Glomerulonephritis

APPROVED

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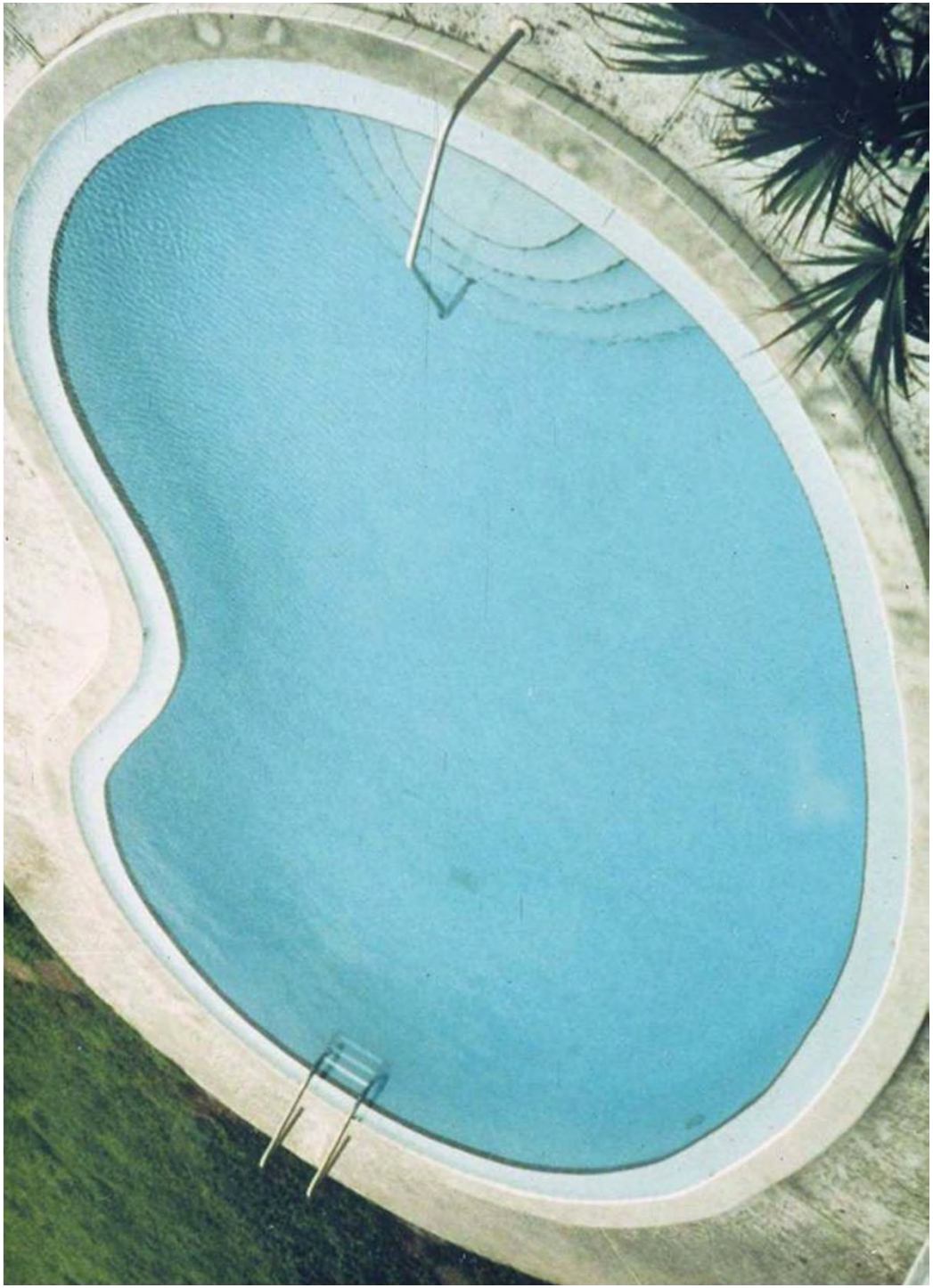
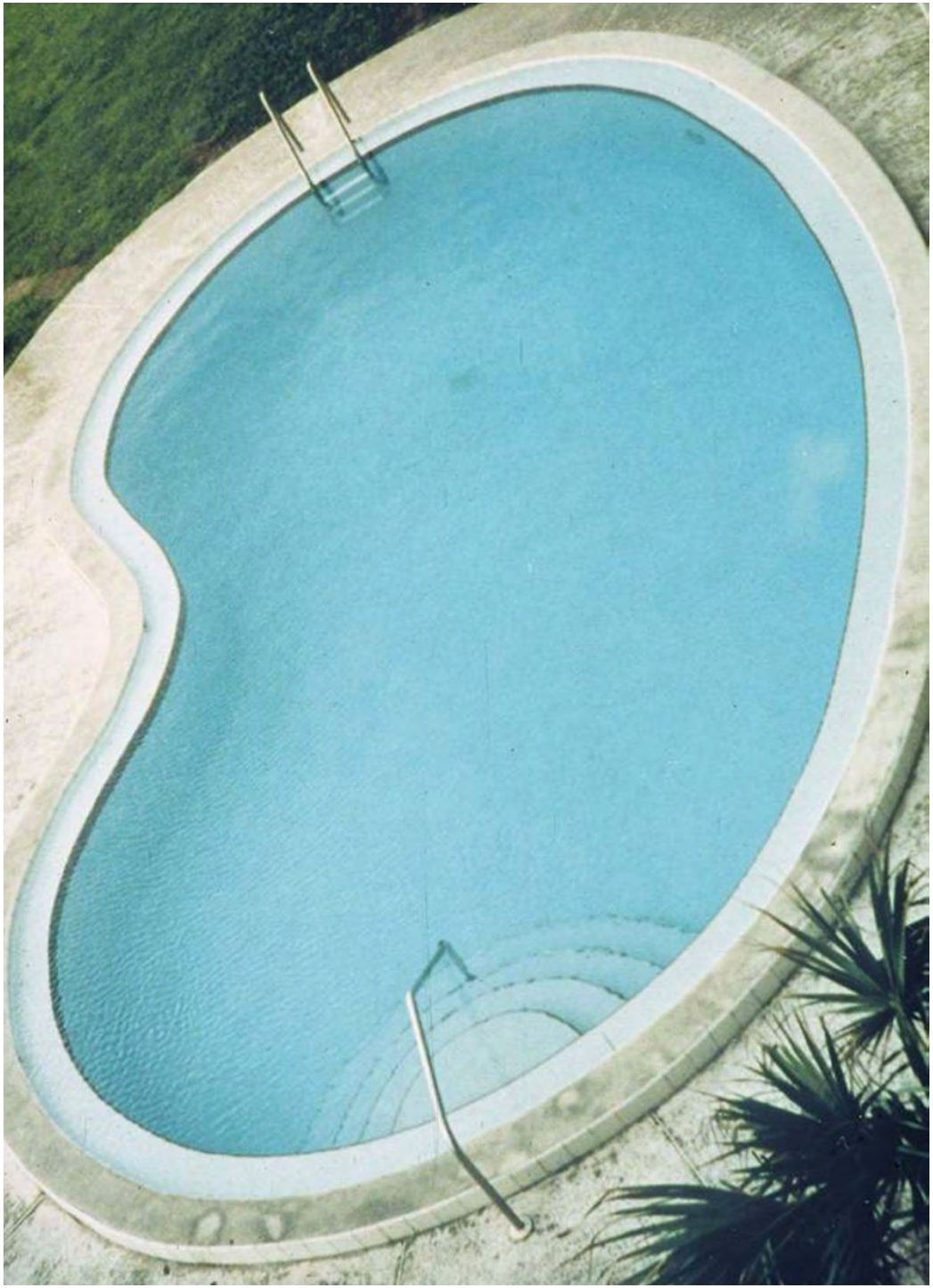
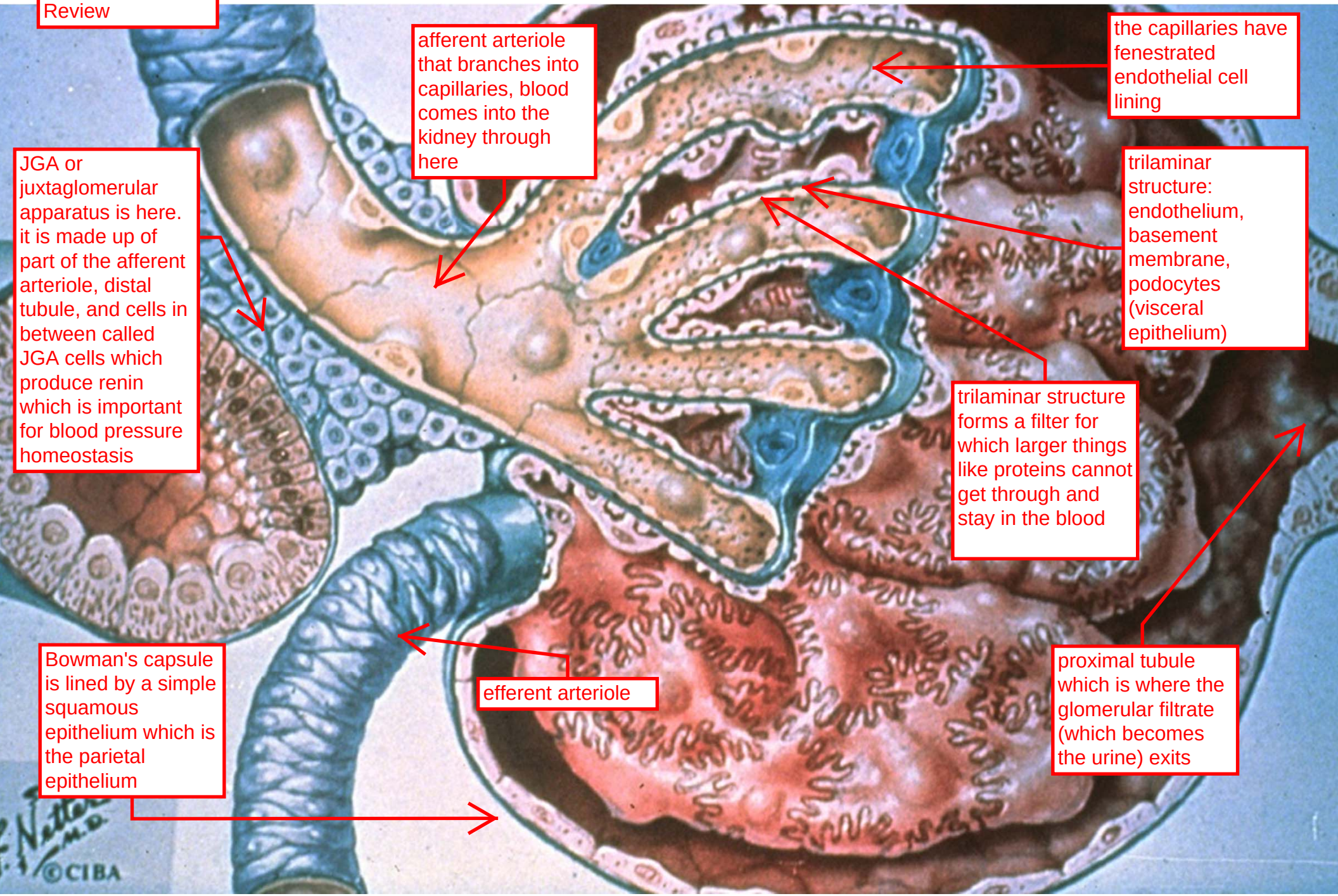
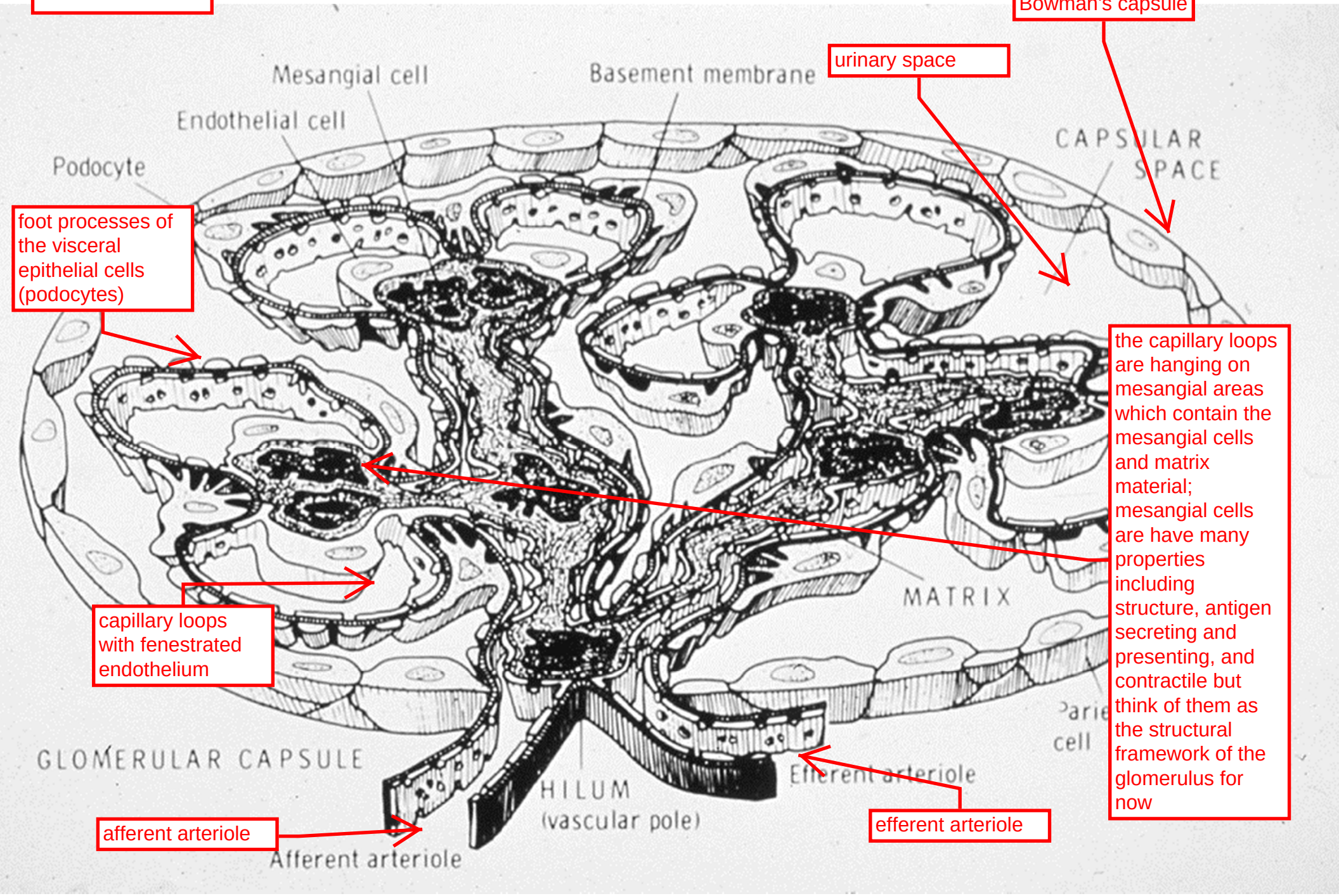
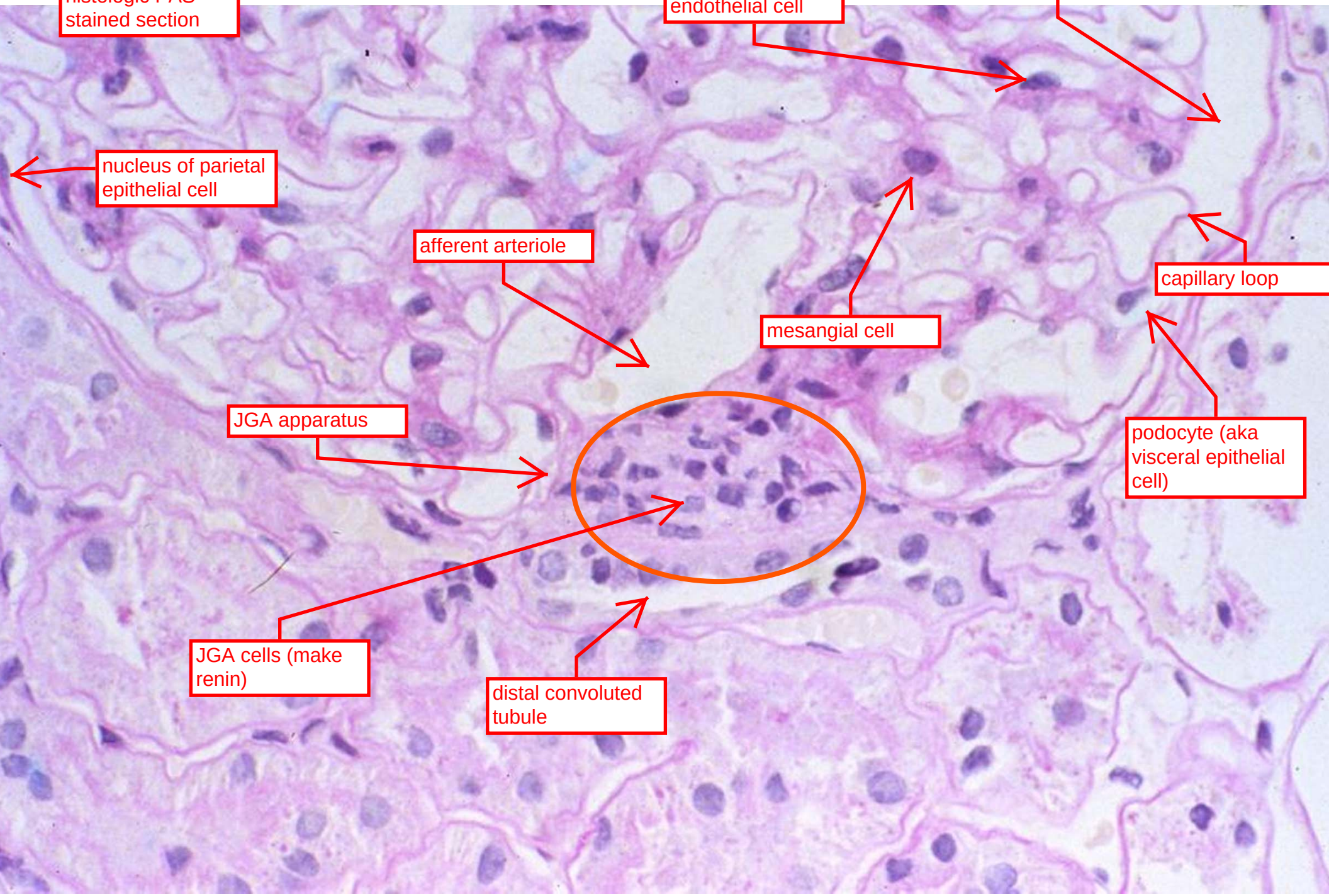
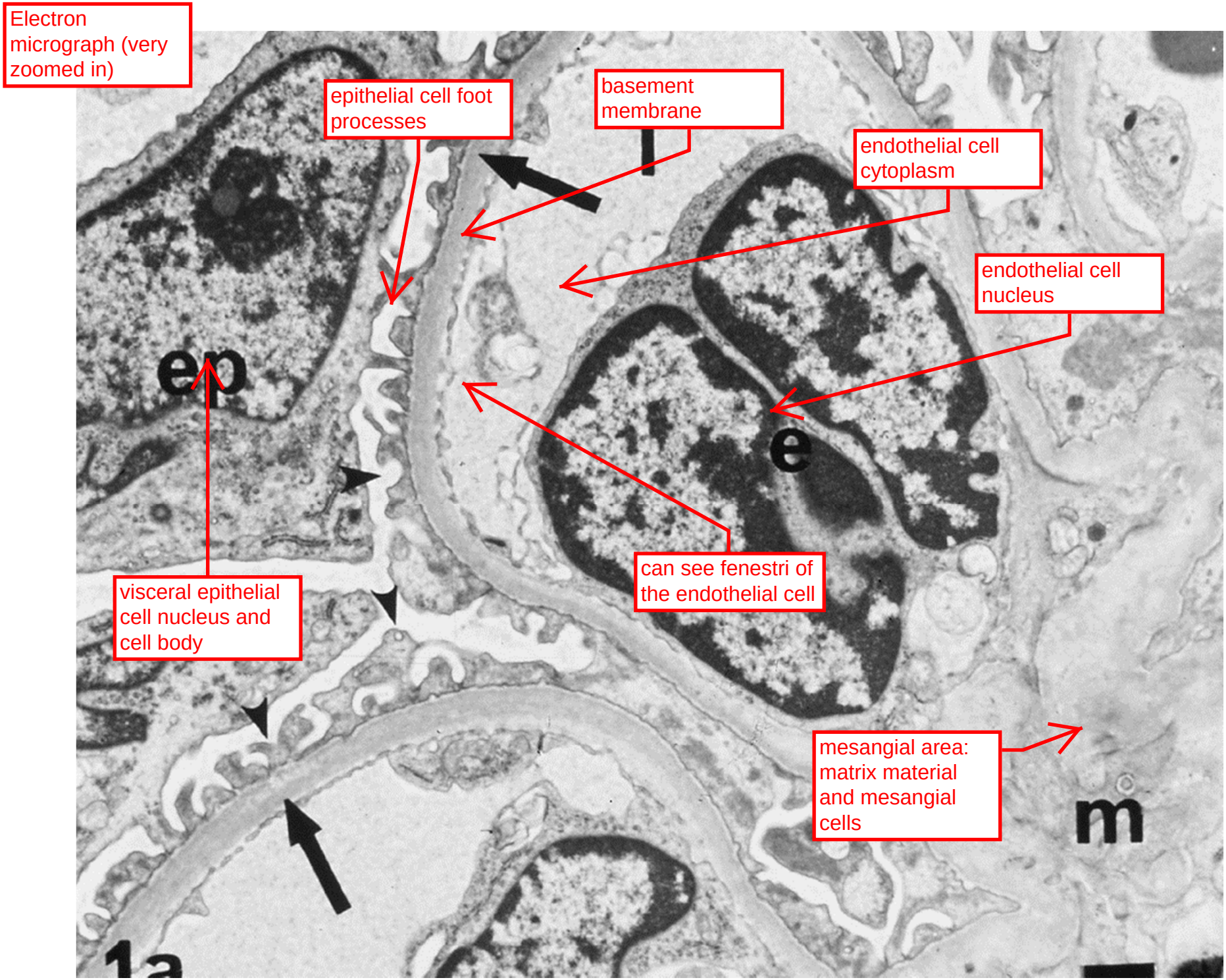





