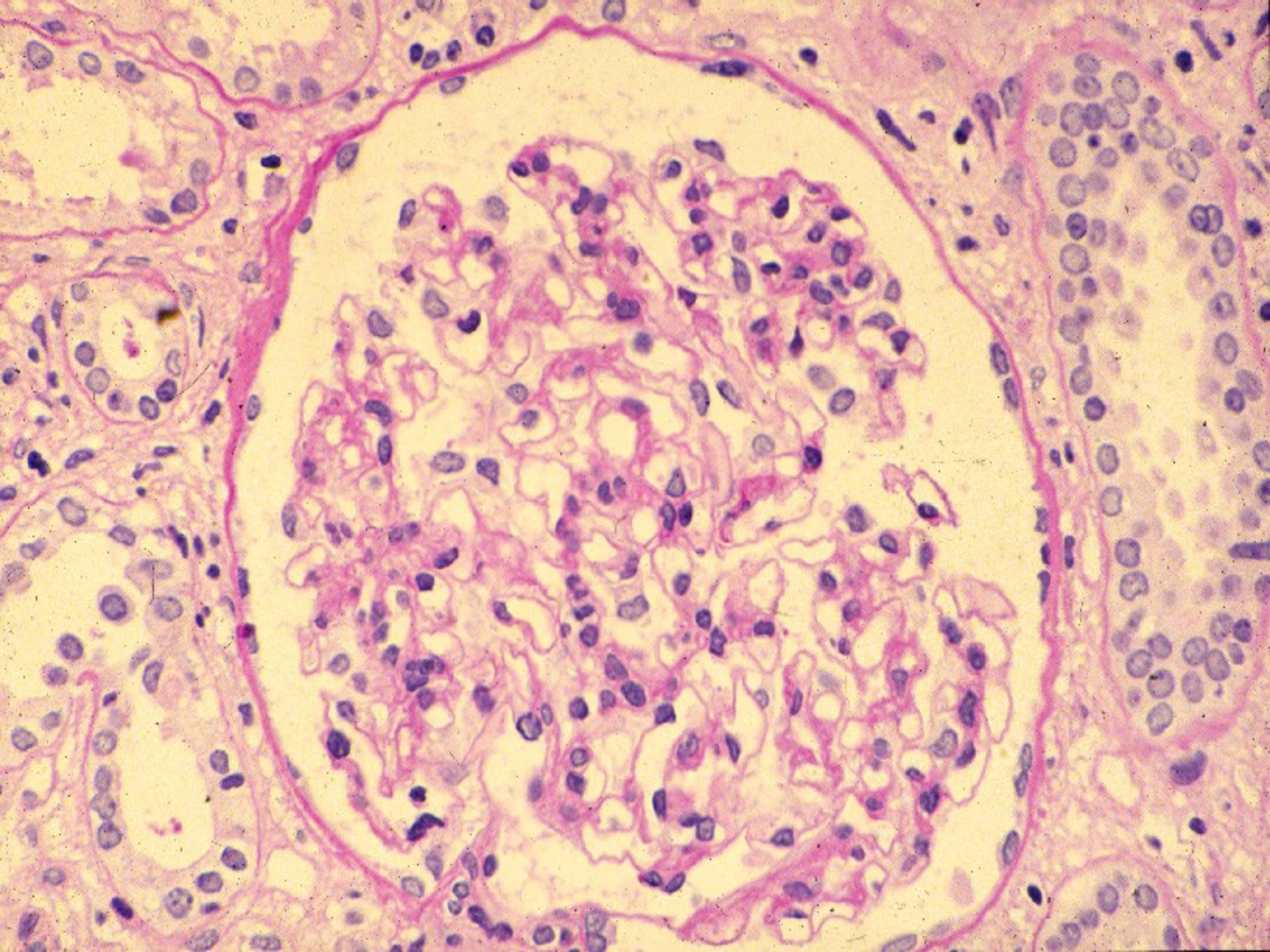
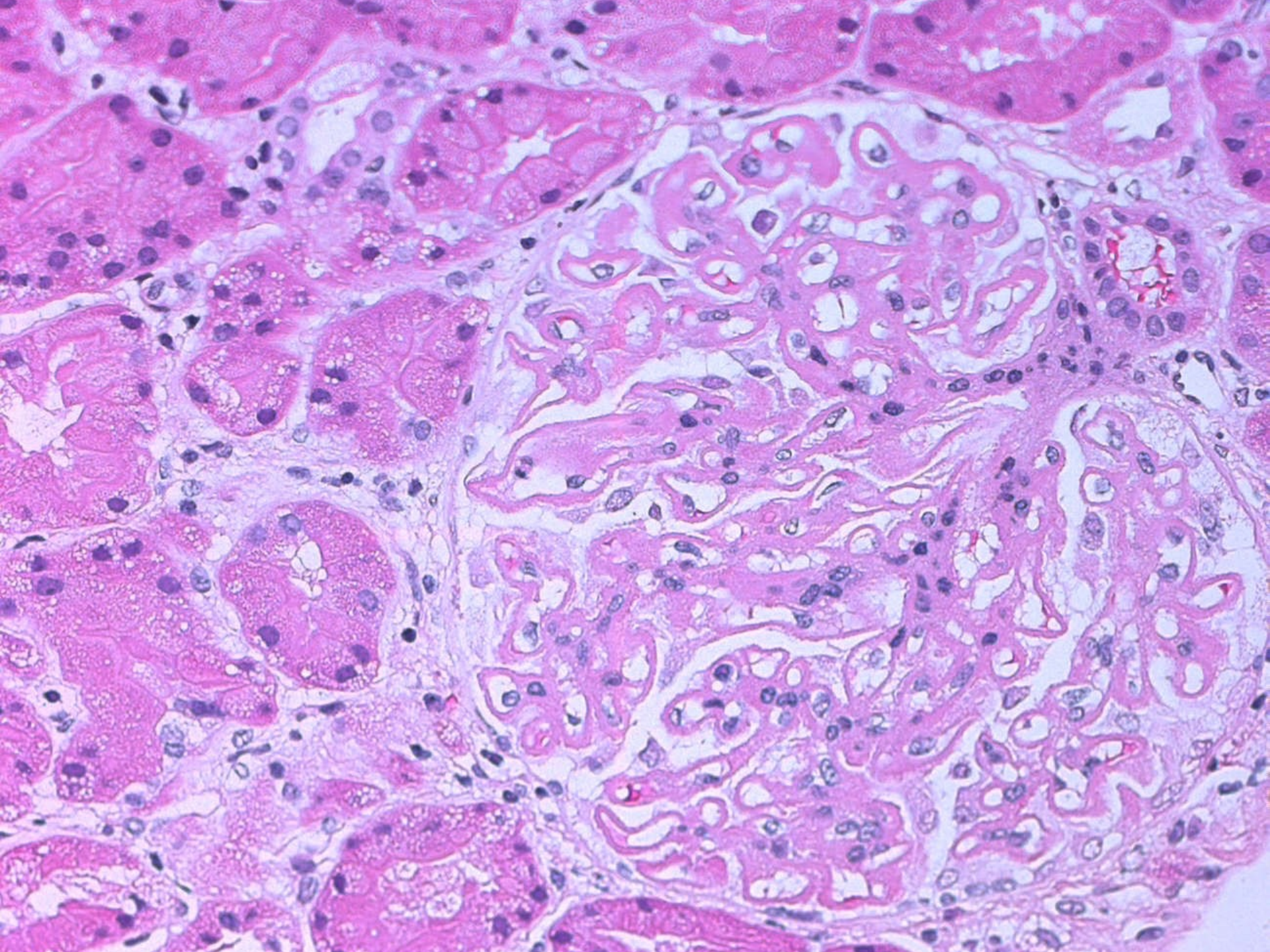
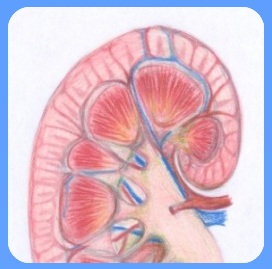
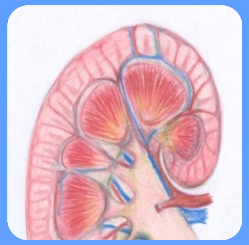






Membranous glomerulonephritis.

(MGN)



MGN

What are the conditions associated with MGN?

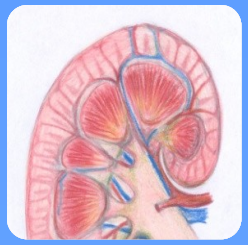
1:Autoimmune diseases.

2:Infectious diseases.

3:Drugs.

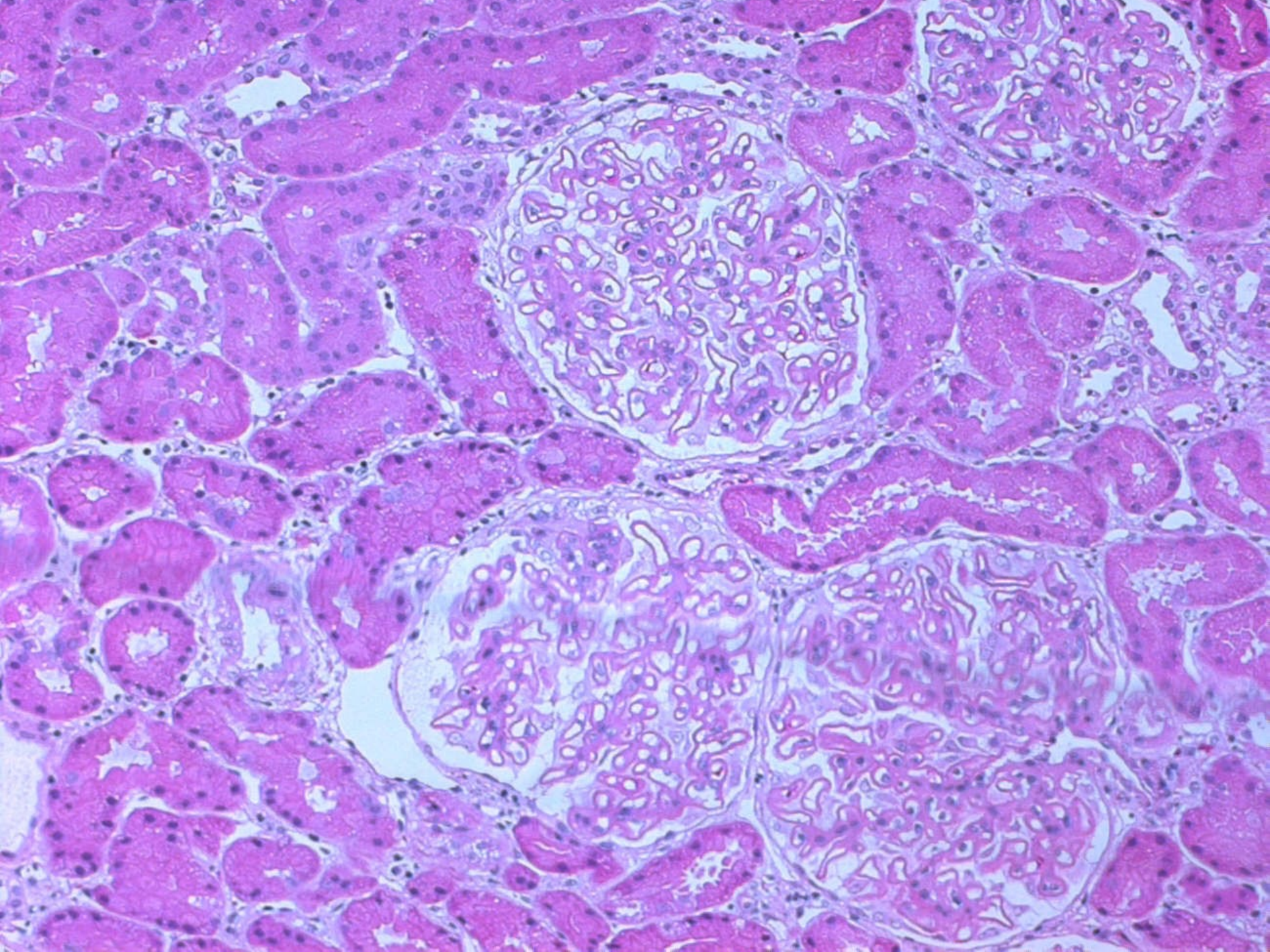
4:Miscellaneous.

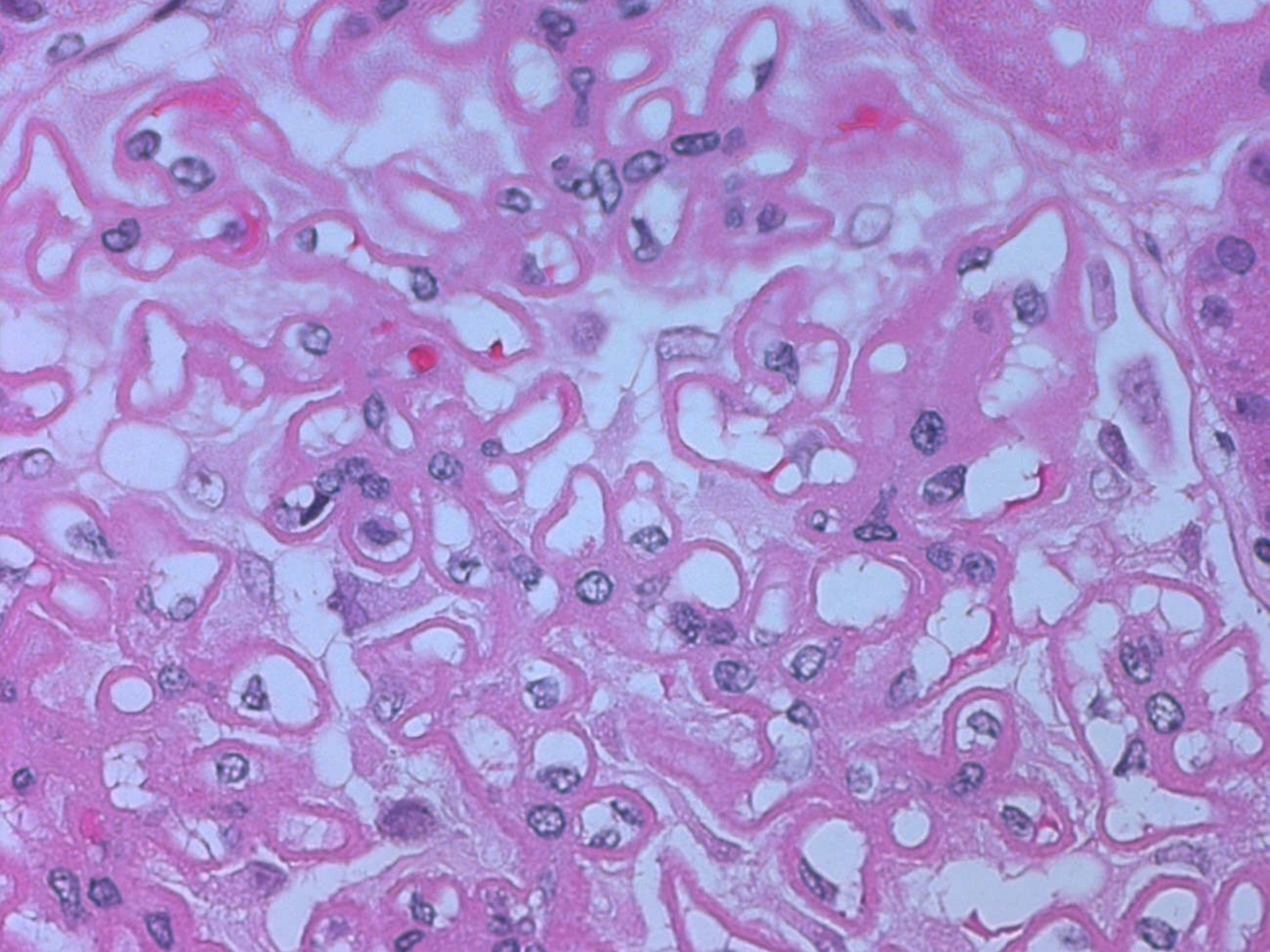
IDIOPATHIC MGN.

