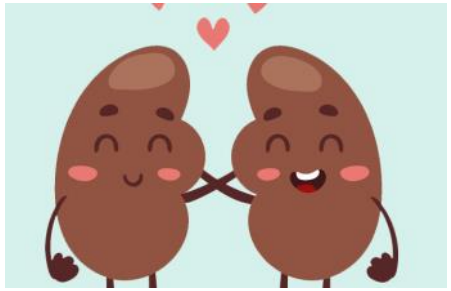
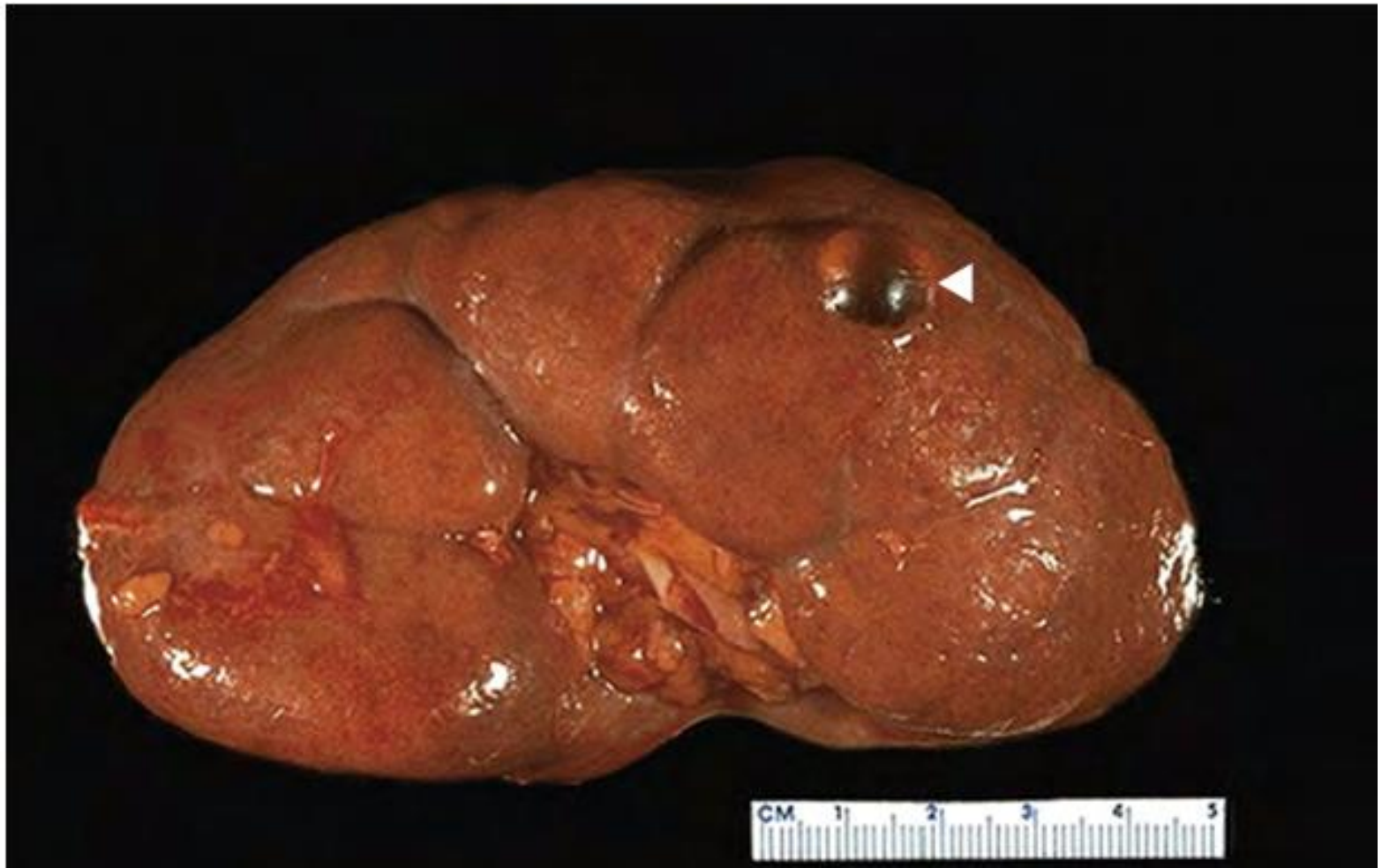
PATHOLOGY OF RENAL SYSTEM, LAB 1

Dr. Manar Rizik Al-Sayyed, M.D, Jordanian board

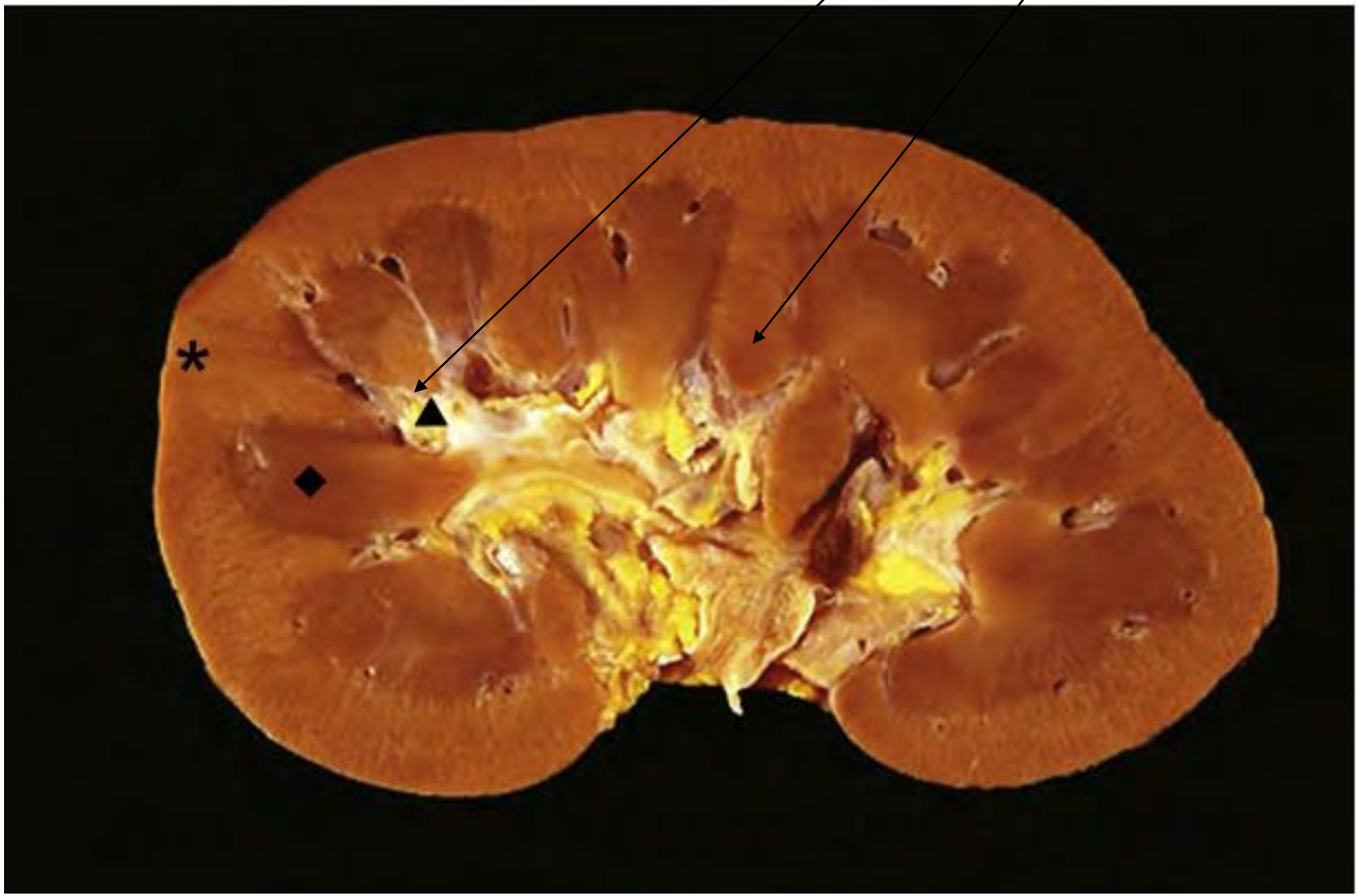


NORMAL KIDNEY, GROSS

- This normal adult kidney has a pattern of fetal lobulations that still persists, as it sometimes does in adults. The hilum at the center contains some adipose tissue. On the right is a smooth-surfaced, small, clear fluid–filled simple renal cyst (◄).

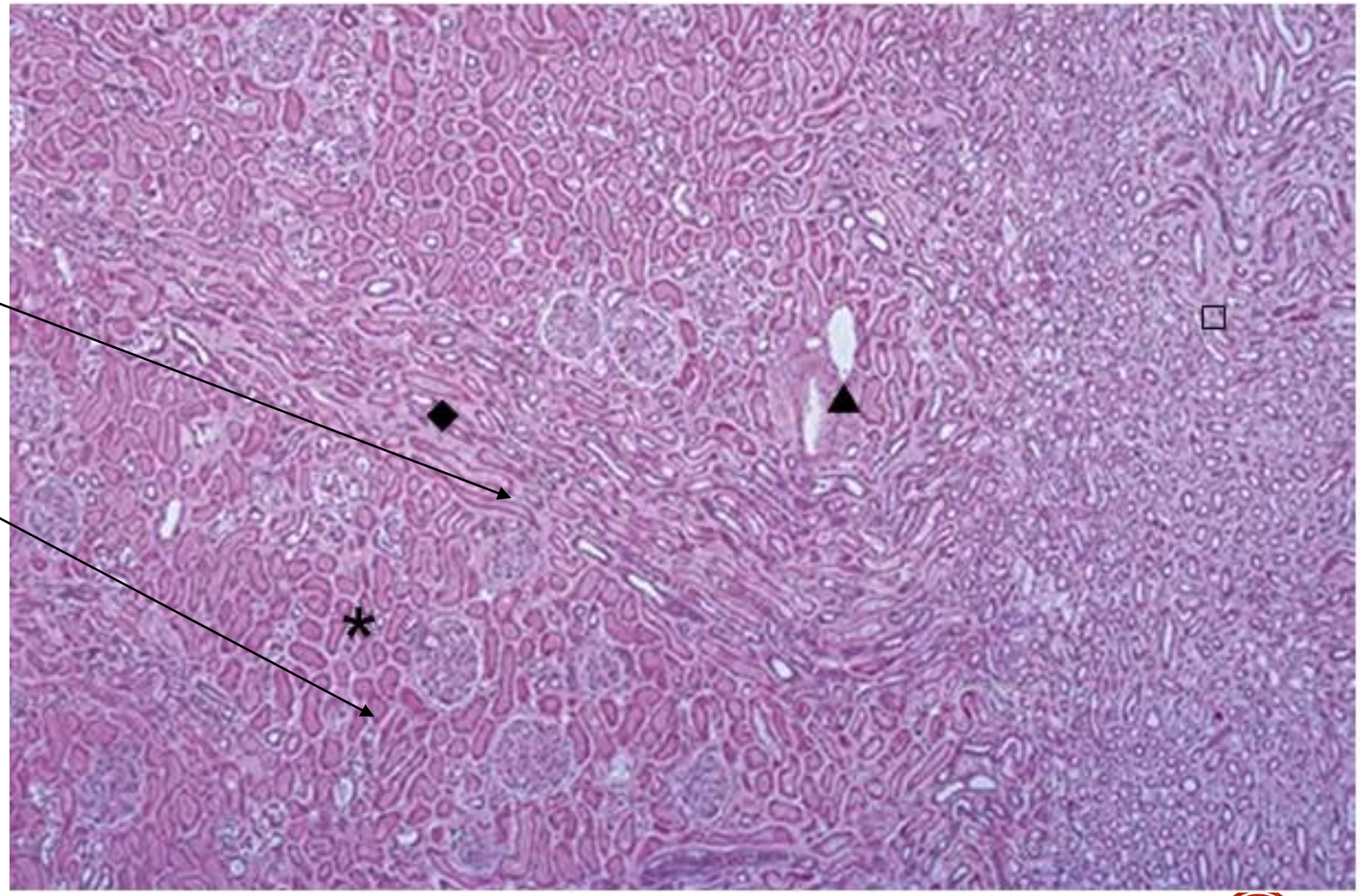


- In cross-section, this normal adult kidney shows the lighter outer renal cortex (*), normally 5 to 10 mm in thickness, and darker inner medulla ( ) with central pelvis containing adipose tissue. Note the renal papillae ( ) projecting into the calyces, through which collecting ducts drain the excreted urine into the renal pelvis.

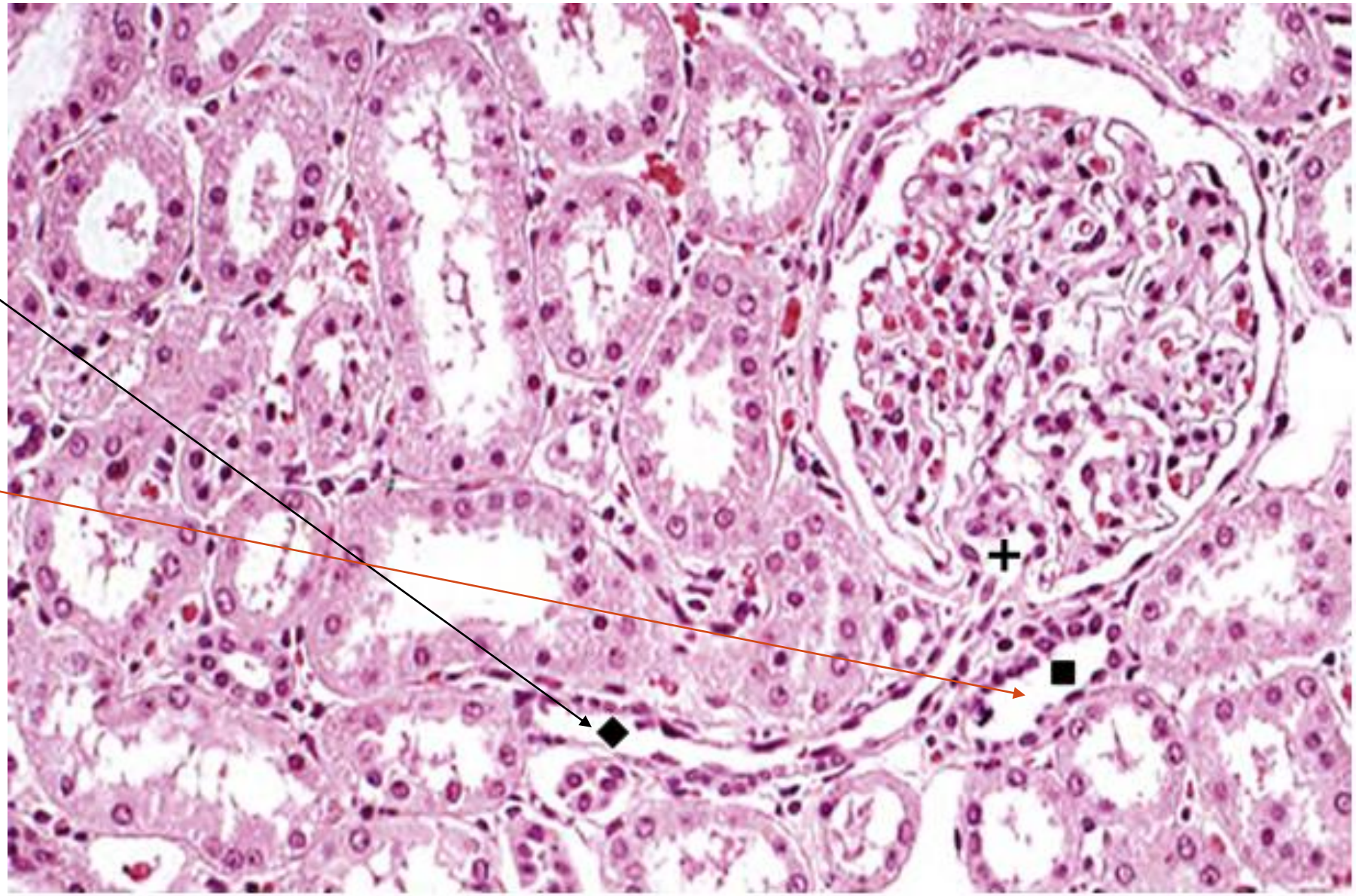


NORMAL KIDNEY, MICROSCOPIC

- The corticomedullary junction of the kidney is shown. The cortex contains a medullary ray—a renal column extending to the medulla. Within the cortex are glomeruli and tubules.