Kidney Anatomy Review
afferent arteriole that branches into capillaries, blood comes into the kidney through here
the capillaries have fenestrated endothelial cell lining
JGA or juxtaglomerular apparatus is here. it is made up of part of the afferent arteriole, distal tubule, and cells in between called JGA cells which produce renin which is important for blood pressure homeostasis
trilaminar structure: endothelium, basement membrane, podocytes (visceral epithelium)
trilaminar structure forms a filter for which larger things like proteins cannot get through and stay in the blood
Bowman's capsule is lined by a simple squamous epithelium which is the parietal epithelium
efferent arteriole
proximal tubule which is where the glomerular filtrate (which becomes the urine) exits
©CIBA


cross section view
Bowman's capsule
urinary space
Mesangial cell
Basement membrane
Endothelial cell
Podocyte
CAPSULAR SPACE
foot processes of the visceral epithelial cells (podocytes)
the capillary loops are hanging on mesangial areas which contain the mesangial cells and matrix material; mesangial cells are have many properties including structure, antigen secreting and presenting, and contractile but think of them as the structural framework of the glomerulus for now
MATRIX
capillary loops with fenestrated endothelium
GLOMERULAR CAPSULE
HILUM
(vascular pole)
Efferent arteriole
efferent arteriole
afferent arteriole
Afferent arteriole


histologic PAS stained section
endothelial cell
urinary space
nucleus of parietal epithelial cell
afferent arteriole
capillary loop
mesangial cell
JGA apparatus
podocyte (aka visceral epithelial cell)
JGA cells (make renin)
distal convoluted tubule


Electron micrograph (very zoomed in)
epithelial cell foot processes
basement membrane
endothelial cell cytoplasm
endothelial cell nucleus
ep
e
can see fenestri of the endothelial cell
visceral epithelial cell nucleus and cell body
mesangial area: matrix material and mesangial cells
m
1a

will now talk about 3 ways to classify glomerular disease

protein in the urine: main cause, damage to the filtration barrier for example, podocyte is damaged and allows protein to get through

Classifications of glomerular disease

By clinical presentation

very bad hematuria

blood in the urine: caused by gross abnormalities for example inflammation of the glomerulus lets blood into the urine, also heritable disorders of the basement membrane causing breaks in it

- **Symptom complexes**
  - **Proteinuria**
  - **Hematuria**
  - **Nephrotic syndrome (severe proteinuria, hypoalbuminemia, edema)**
  - **Nephritic syndrome (hematuria, variable degree of renal insufficiency)**
  - **Rapidly progressive glomerulonephritis (severe form of nephritic syndrome)**
  - **Acute renal failure (oliguria, azotemia)**
  - **Chronic renal failure**
- **Acute vs. chronic**
- **Primary (renal) vs. secondary (systemic)**

very bad proteinurea

because peeing out the albumin

don't put out much urine

build up of nitrogenous wastes in the blood

diabetes and hypertension are major causes of this

possible causes include drug reaction in acute interstitial nephritis, renal calculus blocking the urethra, prostatic disease (by blocking the bladder outlet)

because low albumin in the blood (cannot maintain colloid osmotic pressure of the blood serum)

Classifications of glomerular disease

By histologic pattern

proliferation of cells in the glomerular tuft

do it a lot

some

not as much

can happen in a lot of diseases but mainly in immune complex diseases, immune complexes deposit in the glomerulus

Acute alterations

- Intrinsic (mesangial, endothelial, visceral epithelial) cell proliferation
- Extrinsic (parietal epithelial) cell proliferation (crescent formation)
- Inflammatory cell infiltration
- Necrosis