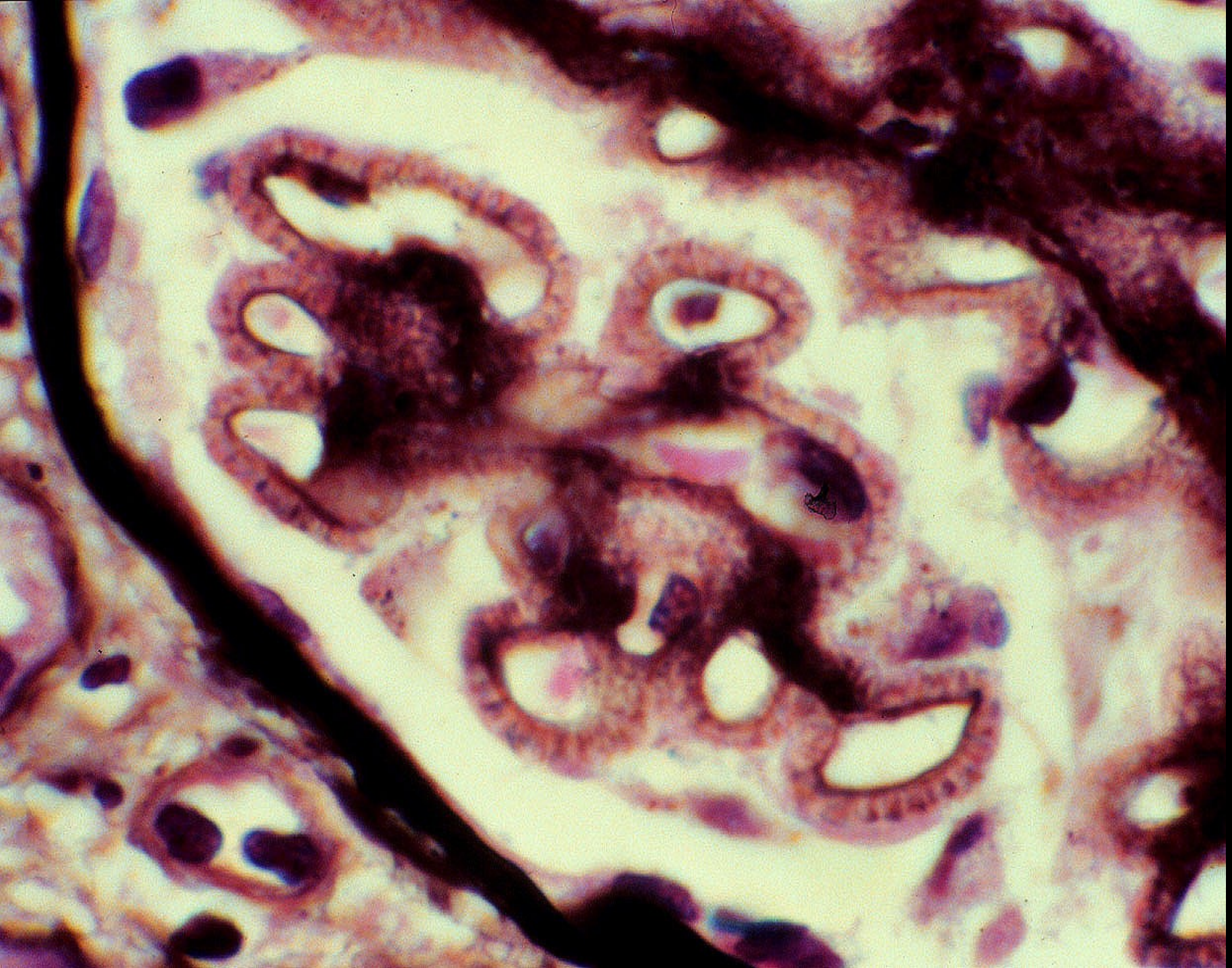


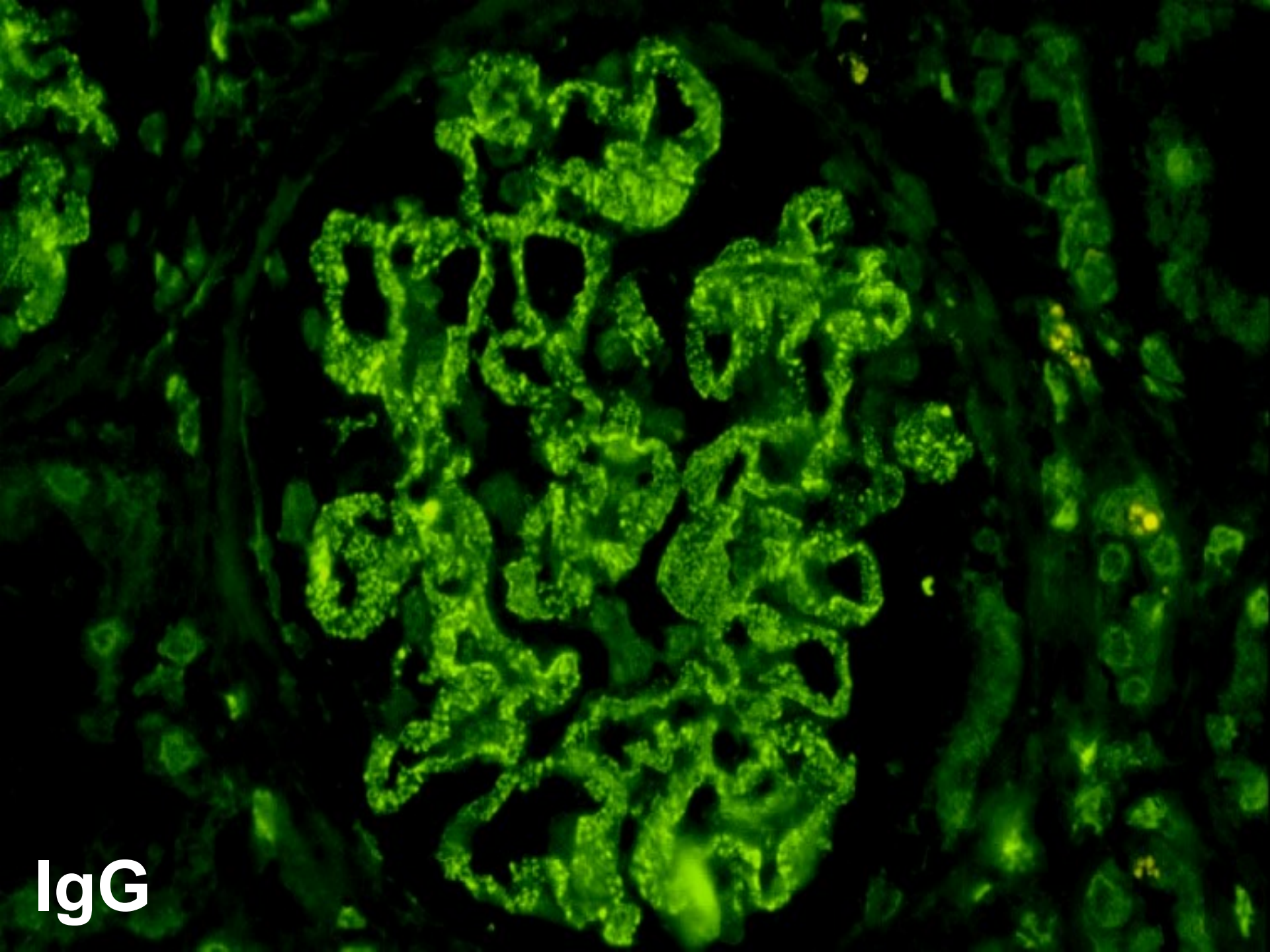
Conclusion

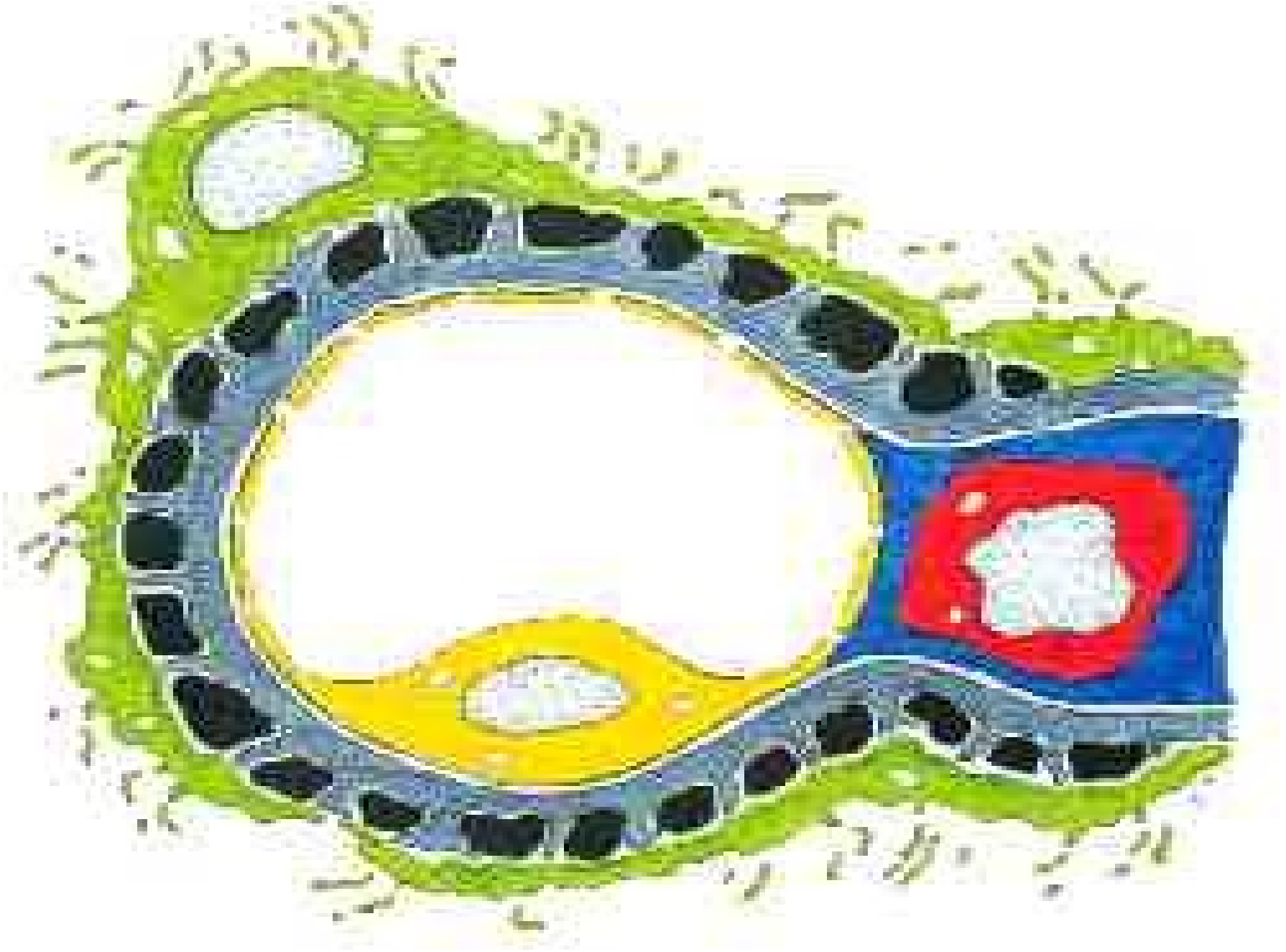
The variety of causes linked to MGN minimizes the fact that in many instances the relationship is tentative and the etiologic implication is unproven.

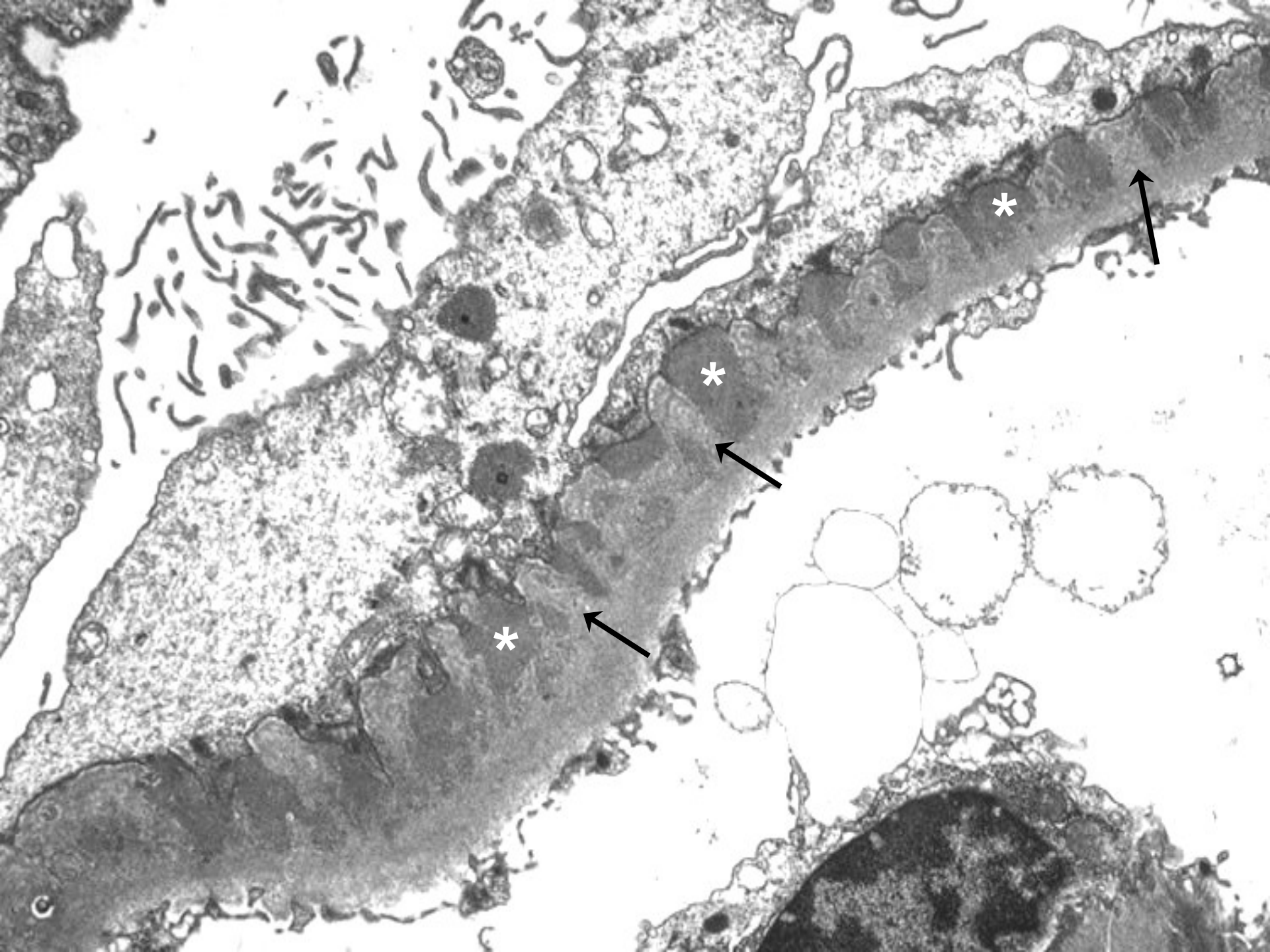


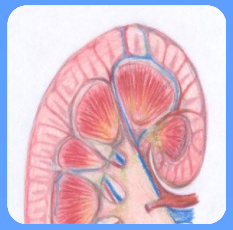




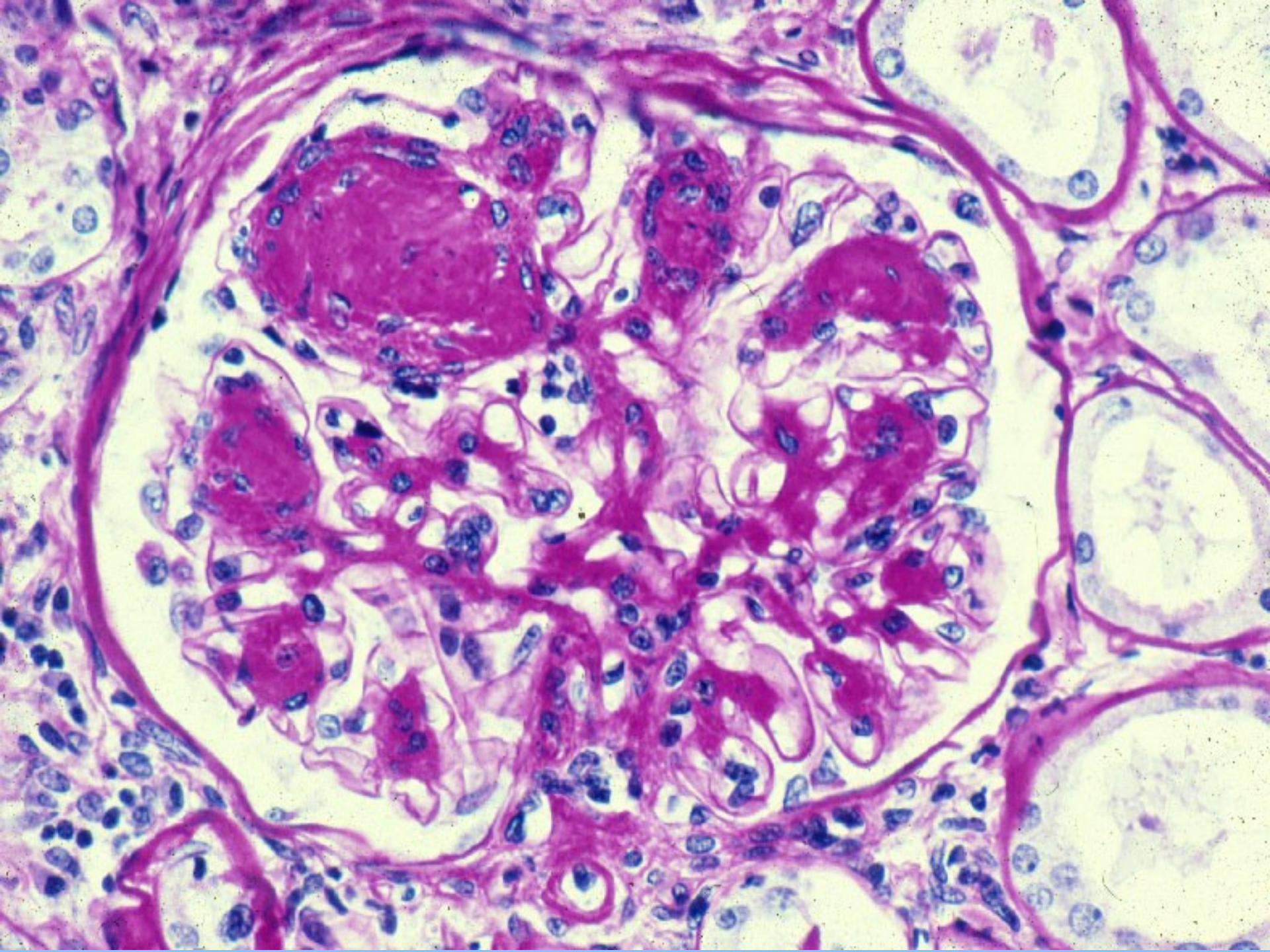

IgG

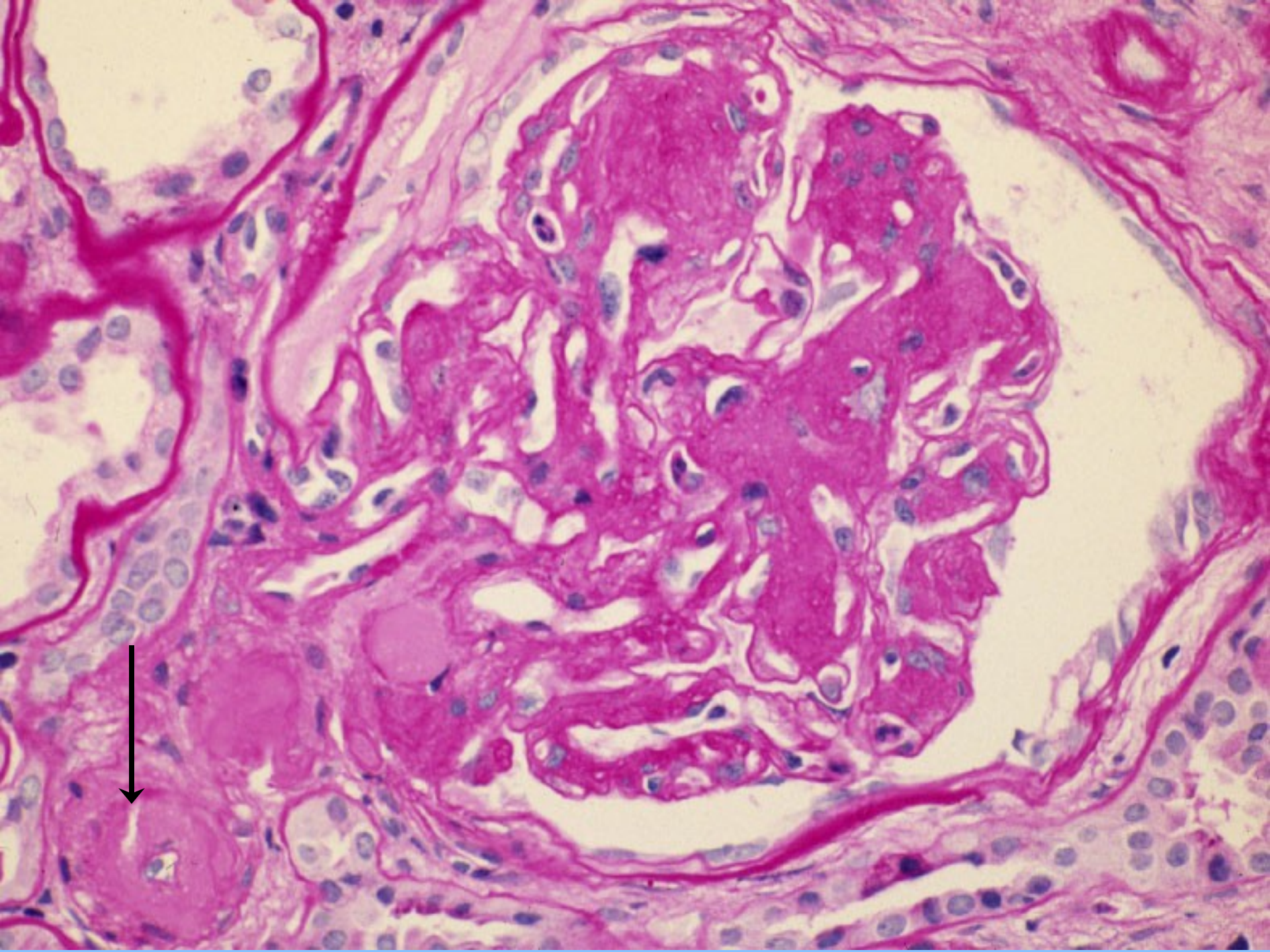


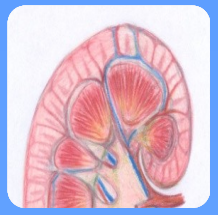




Diabetic Nephropathy





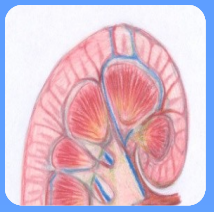


Acute Nephritic Syndrome

1-Acute post-streptococcal GN

2-Membrano-Proliferative Glomerulonephritis

3-Systemic Lupus Erythematosus

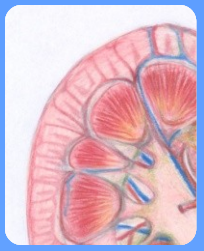


A. **Post infectious glomerulonephritis (syn. post-streptococcal glomerulonephritis)**

1. **One of most frequent causes of nephritic syndrome in childhood. May be seen in adults in whom clinical course may be less typical.**

2. **Most frequently associated with group A Streptococcal infection (pharyngitis or cutaneous) of "nephritogenic" serotype; less commonly, other infections (e.g. Staph, pneumococcus, mycoplasma, viral hepatitis, etc.) may precede glomerulonephritis.**

3. **Clinically, in fully developed cases, the abrupt onset of hematuria ("tea colored urine"), oliguria, edema, and hypertension are found; serum C3 is depressed and serology for infectious agents is positive (antistreptolysin O, antihyaluronidase titre, anti-DNAase B).**