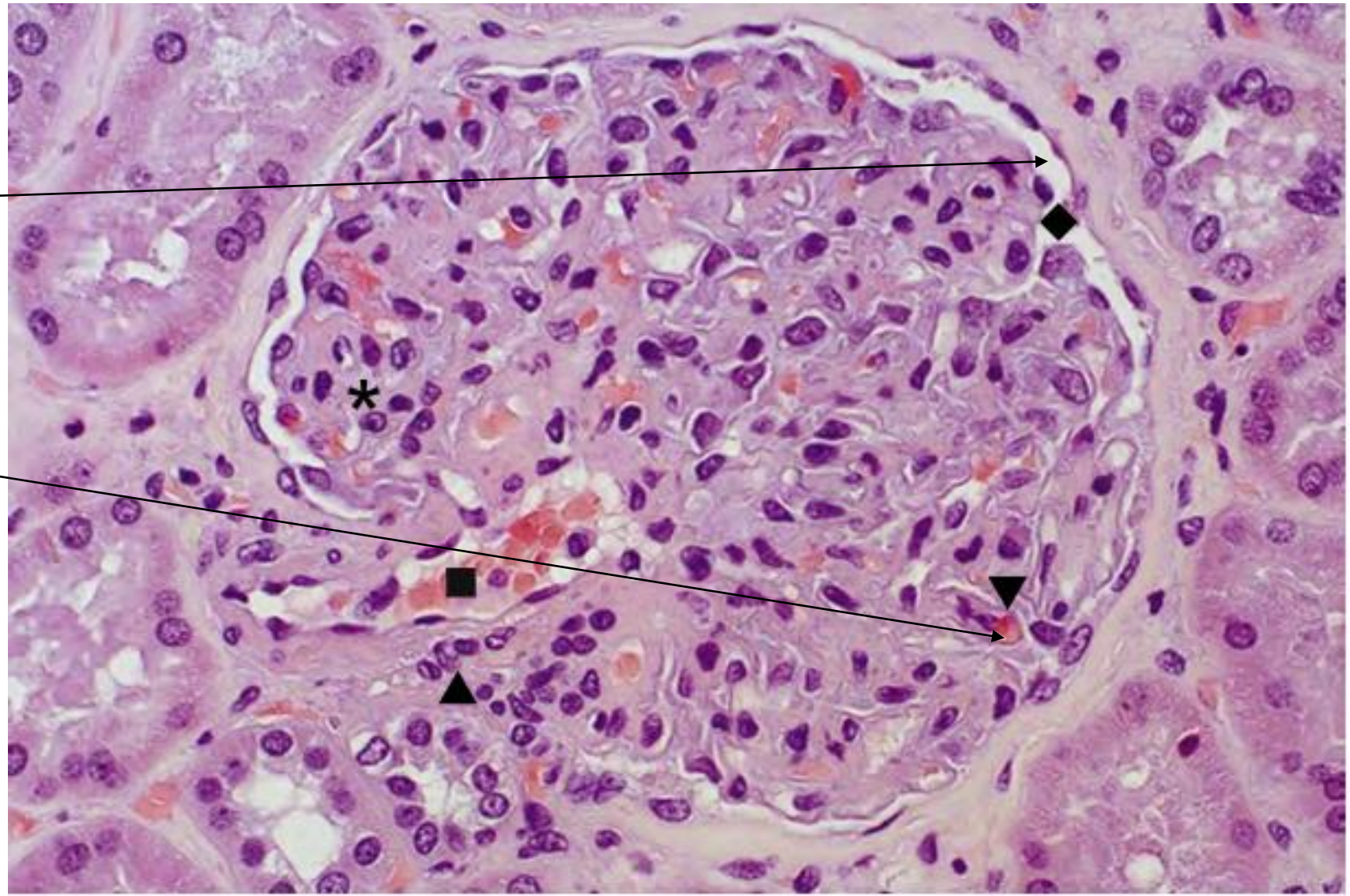


- Afferent arteriole
- Vascular pole +
- Distal convoluted tubule



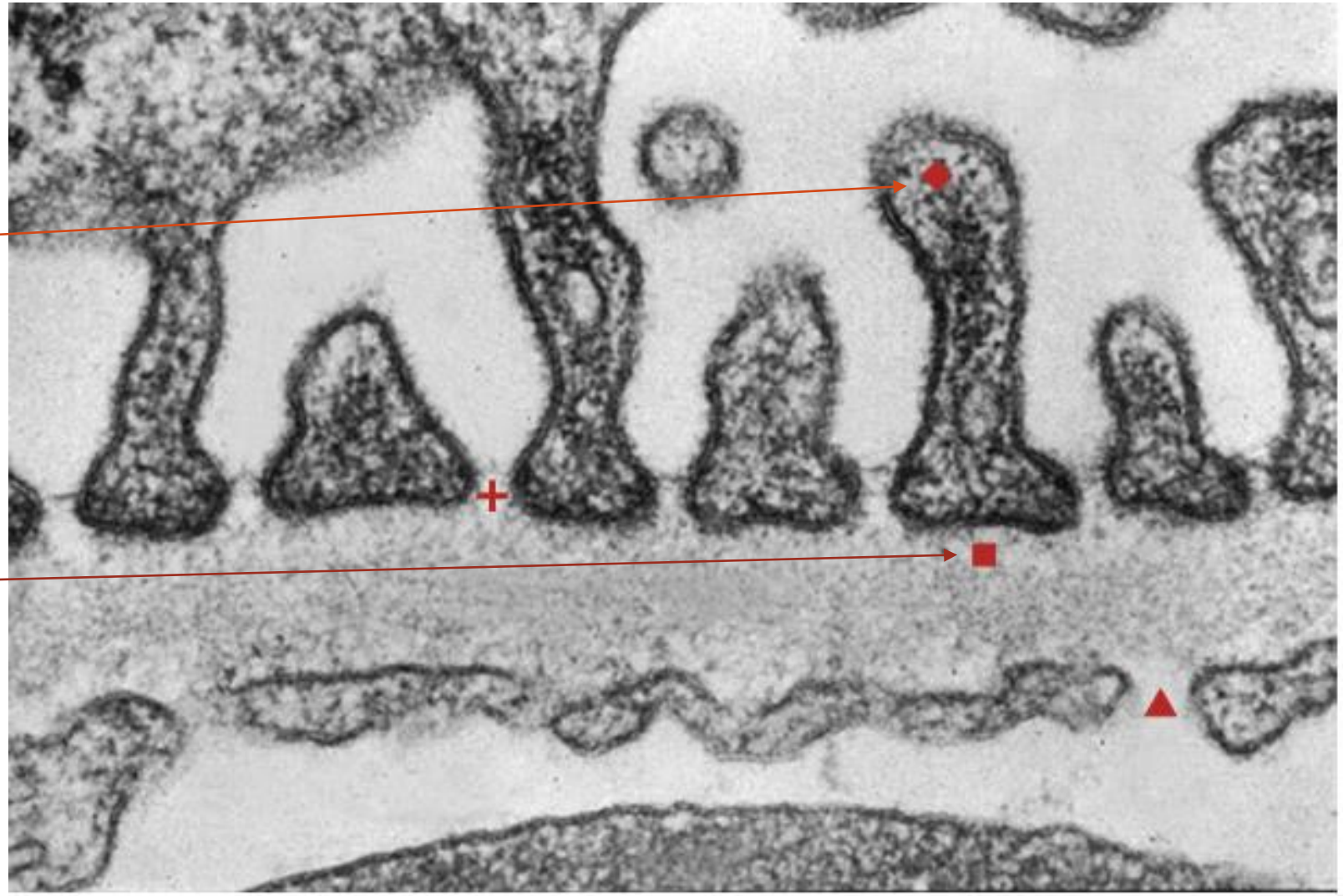
NORMAL KIDNEY, MICROSCOPIC

- Mesnagium *
- Bowman space
- Visceral epithelail cells (podocytes) surround the capillary loops



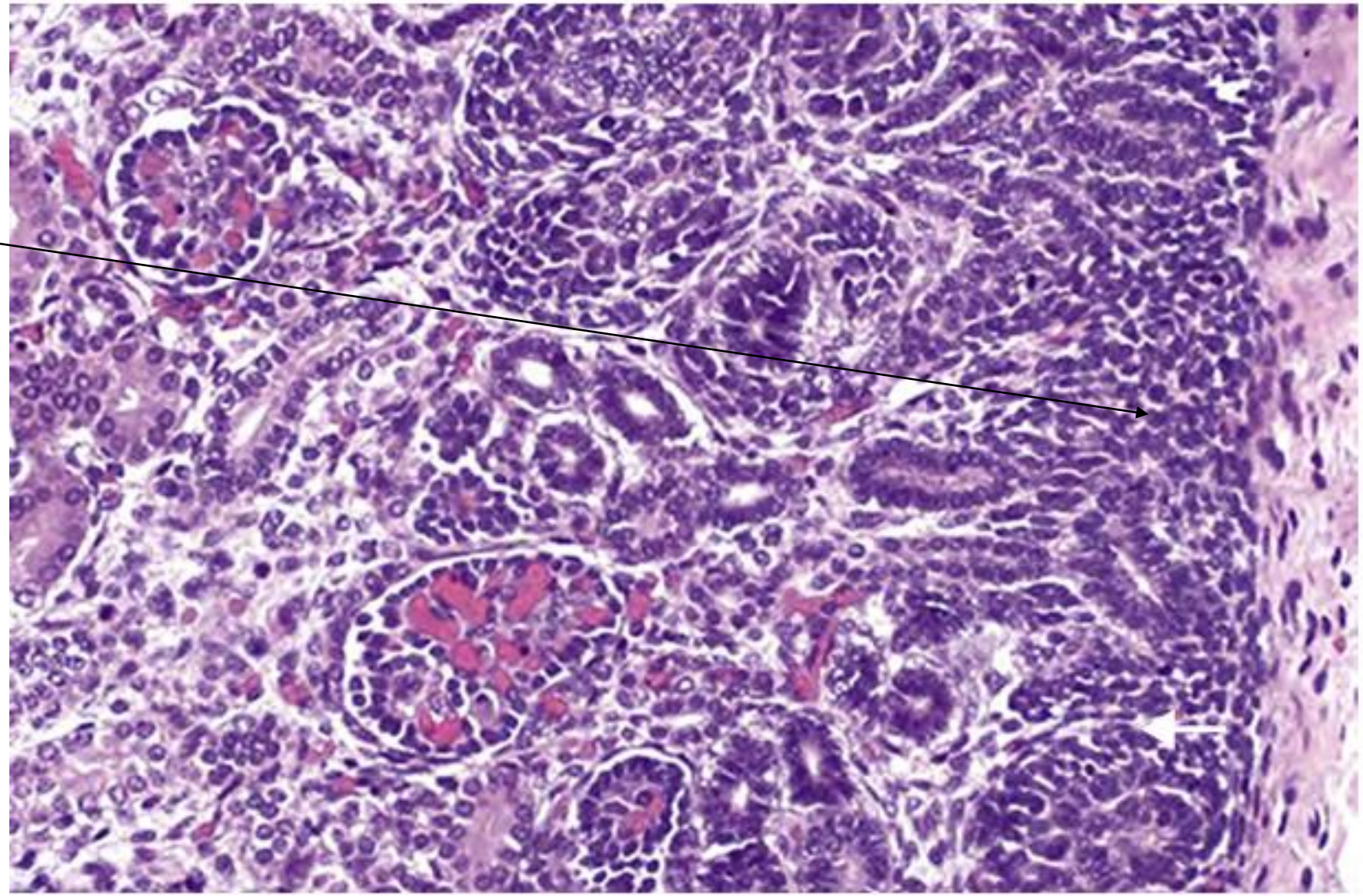
NORMAL KIDNEY, ELECTRON MICROSCOPY

- A glomerular capillary loop at high magnification has a visceral epithelial cell (podocyte) with interdigitating foot processes embedded in and adherent to the lamina rara externa of the basement membrane.



NORMAL FETAL KIDNEY, MICROSCOPIC

- Beneath the capsule of the developing fetal kidney is a nephrogenic zone composed of primitive **dark-blue** cells in which development of glomeruli and tubules is taking place and from which the new cortex forms.

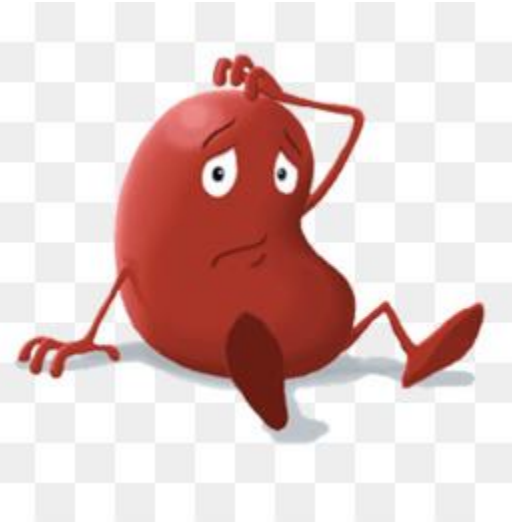


GLOMERULAR DISEASES

ACUTE VS. CHRONIC GLOMERULONEPHRITIS

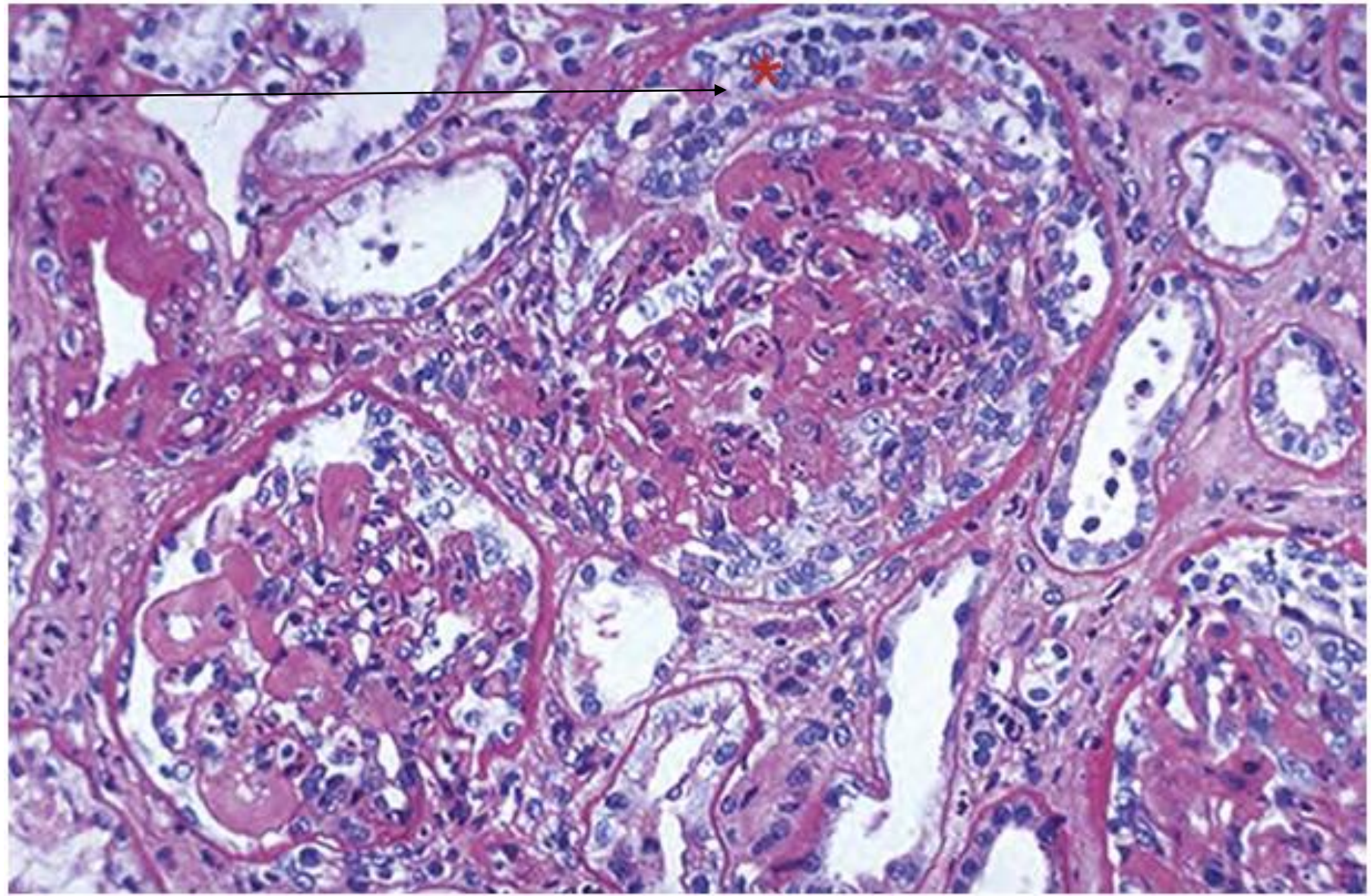
1. Acute (and rapidly progressive) glomerulonephritis