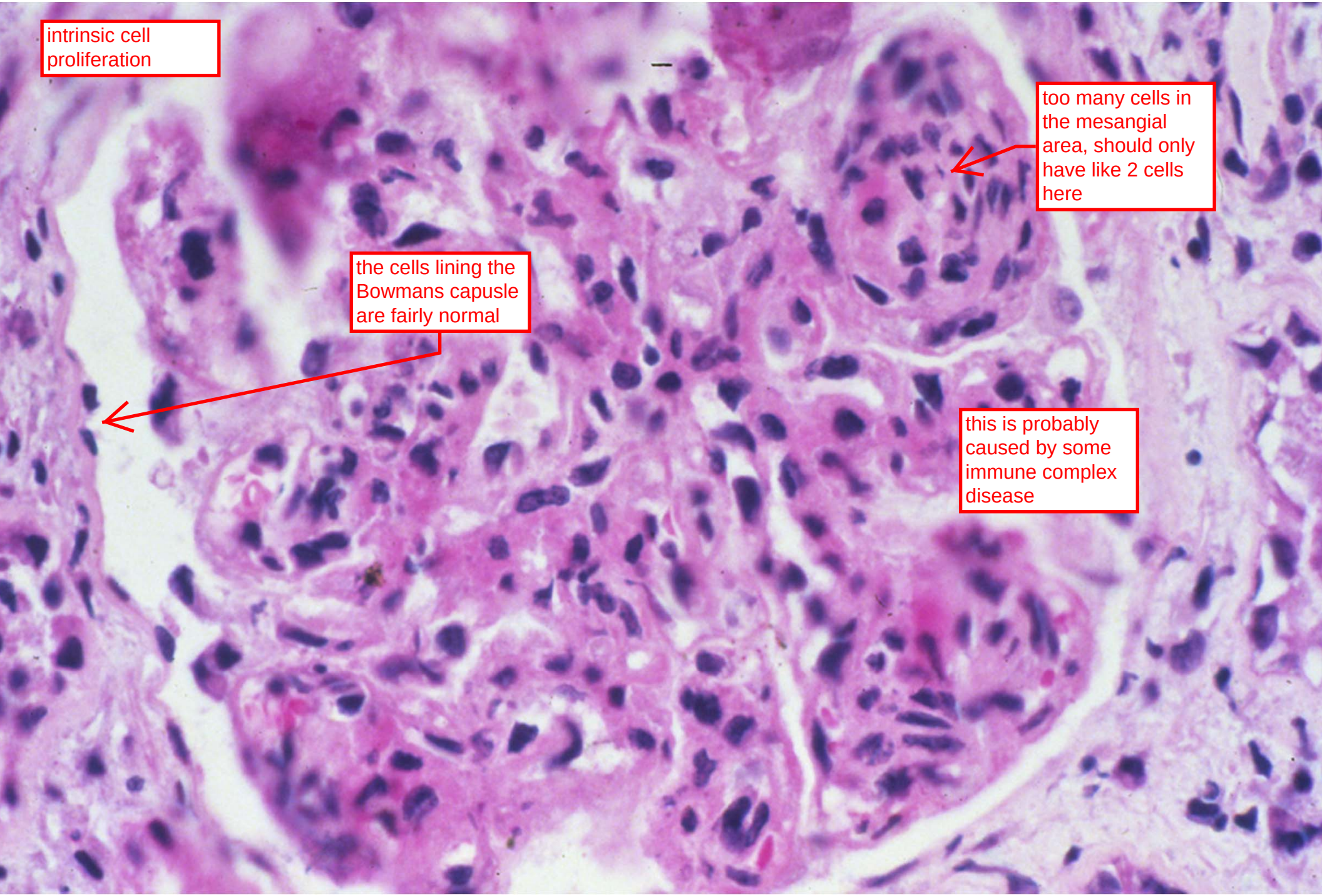
Chronic alterations

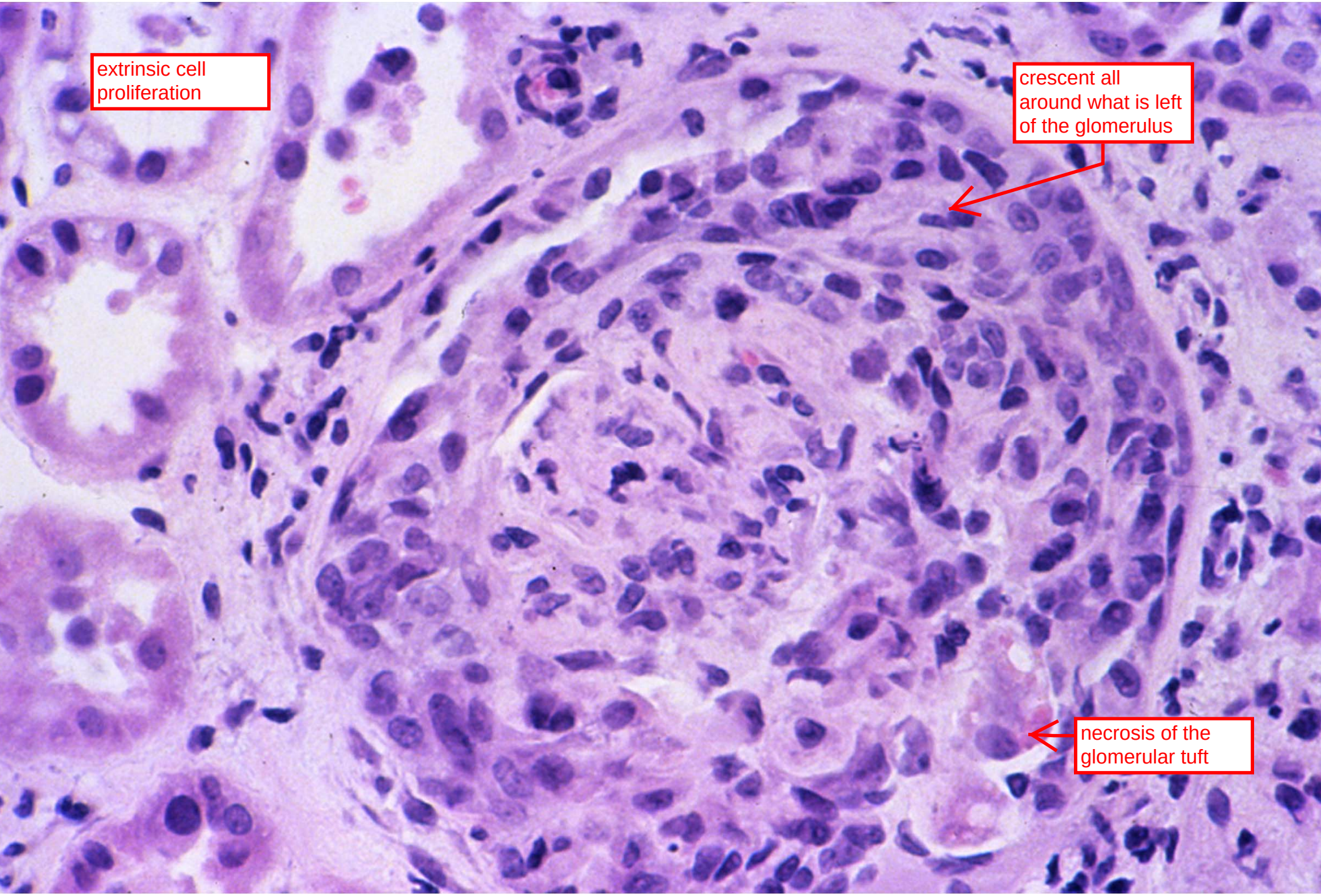
- Mesangial matrix/capillary basement membrane expansion
- Fibrosis (scarring in areas of antecedent necrosis)
- Sclerosis (collapse of glomerular tufts)

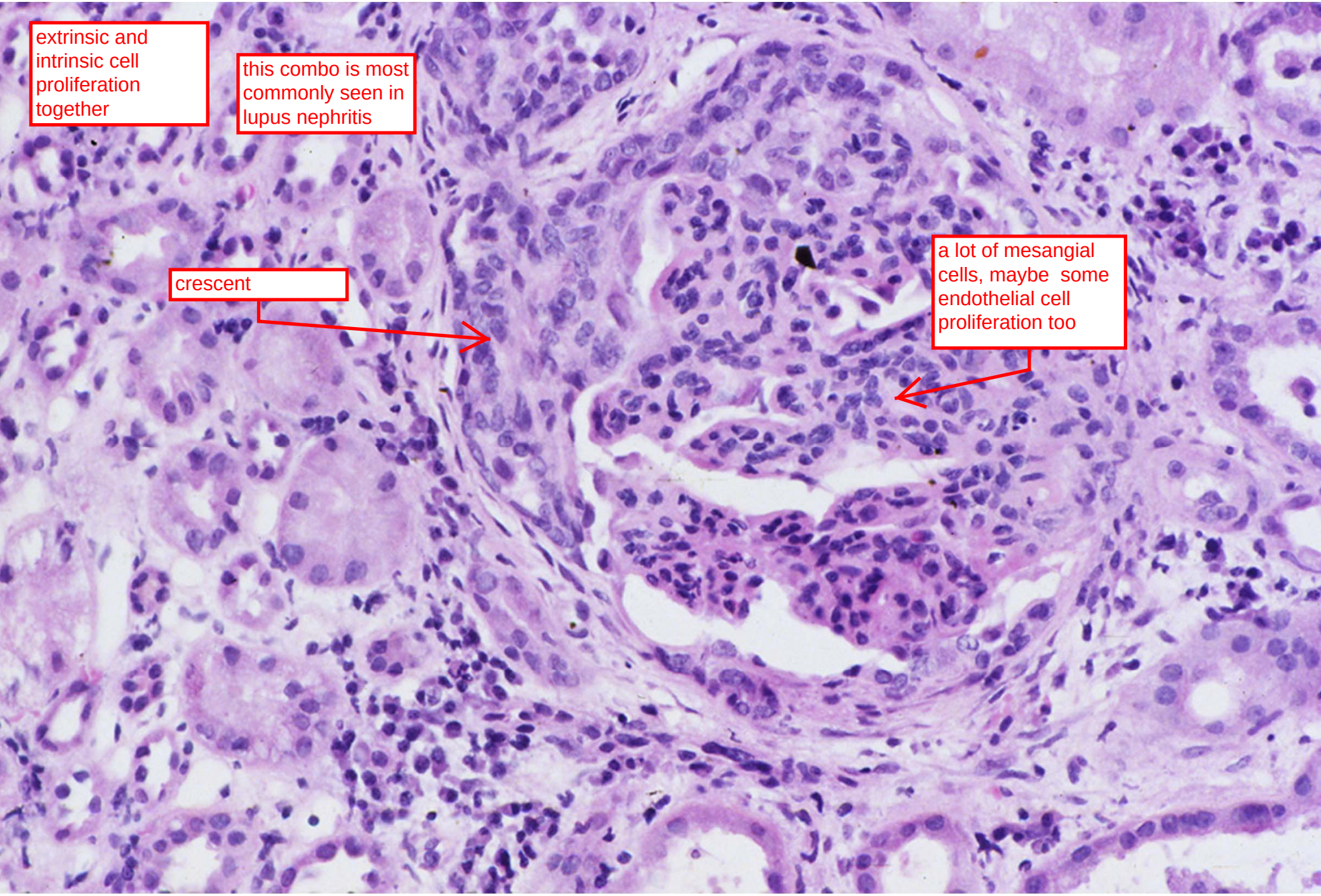
cresent formation results from necrosis to the glomerular tuft and liberation of fibrin into the Bowman's capsule and excites the epithelial cells

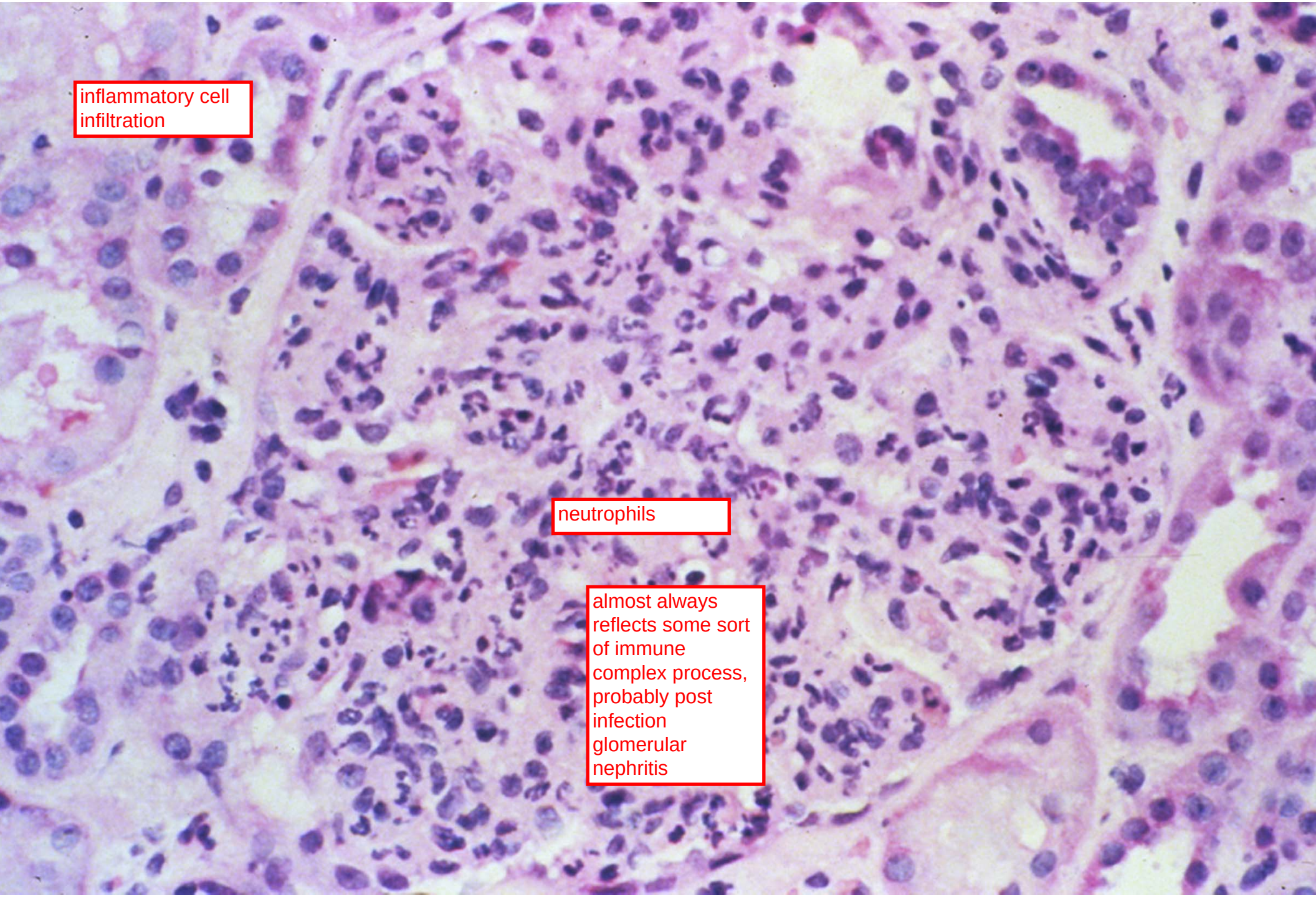
overgrowth of the glomerulus with fibrous tissue

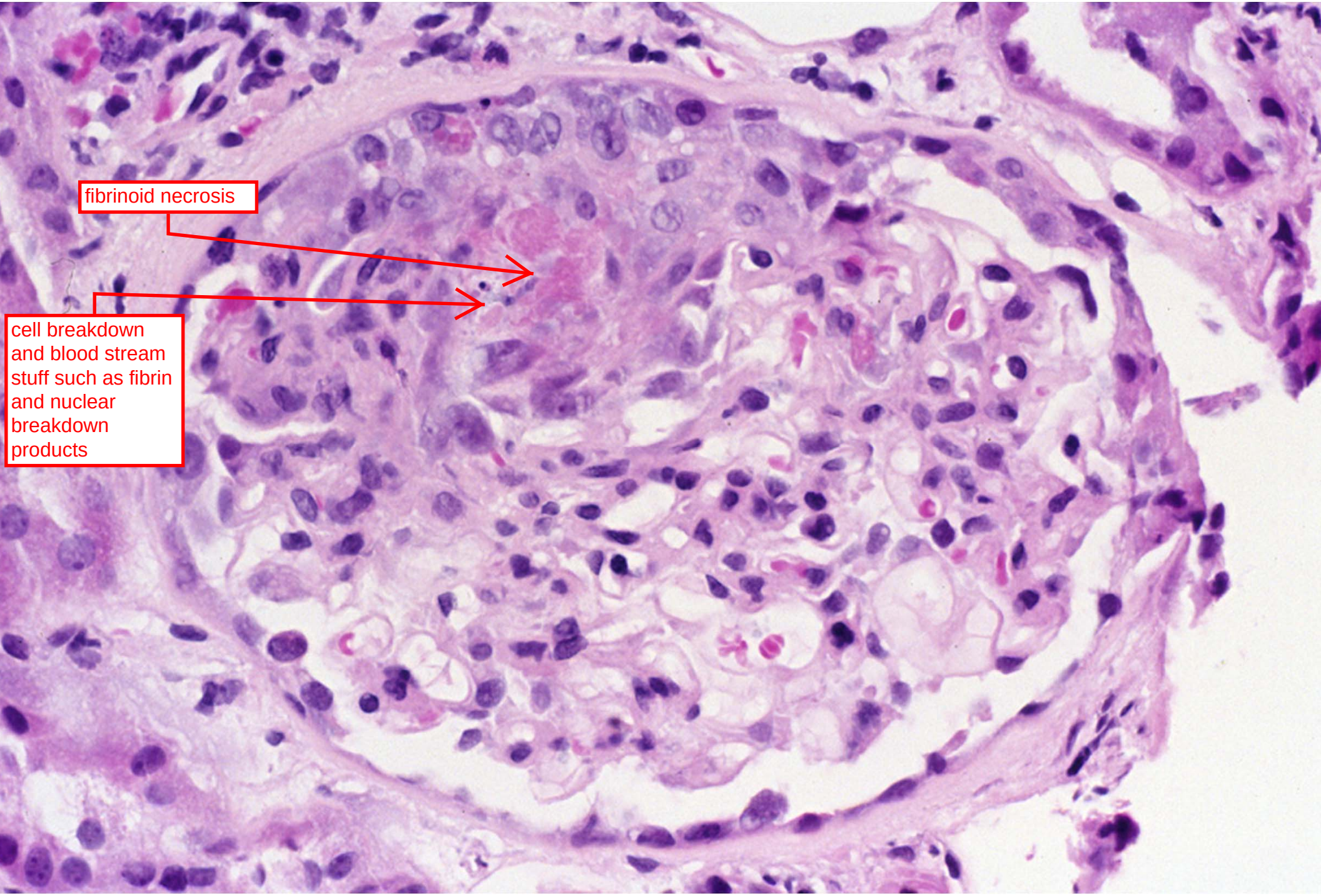
these two look similar but are different