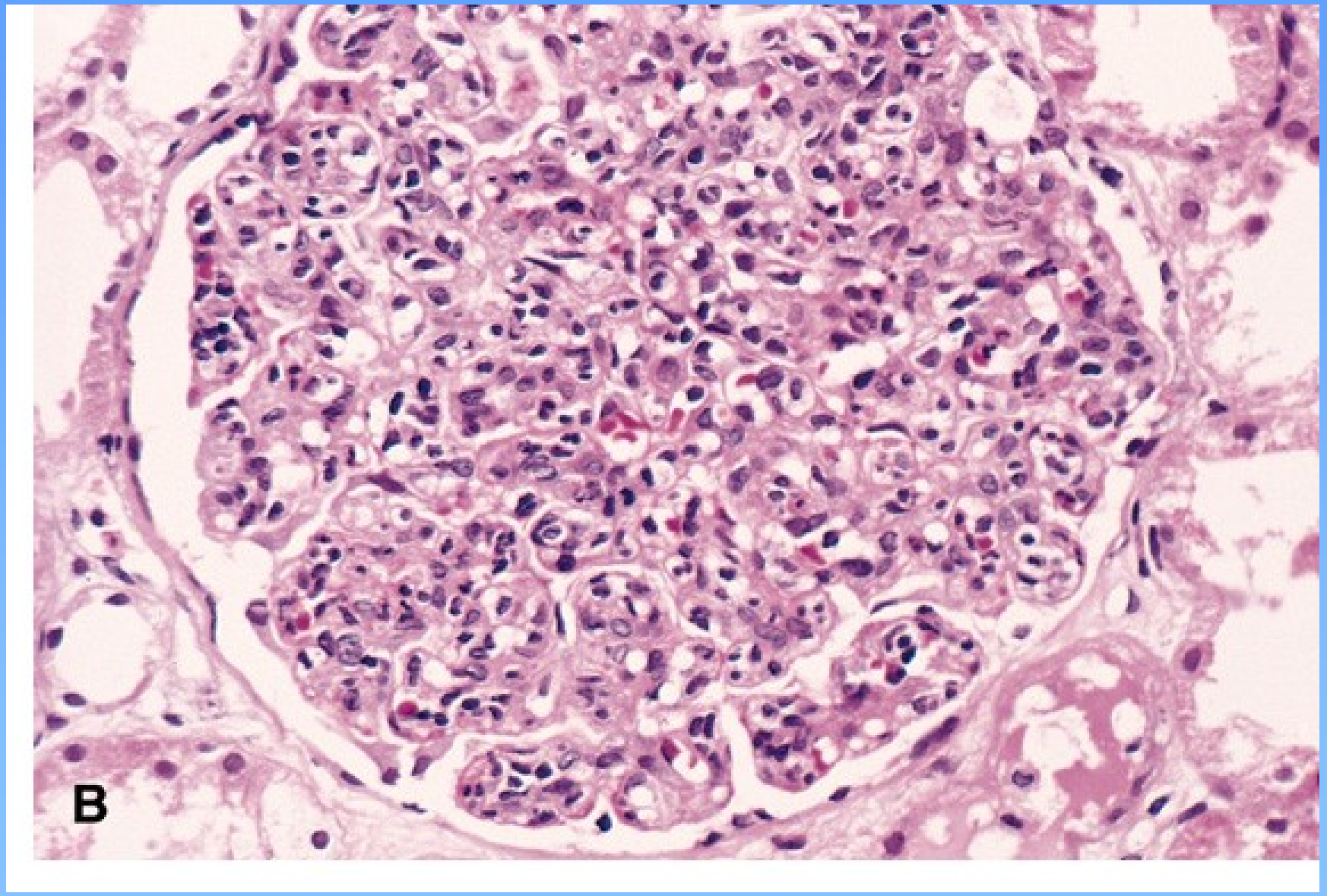


A. **Post infectious glomerulonephritis**

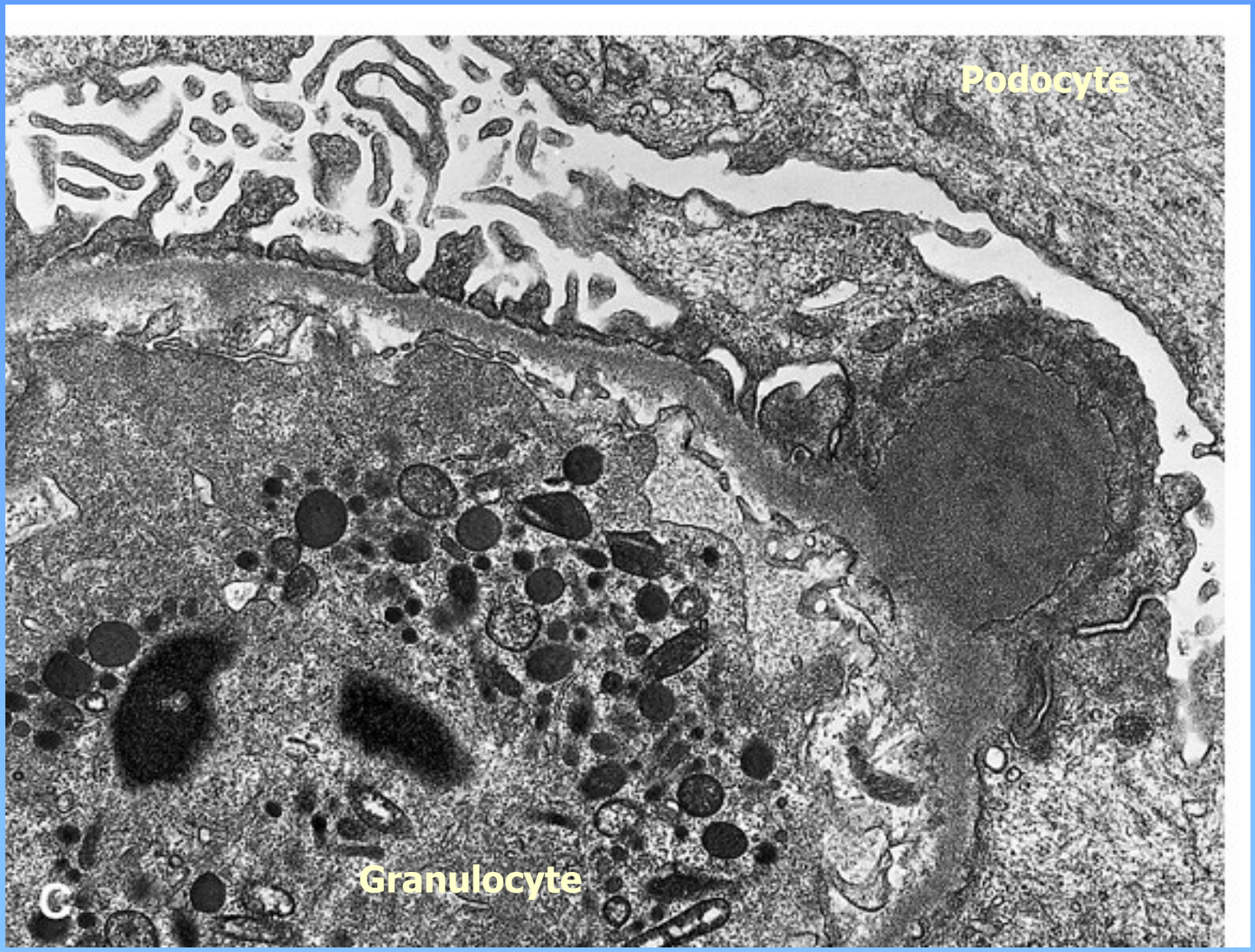
4. **Morphologically glomeruli are enlarged and hypercellular with numerous polys. Mesangial and endothelial cells increased. Epithelial crescents are uncommon. IF demonstrates classic "lumpy bumpy" pattern staining for IgG or C3.**

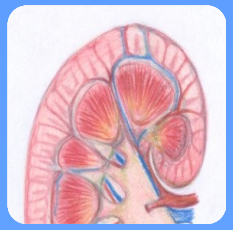
5. **Most children recover with disappearance of proteinuria and hematuria over several months. Clinical improvement usual within several weeks. Rarely the course is that of rapidly progressive glomerulonephritis or of slow progression to chronic renal failure.**

Acute proliferative glomerulonephritis



Acute proliferative glomerulonephritis - subepithelial deposit

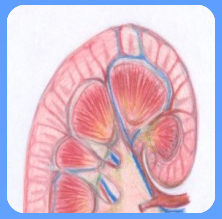




Membranoproliferative

Glomerulonephritis.

MPGN



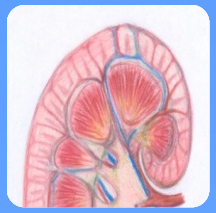
MPGN

MPGN as the name indicates involves both the glomerular capillary wall (Thickening,Double contour) and the glomerular tuft (proliferation).

MPGN

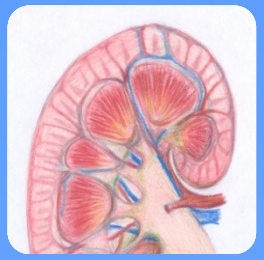
Clinical aspect:

- Proteinuria.
- Nephrotic Syndrome.
- Nephritic Syndrome.
- Hematuria .
- Decreased C3 level.
- Increased ASO titer.
- The disease mostly affects children.

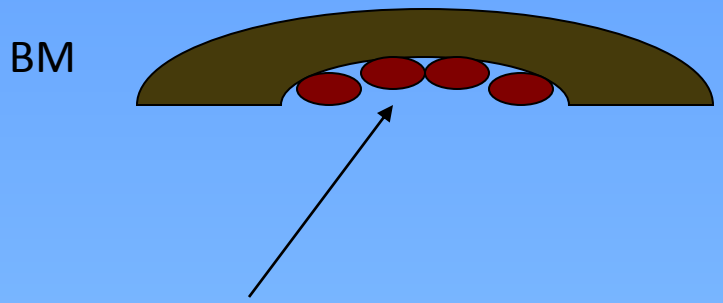


MPGN

- Secondary MPGN:
- Hepatitis B
- Hepatitis C
- Sickle cell Disease or Trait
- Malignancy…

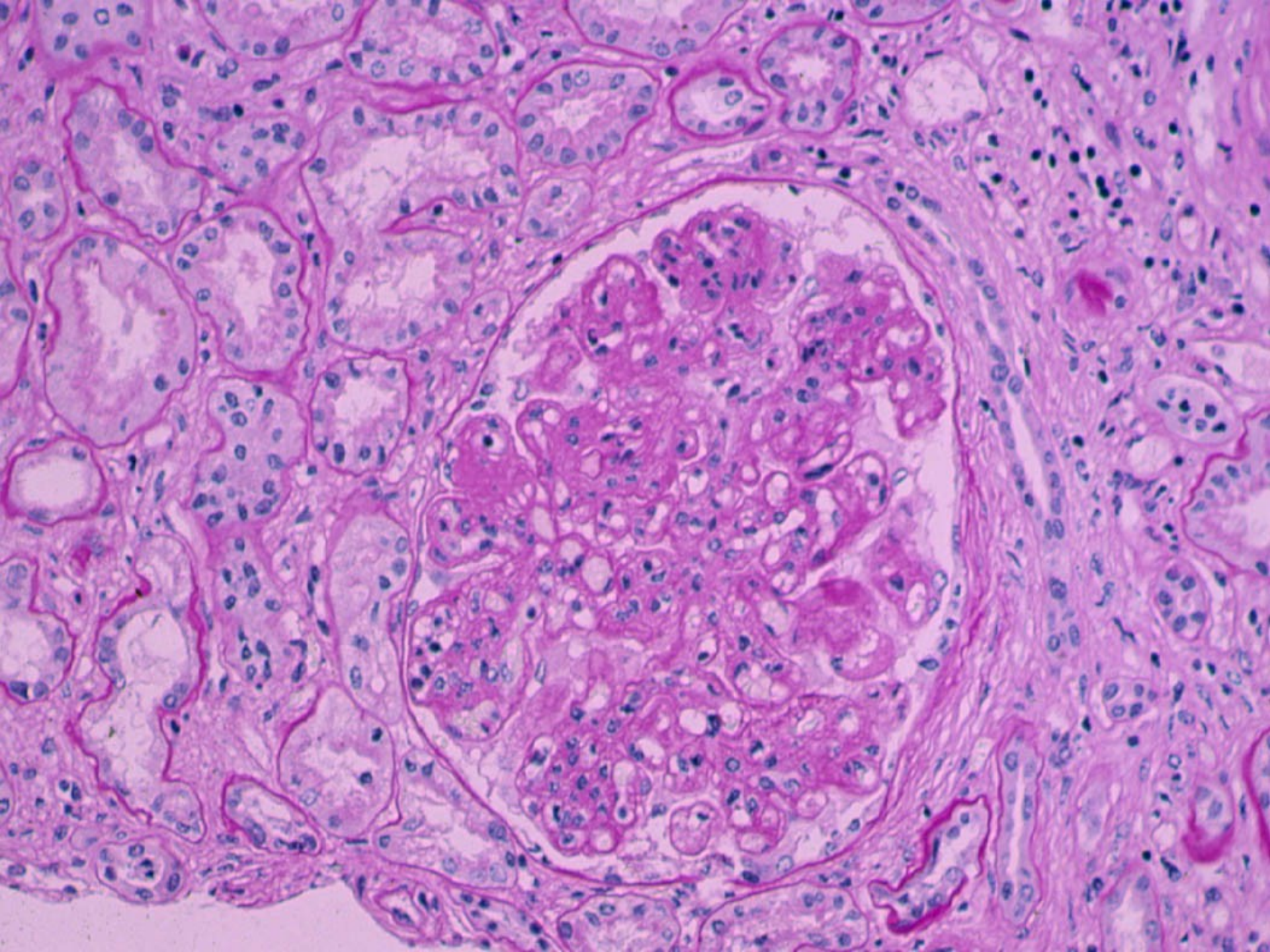


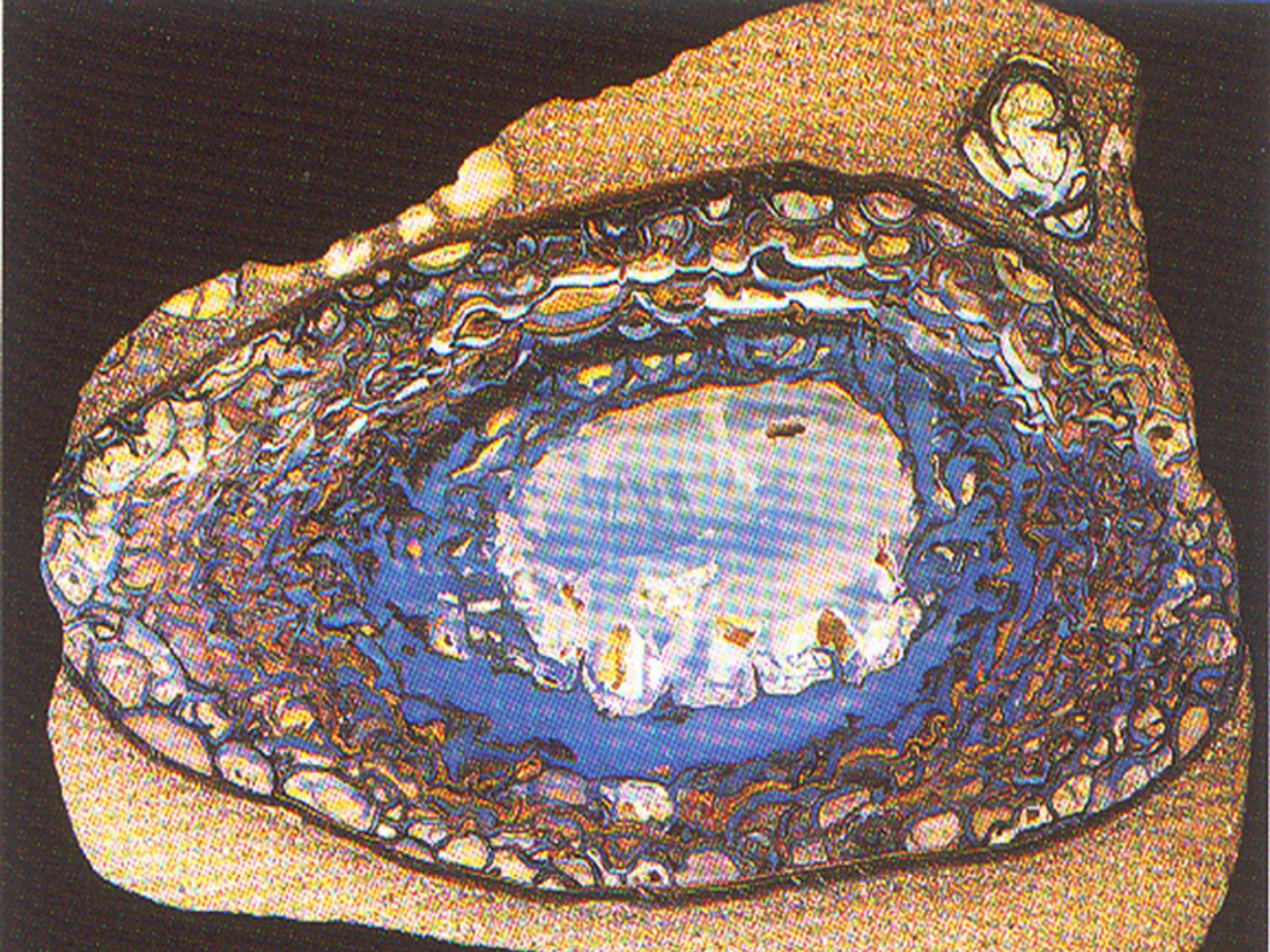
MPGN

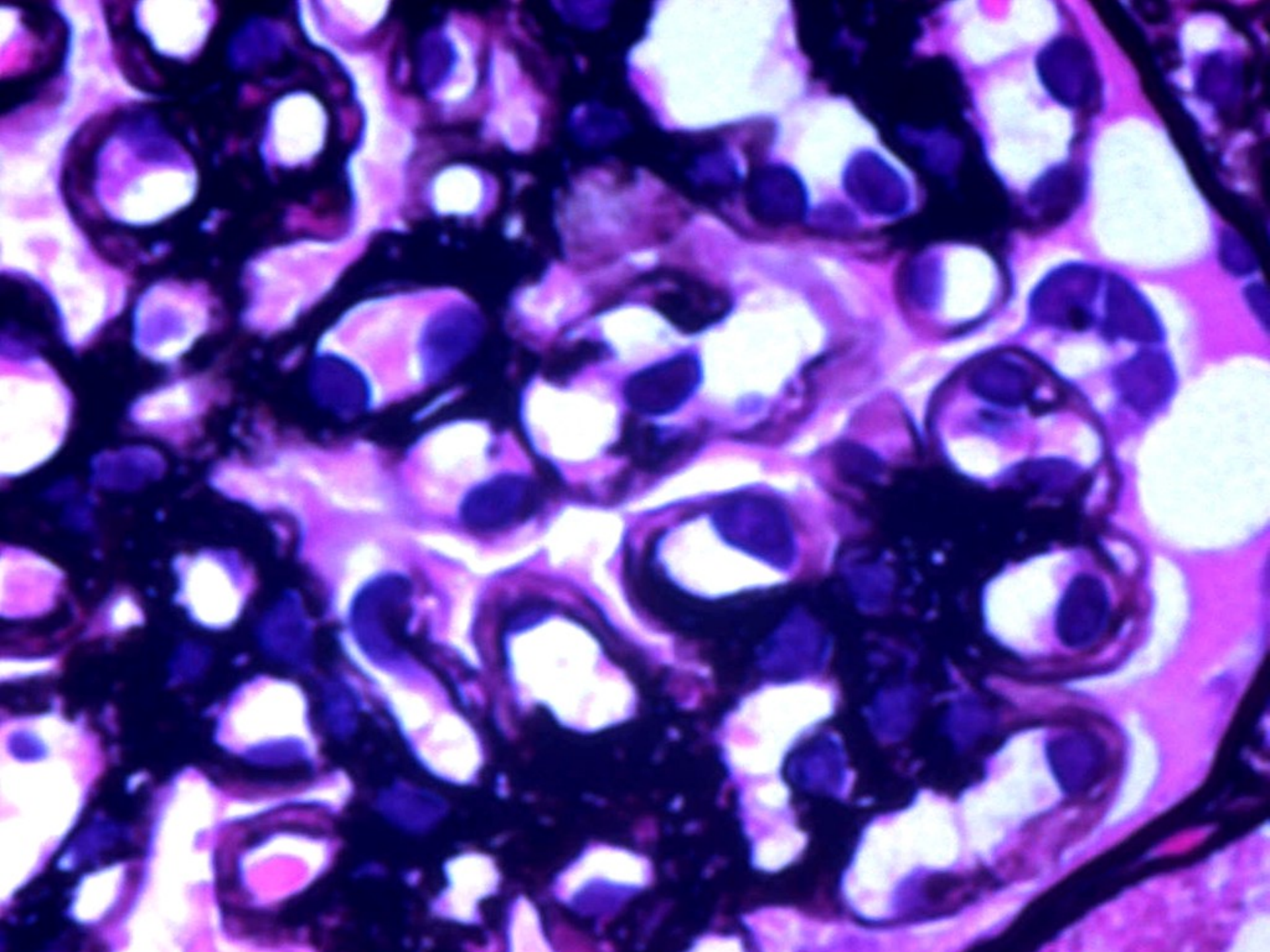


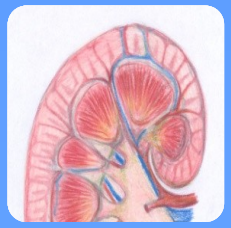
CIC of known,unknown or suspected origin.