- Based on LM,IF, and EM, there are 3 etiologies:
  1. Anti-GBM disease = Goodpasture syndrome
  2. Immune complexes GN: post strep, SLE
  3. Pauci-immune form of RPGN= ANCA disease: Microscopic polyangitis



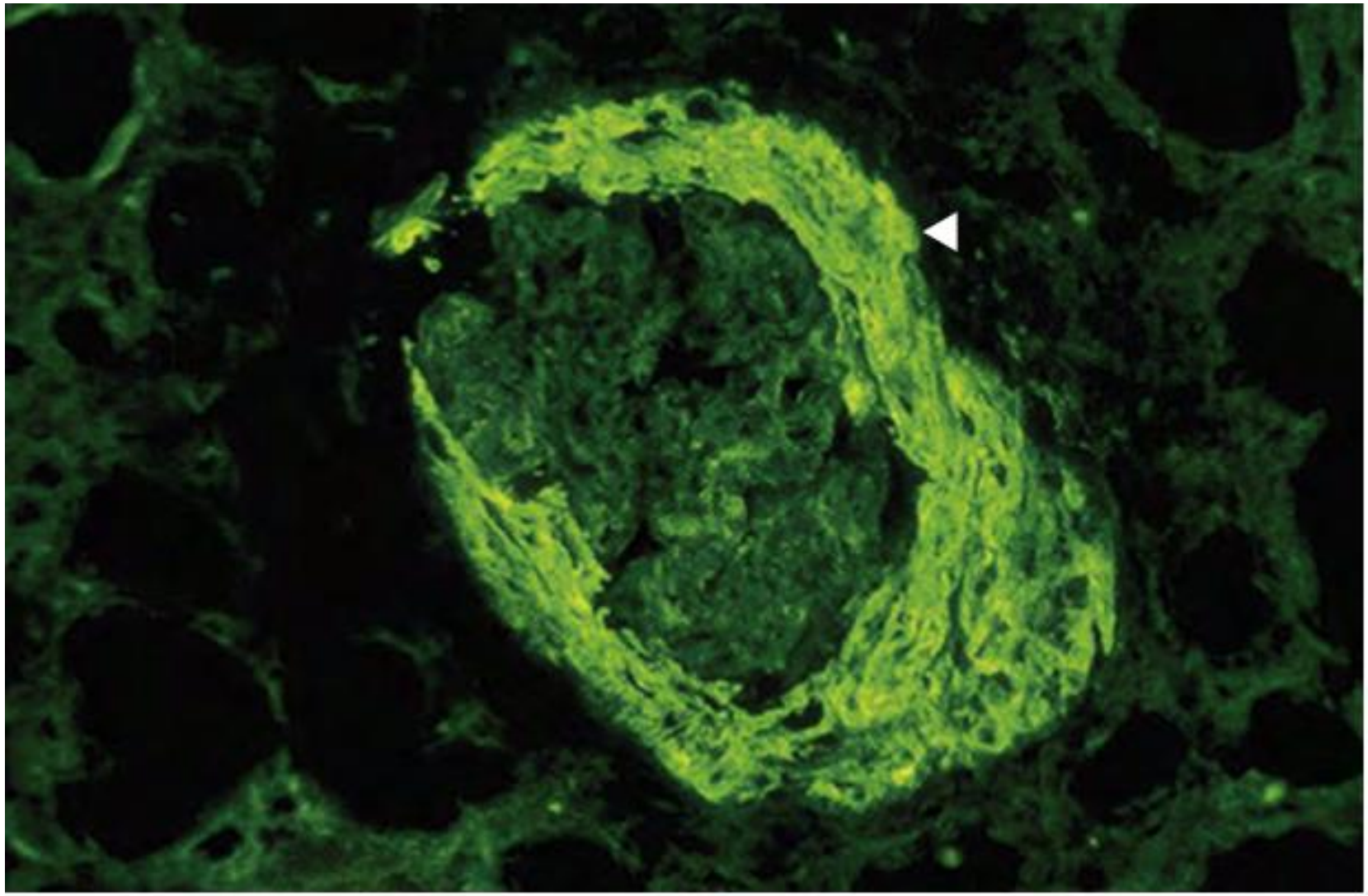
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN)

- =Crescentic GN
- **Crescent** = proliferating parietal epithelial cells.



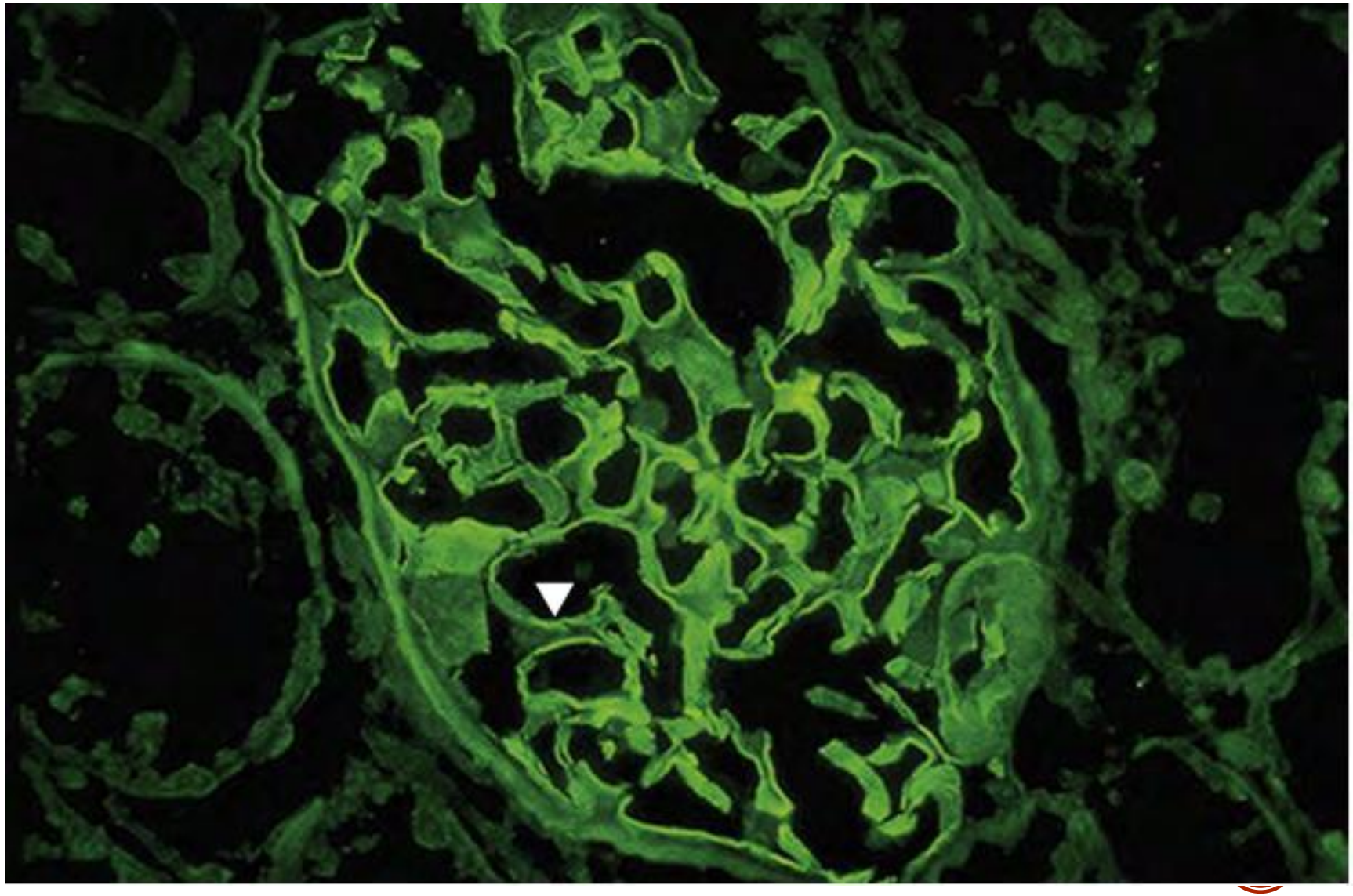
RPGN, IMMUNOFLUORESCENCE

- This glomerulus shows bright green immunofluorescence (◄) with antibody to fibrinogen.



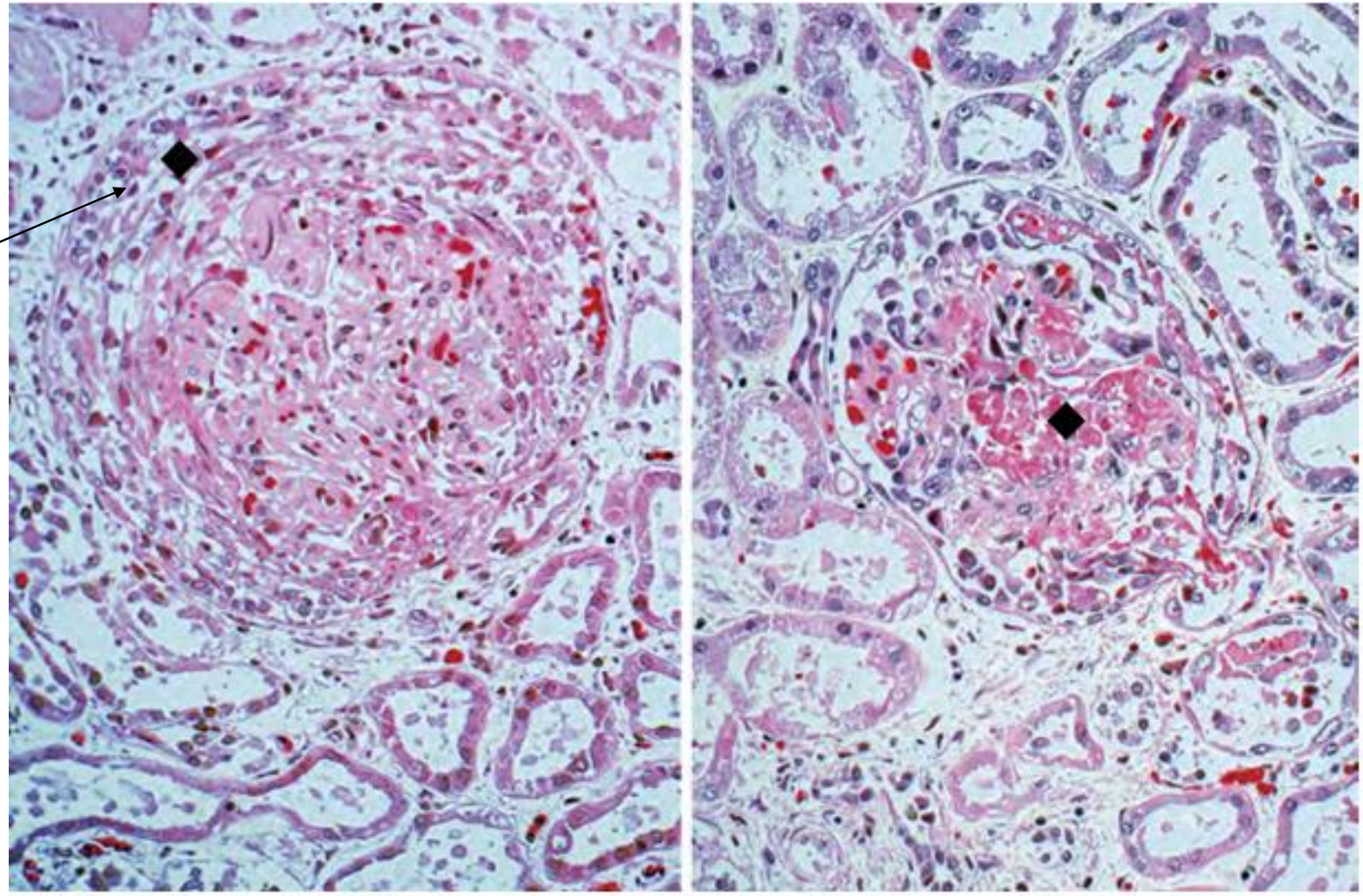
ANTI-GBM DISEASE IMMUNOFLUORESCENCE

- There is bright green positivity with antibody to IgG with a smooth, diffuse, **linear** pattern that is characteristic of RPGN caused by circulating anti-GBM antibody with Goodpasture syndrome.



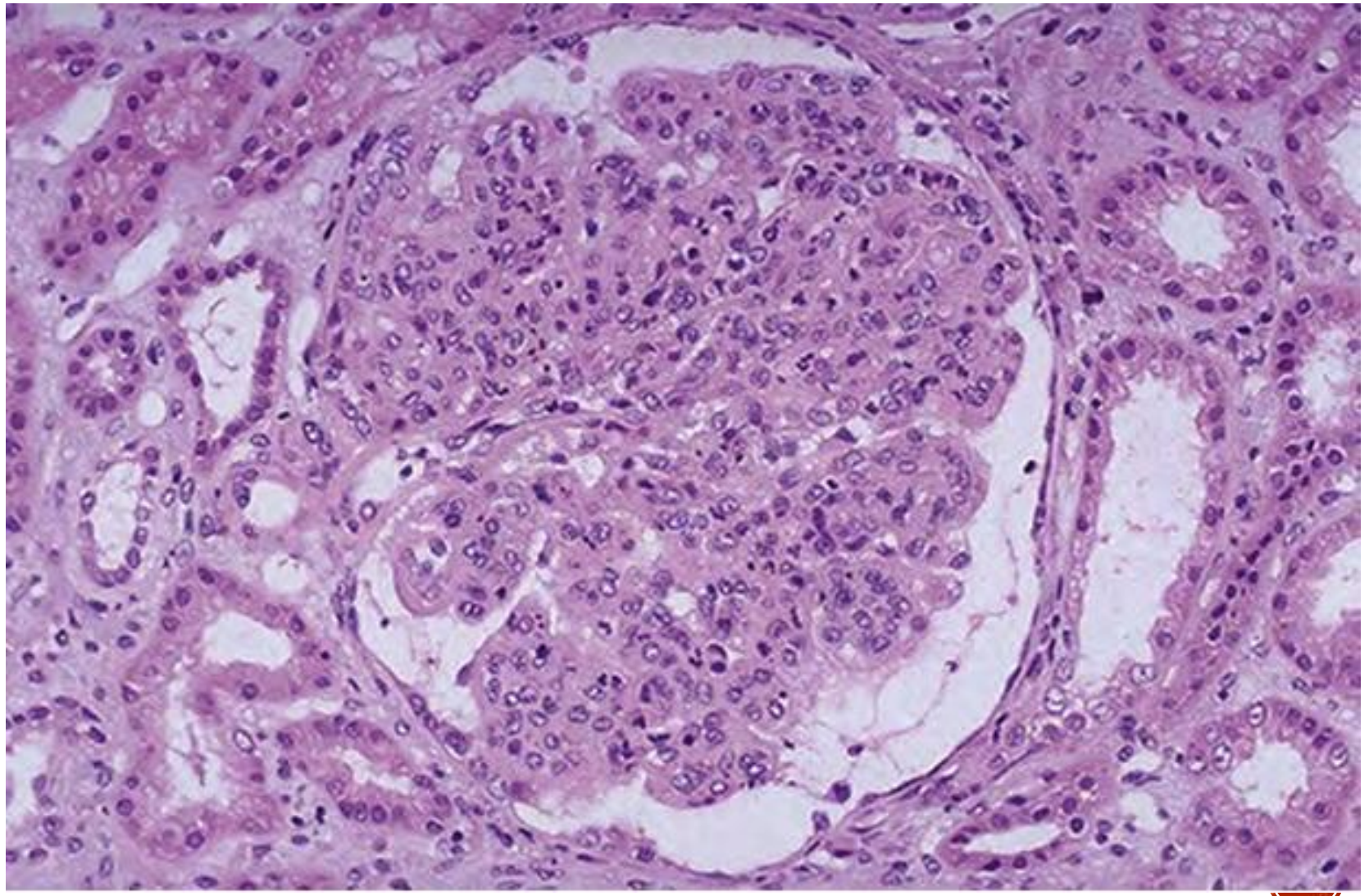
PAUCI-IMMUNE FORM OF RPGN, MICROSCOPIC POLYANGITIS

- Note the focal segmental necrotizing GN in the right panel and
- A glomerular crescent in the left panel in this case of (ANCA)–associated GN. Tubular atrophy is also present.