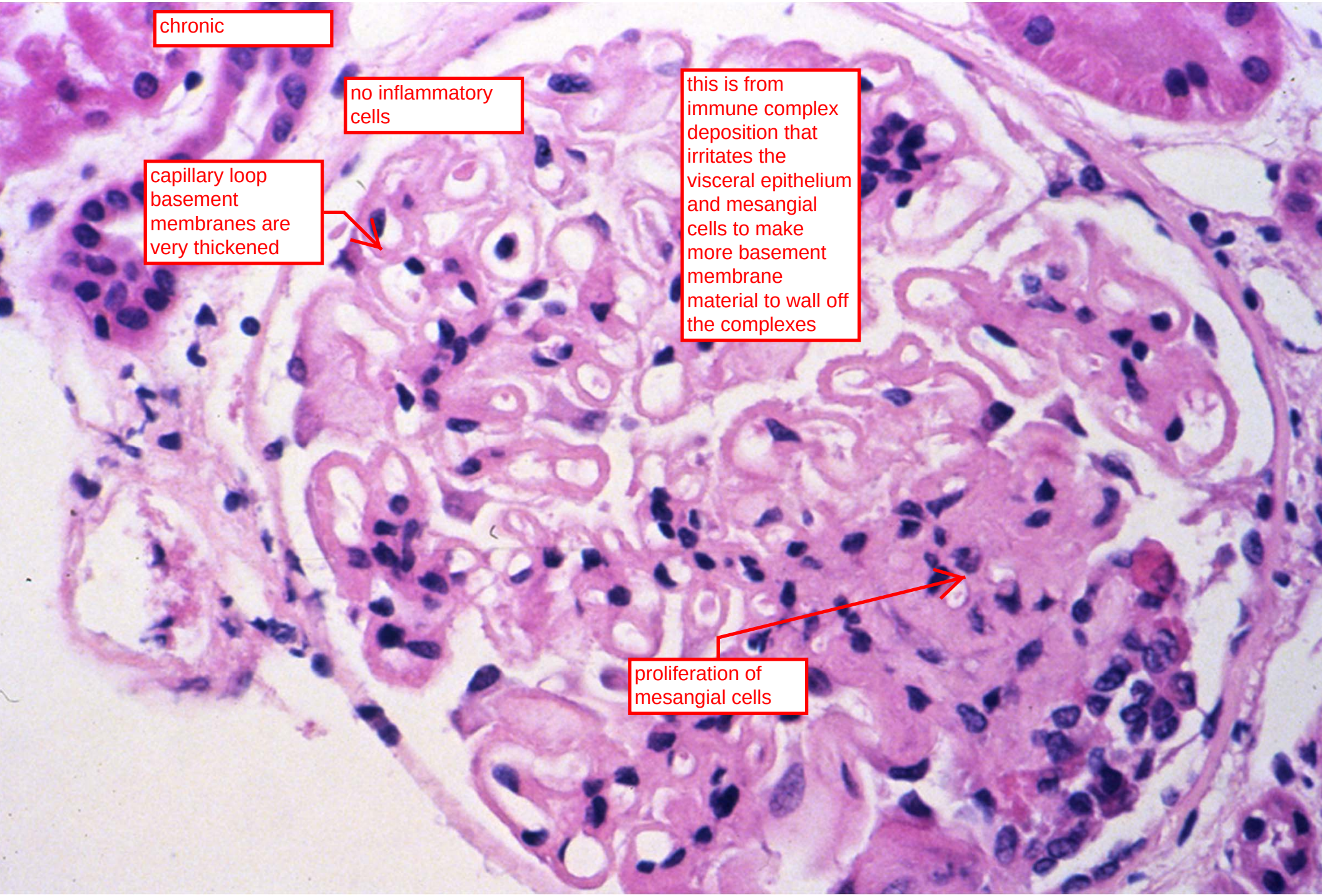

intrinsic cell proliferation
too many cells in the mesangial area, should only have like 2 cells here
the cells lining the Bowmans capusle are fairly normal
this is probably caused by some immune complex disease

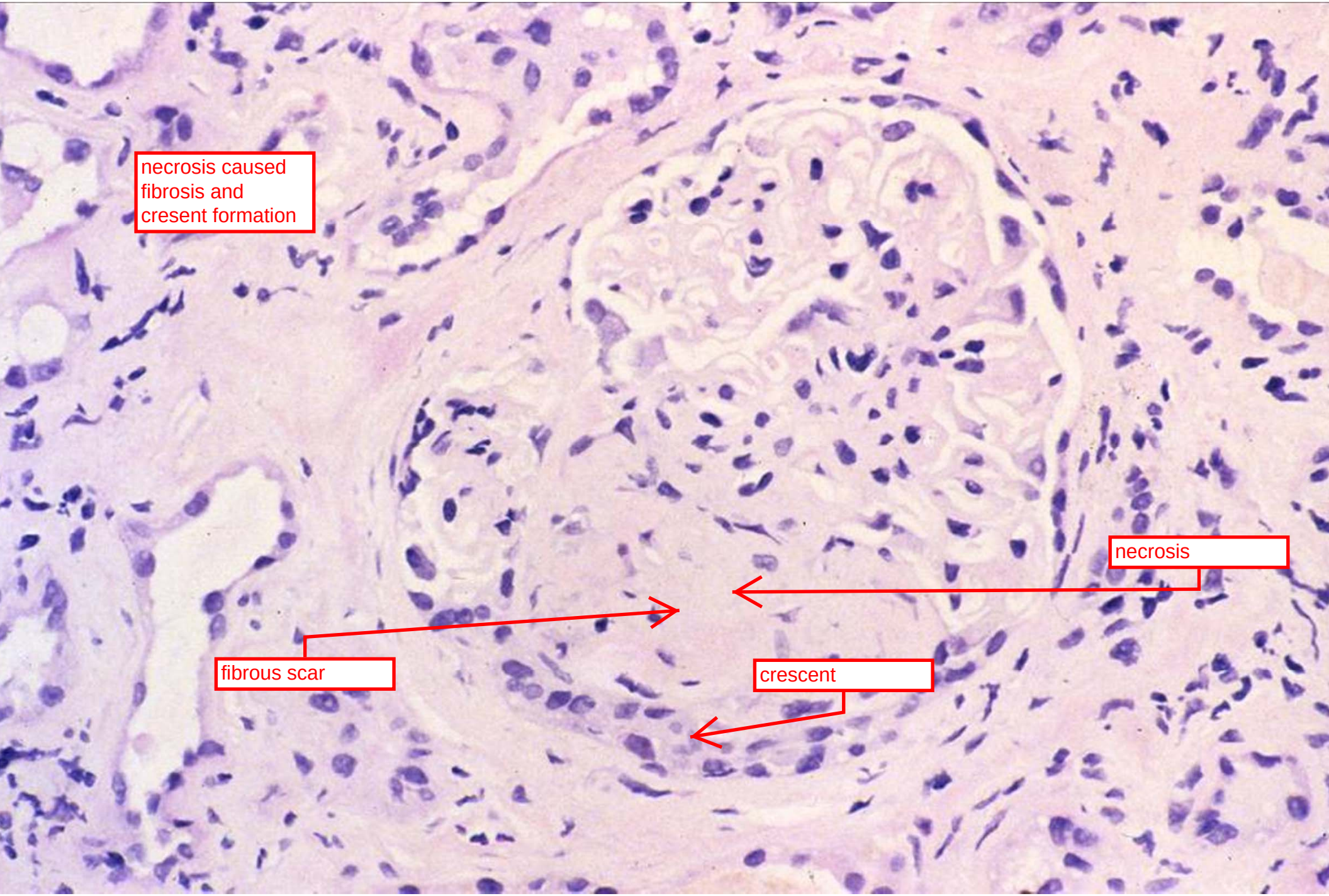

extrinsic cell proliferation
crescent all around what is left of the glomerulus
necrosis of the glomerular tuft

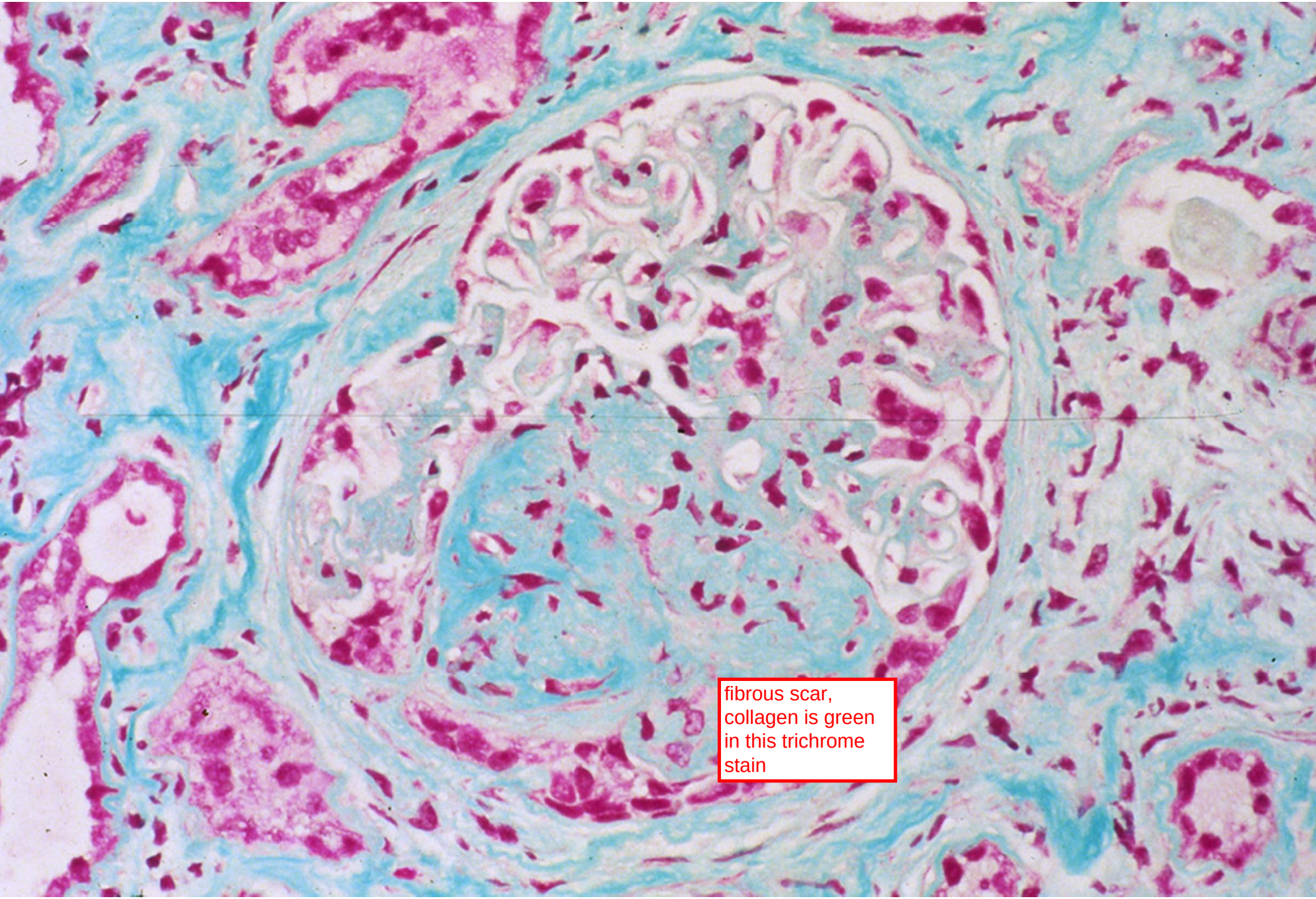

extrinsic and intrinsic cell proliferation together
this combo is most commonly seen in lupus nephritis
crescent
a lot of mesangial cells, maybe some endothelial cell proliferation too