C’ activation







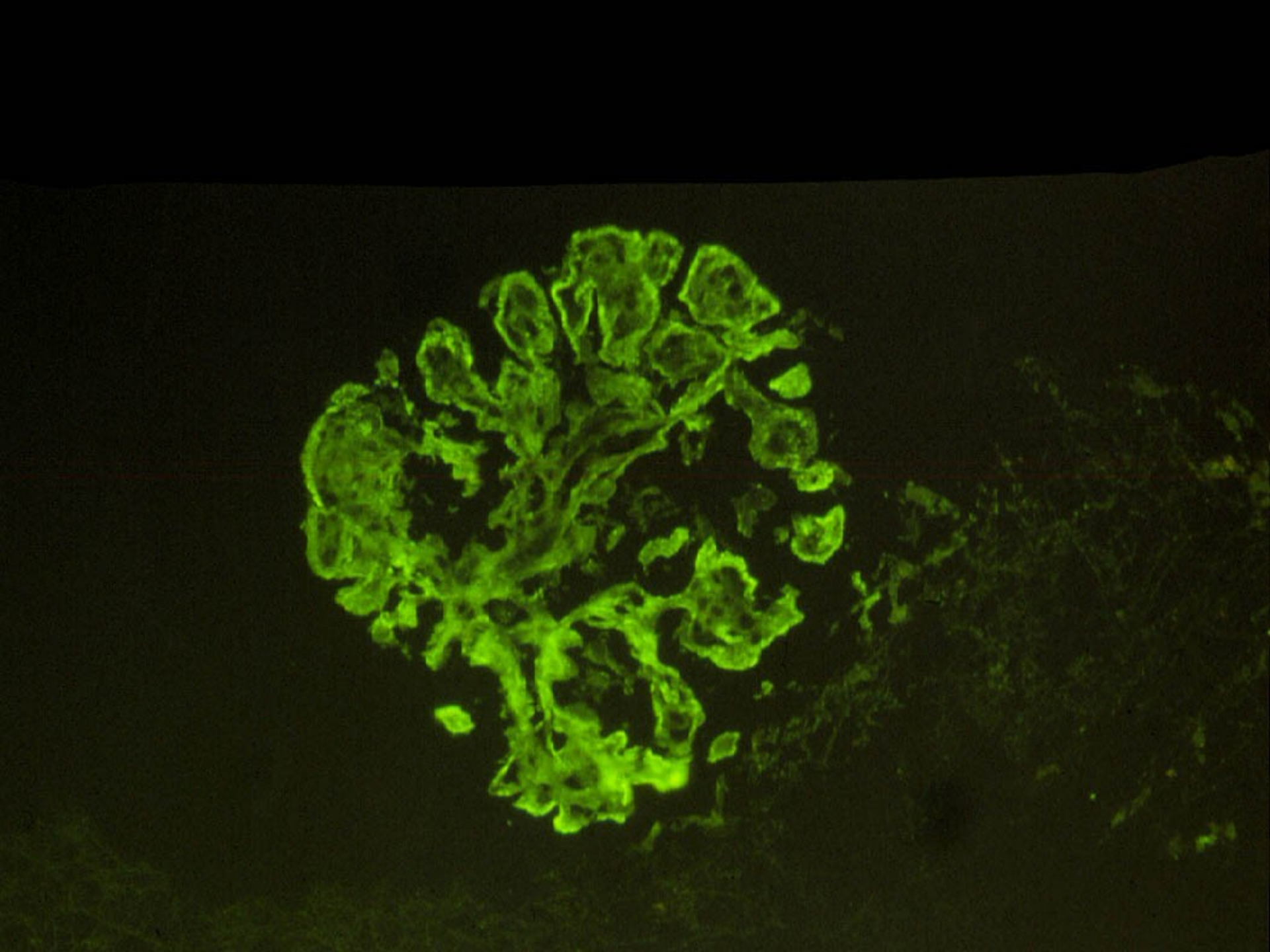


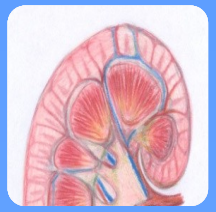
MPGN

Immunofluorescent microscopy

C3 : Peripheral lobular pattern

IgG: Similar pattern

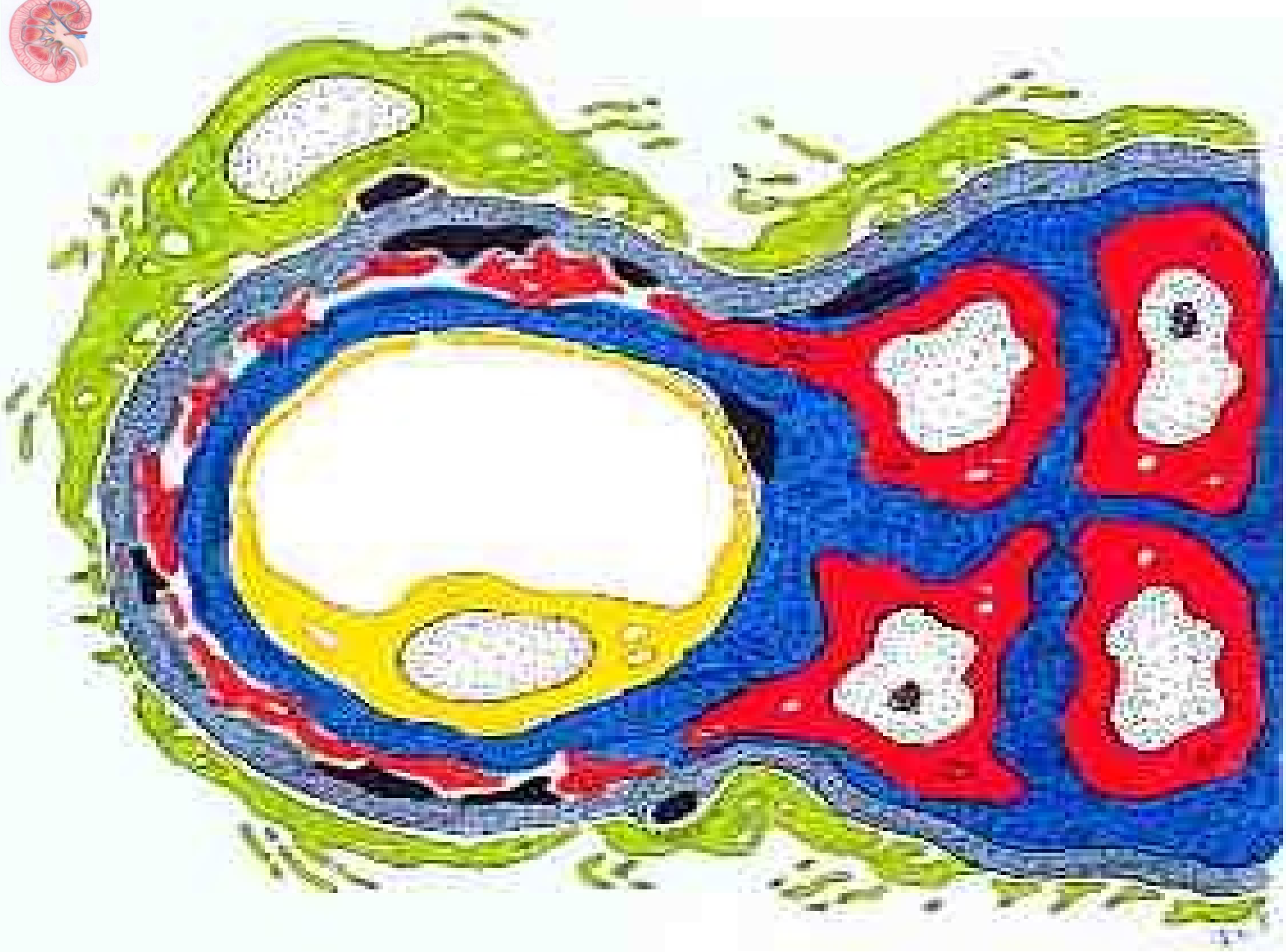


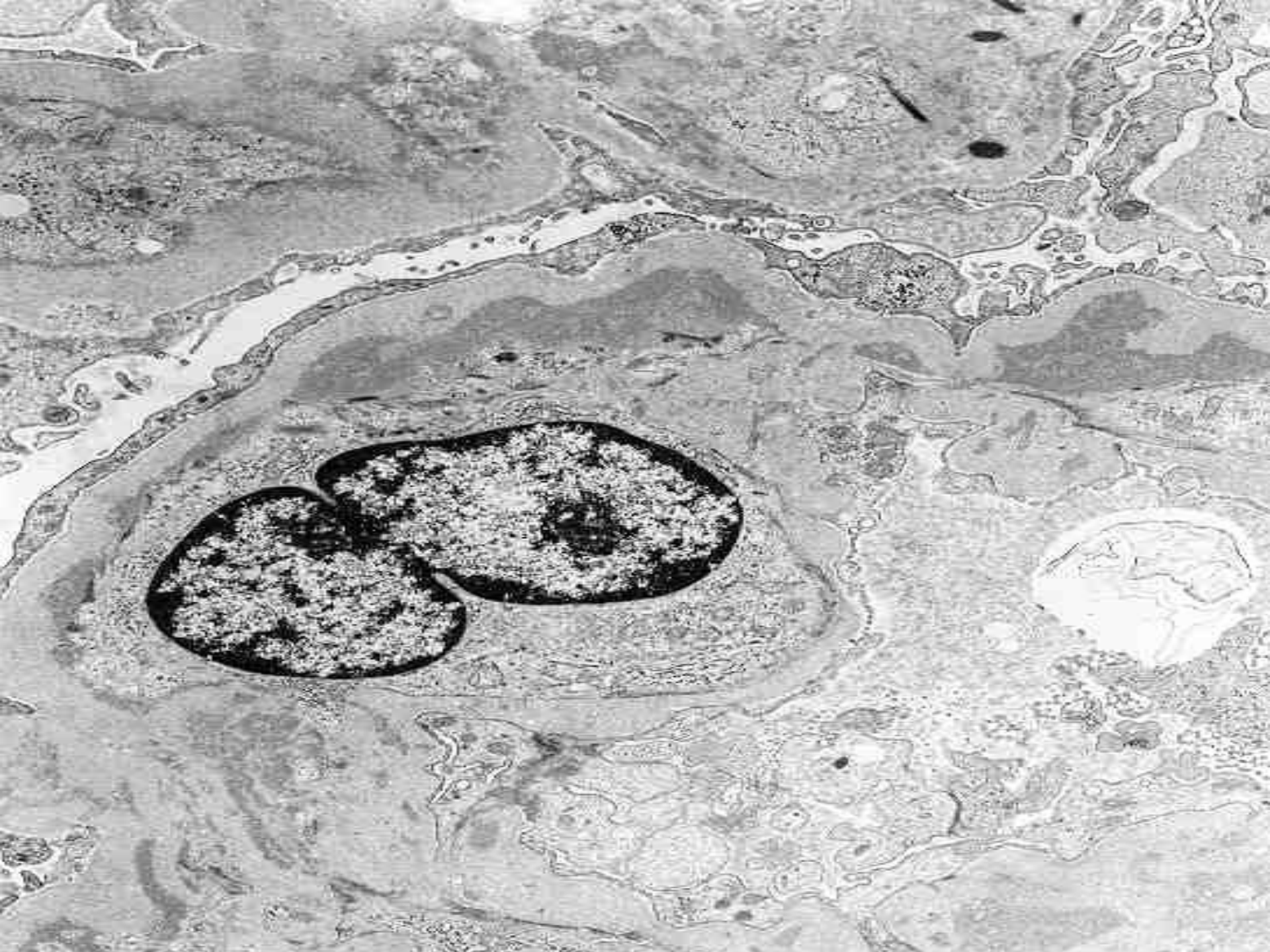


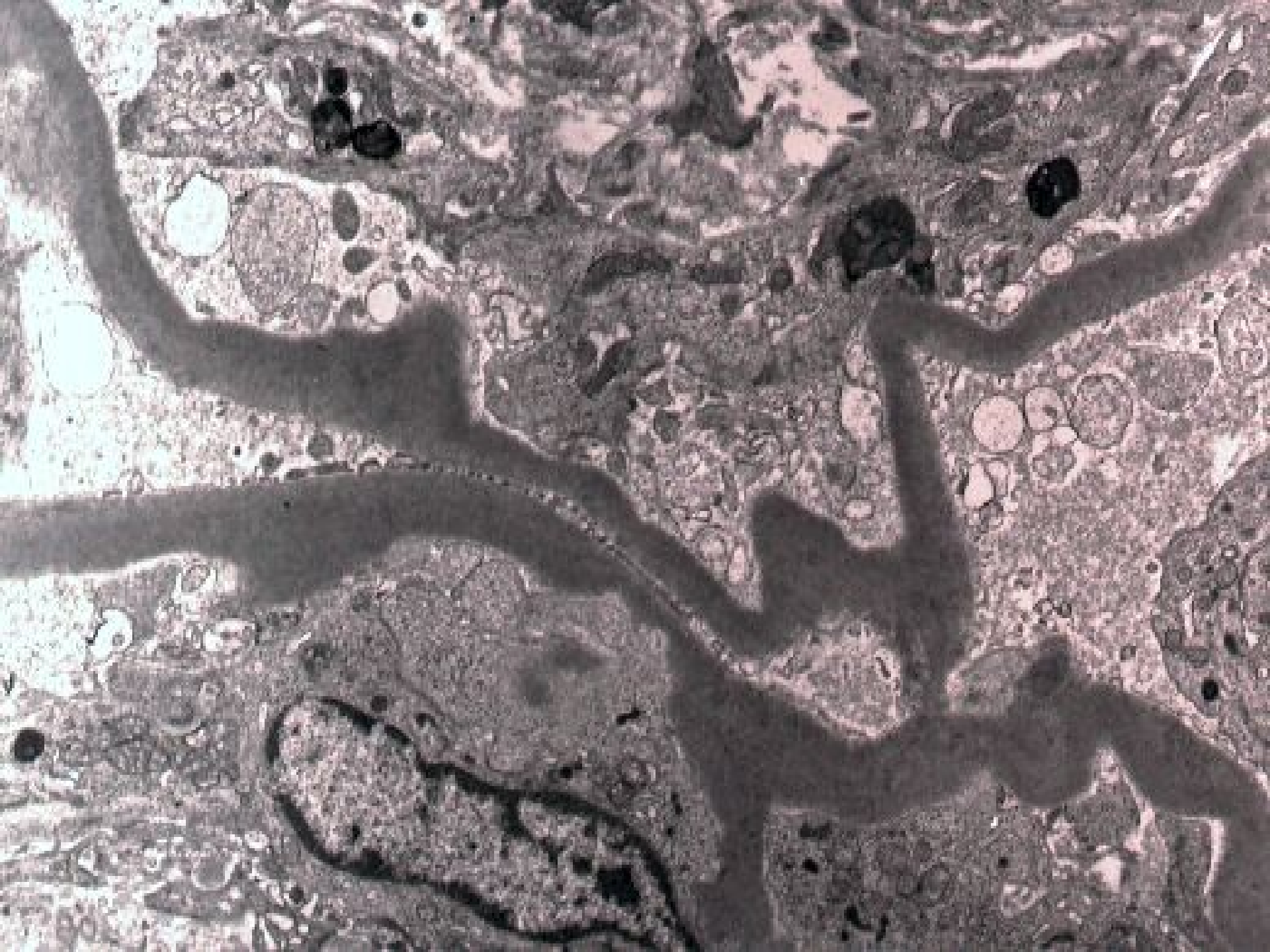
MPGN

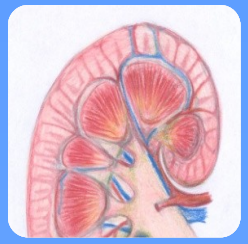
Electron microscopy findings

What are the electron microscopy findings?









MPGN (II)

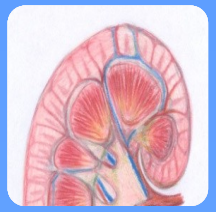
Clinical features:

-Mainly in children and young adults.

-Nephritic Syndrome.

-Renal insufficiency.

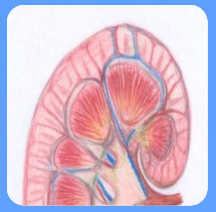
Prognosis ?



MPGN (II)

Pathogenesis:

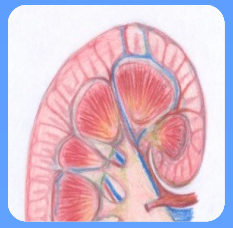
-C3 nephritic factor (IgG autoantibody against ACP convertase,C3bBb).



MPGN (II)

MPGN Type II Or Dense Deposit Disease (DDD).

What is the characteristic of this disease?

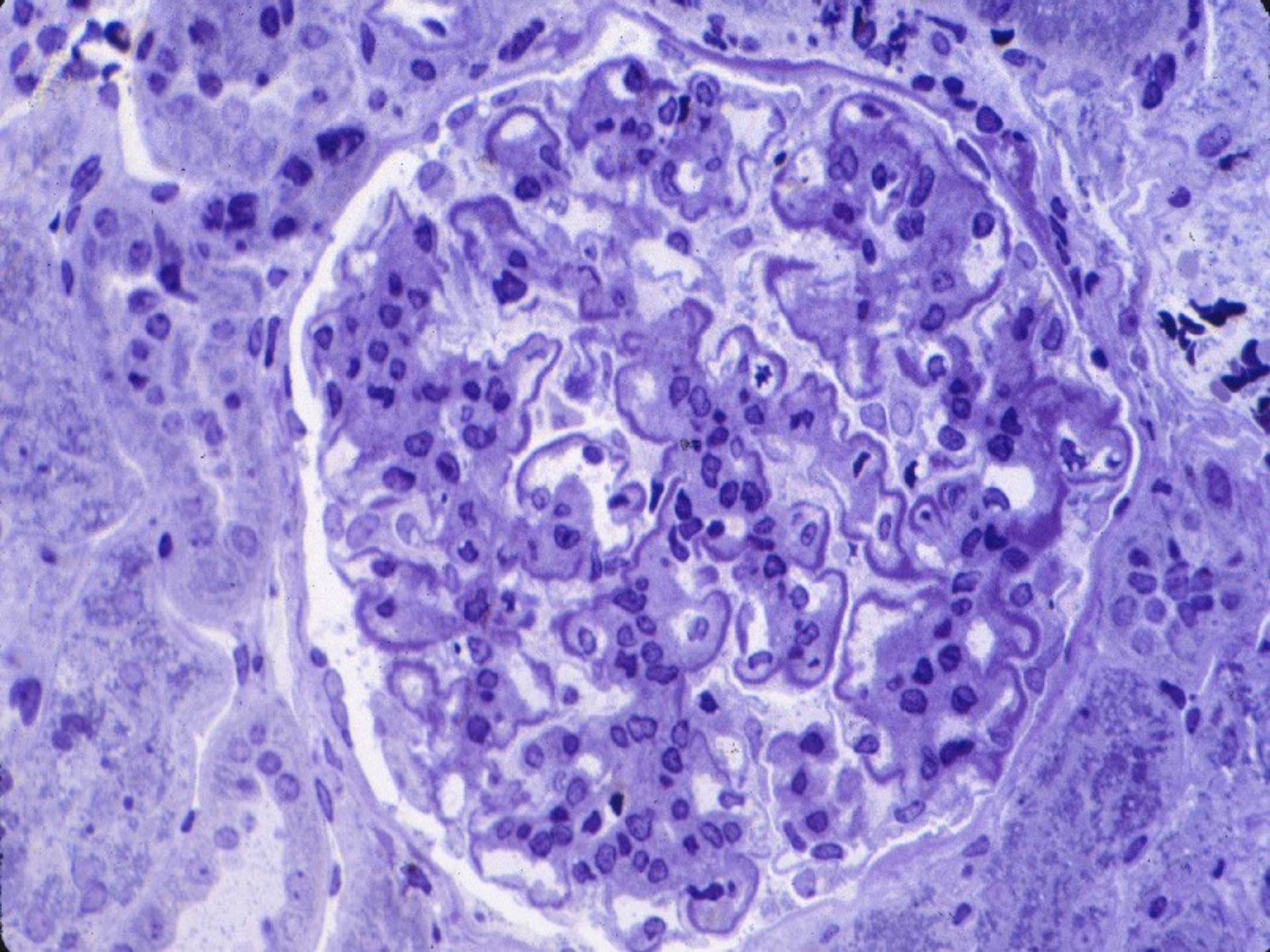


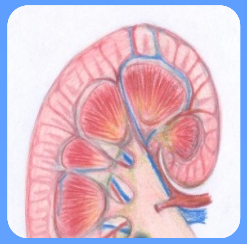
MPGN (II)

Dense deposit:

-Not of immune complex origin.