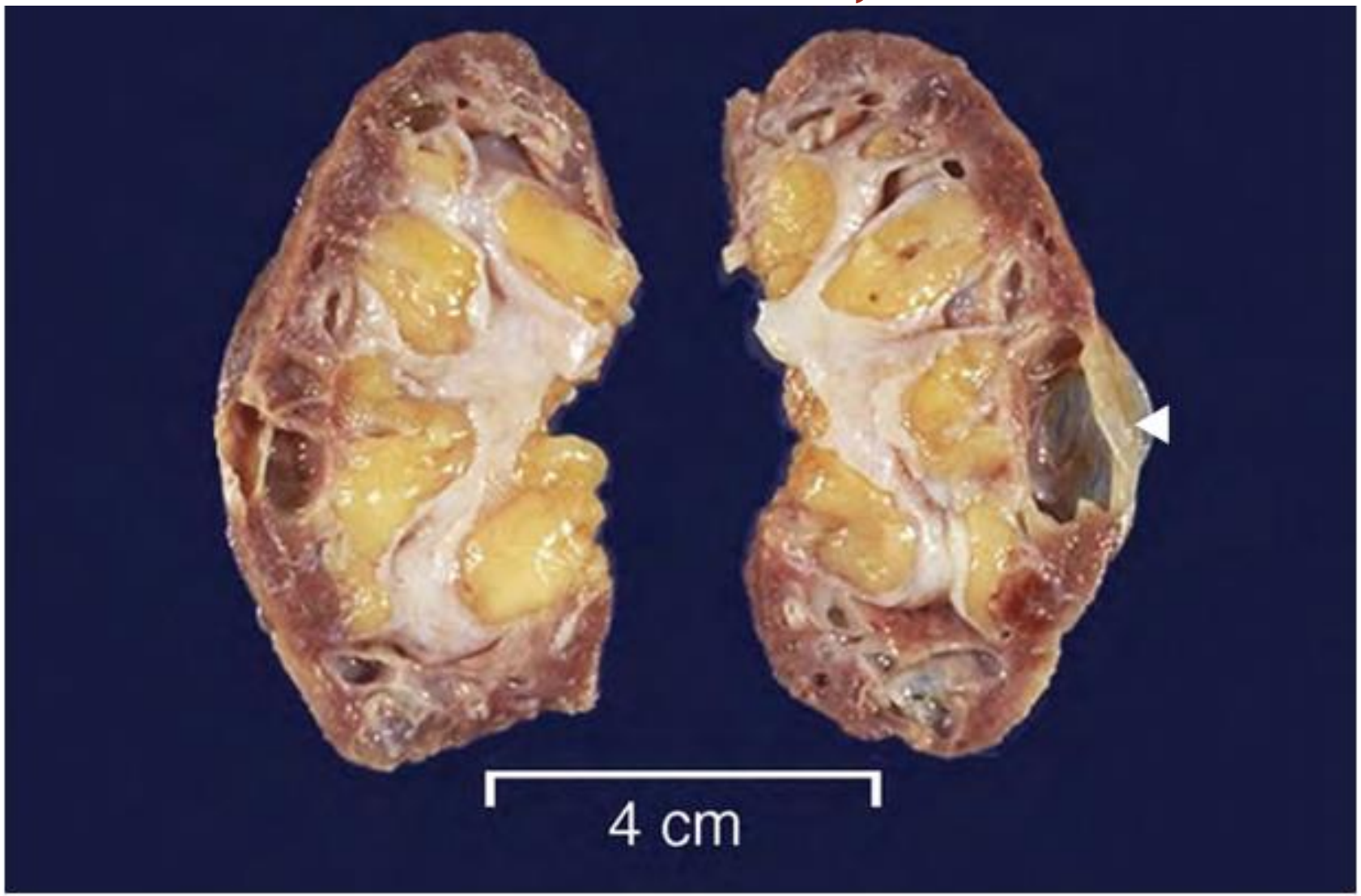
POSTINFECTIOUS GLOMERULONEPHRITIS

- Postinfectious glomerulonephritis (GN) is hypercellular with increased inflammatory cells, and capillary loops are poorly defined.



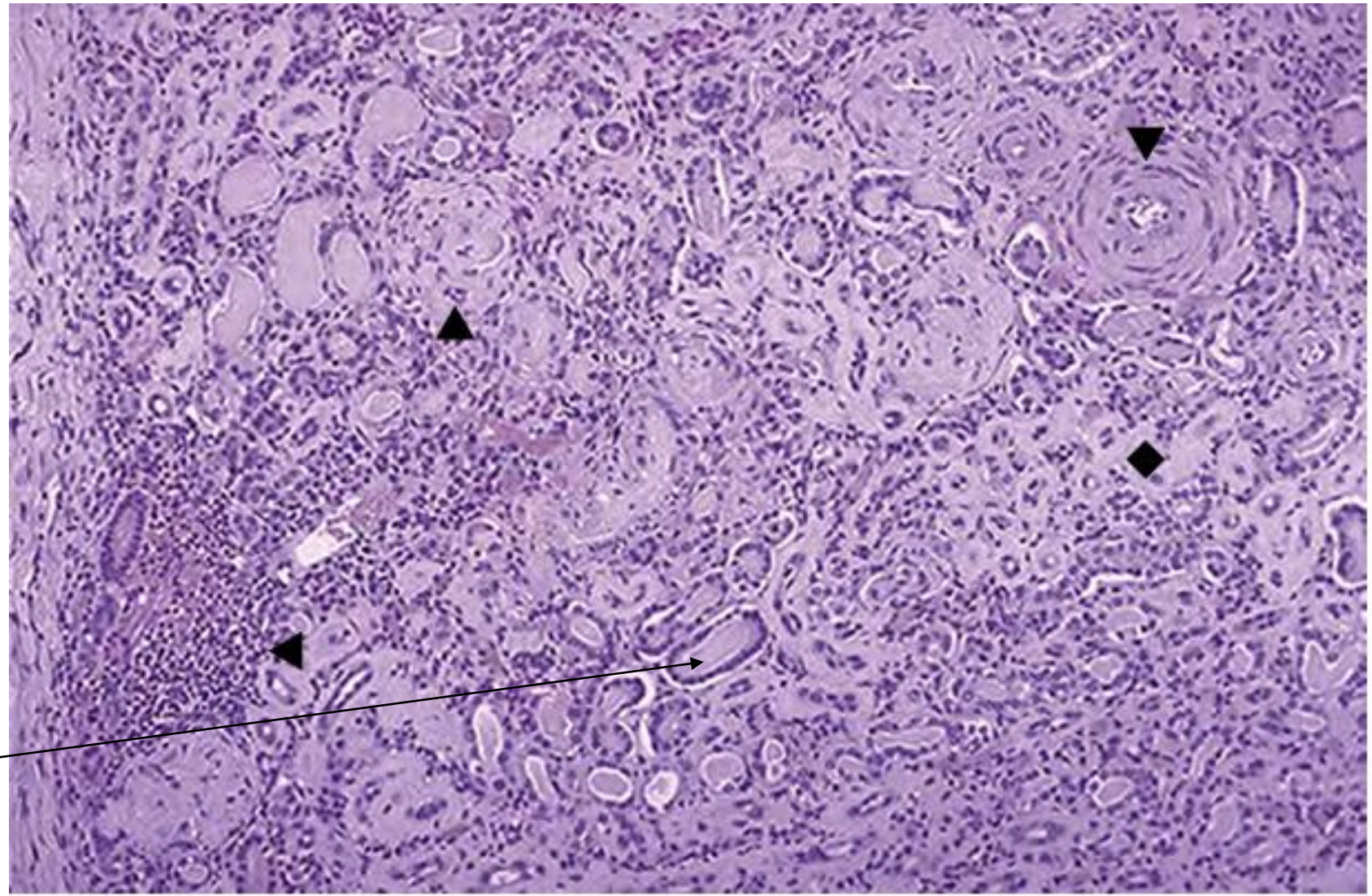
2- CHRONIC GLOMERULONEPHRITIS, GROSS

- Here are atrophic kidneys with thin cortices from a patient with CRF.
- Some incidental simple cysts (◄) are also seen.



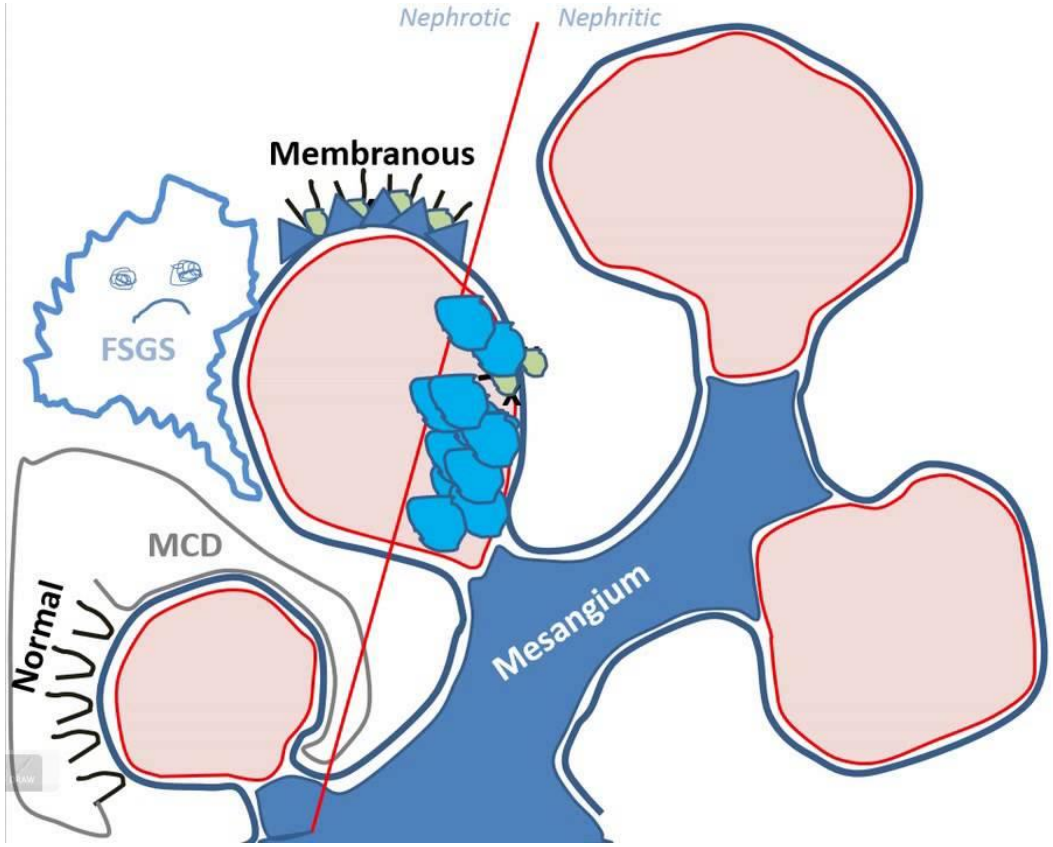
END-STAGE RENAL DISEASE, MICROSCOPIC

- The cortex is fibrotic, the glomeruli are sclerotic from hyaline obliteration, there are scattered interstitial chronic inflammatory cell infiltrates (◄), and the arteries are thickened.
- Tubules are often dilated and filled with pink casts and give an appearance of "**thyroidization**."



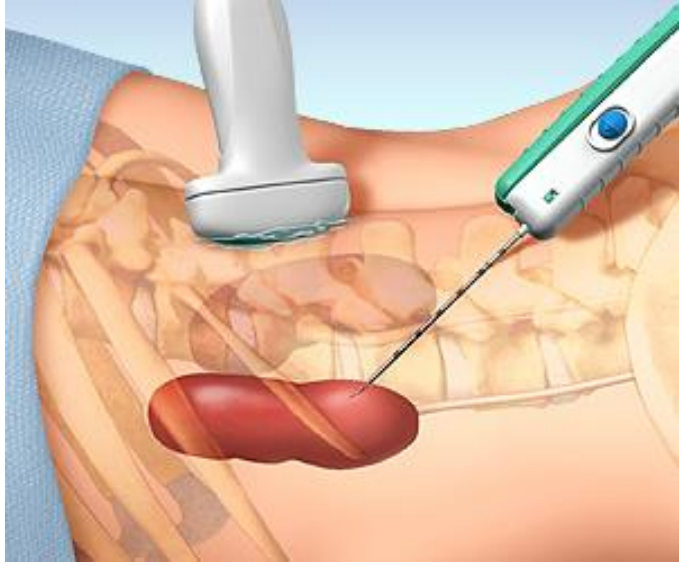
GLOMERULAR DISEASES

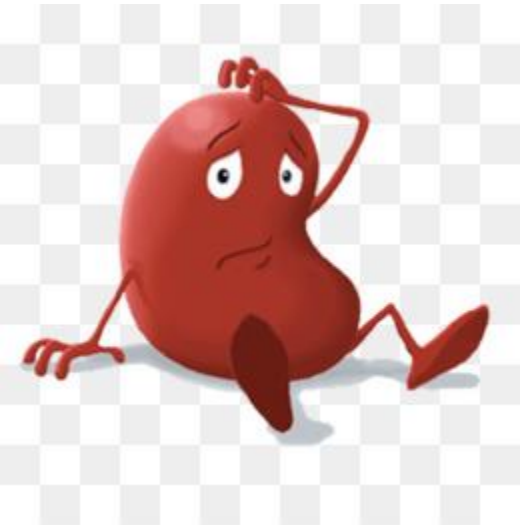
- 1ry:
  - Nephrotic: MCD, FSGS, MG
  - Nephritic: RPGN, IgA nephropathy
- 2ry: DM, SLE, Amyloidosis



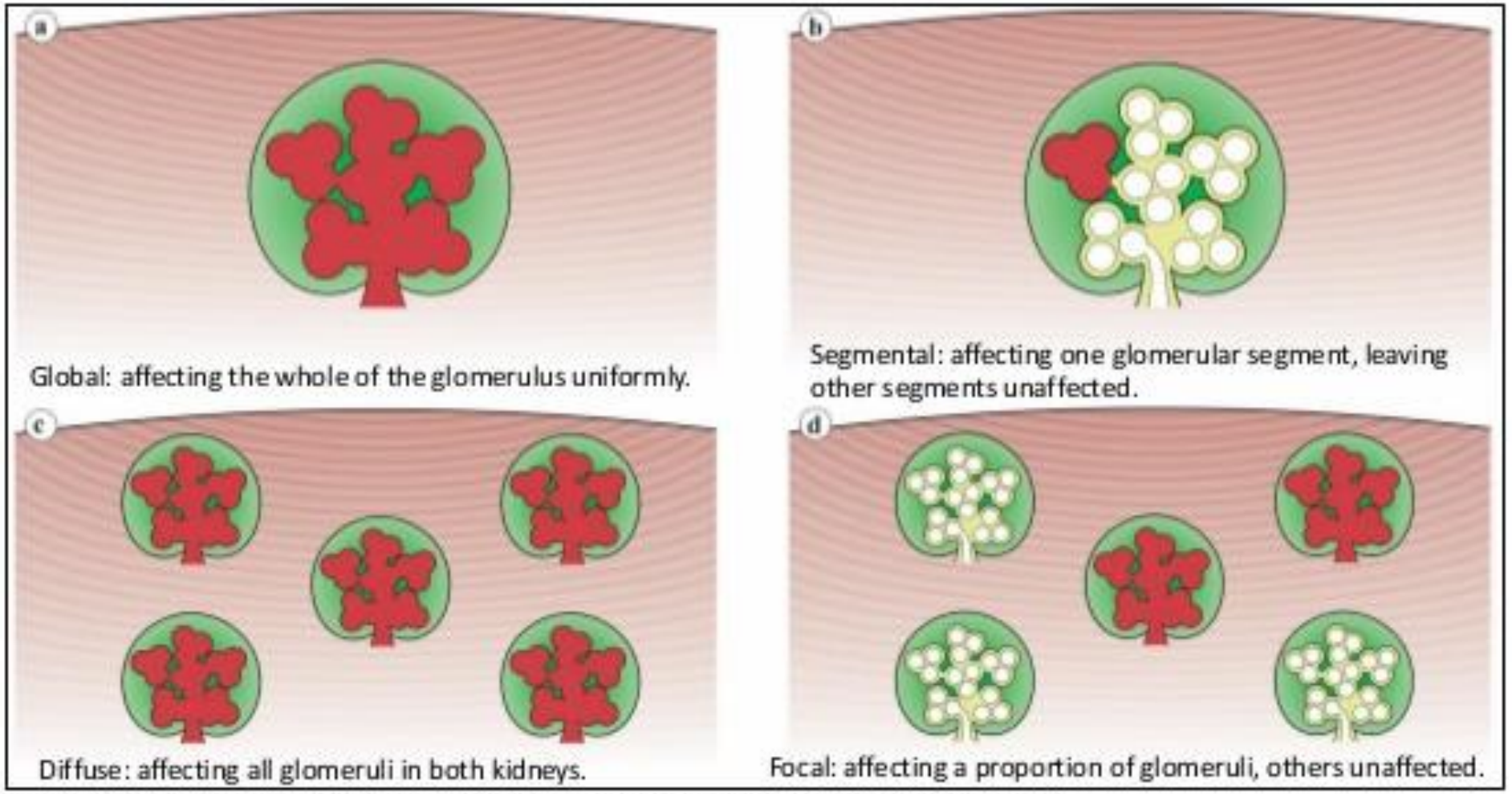
DIAGNOSIS

- Clinical manifestations
- Light microscopy
- Immunofluorescence
- Electron microscopy