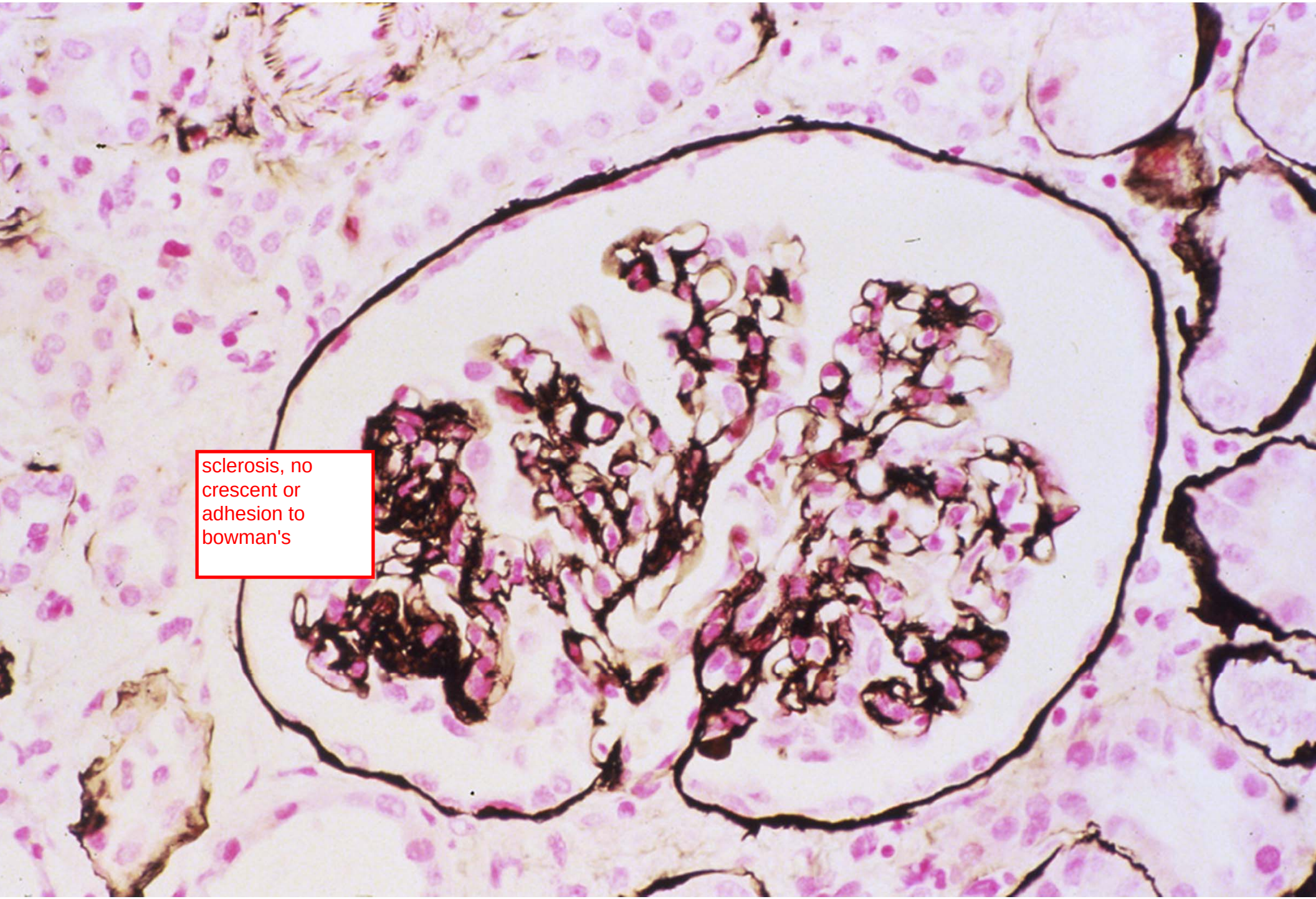

inflammatory cell infiltration
neutrophils
almost always reflects some sort of immune complex process, probably post infection glomerular nephritis


fibrinoid necrosis
cell breakdown and blood stream stuff such as fibrin and nuclear breakdown products


chronic
no inflammatory cells
capillary loop basement membranes are very thickened
this is from immune complex deposition that irritates the visceral epithelium and mesangial cells to make more basement membrane material to wall off the complexes
proliferation of mesangial cells


necrosis caused
fibrosis and
cresent formation
necrosis
fibrous scar
crescent

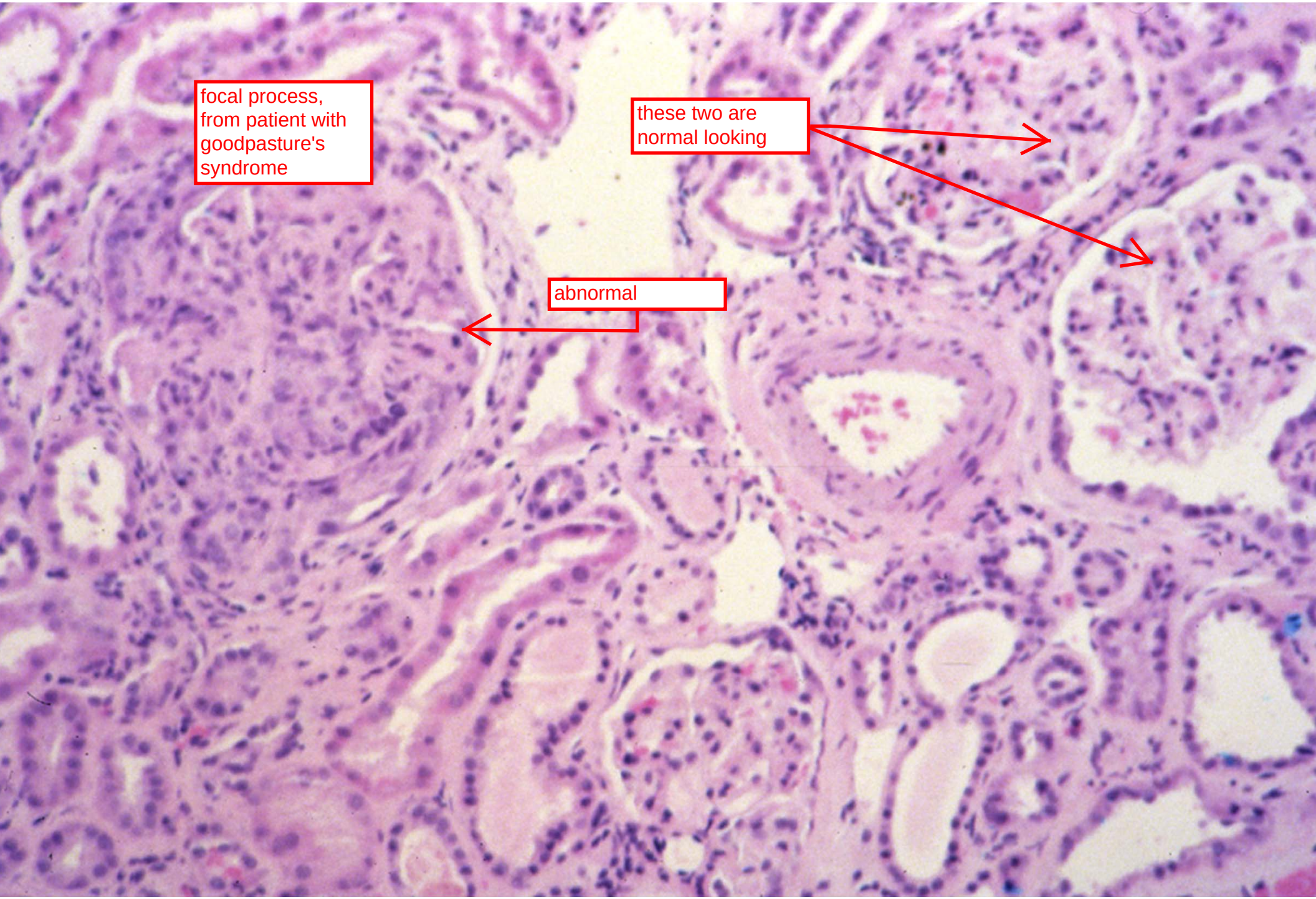

fibrous scar,
collagen is green
in this trichrome
stain

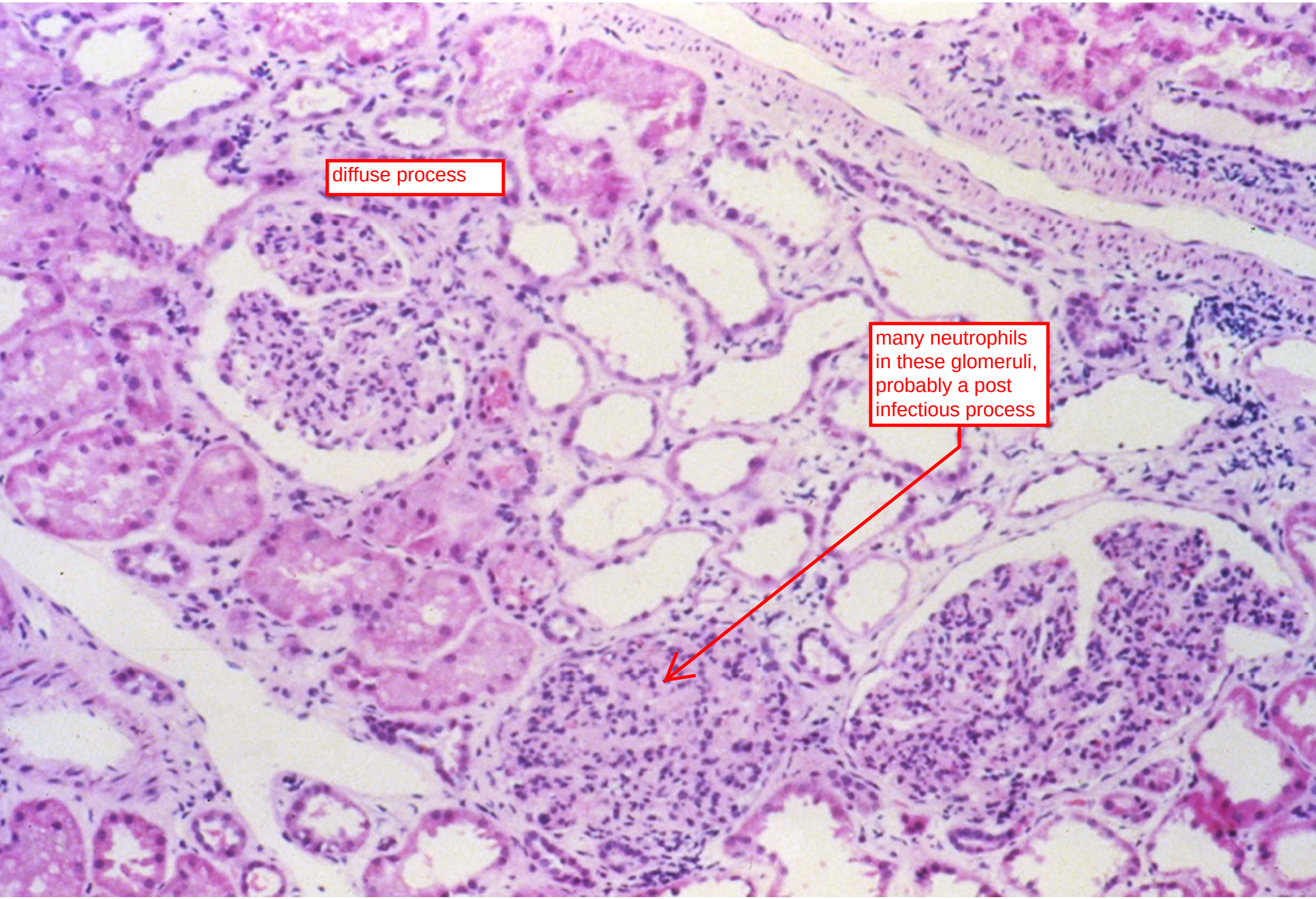

sclerosis, no crescent or adhesion to bowman's

read it

Classifications of glomerular disease
By histologic pattern

- **Percentage of glomeruli involved**
  - **Focal (less than 75%)**
  - **Diffuse (75% or more)**

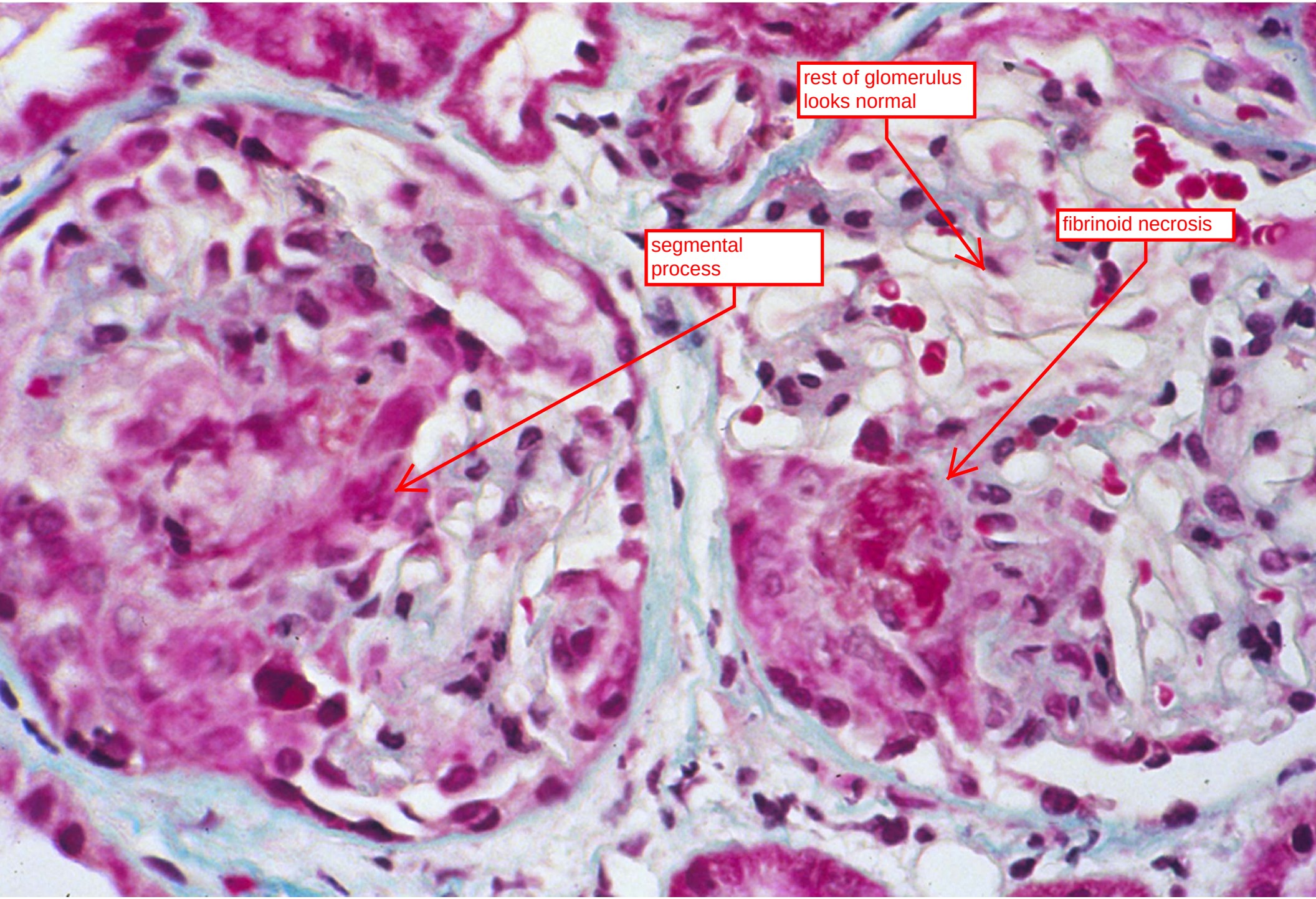

focal process, from patient with goodpasture's syndrome
these two are normal looking
abnormal