-Not deposits but alteration in the BM material.

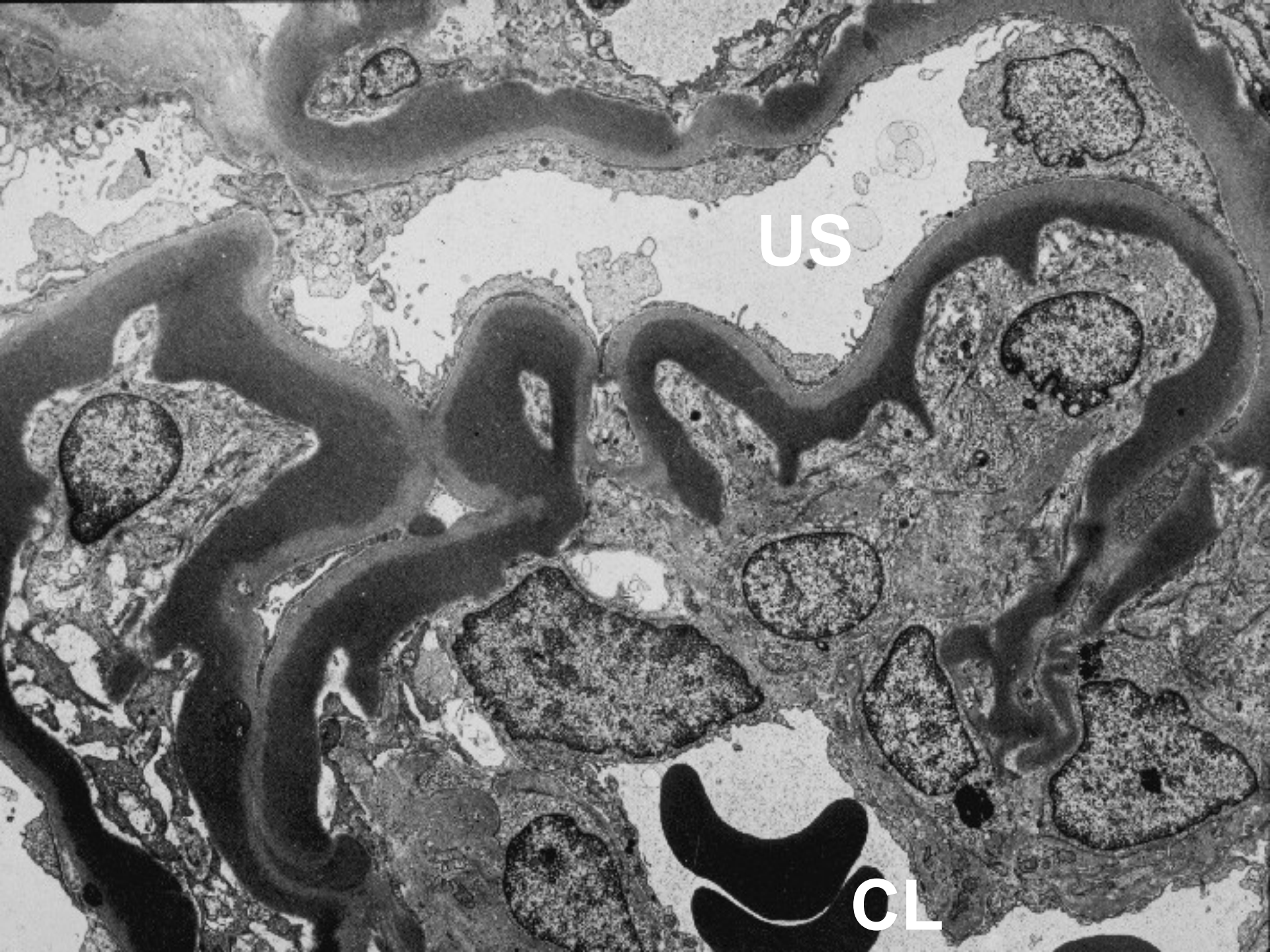


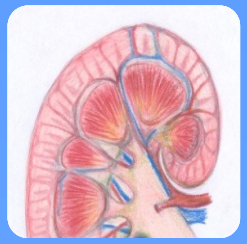


MPGN (II)

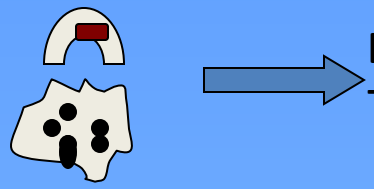
Immunofluorescent microscopy:

Widespread deposition of C3

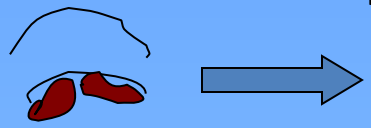

US
CL



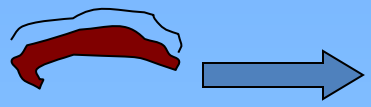
MPGN



Double contour (Tram Track)
Tuft (Hypercellularity).

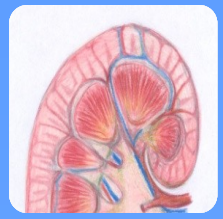


Type I:Subendothelial deposits

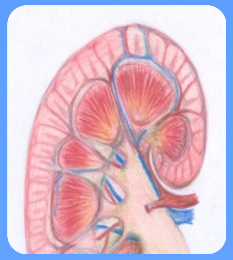


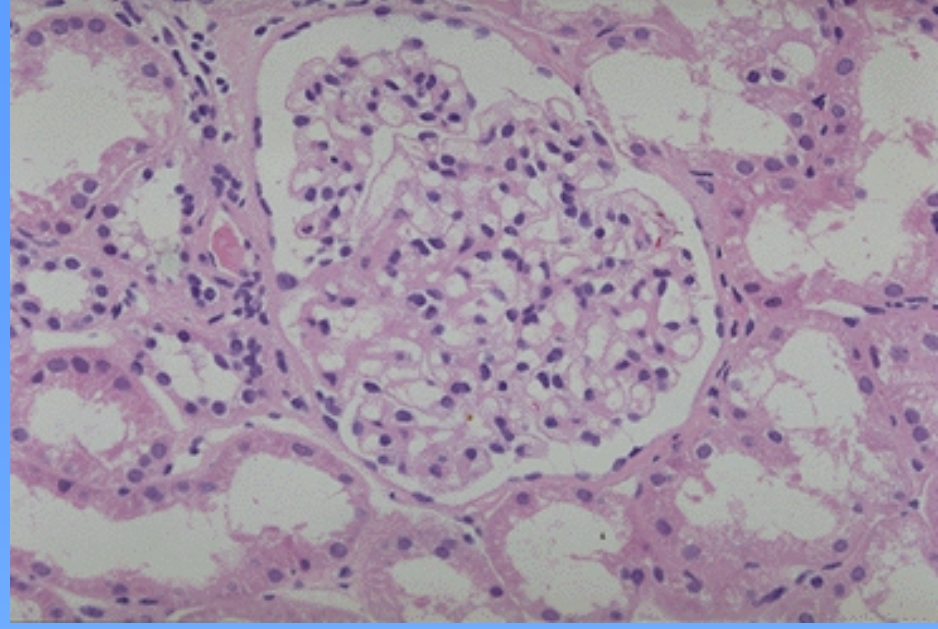
Type II:Dense Deposit Disease

3. Lupus nephritis

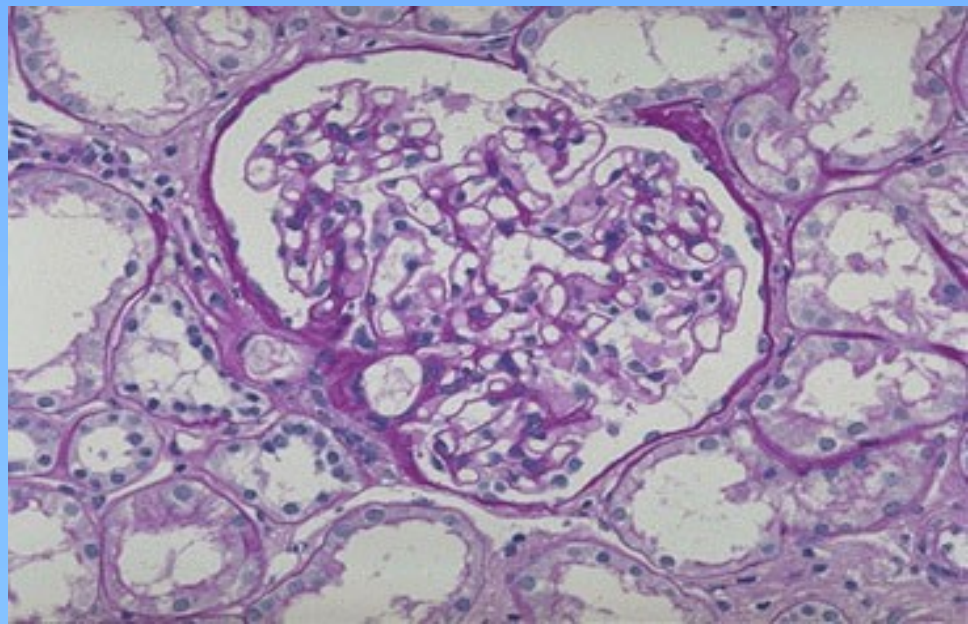


- **Renal involvement occurs in about 70% of SLE patients. Most patients have anti-dsDNA antibodies and are hypocomplementemic.**
- **The histological changes in lupus nephritis vary from mild mesangial cell proliferation to diffuse proliferative glomerulonephritis.**
- **About half of the patients with lupus nephritis have the diffuse proliferative form (i.e. the most severe form).**
- **IF and EM reveal mesangial and subendothelial immune complex deposits containing IgG, IgM, IgA, and C3. These complexes often contain ss- and ds- DNA.**

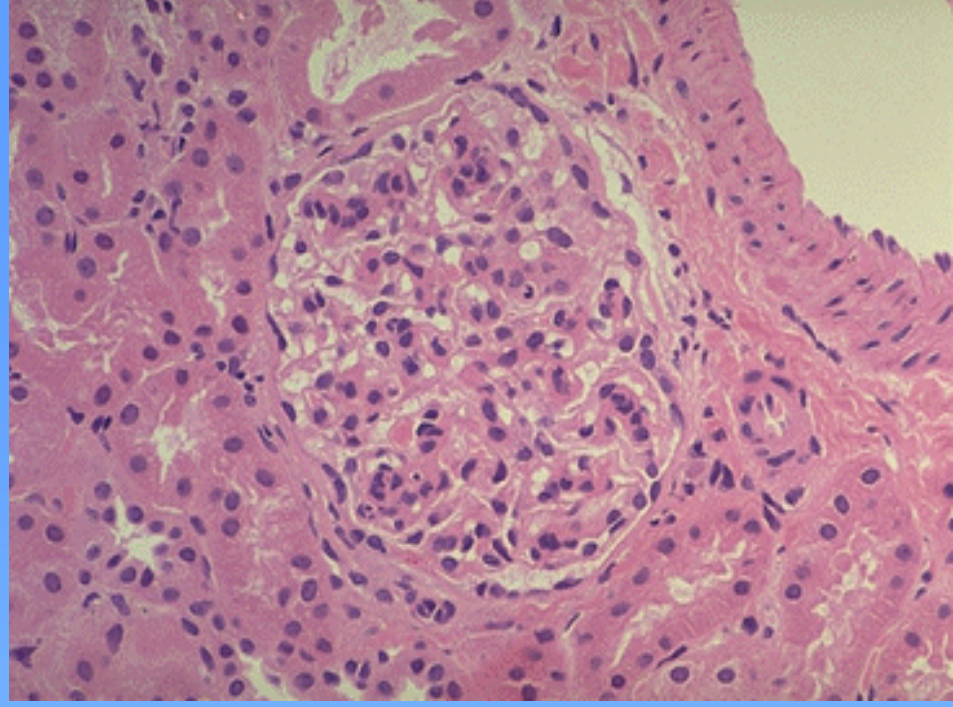


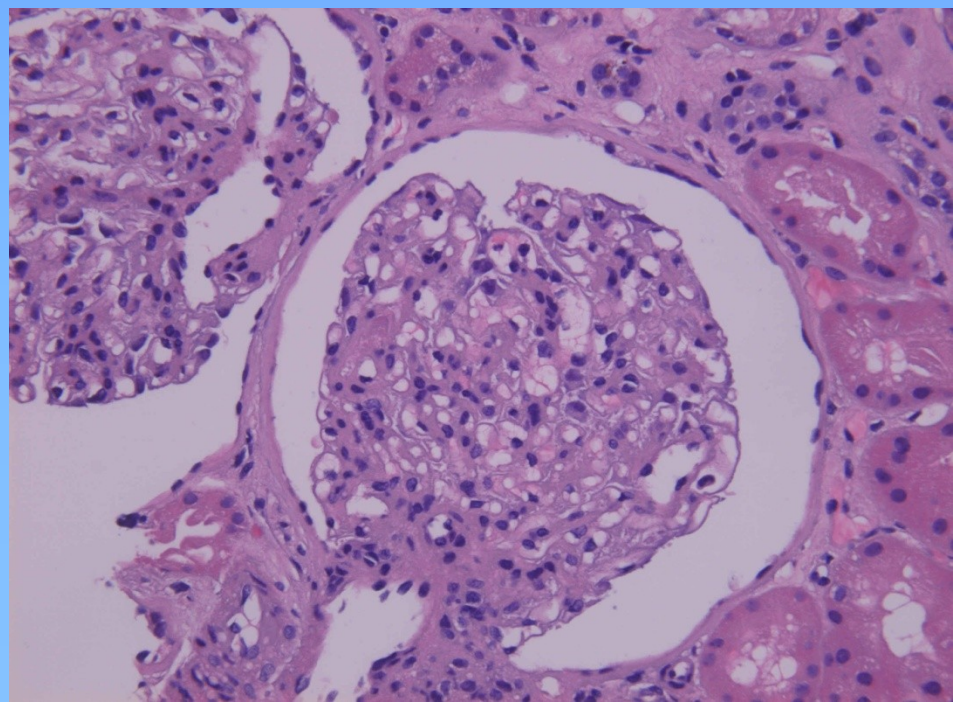


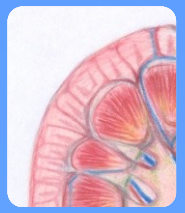
- Class I
- Minimal mesangial lupus nephritis