Patterns of glomerular disease



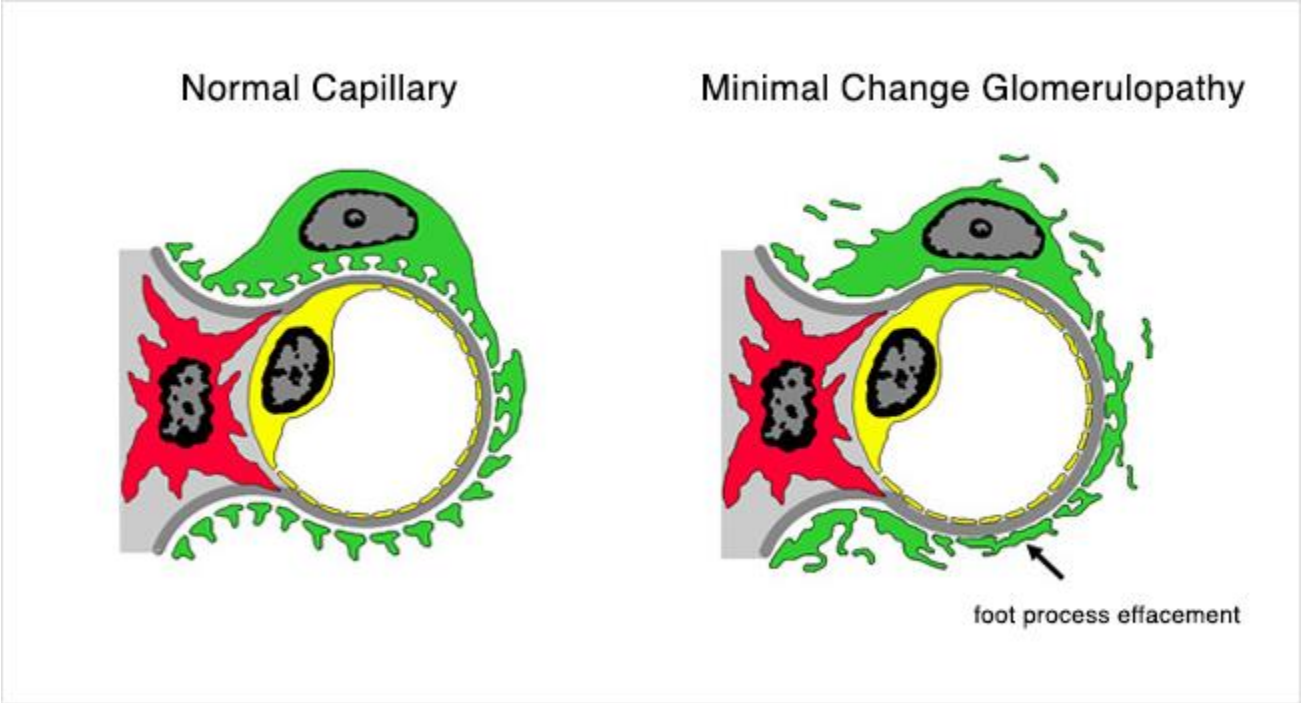
Modified from: Stevens A, Lowe J, Scott I. *Core Pathology, 3rd Ed.* St. Louis: Mosby-Elsevier, 2009; 367.

TRIGGER CASE

- A 5-year-old boy presents to the emergency room with a 1-week hx of generalized edema and fatigue. He suffered from a viral URI 1 week before this visit. You suspect that a renal biopsy would show normal-appearing glomeruli except for epithelial foot processes fusion on electron microscopy and you begin the child on prednisone.
- **What is the Diagnosis?**

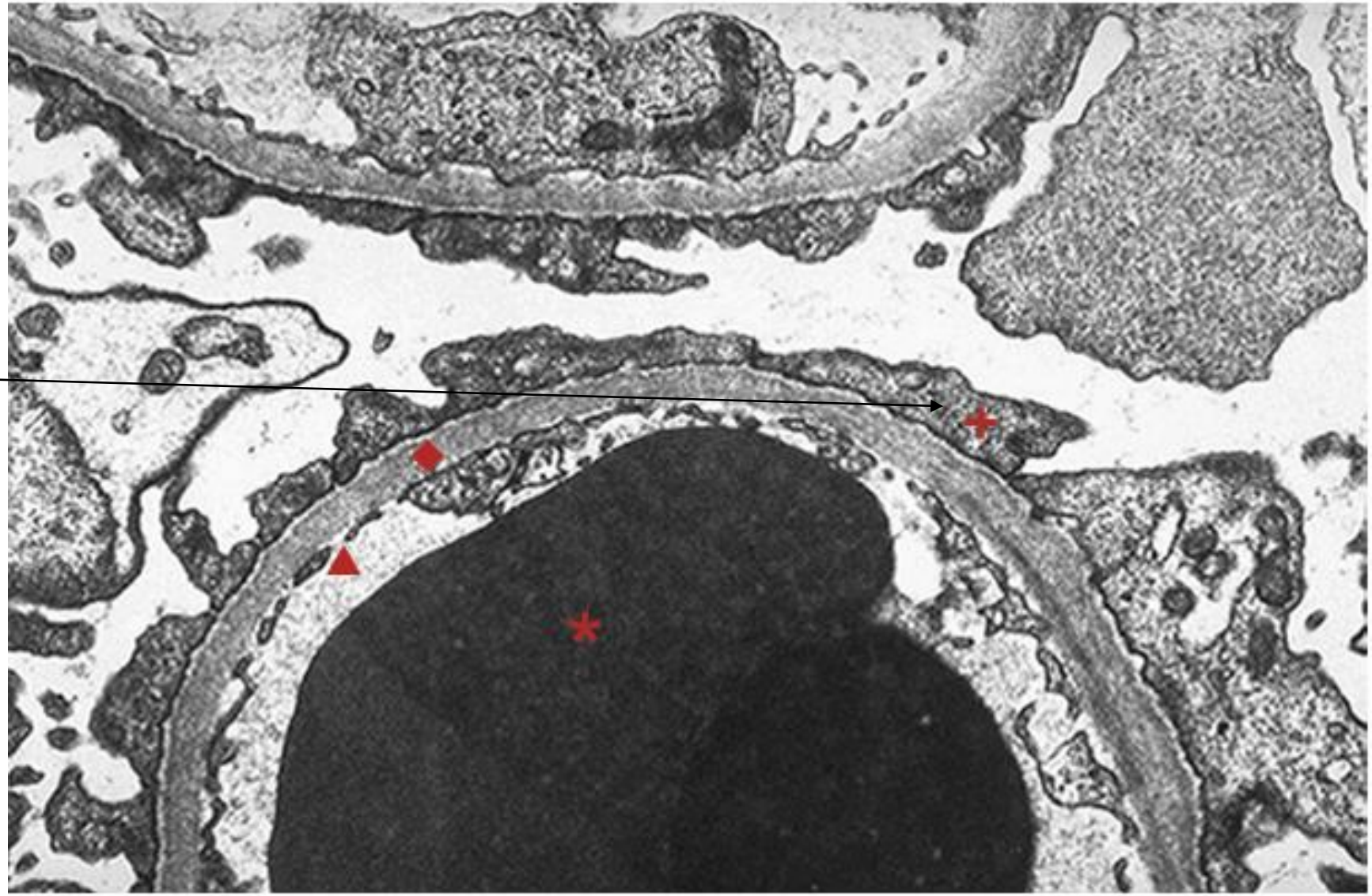
MINIMAL CHANGE DISEASE (MCD)

- It is the **most common** cause of nephrotic syndrome in children.
- Light microscopy: **normal**
- Immunofluorescence: **normal**
- **Electron microscopy**: effacement of podocytes foot processes



MCD, ELECTRON MICROSCOPY

- The epithelial cell (podocyte) foot processes are effaced (giving the appearance of fusion) and run together (+).

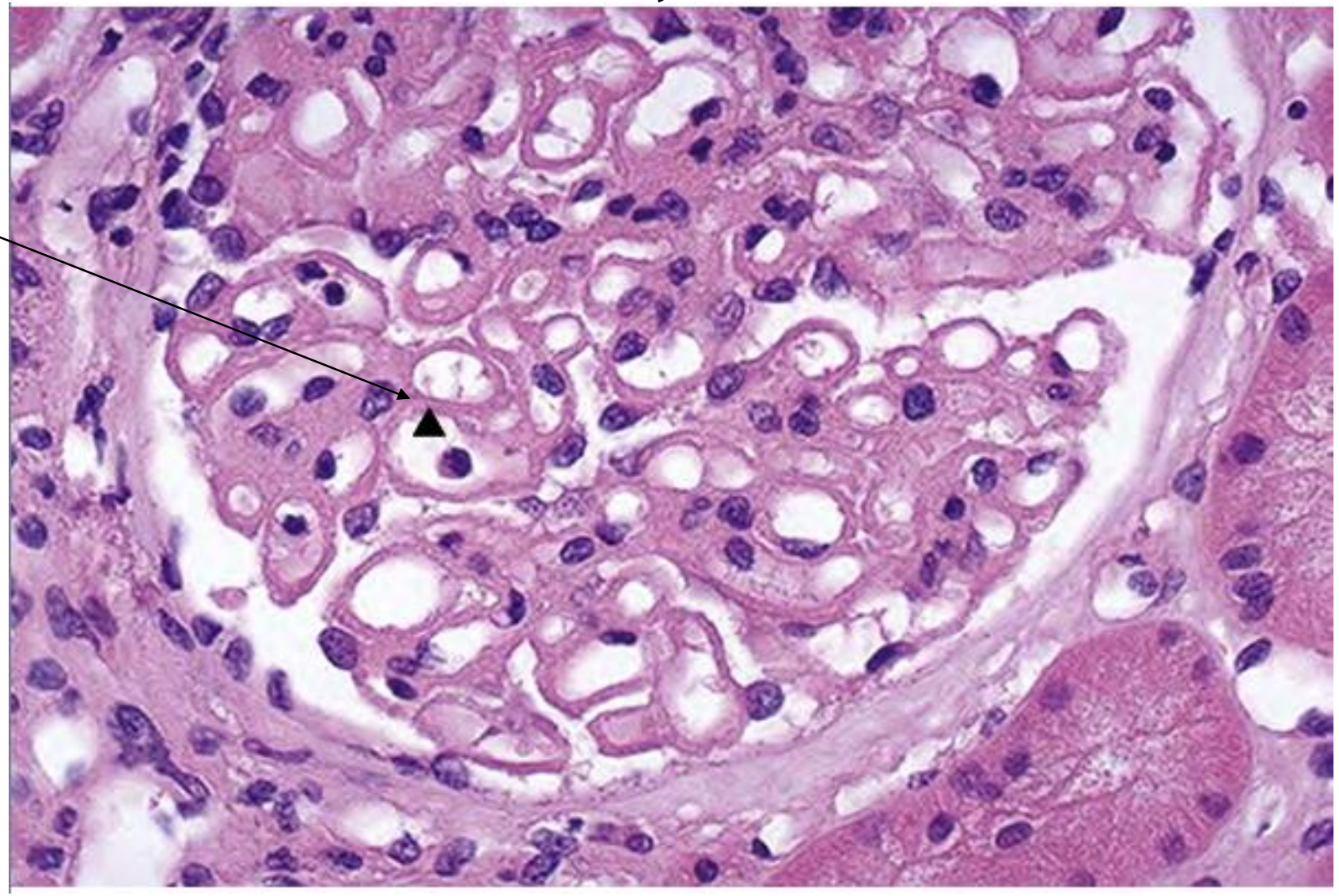


MEMBRANOUS NEPHROPATHY

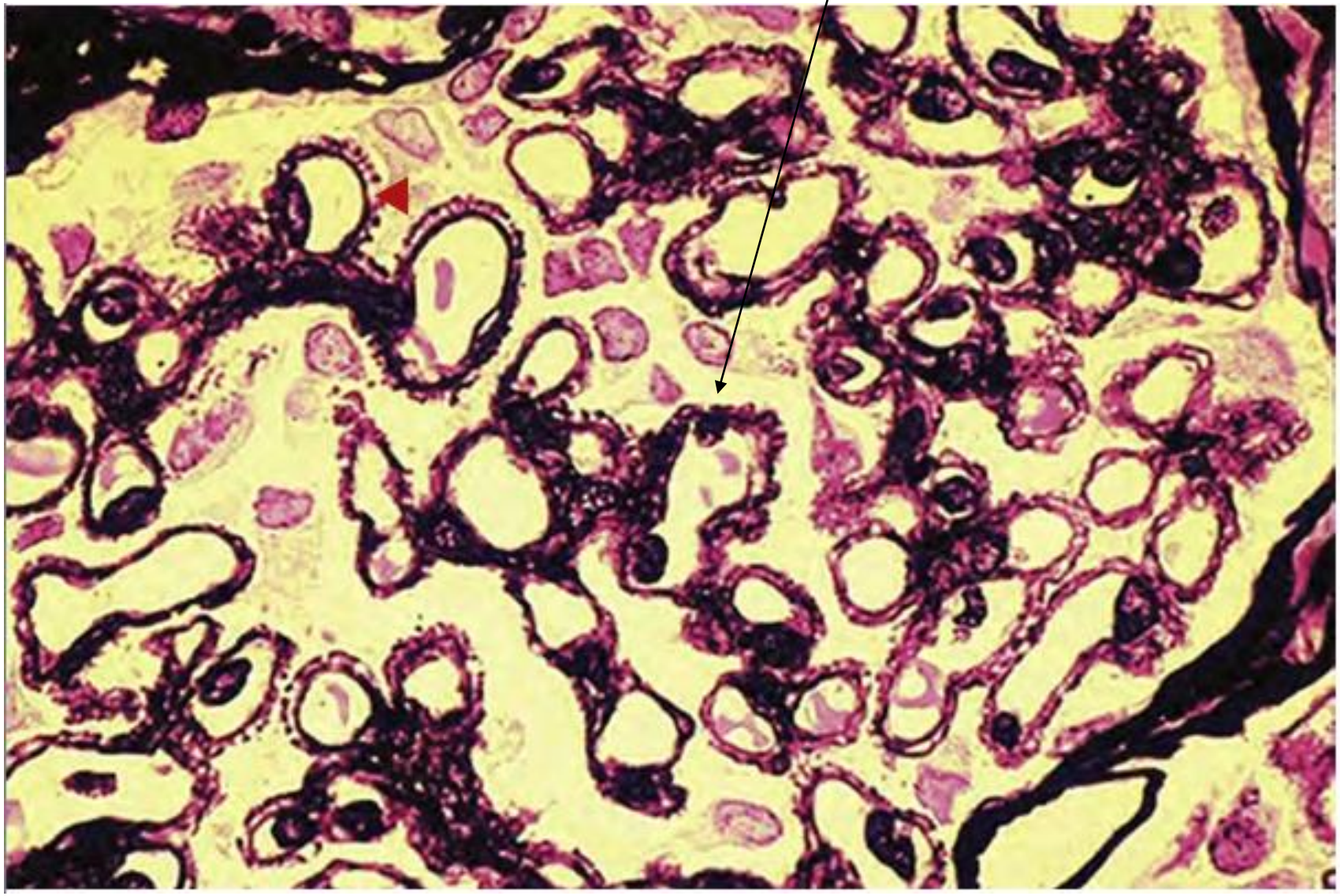
- It is the **most common** cause of nephrotic syndrome in adults.
- LM: diffuse capillary wall and basement membrane thickening
- IF: granular pattern of IgG or C3 deposits (lumpy-bumpy)
- EM: subepithelial immune complex deposition (spike and dome)

MEMBRANOUS NEPHROPATHY, MICROSCOPIC

- These capillary loops are **diffusely thickened** and prominent.