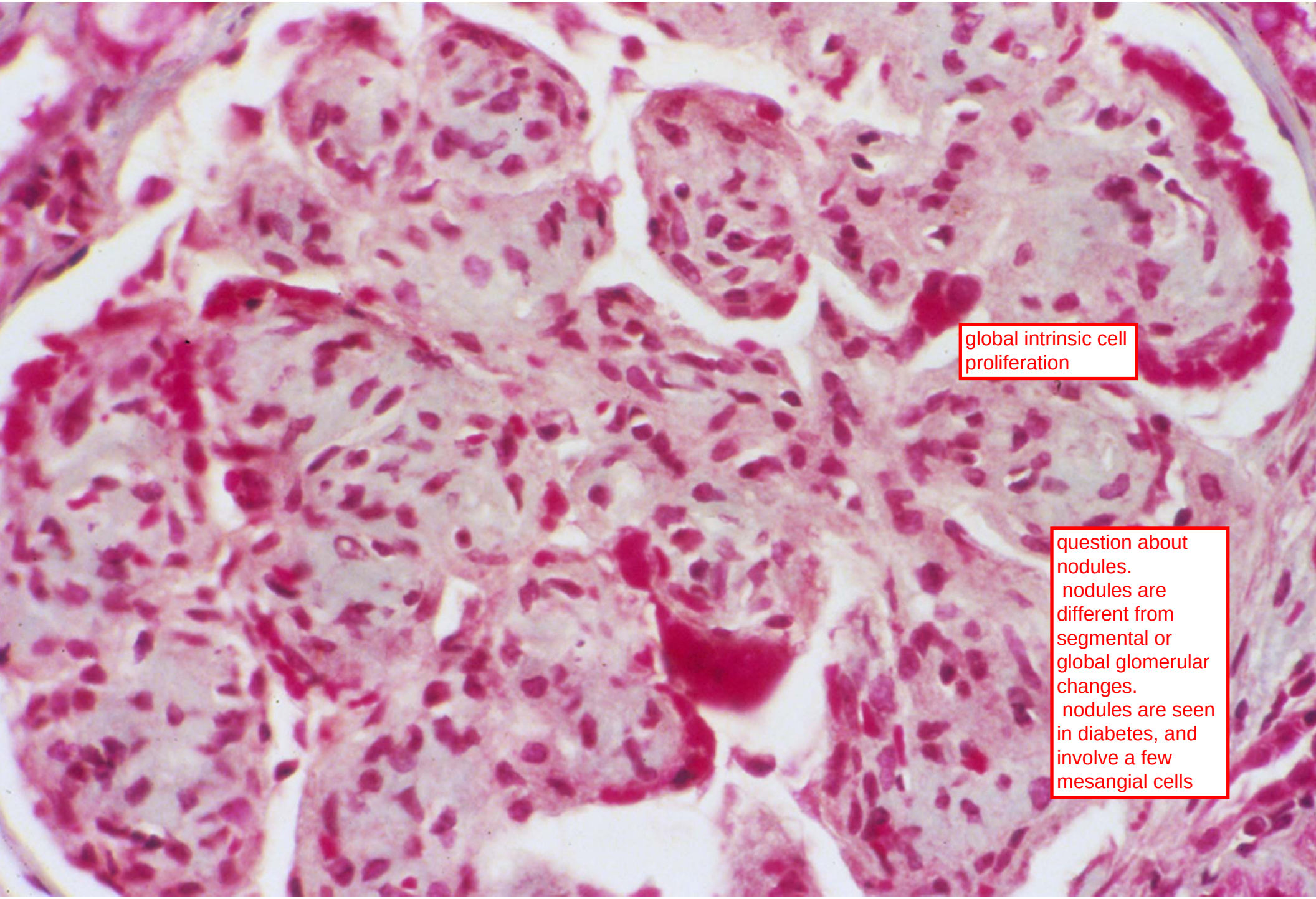

diffuse process
many neutrophils in these glomeruli, probably a post infectious process

read slide

Classifications of glomerular disease
By histologic pattern

- **Extent of involvement of individual glomeruli**
  - **Segmental (portions of glomeruli affected)**
  - **Global (entire glomeruli affected)**

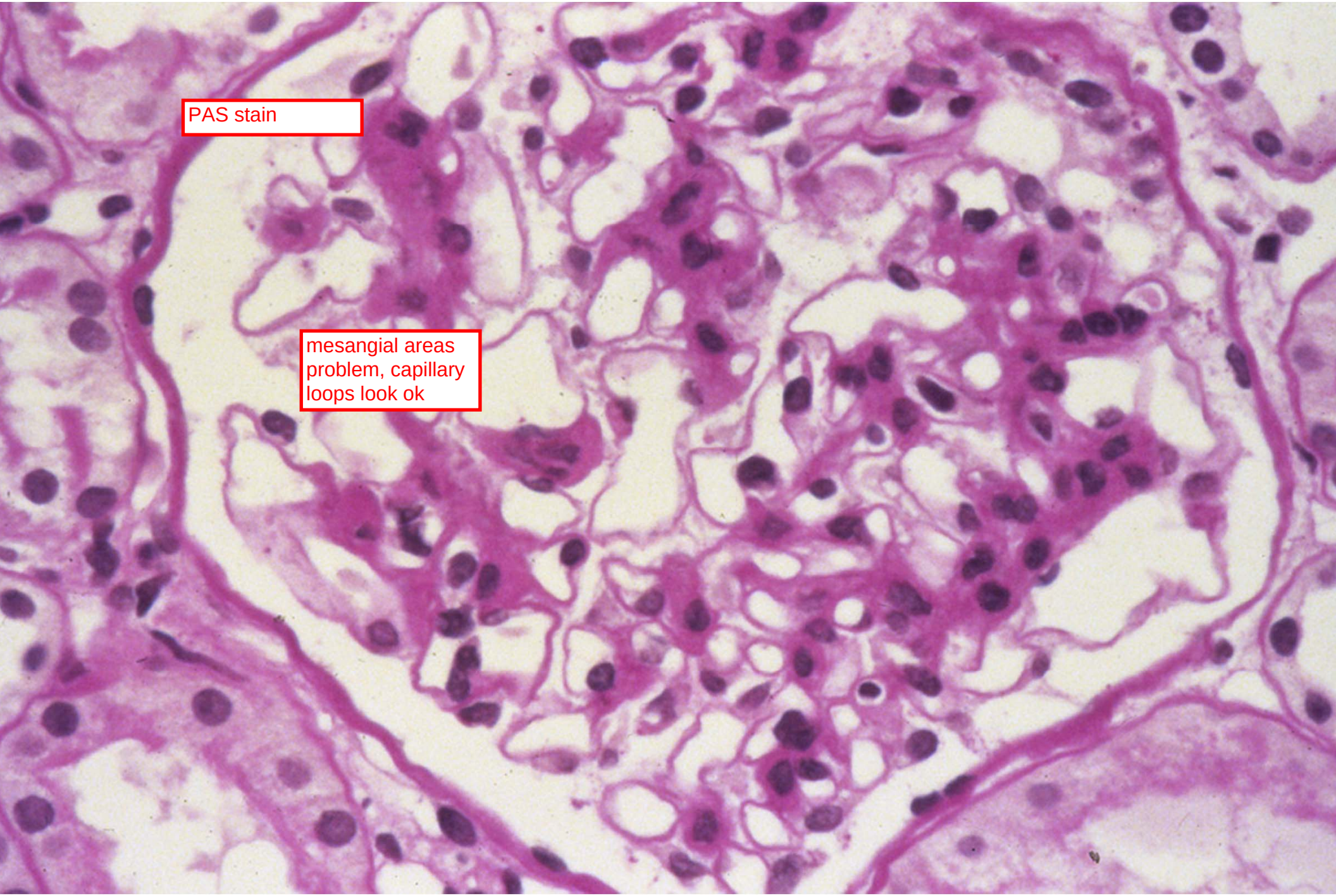

rest of glomerulus looks normal
fibrinoid necrosis
segmental process

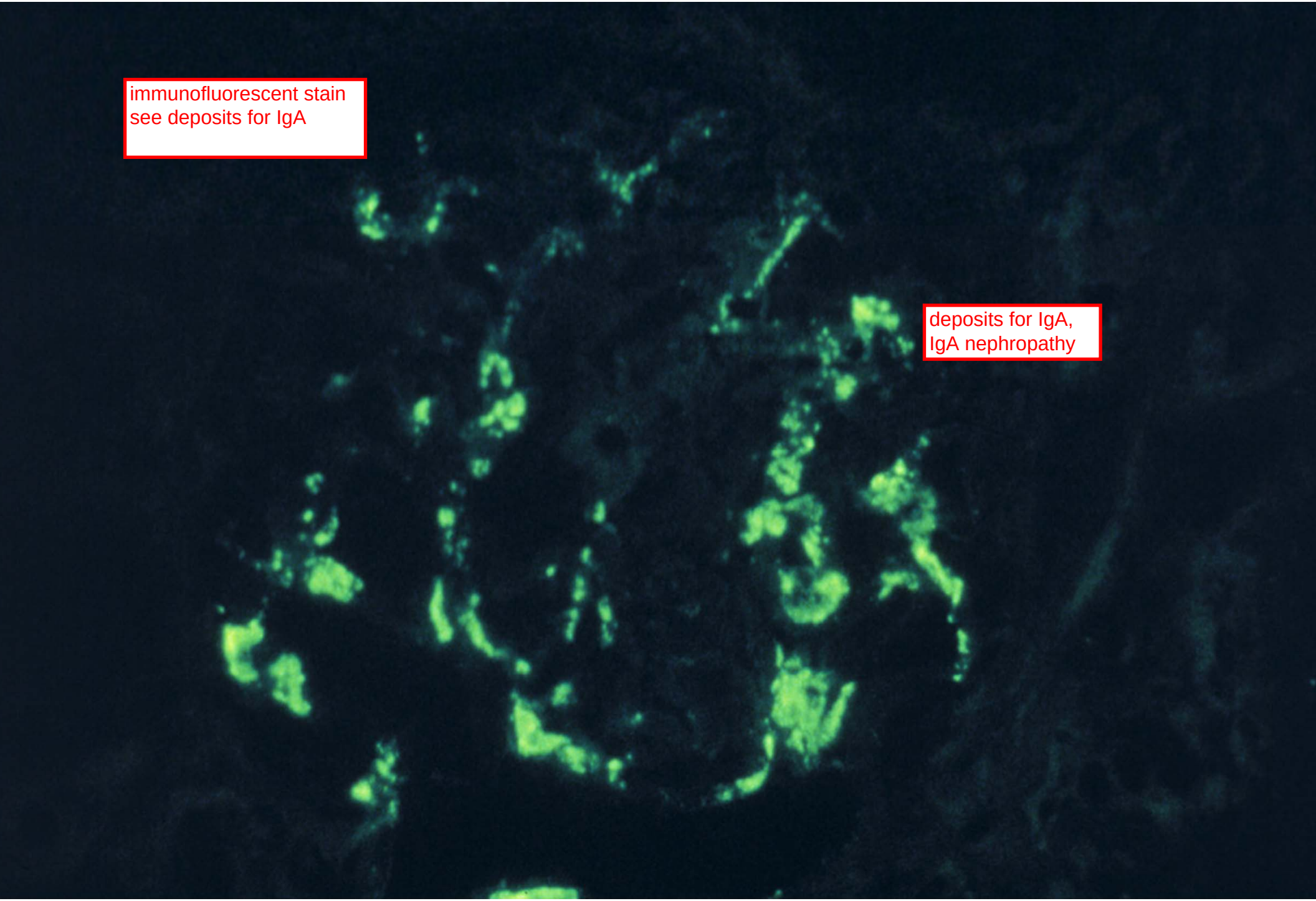

global intrinsic cell proliferation
question about nodules.
nodules are different from segmental or global glomerular changes.
nodules are seen in diabetes, and involve a few mesangial cells