- Class II
- Mesangial proliferative lupus nephritis

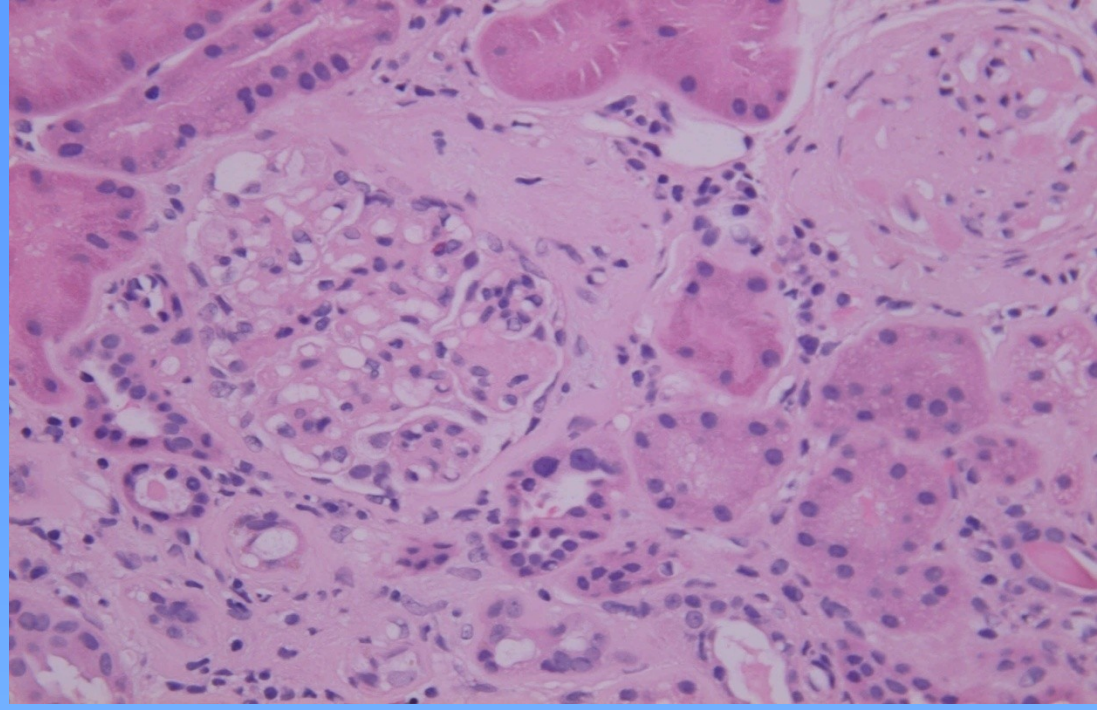


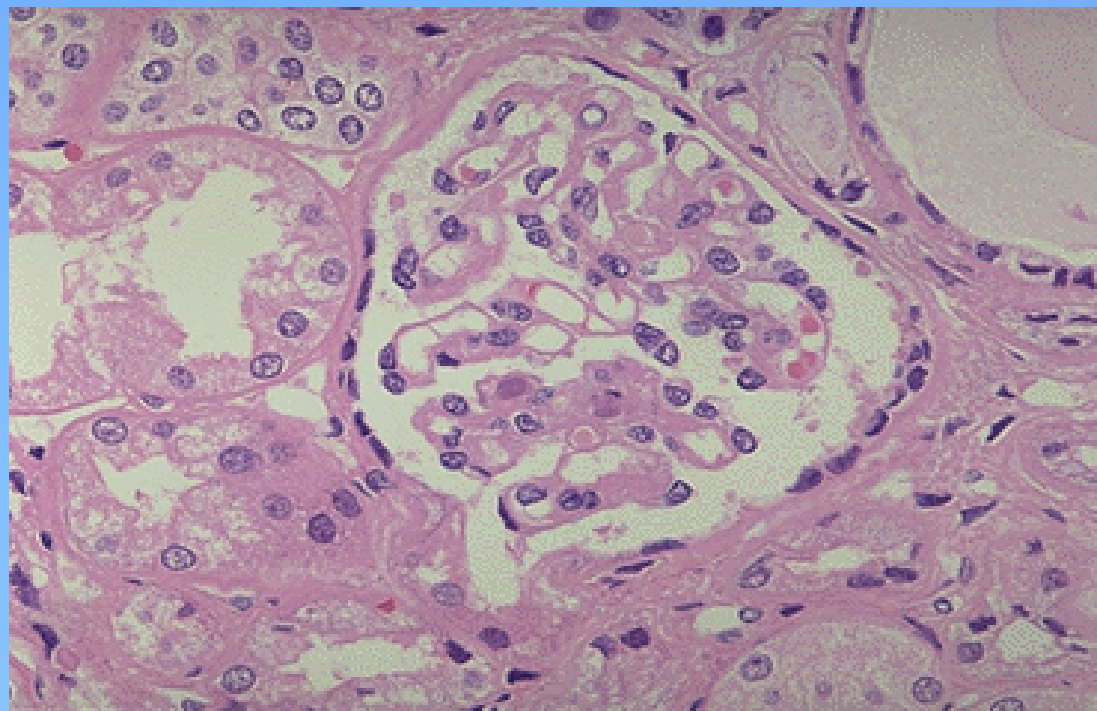


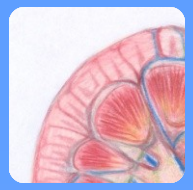


Class III

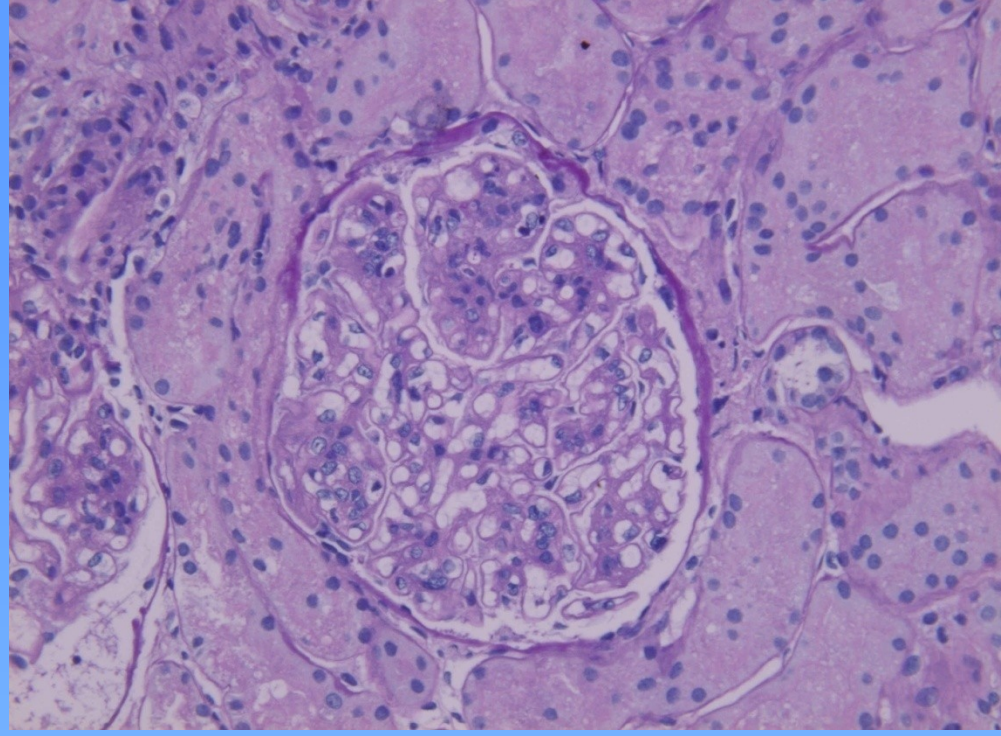
- Focal lupus nephritis

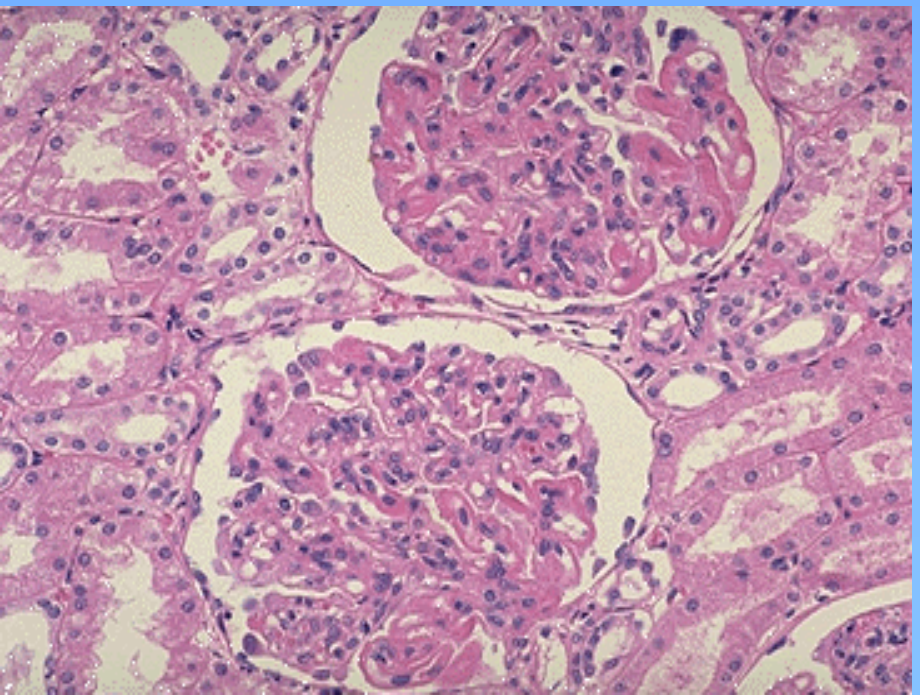


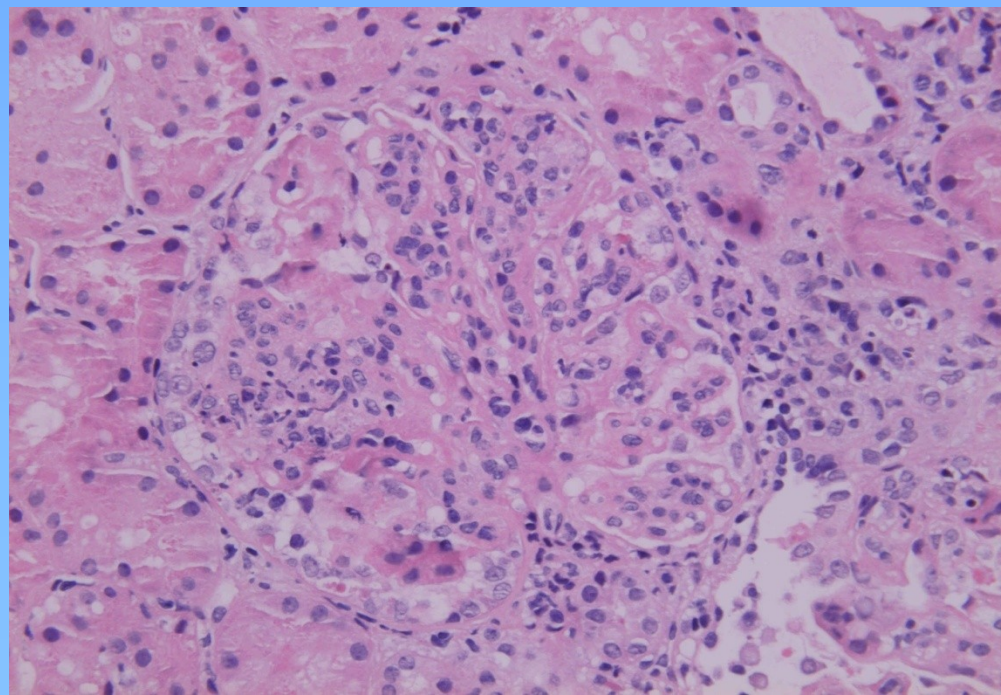




- Class IV
- Diffuse segmental (IV-S) or global (IV-G) lupus nephritis

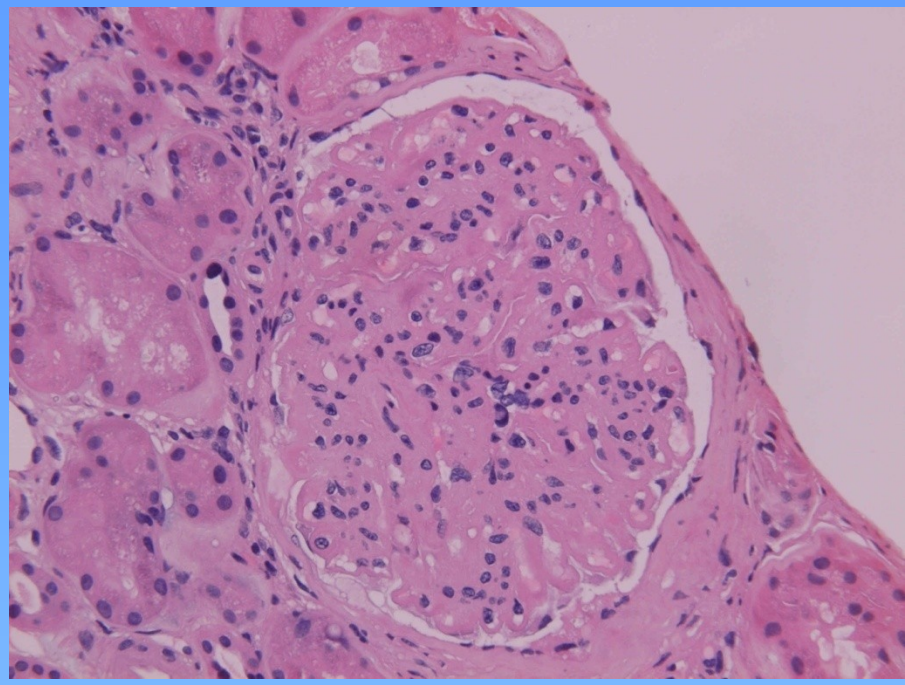


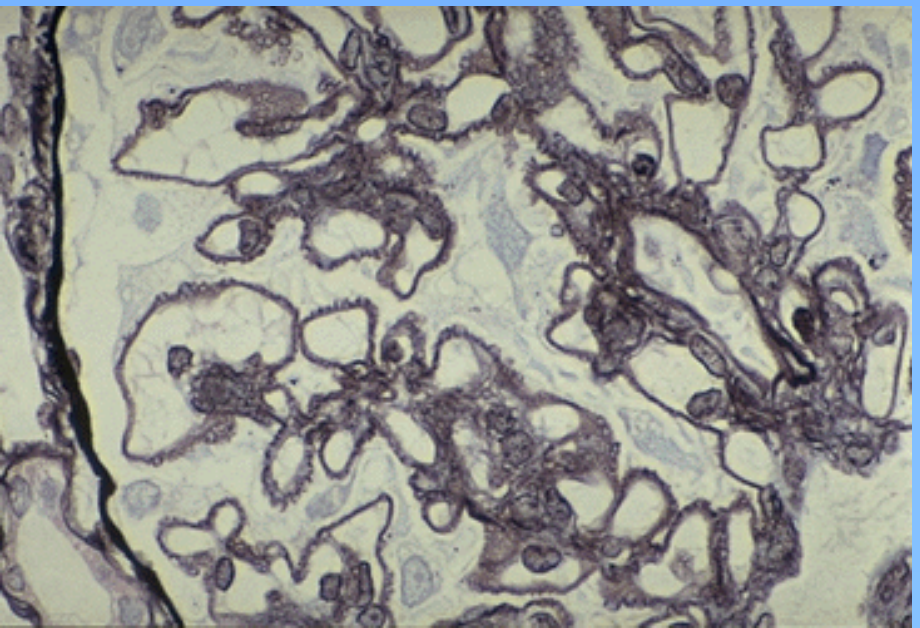




- Class V

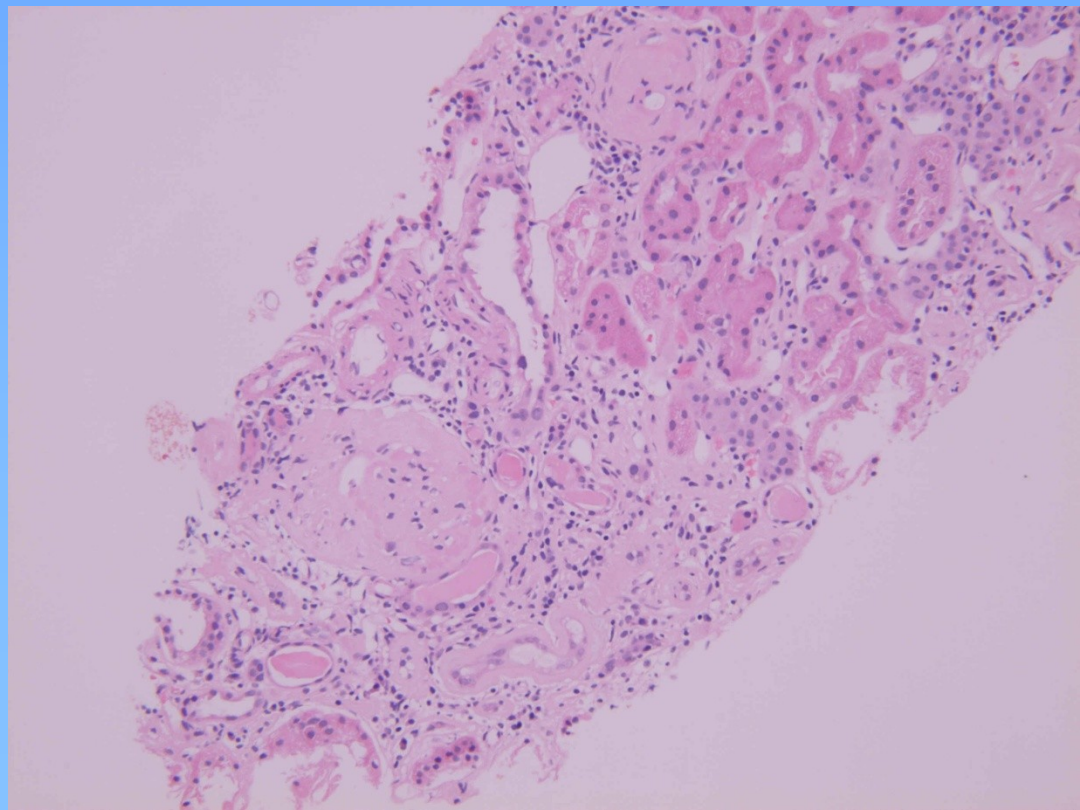
- Membranous lupus nephritis





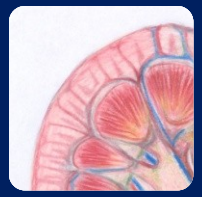
- Class VI

- Advanced sclerosing lupus nephritis



RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Clinical conditions that evolve with rapidly progressive decline in renal function and an active urine sediment are usually characterized by an inflammatory process that results in the formation of cellular crescents within Bowman's space (crescents).



RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Rapid decline in renal function (over several days or few weeks)

Active urine sediment

Usually no edema and no hypertension

CRESCENTIC GLOMERULONEPHRITIS

Idiopathic or primary crescentic glomerulonephritis:

- Type I, anti-GBM disease
- Type II, immune complex-mediated
- Type III, pauci immune (ANCA-associated)
  - Vasculitides (ANCA-associated):
    - microscopic form of polyarteritis nodosa,
    - Wegener's granulomatosis
    - Churg-Strauss syndrome
    - Drug-induced vasculitides

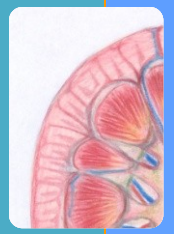
Other primary glomerulonephritides:

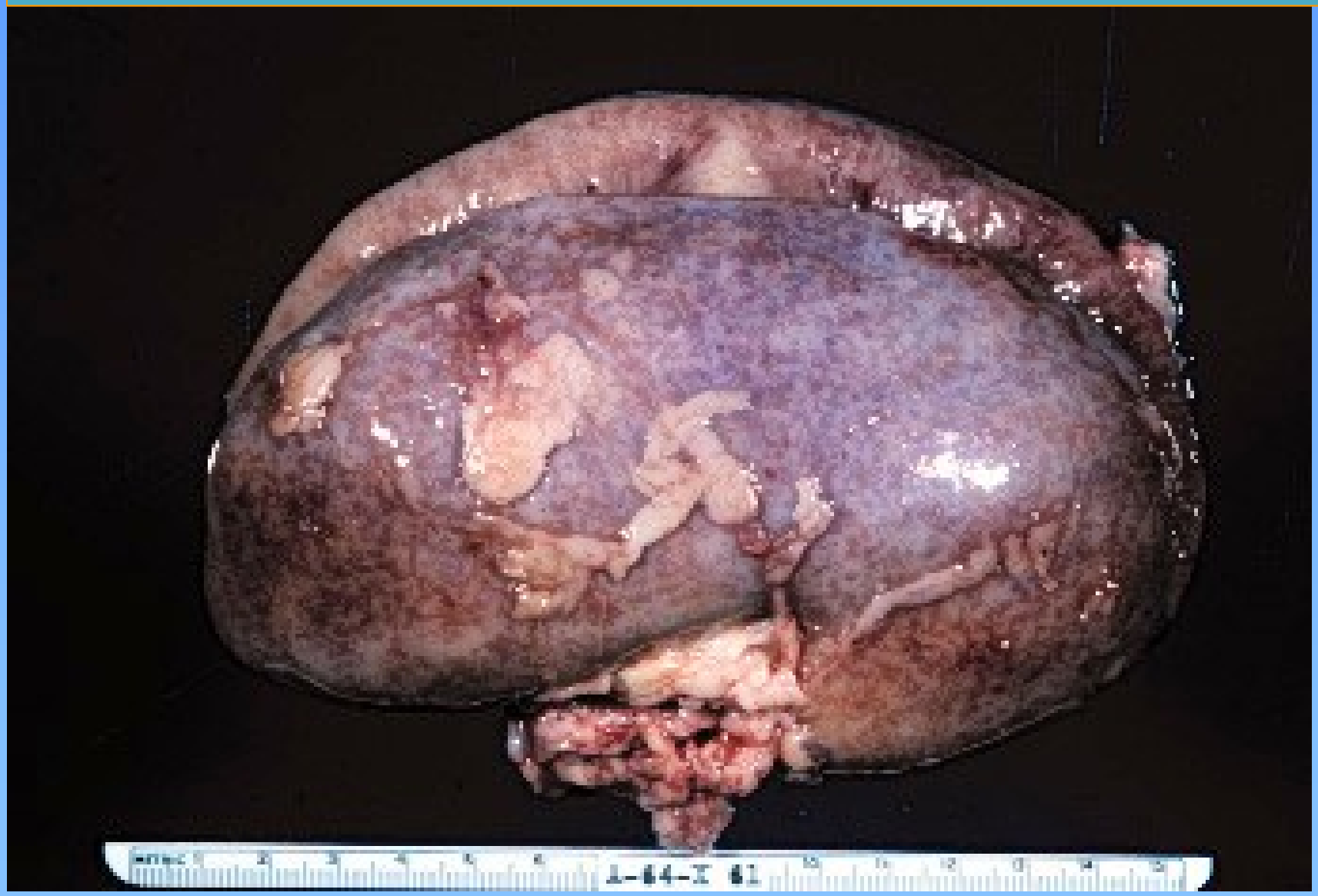
- post-infectious GN, IgA nephropathy, MPGN, etc.

Systemic diseases (SLE, RA, H-S purpura)

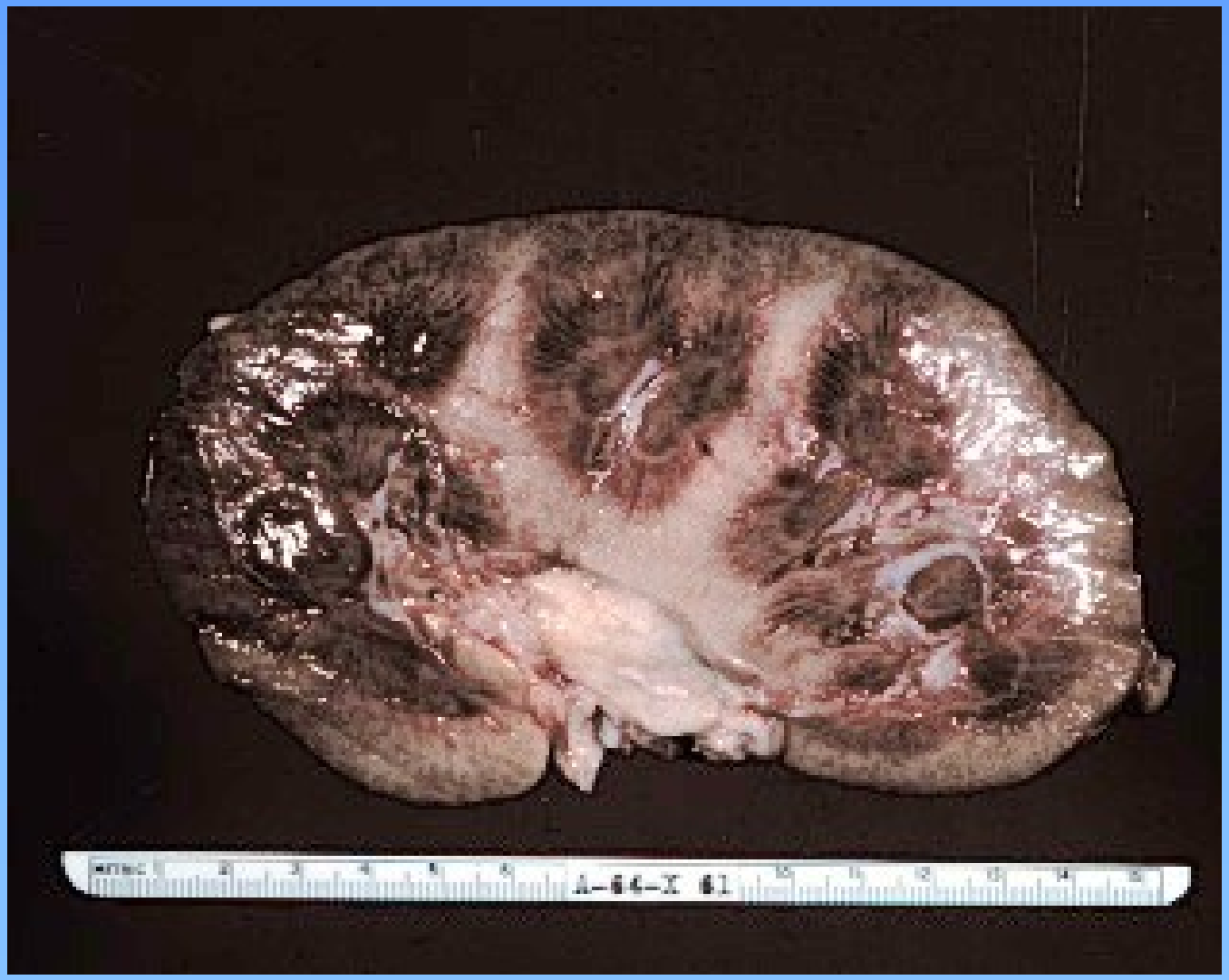
The kidney of rapidly progressive glomerulonephritis.