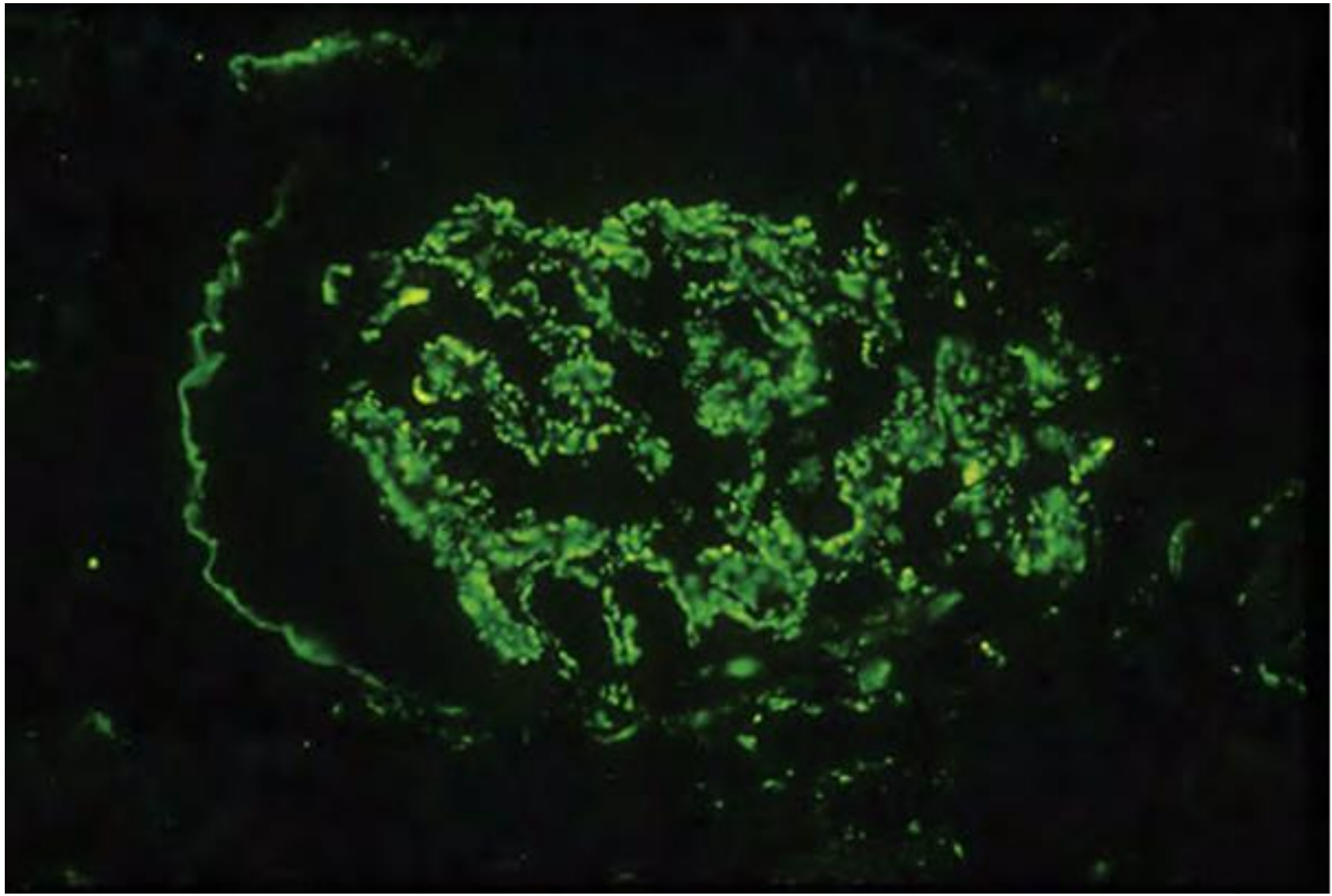


- A Jones **silver stain** of this glomerulus highlights the proteinaceous basement membranes of capillary loops in black. There are characteristic "**spikes**" involving the capillary loops with membranous nephropathy.



IMMUNOFLUORESCENCE

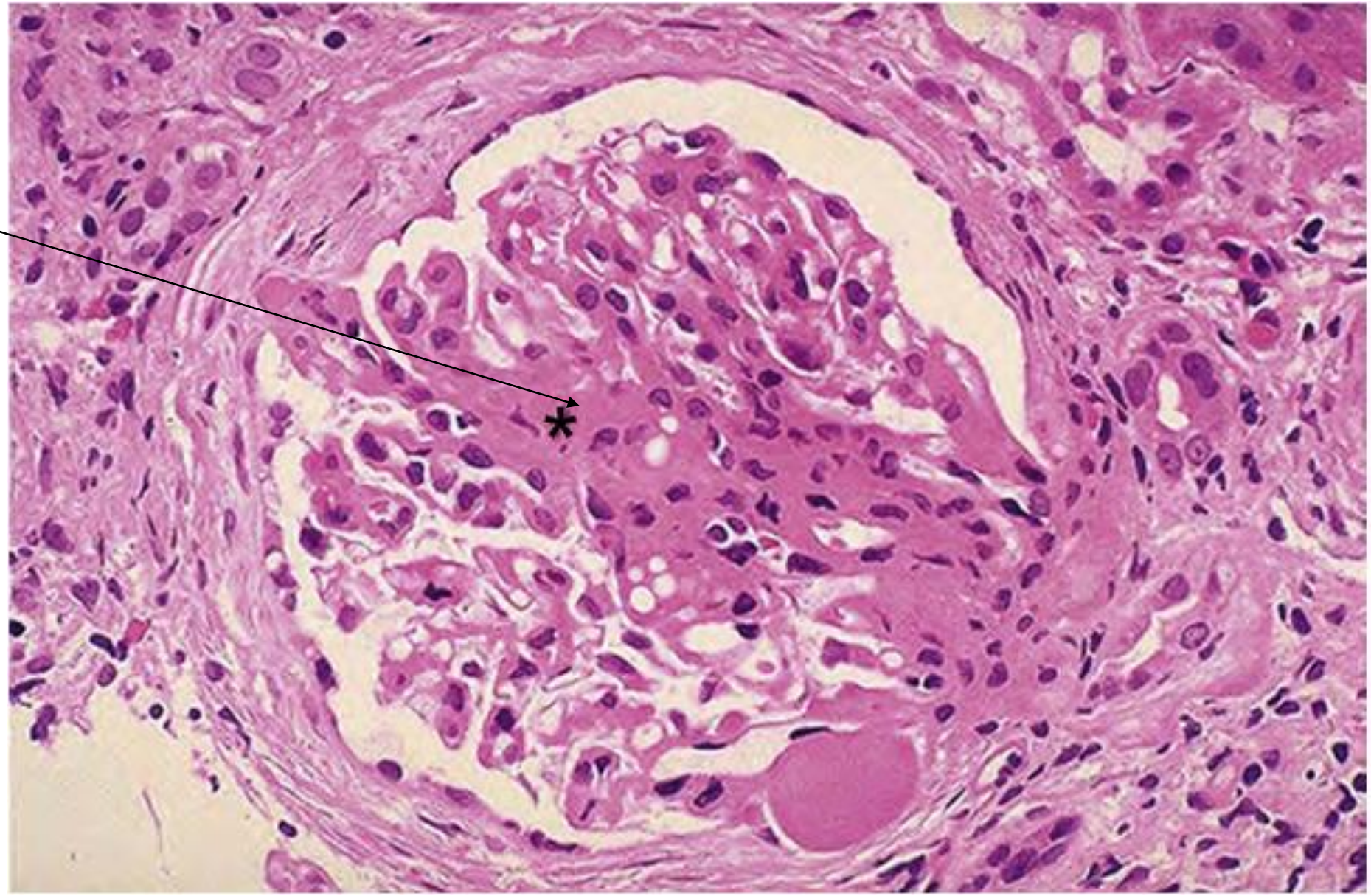
- The immunofluorescence pattern here has a "bumpy" or **granular** staining pattern as a result of irregular deposition of immune complexes within the basement membranes of the glomerular capillary loops.



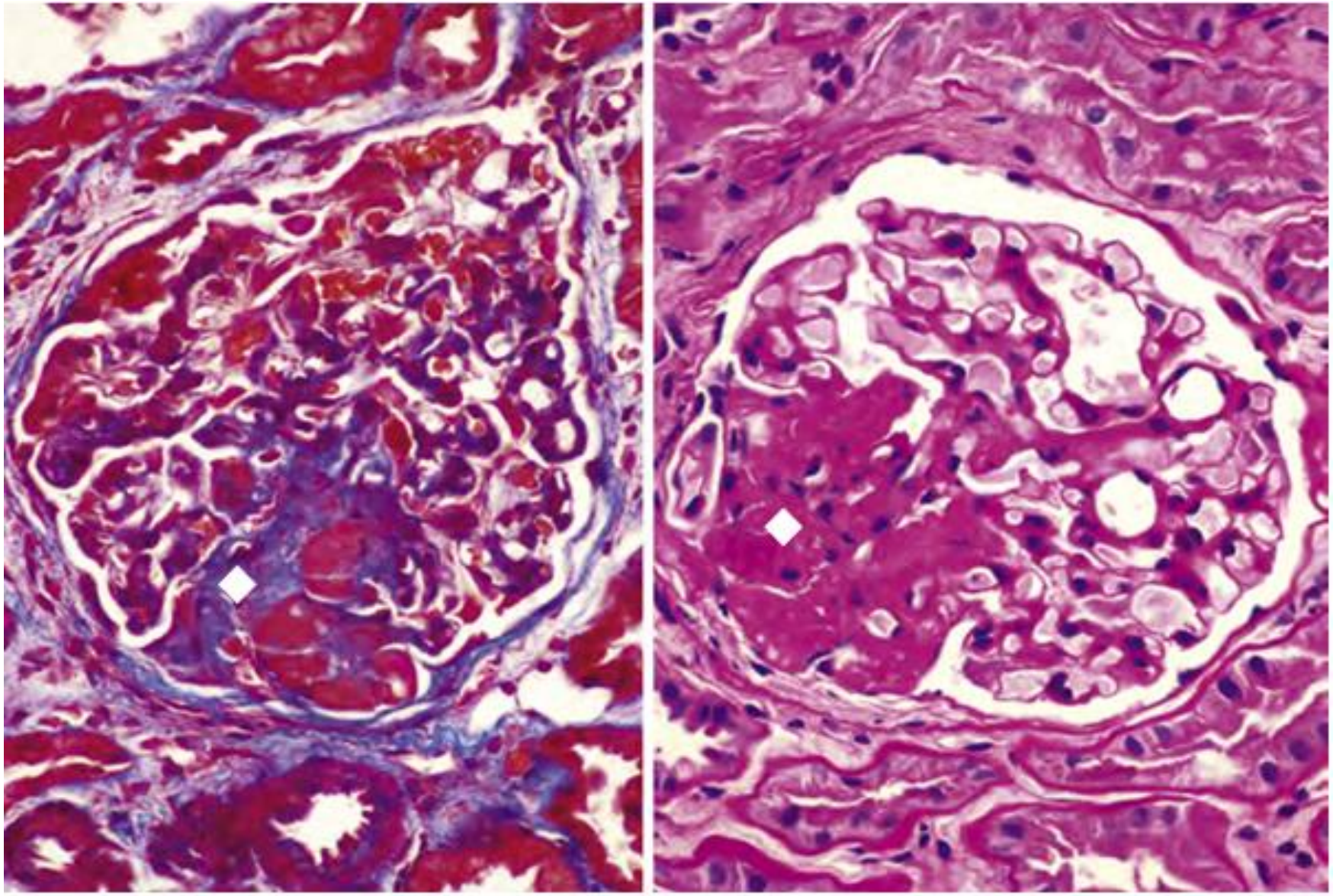
FOCAL SEGMENTAL GLOMERULOSCLEROSIS

- LM: focal and segmental **sclerosis** within capillary tufts and **hyalinosis**.
- IF: **granular mesangial IgM** and C3 deposits
- EM: podocytes foot precesses fusion

- An area of **collagenous sclerosis** traverses the middle segment of this glomerulus.



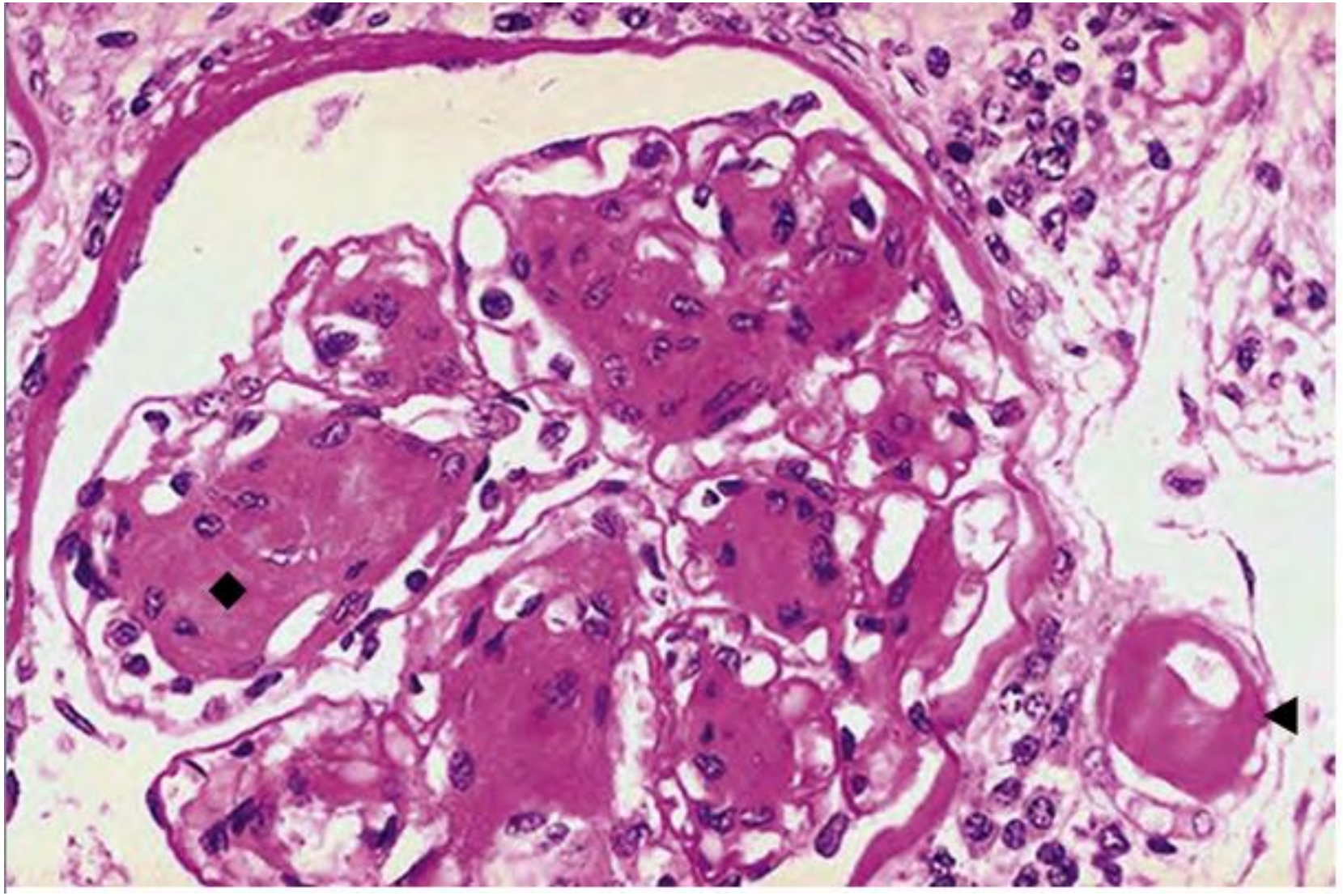
- The trichrome stain (blue, left panel) and PAS stain (red, right panel) of a glomerulus in a patient with FSGS shows focal collagen deposition at the vascular pole.