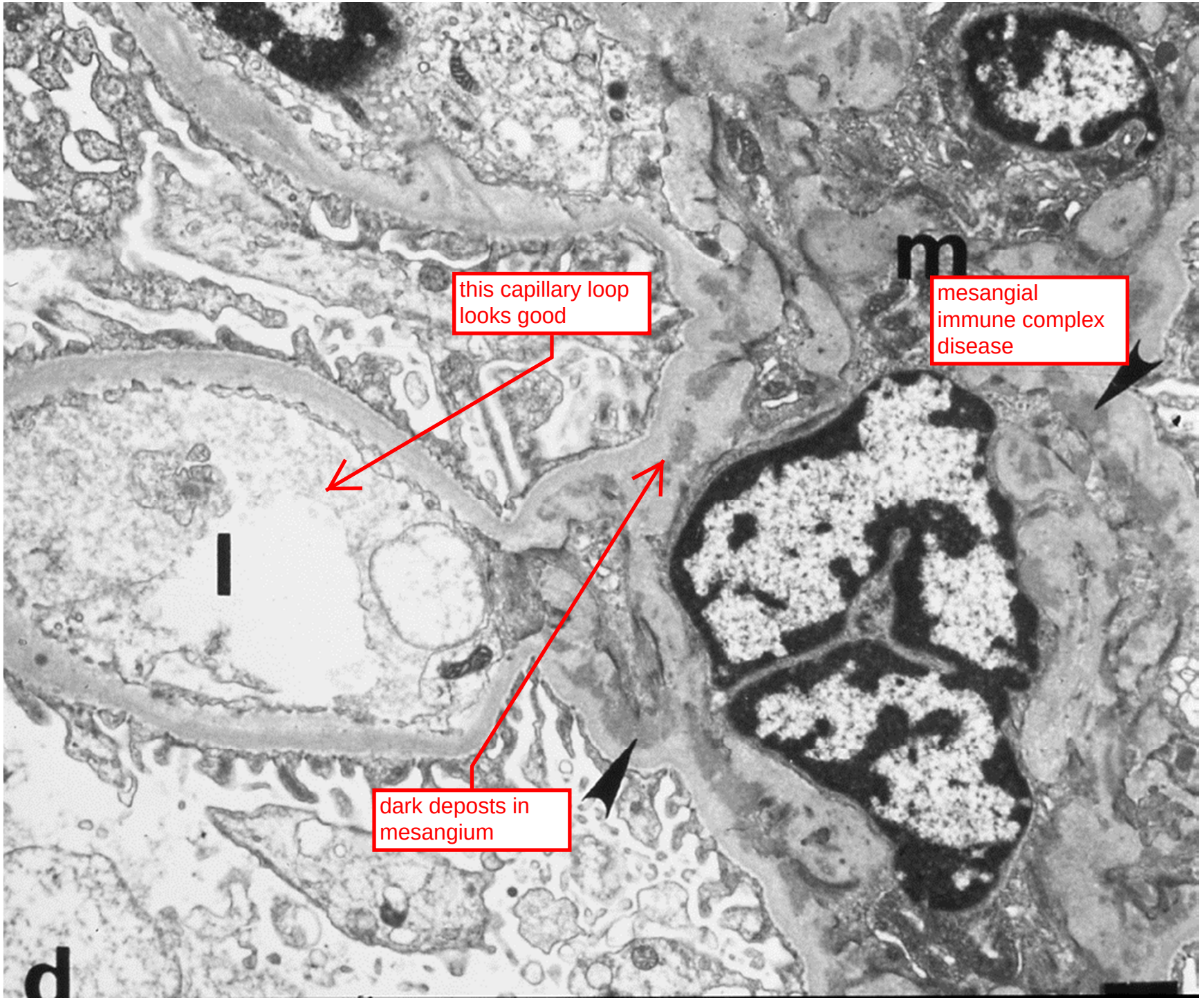
read slide

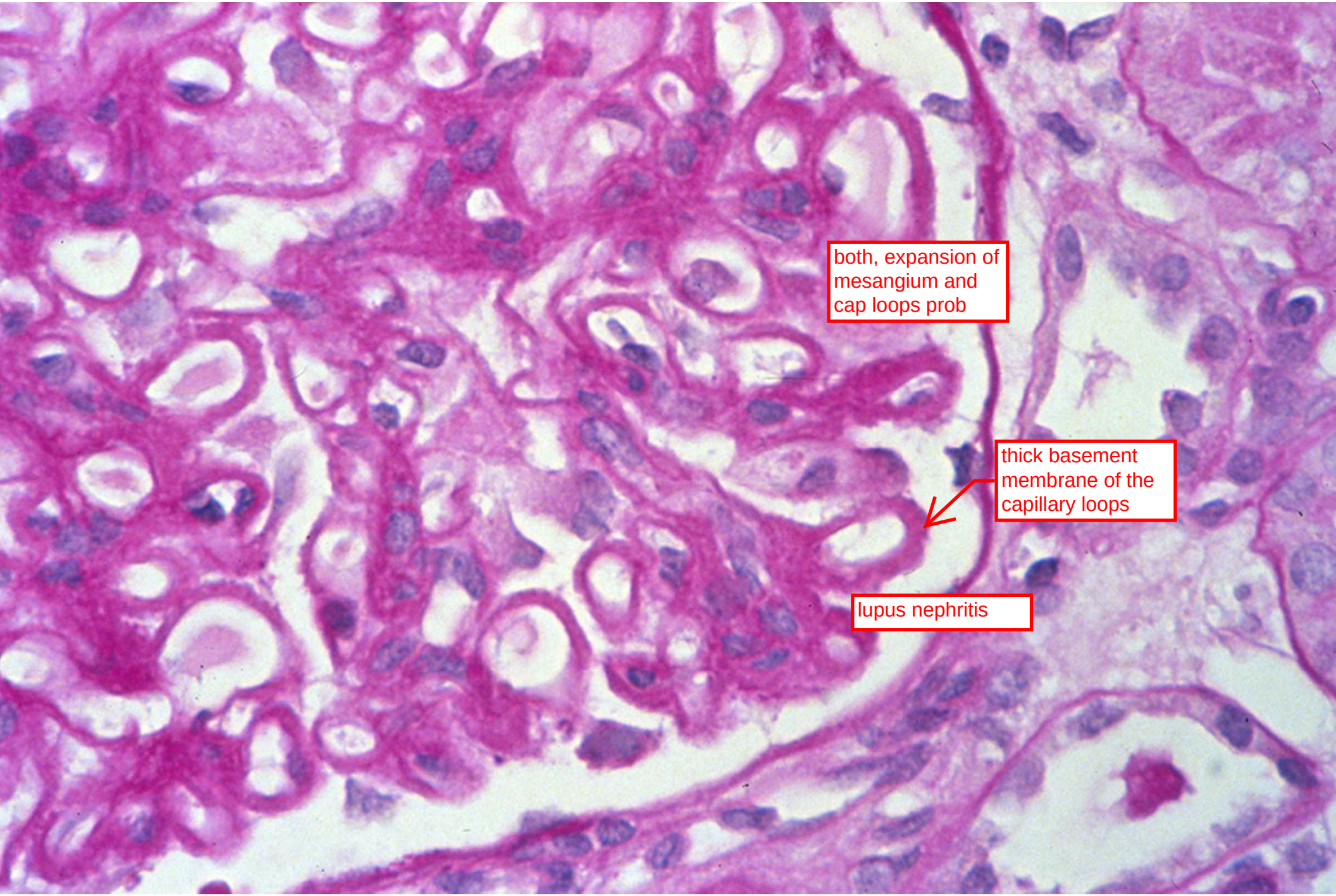
Classifications of glomerular disease
By histologic pattern

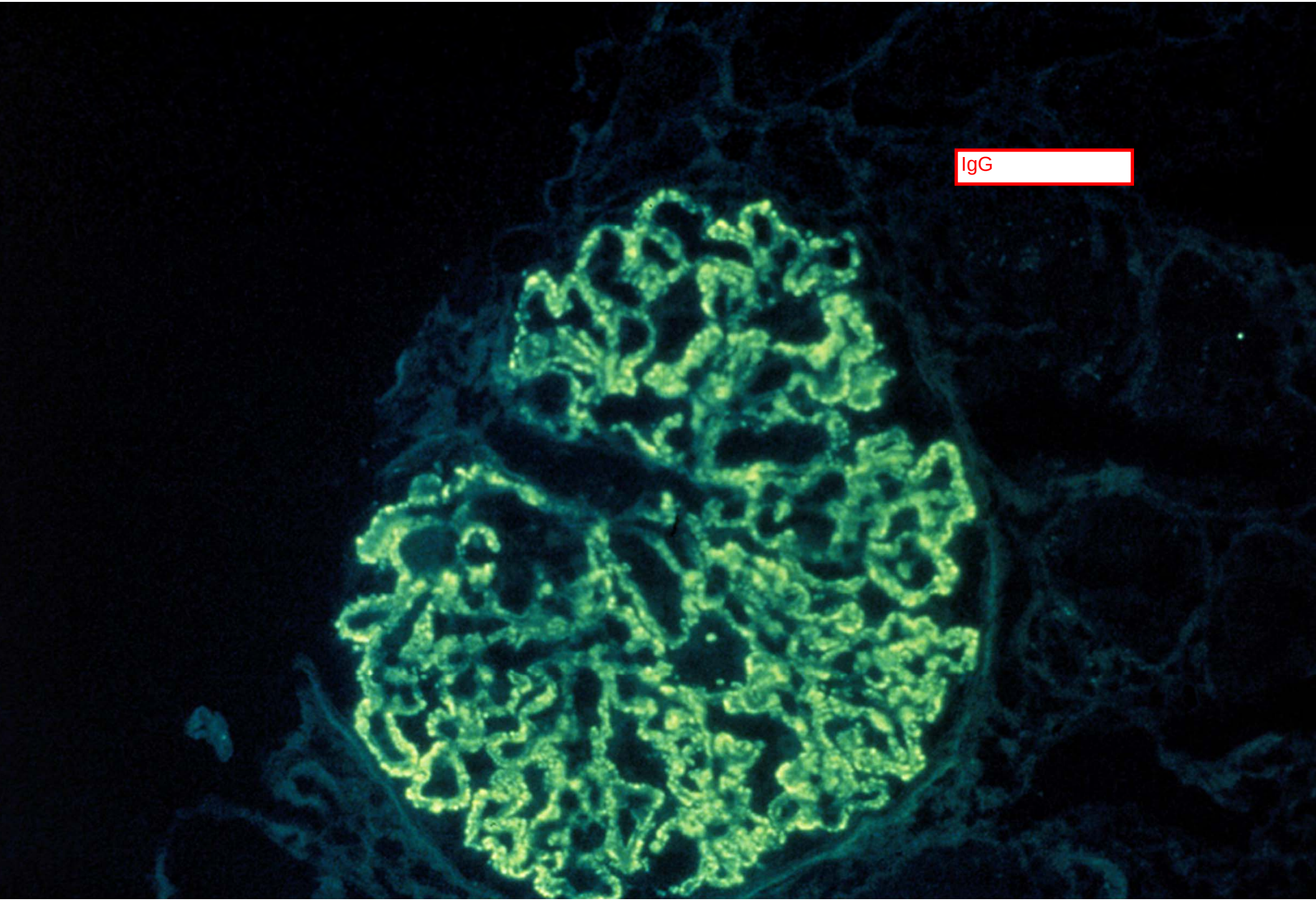
- **Glomerular compartment(s) involved**
  - **Capillary loops**
  - **Mesangium**
  - **Bowman's space**