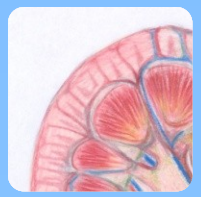
It measures 9 or 10 cm from pole to pole the surface is pale and smooth, very different from the kidney of chronic glomerulonephritis - prognosis is very poor

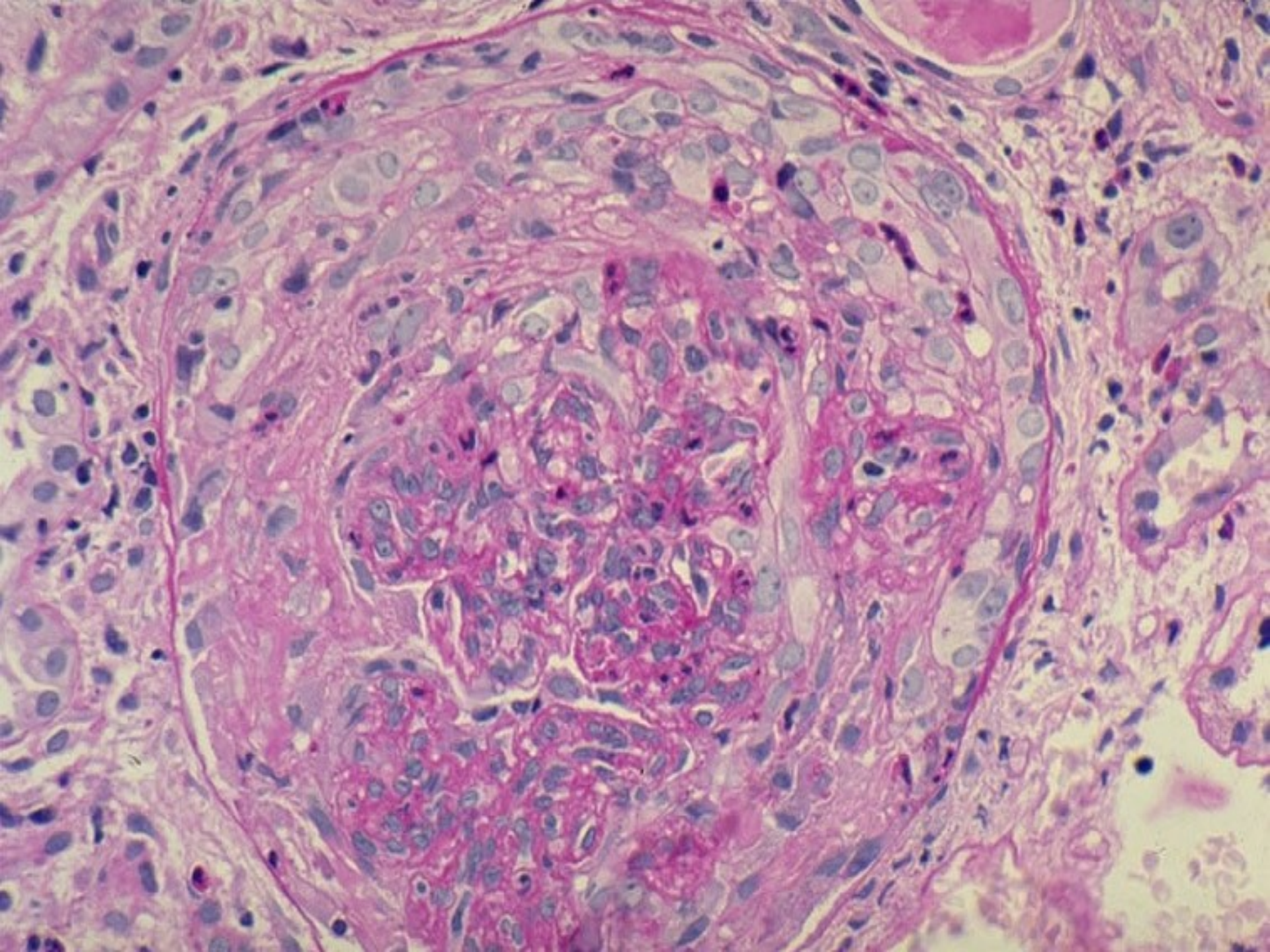


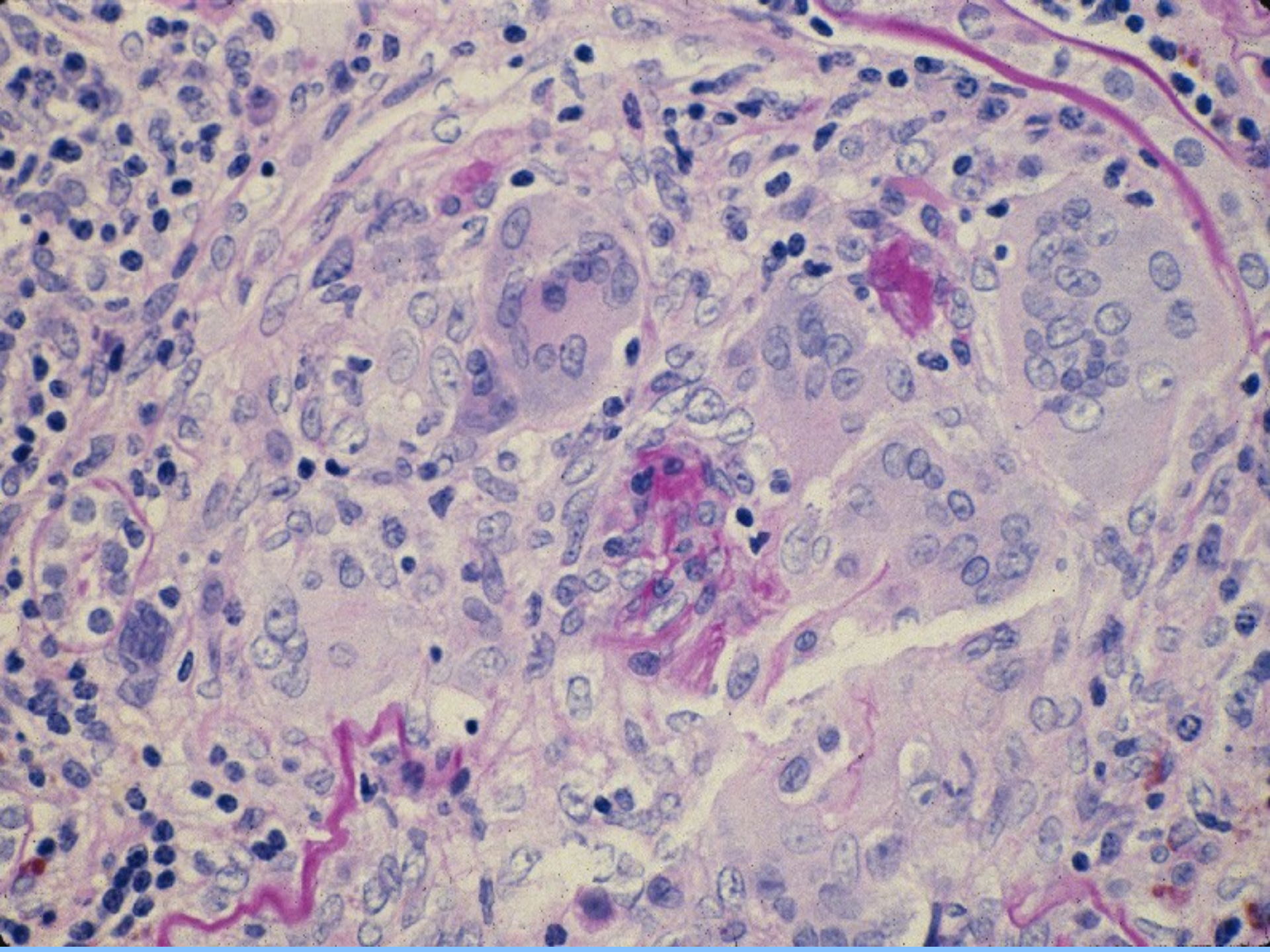


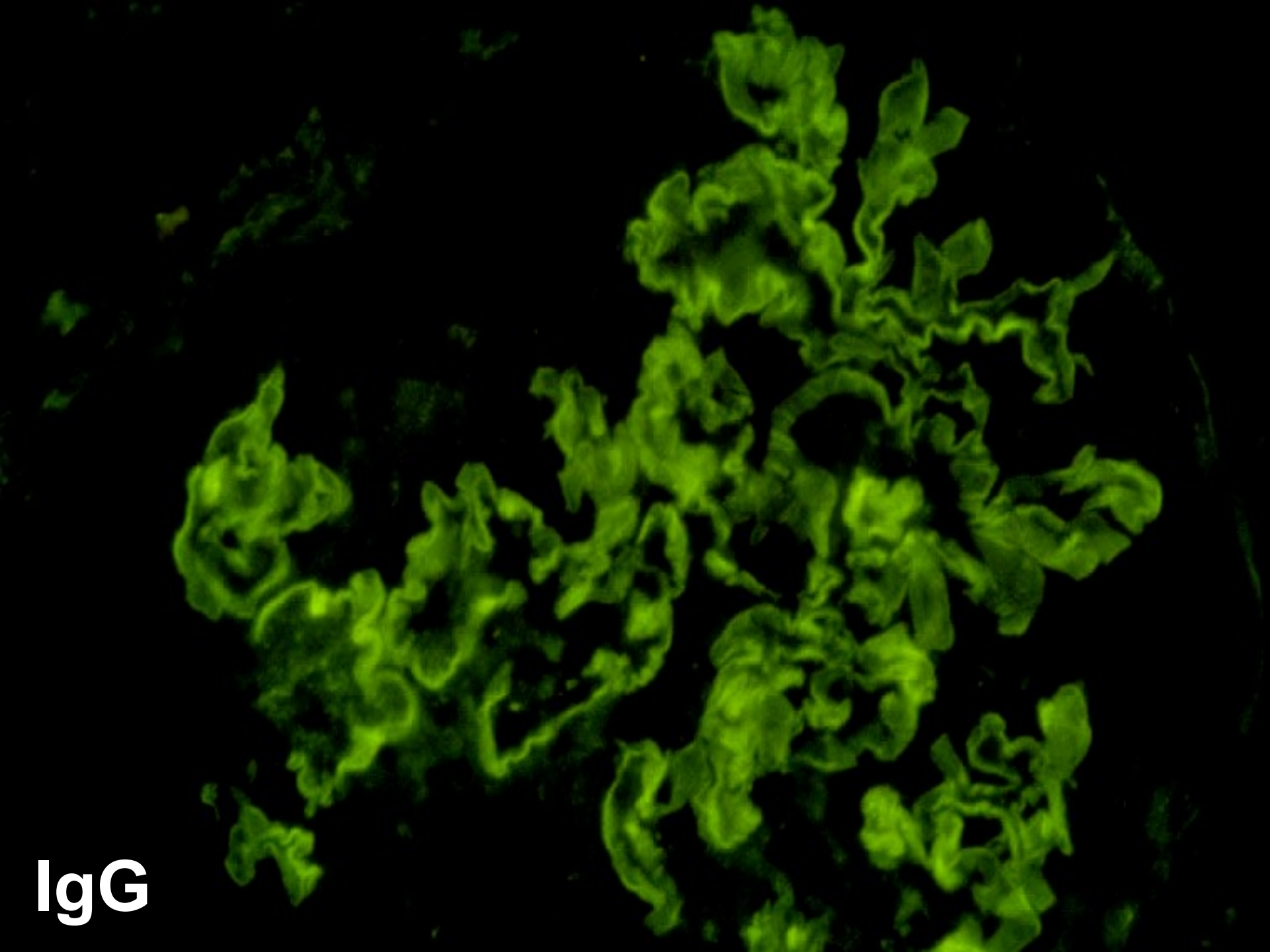
Cross-section of a kidney with rapidly progressive glomerulonephritis: the cortex is pale and swollen. Disease is characterized by epithelial crescents around the glomeruli.

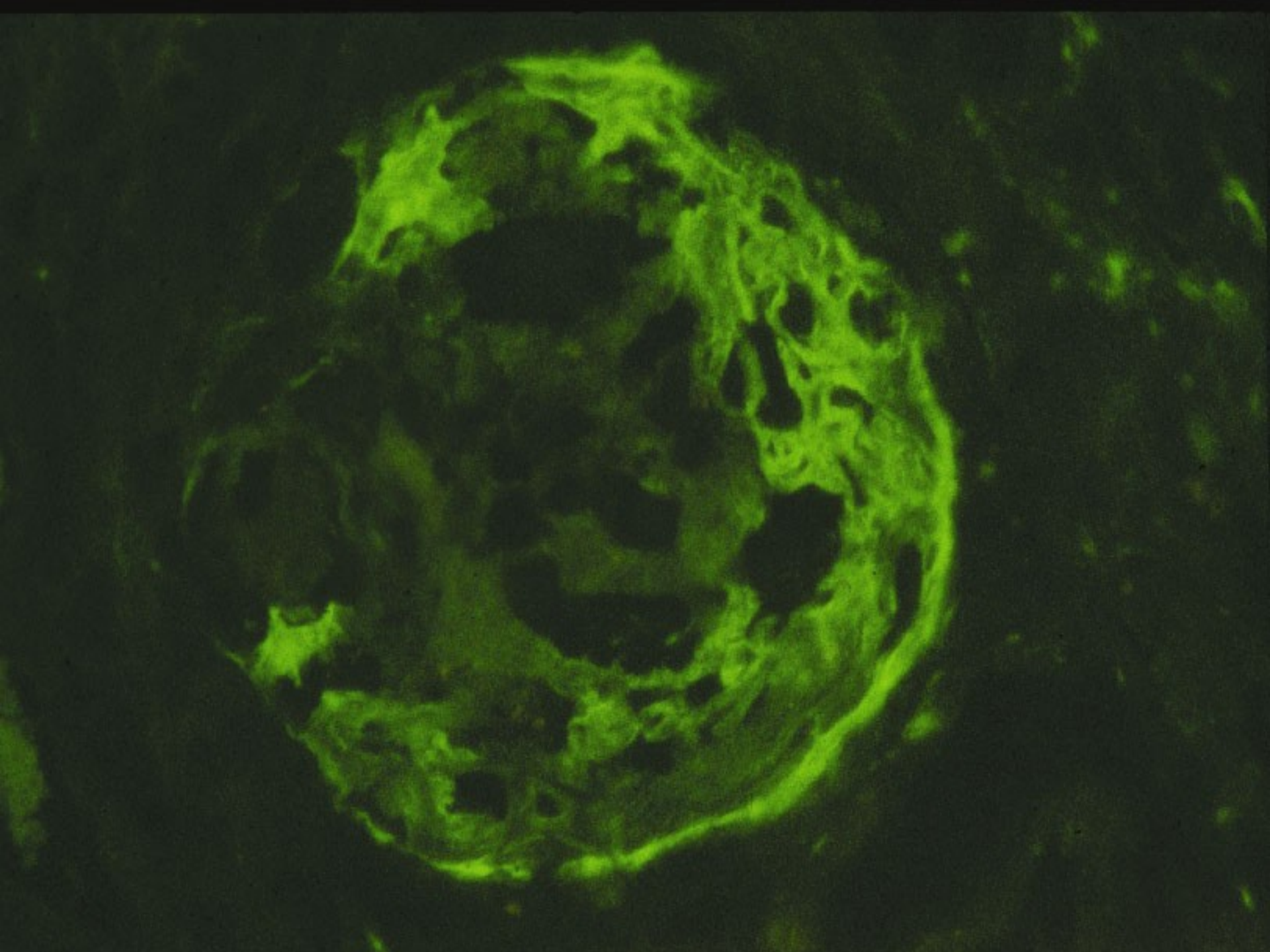


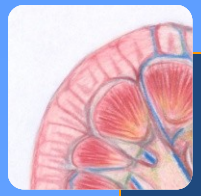







IgG



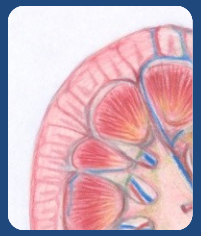


ASYMPTOMATIC HEMATURIA (PROTEINURIA)

Hematuria or proteinuria (persistent microhematuria)

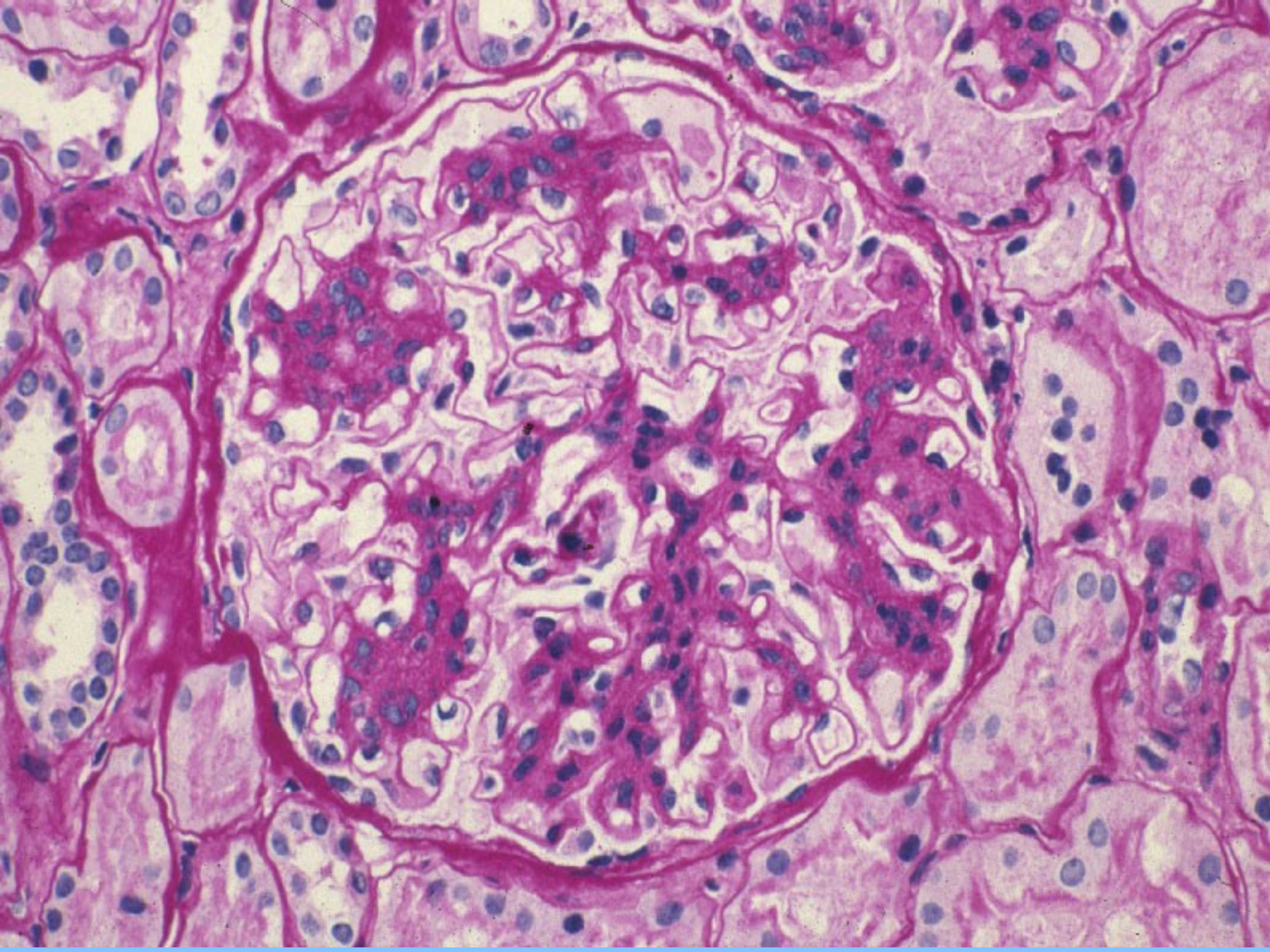
Usually normal renal function (early during the course)