DIABETIC NEPHROPATHY

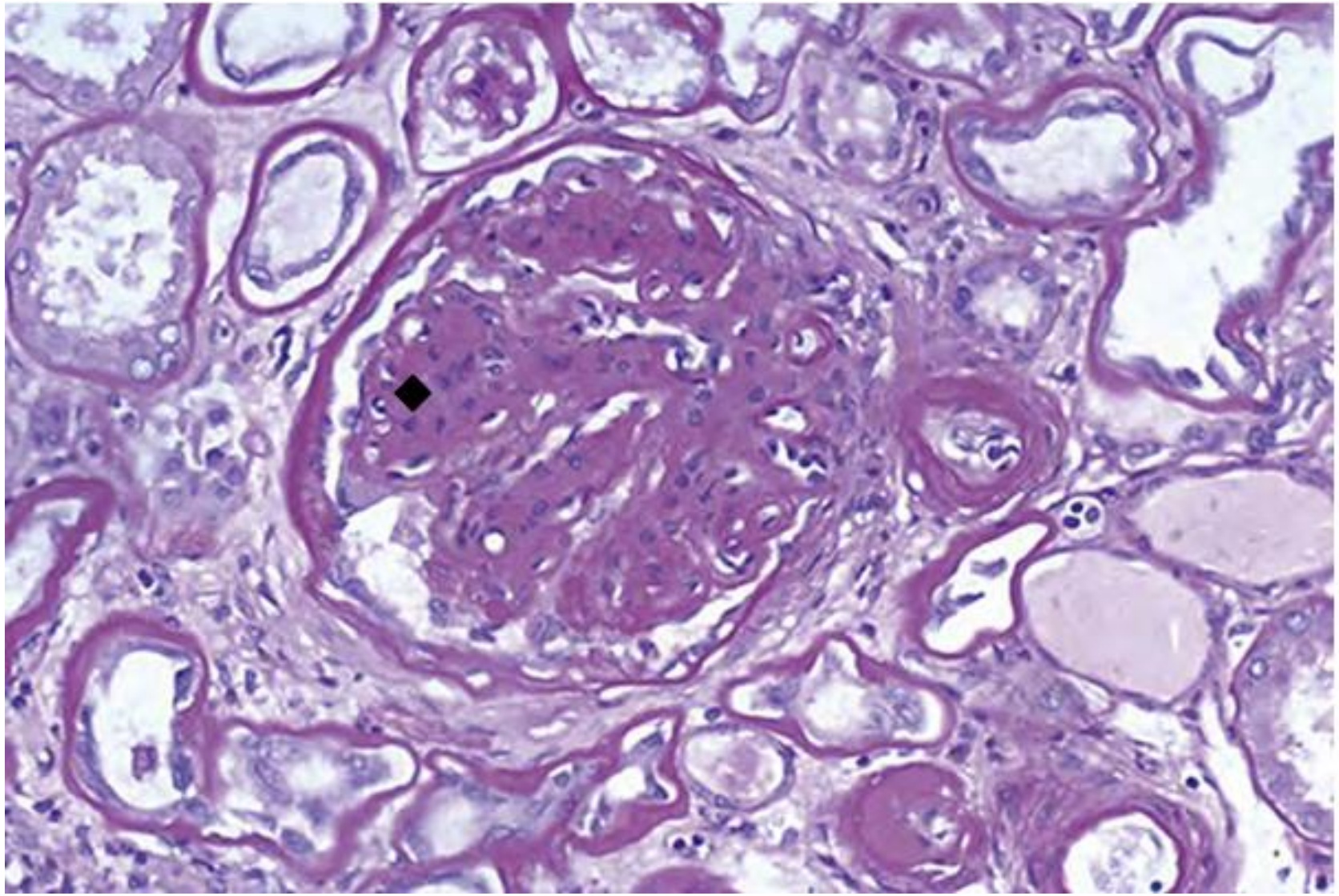
- LM:
  1. Mesangial matrix expansion
  2. Nodular glomerulosclesosis (Kimmelstiel-Wilson nodules)
  3. Diffuse glomerulosclesosis
- IF: Not specific
- EM: striking increase in GBM thickening

NODULAR GLOMERULOSCLEROSIS (KIMMELSTIEL-WILSON DISEASE)



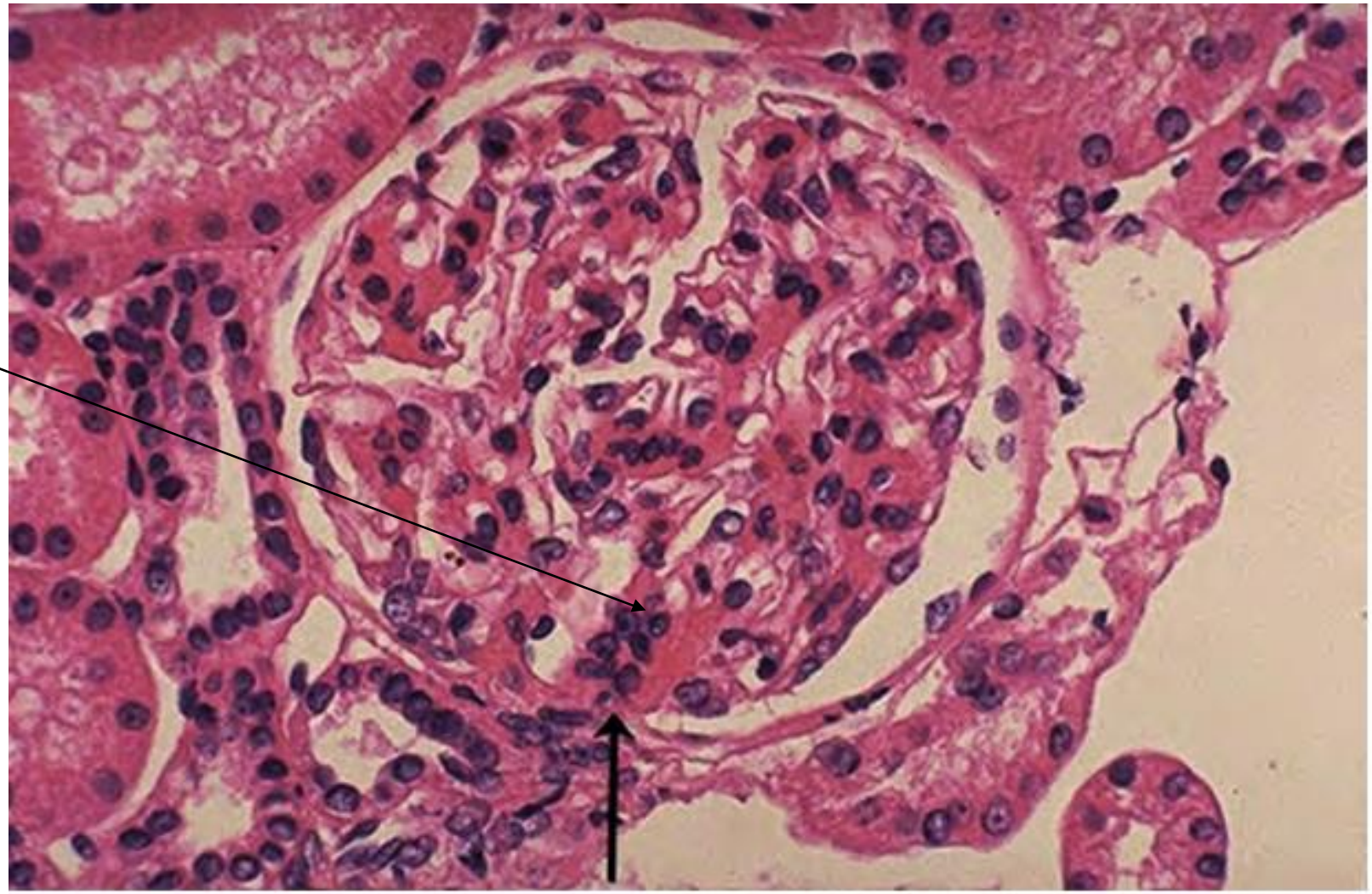
DIFFUSE GLOMERULOSCLEROSIS

- A PAS stain highlights an **increase in mesangial matrix**, a slight increase in mesangial cellularity, and capillary basement membrane thickening.



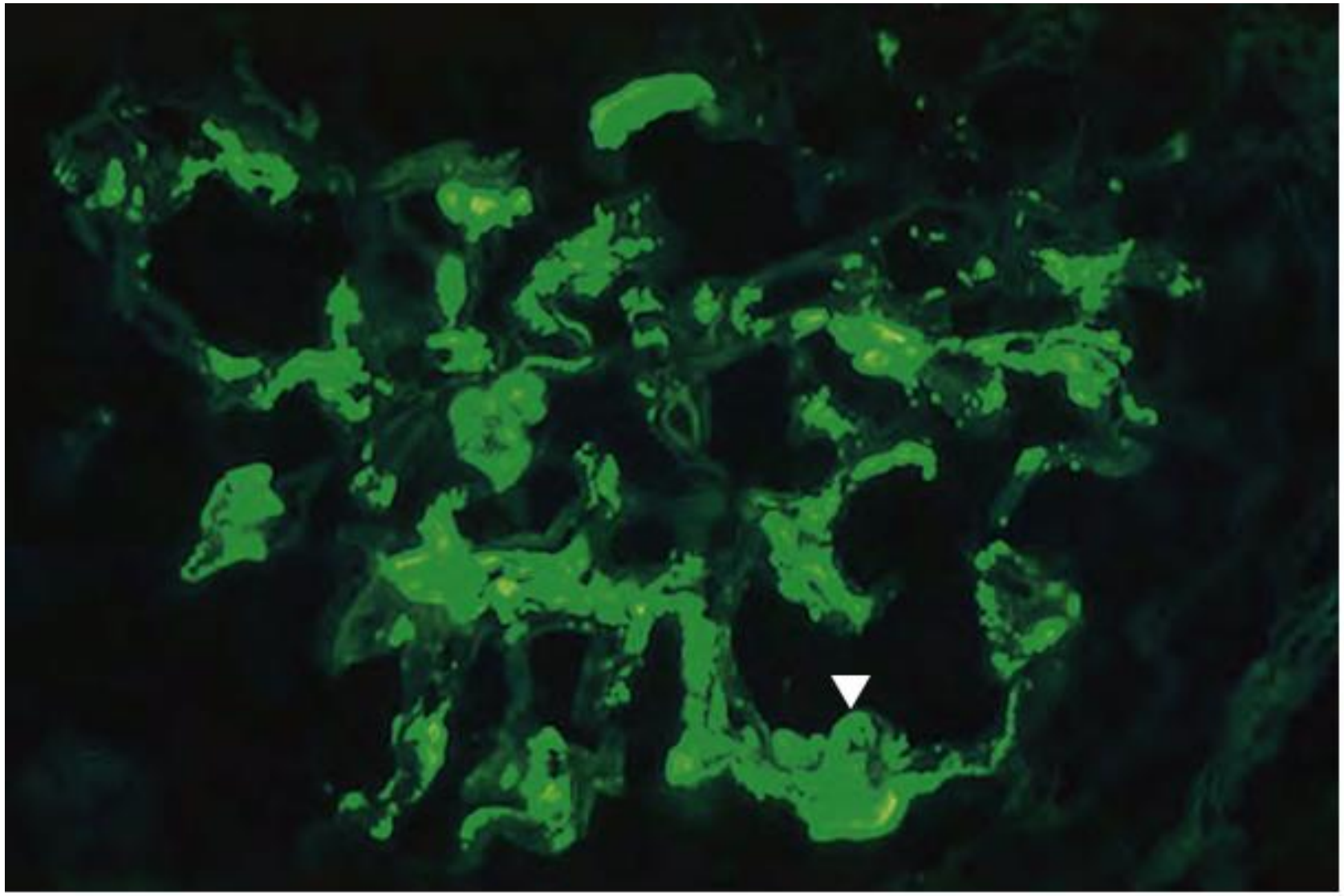
IGA NEPHROPATHY (BERGER DISEASE)

- LM: mesangial expansion and mild hypercellularity
- IF and EM: **mesangial IgA** deposition



IGA NEPHROPATHY, IMMUNOFLOURESCENCE

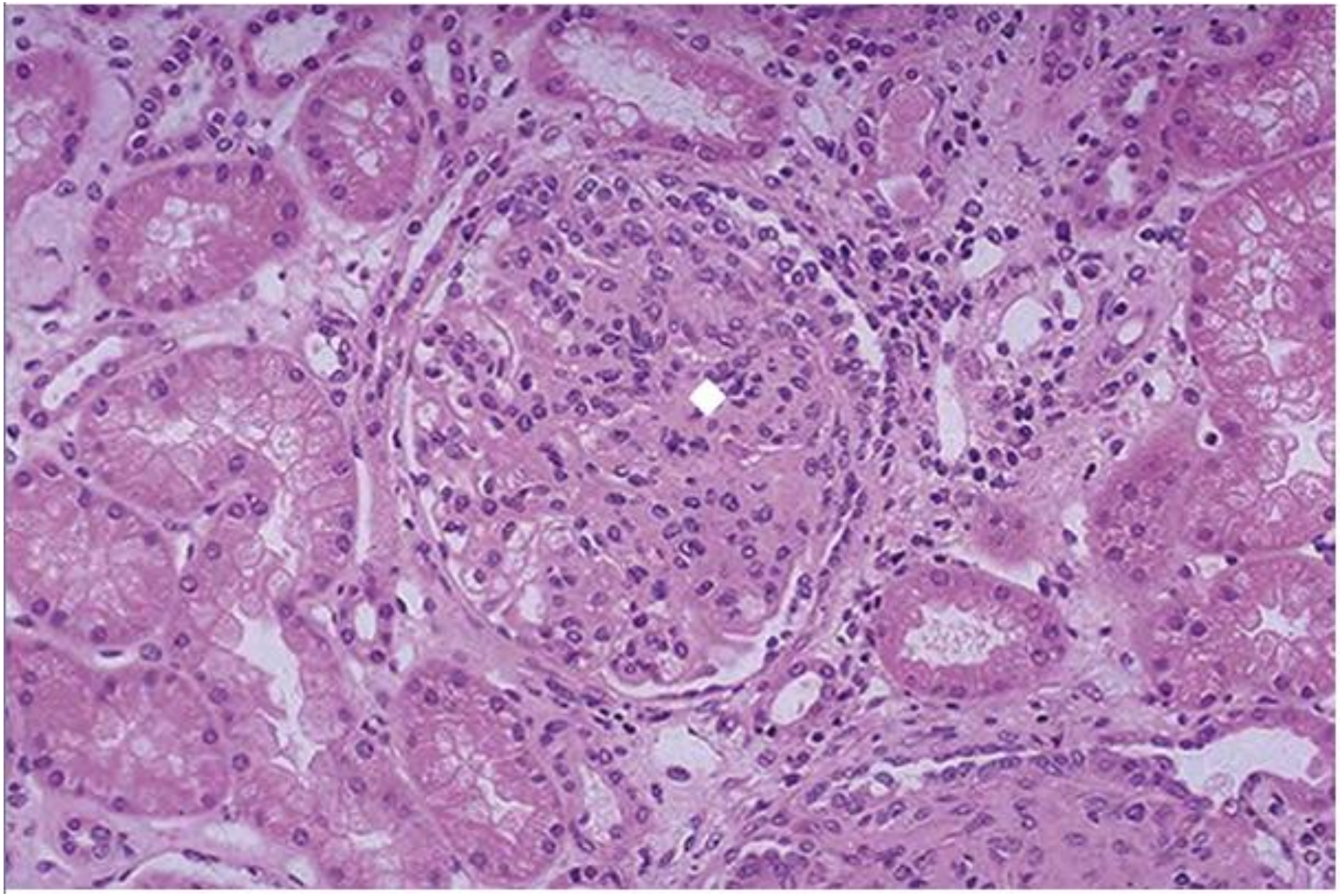
- IgA mesangial deposits



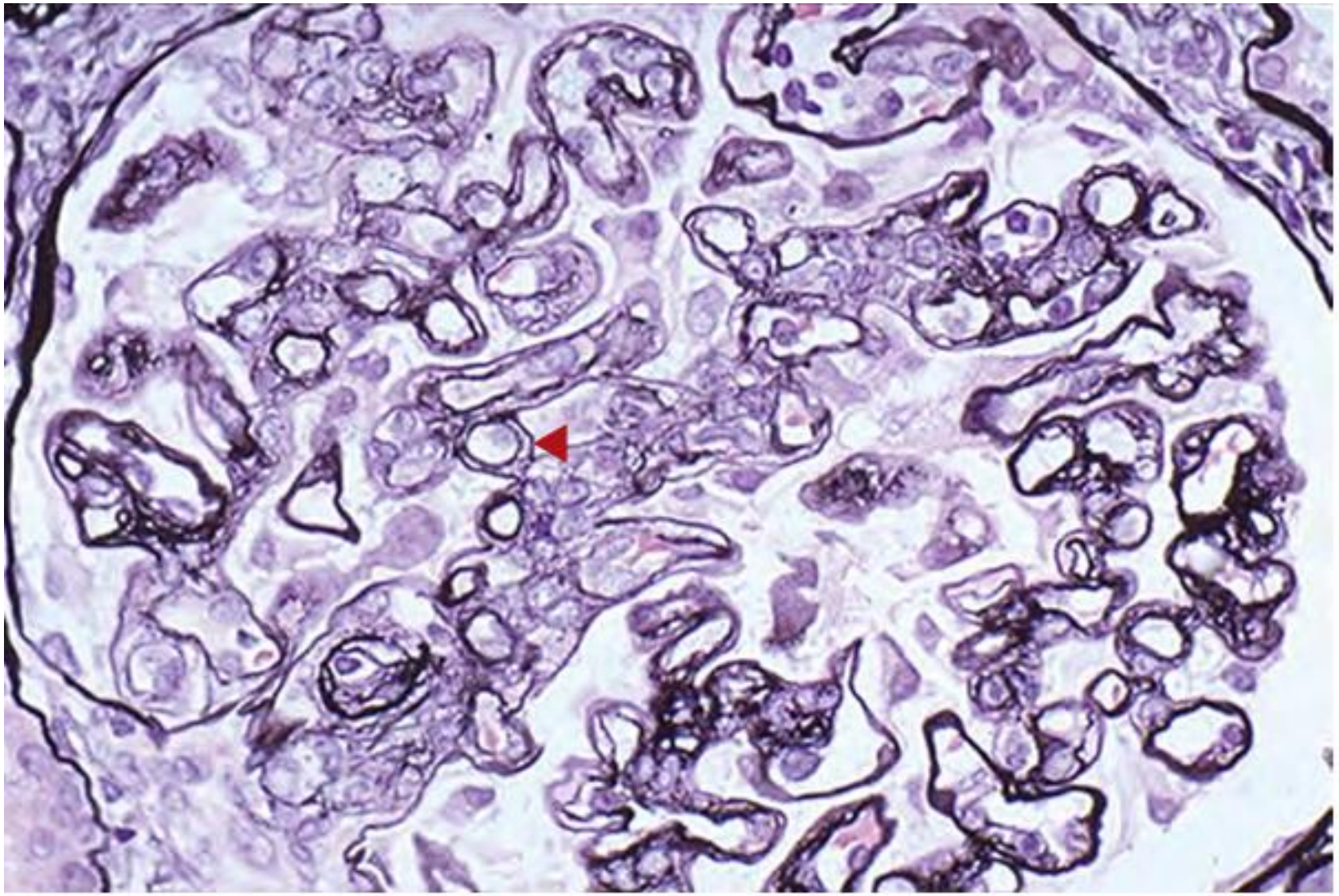
MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

- LM:
  1. Reduplication of basement membrane (**splitting**)
  2. Lobular proliferation of mesangial matrix into capillary loops (**tram-track appearance**)
- IF and EM: **subendothelial** deposits

- On light microscopy, there is **mesangial proliferation, increased mesangial matrix**, accentuation of the lobular architecture, and increased leukocytes.

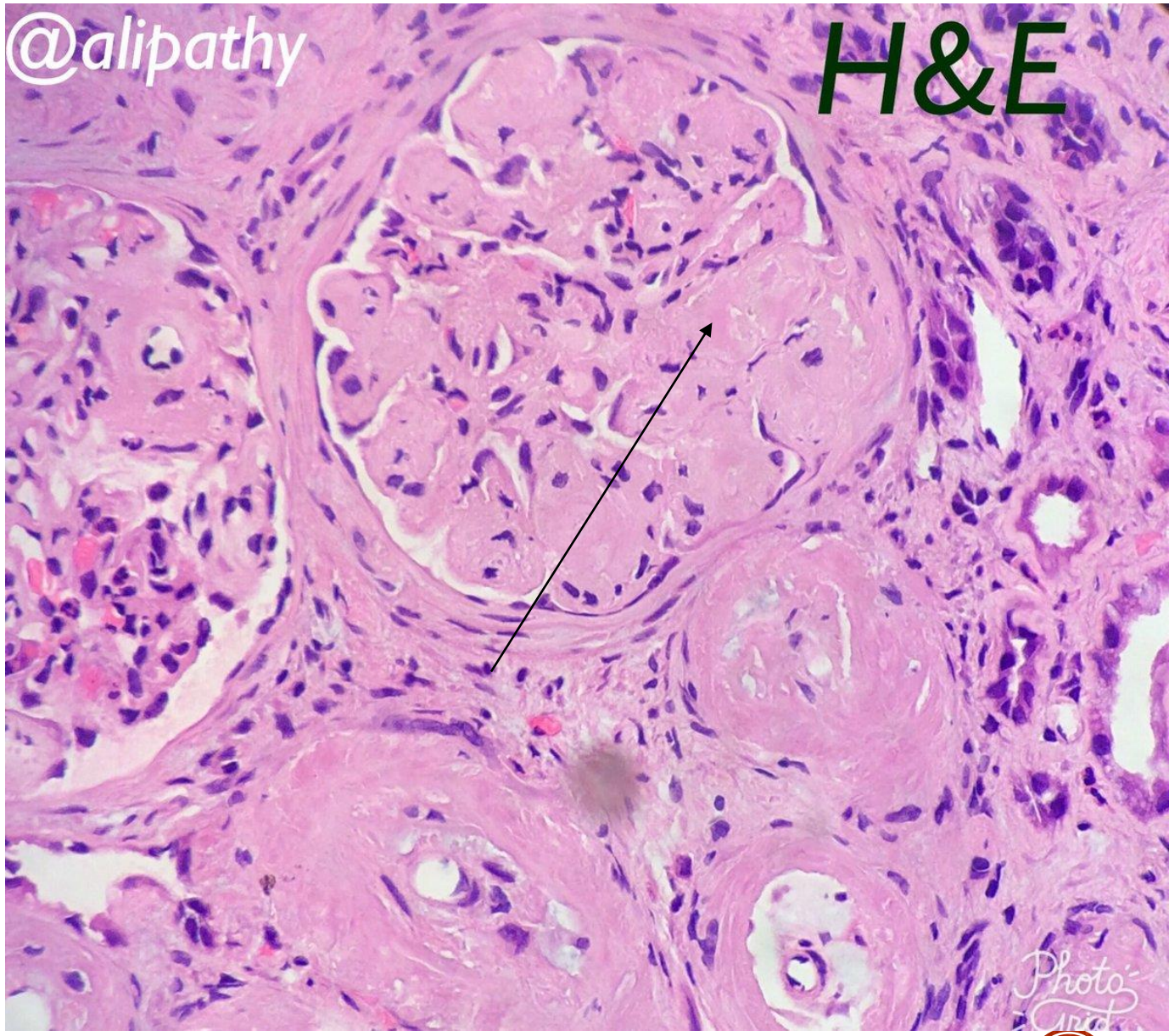


- This Jones silver stain shows a double contour to many basement membranes, or the "**tram- tracking**" that is characteristic of membranoproliferative glomerulonephritis (MPGN), which results from **basement membrane reduplication.**



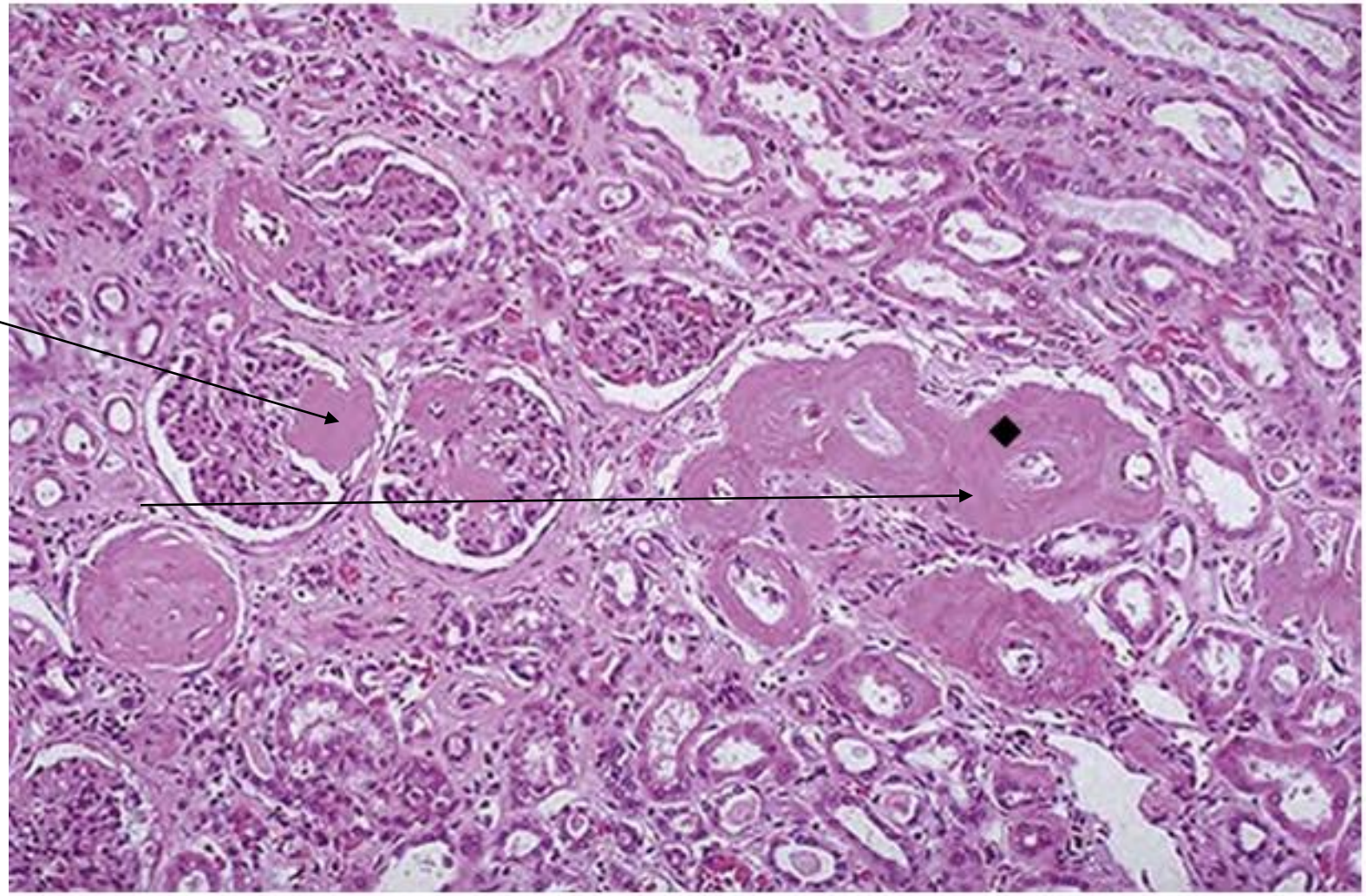
TRIGGER CASE

- A 60-year-old man complains of chronic back pain, fatigue, and excessive urination. X-ray reveals numerous lytic lesions in the lumbar vertebral bodies. Lab tests show hypoalbuminemia, mild anemia, and thrombocytopenia. A monoclonal immunoglobulin light-chain peak is demonstrated on serum electrophoresis. A bone marrow biopsy shows foci of plasma cells, account for 20%. A kidney biopsy is obtained.
- **What is the Diagnosis?**



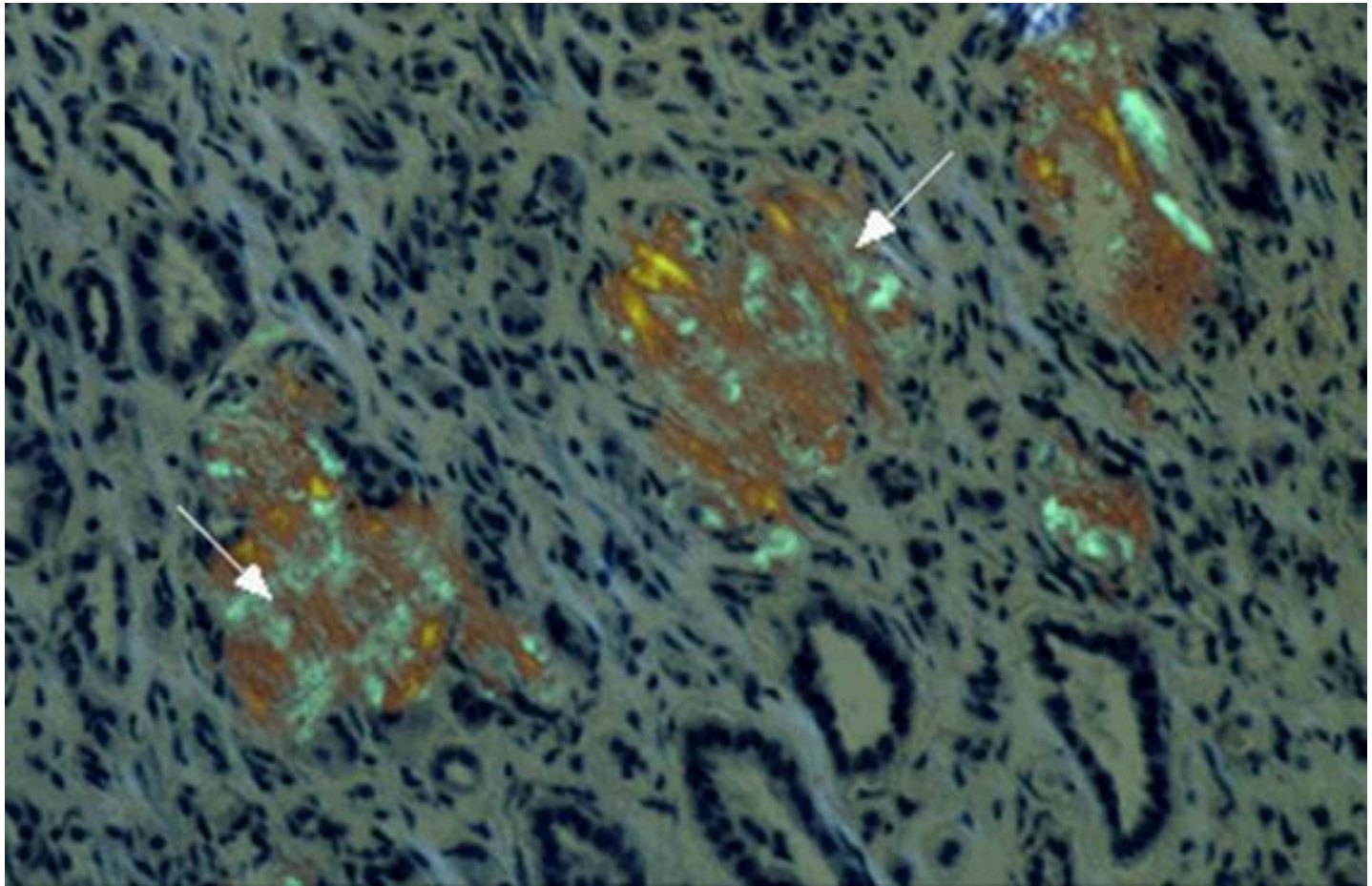
RENAL AMYLOIDOSIS, MULTIPLE MYELOMA

- In the renal cortex, pale pink deposits of **amyloid** and small renal arterial branches that have become thickened are visible within glomeruli. The **amorphous pink deposits** of amyloid may be found in and around arteries, in interstitium, or in glomeruli.



RENAL AMYLOIDOSIS

- Congo red special stain shows **apple-green** colored amyloid under polarized microscope.



THANK YOU ☺