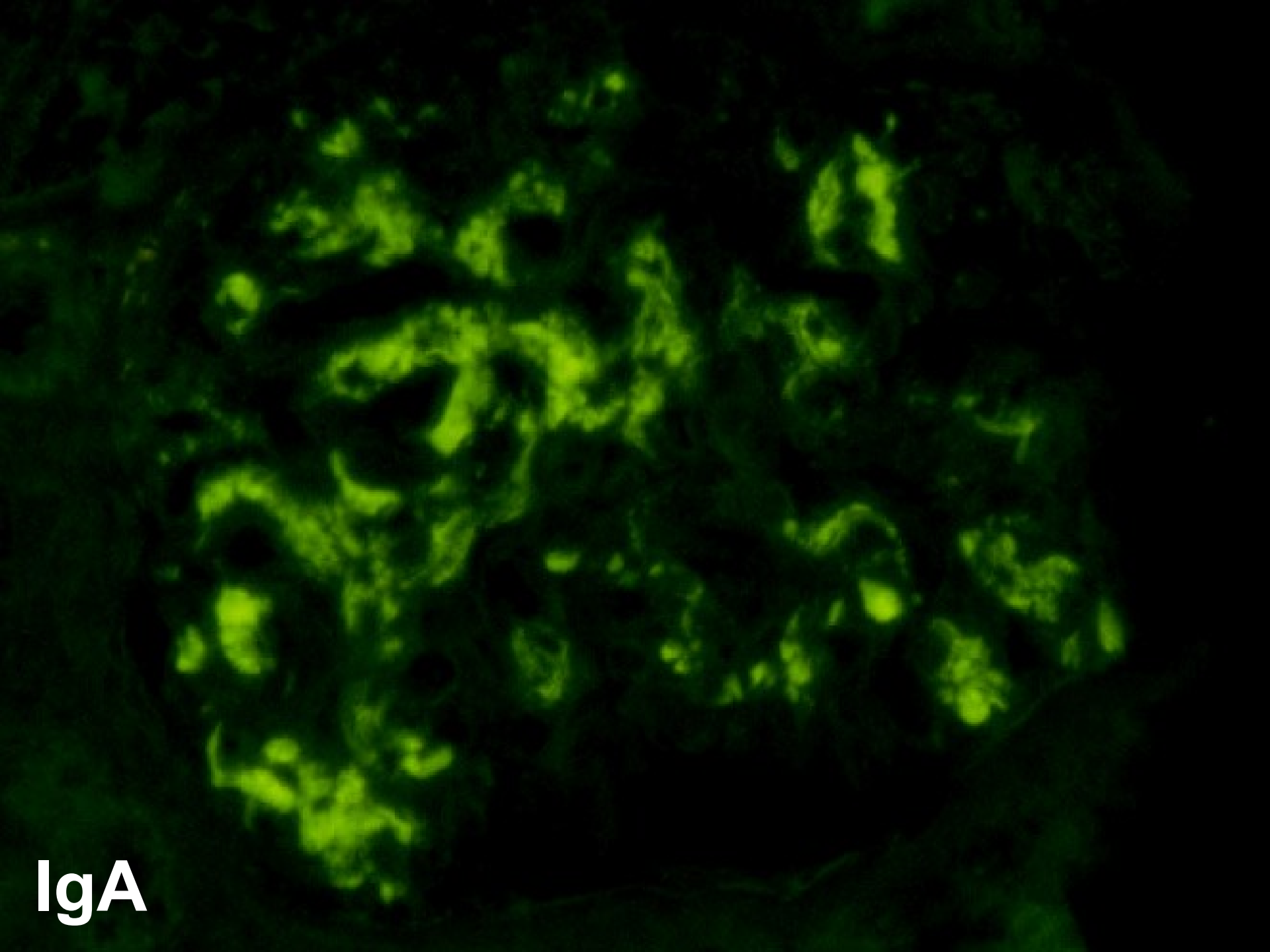
Usually no hypertension or edema

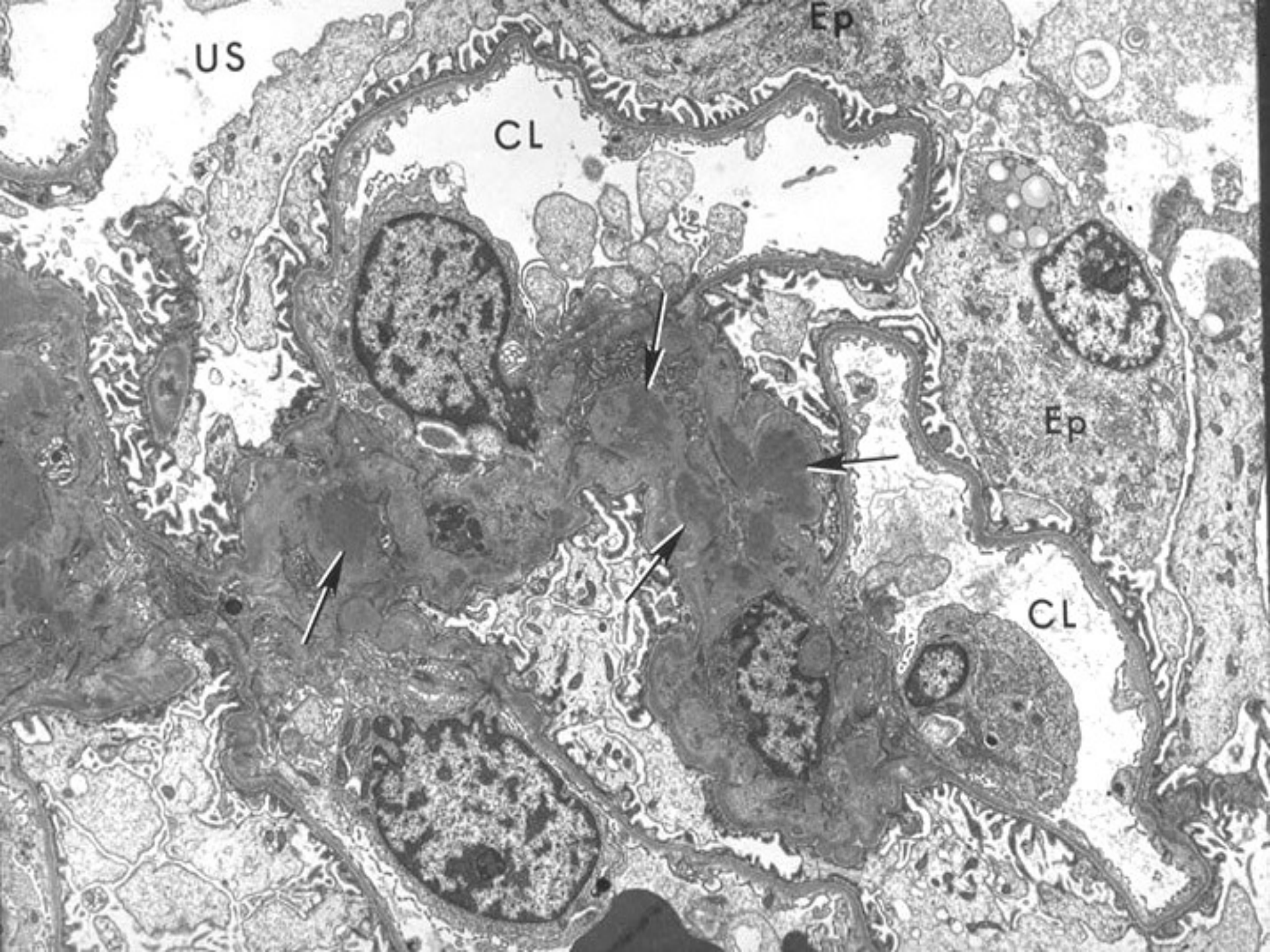


ASYMPTOMATIC HEMATURIA/PROTEINURIA

These conditions are characterized morphologically either by focal necrotizing and/or inflammatory lesions of the glomeruli or by basement membrane anomalies that result in greater capillary fragility.




IgA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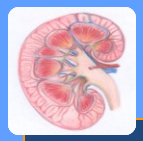


CHRONIC NEPHRITIC SYNDROME

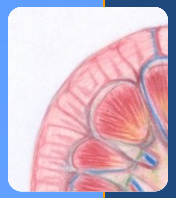
Azotemia

Active urine sediment (variable)

Proteinuria (variable)

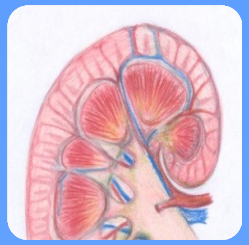
Past history of RPGN, nephrotic syndrome, or nephritic syndrome

Hypertension



CHRONIC RENAL FAILURE
CHRONIC NEPHRITIC SYNDROME

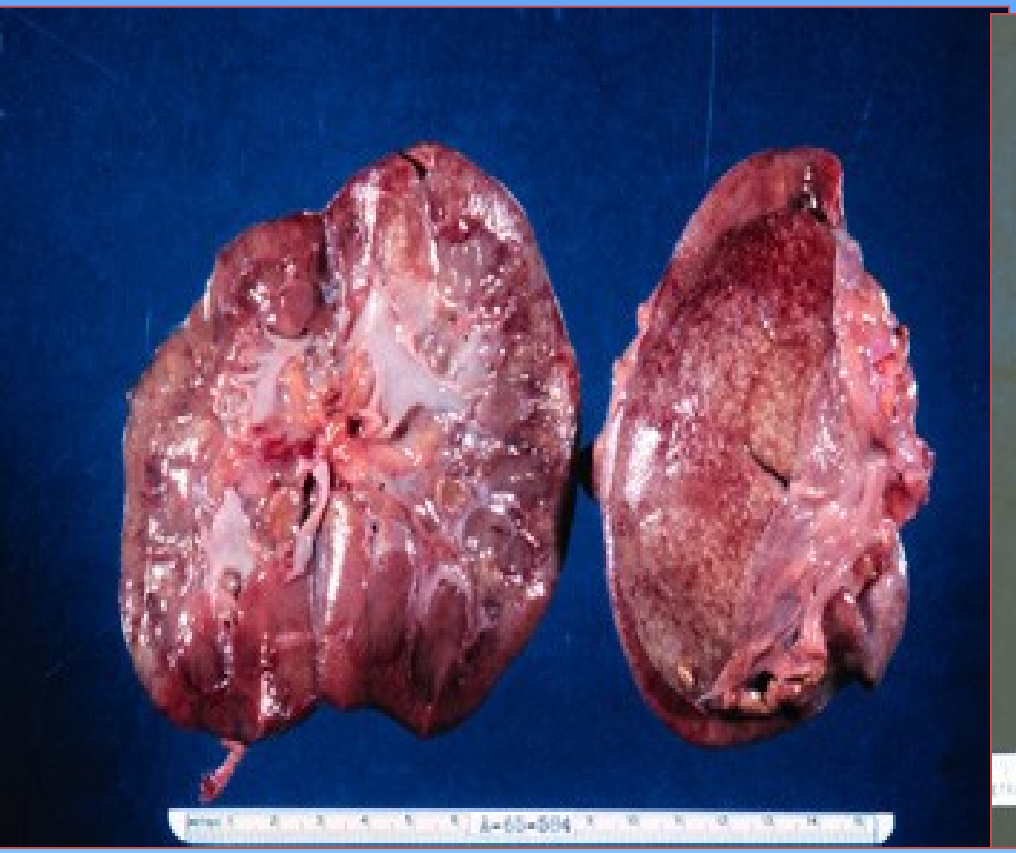
The structural equivalent of this syndrome is end-stage renal disease, with widespread global glomerular obsolescence (sclerosis), tubular atrophy, interstitial fibrosis, and variable degree of arterial and arteriolar sclerosis. A more precise diagnosis can often be established by immunohistochemical and ultrstructural studies.

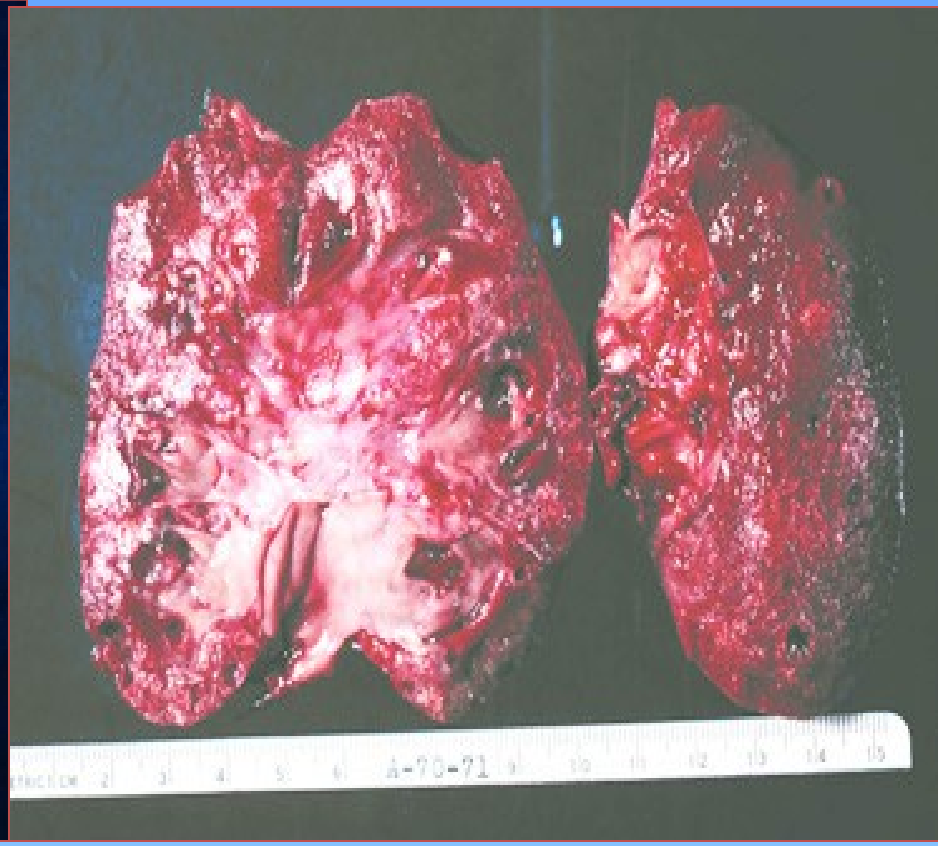


END STAGE RENAL DISEASE

Chronic Renal Failure

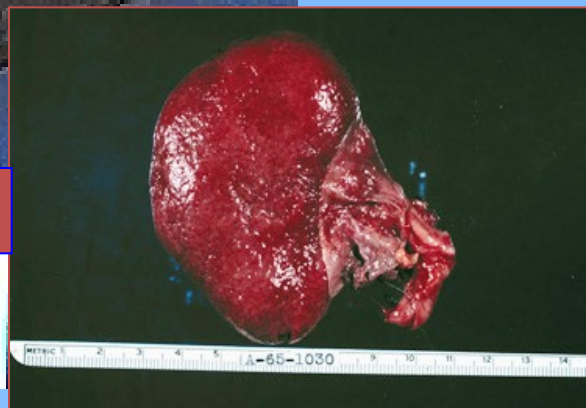
"End stage kidney" of chronic glomerulonephritis. These are severely contracted kidneys each measure about 2 x 3".. Notice the cortices small amount of parenchyma and the finely granular surfaces. Such kidneys are incompatible with life.



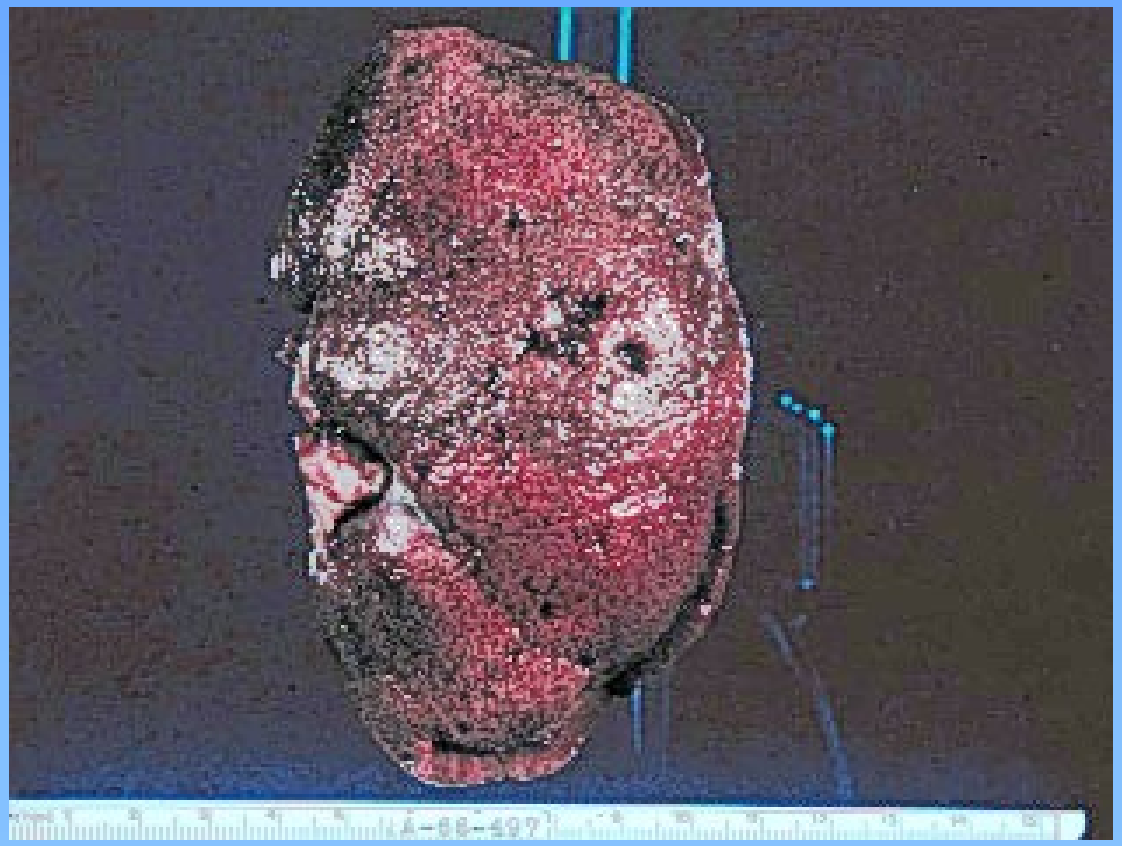


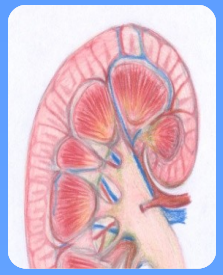
"End stage kidney" of chronic glomerulonephritis. This is the kidney of a 38 year old man who presented with an insidious onset of the three signs of uremia, that is loss of appetite, lethargy, and the laboratory finding of an increased BUN. He had no antecedent history of acute glomerulonephritis.

Extremely contracted and finely granular



Contracted kidney with a finely granular surface representing another glomerular disease, Kimmelsteil-Wilson disease or diabetic glomerulosclerosis. Grossly is indistinguishable from chronic glomerulonephritis. Notice larger scars rather shallow pits on the surface: these represent chronic pyelonephritis another disease that diabetics are apt to develop.





CONCLUSION