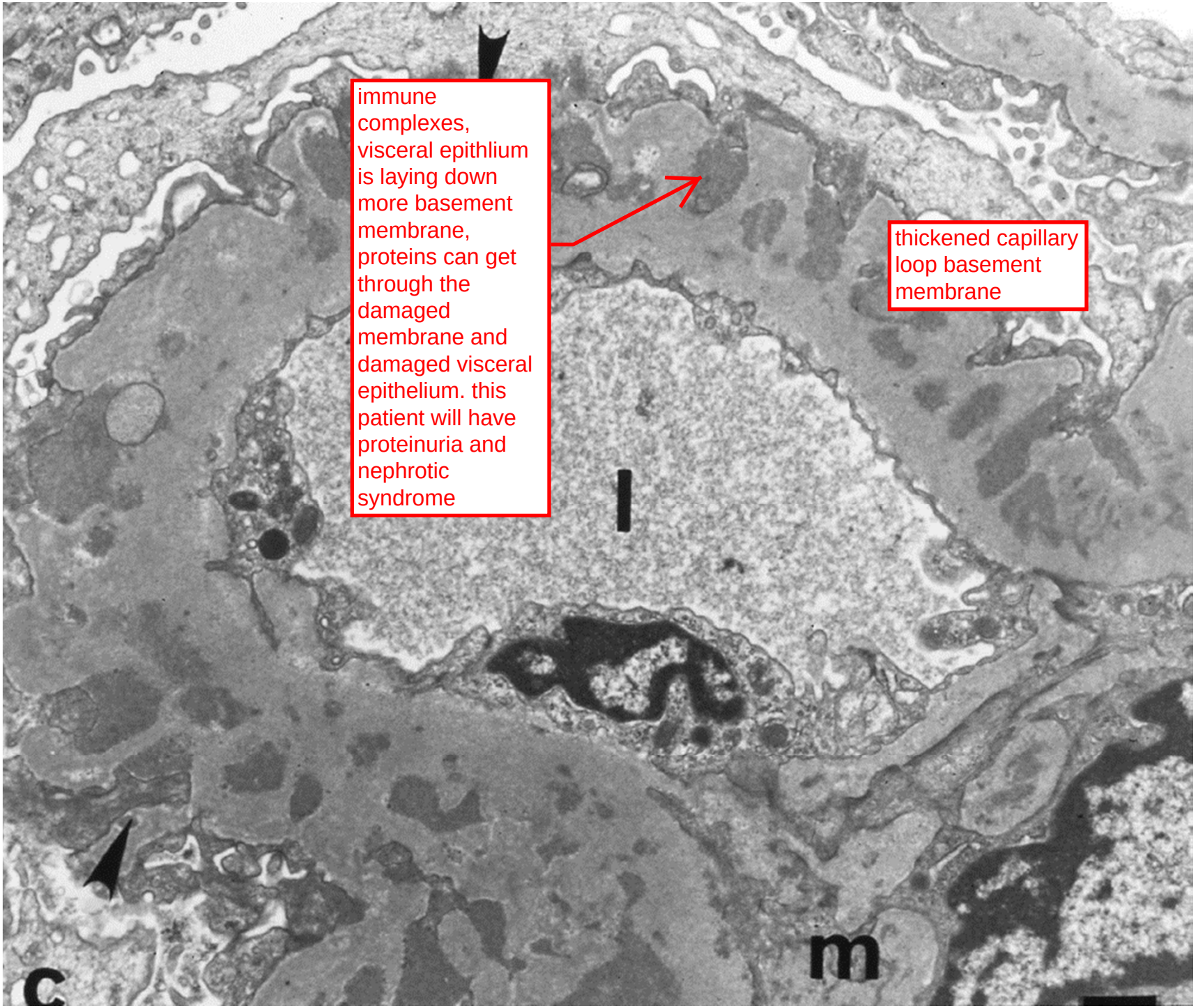

PAS stain
mesangial areas problem, capillary loops look ok

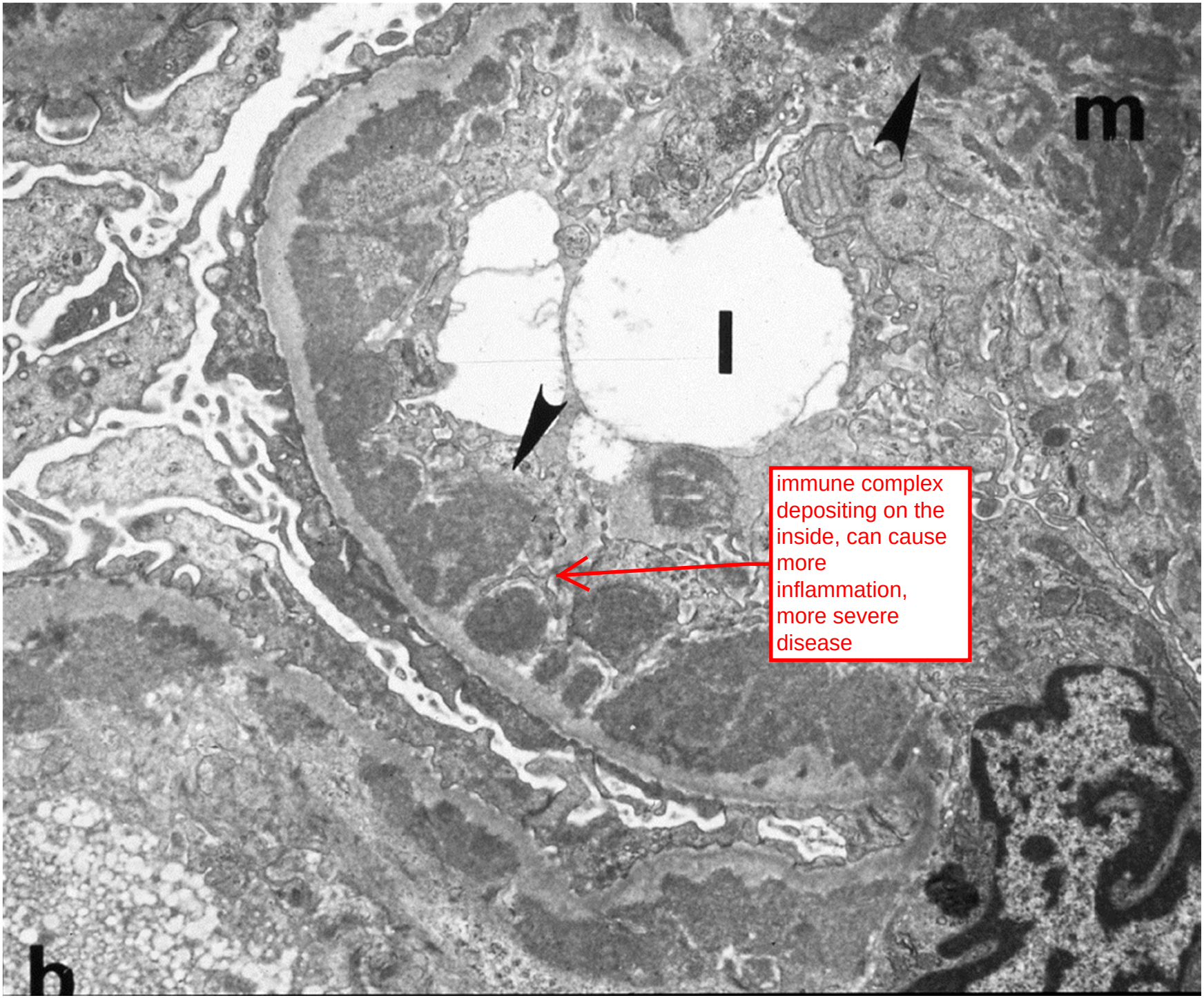

immunofluorescent stain
see deposits for IgA
deposits for IgA,
IgA nephropathy

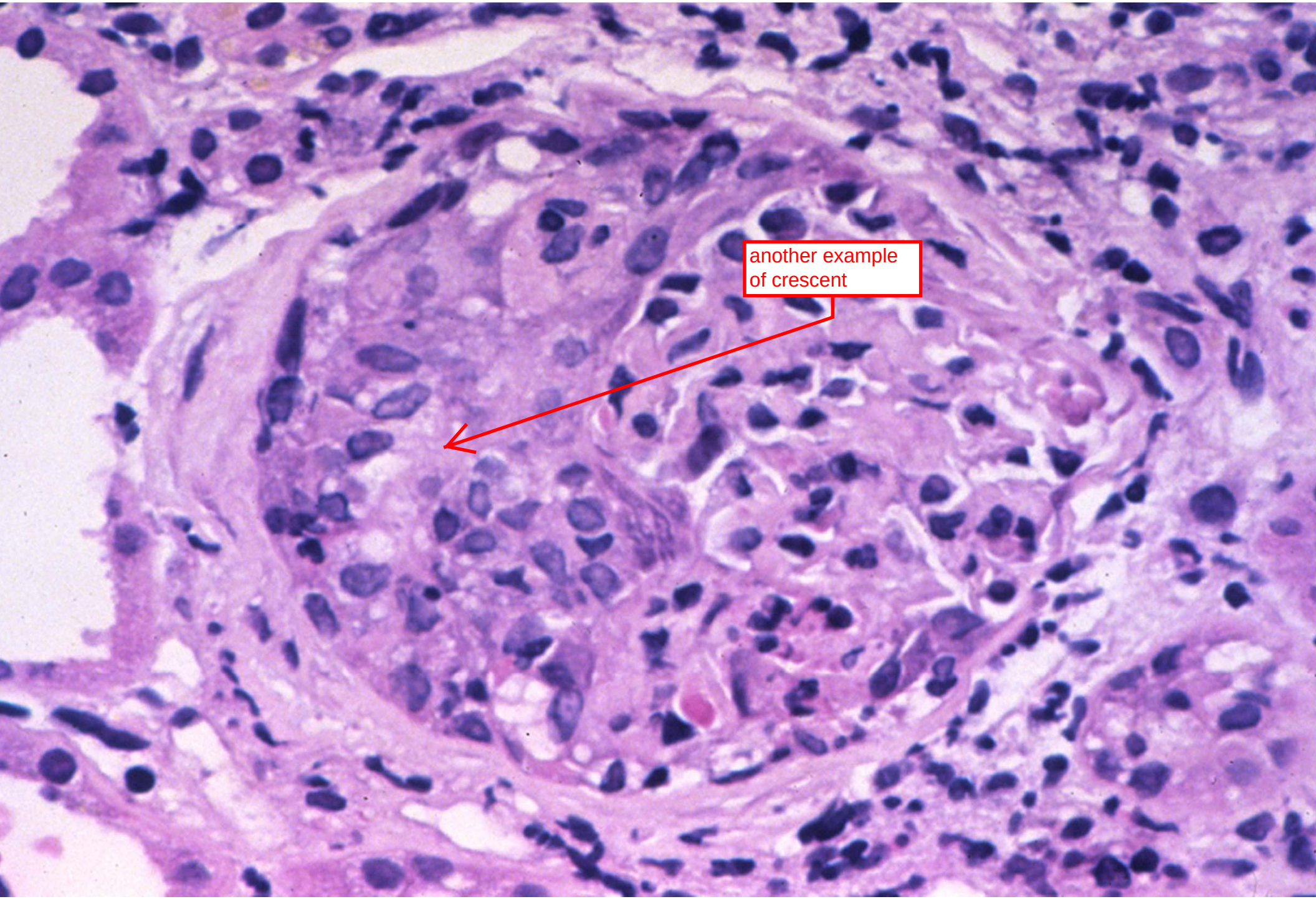

this capillary loop looks good
mesangial immune complex disease
dark deposts in mesangium
l
m
d


both, expansion of mesangium and cap loops prob
thick basement membrane of the capillary loops
lupus nephritis


IgG


immune complexes, visceral epithlium is laying down more basement membrane, proteins can get through the damaged membrane and damaged visceral epithelium. this patient will have proteinuria and nephrotic syndrome
thickened capillary loop basement membrane
m
c


m
l
immune complex depositing on the inside, can cause more inflammation, more severe disease
b


another example
of crescent

Classifications of glomerular disease
By pathogenesis

- Immune complex deposition
- Monoclonal protein deposition/plasma cell dyscrasias
- Epithelial cell damage
- Intrinsic defects of glomerular basement membrane
- Antibodies against glomerular basement membrane
- Endothelial cell damage
- Other vascular damage (e.g., diabetes)

example: amyloidosis

example: heritable collagen biosynthesis diseases

example: minimal change disease

example: HUS

type II hypersensitivity reactions

Immune complex diseases

Classification of Immune Complex Diseases

- **Antigen source**
  - **Autoantigens**
    - Intrinsic glomerular antigens
    - Non-glomerular antigens (e.g. DNA)
  - **Exogenous antigens (e.g. bacterial components)**

in post infectious glomerulonephritis

- **Immune components**
  - **Immunoglobulins (IgG, IgM, IgA)**
  - **Complement components (e.g. C1q, C4, C3)**

unknown why some antibodies in some diseases and not others, can often see all three in lupus

- **Location**
  - **Mesangial**
  - **Subendothelial (between endothelial cell and basement membrane)**
  - **Subepithelial (between epithelial cell and basement membrane)**
  - **Intramembranous**

in IgA nephropathy

as in membranous nephritis

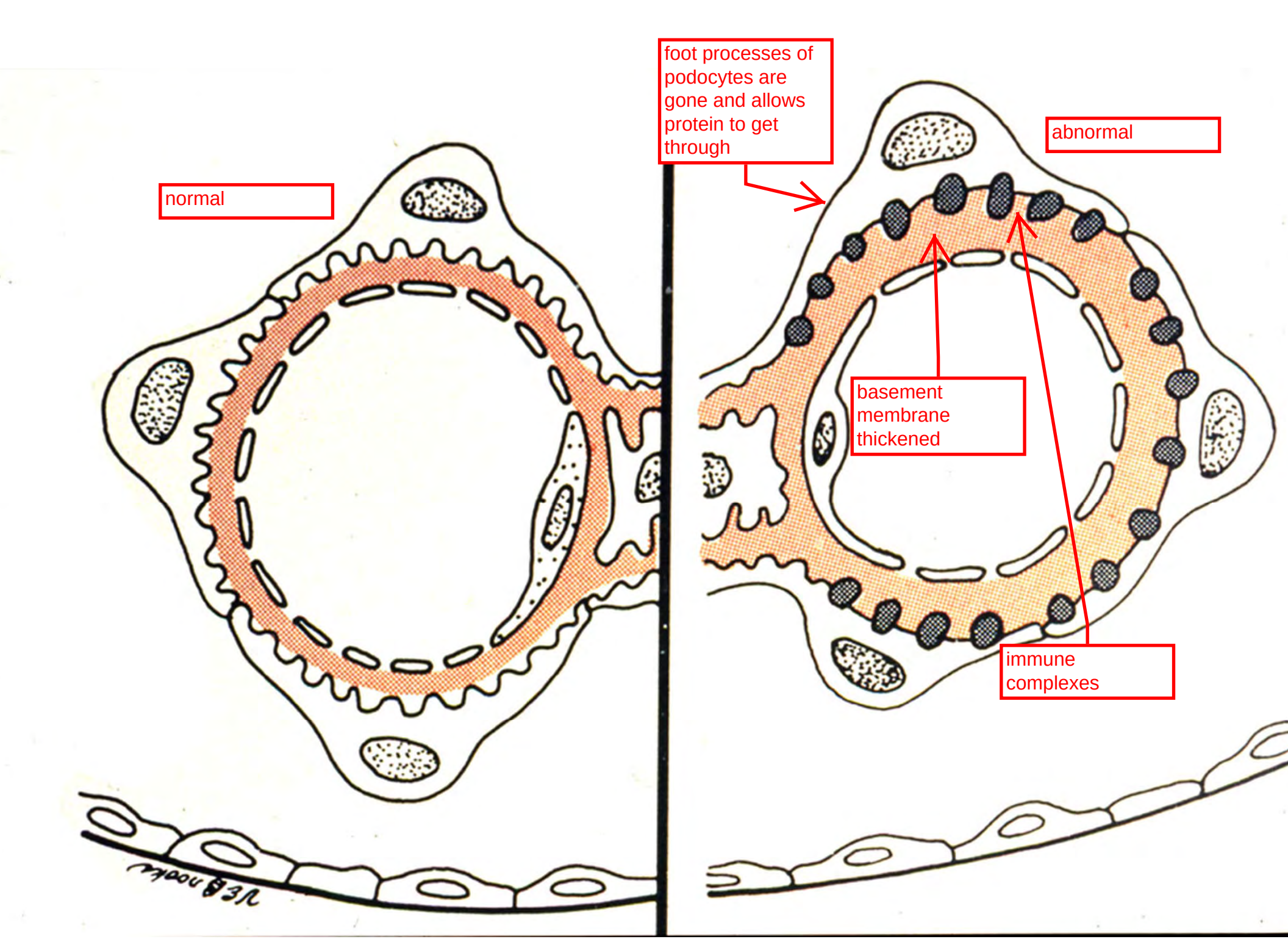
Membranous glomerulonephritis

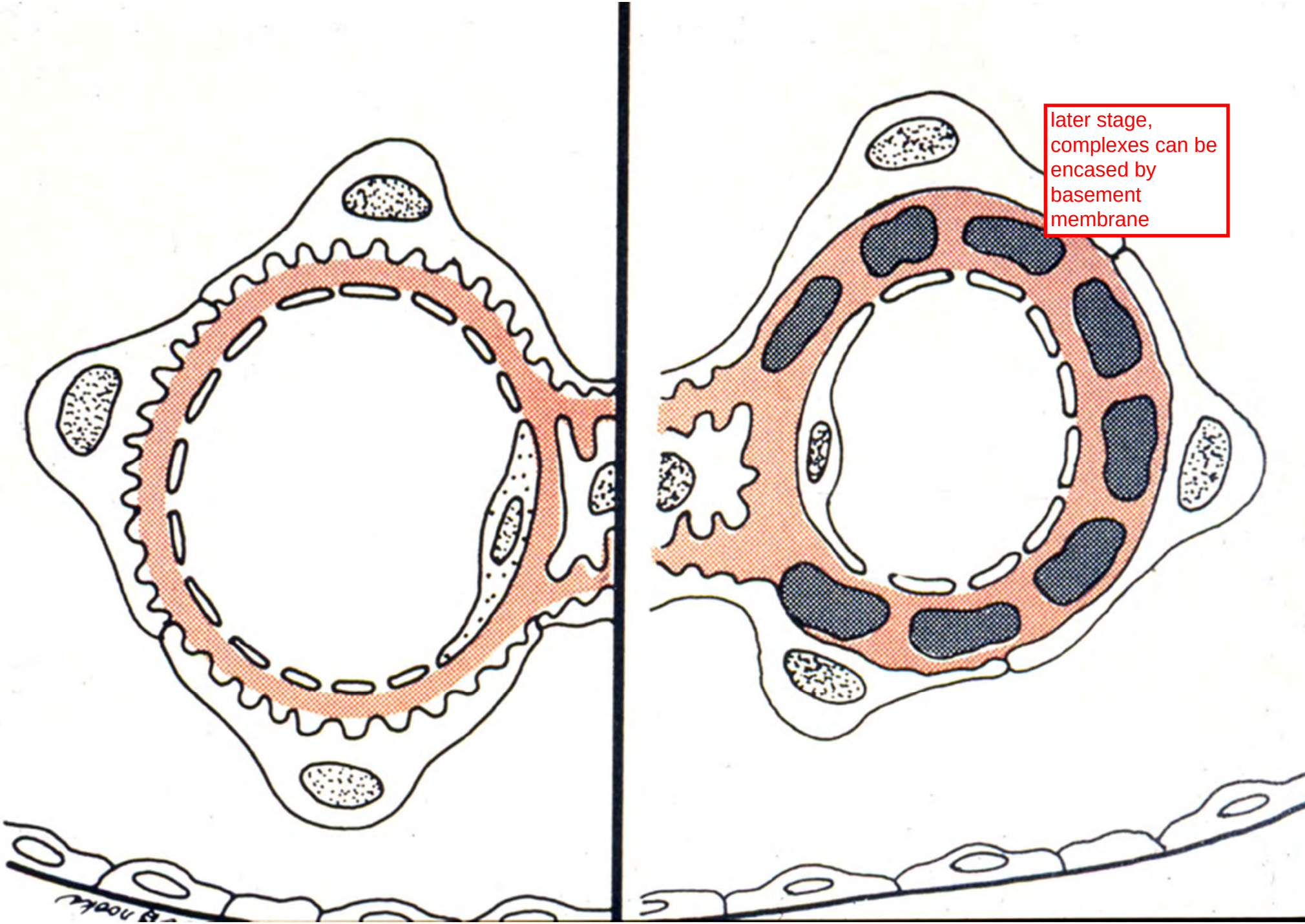
fairly common

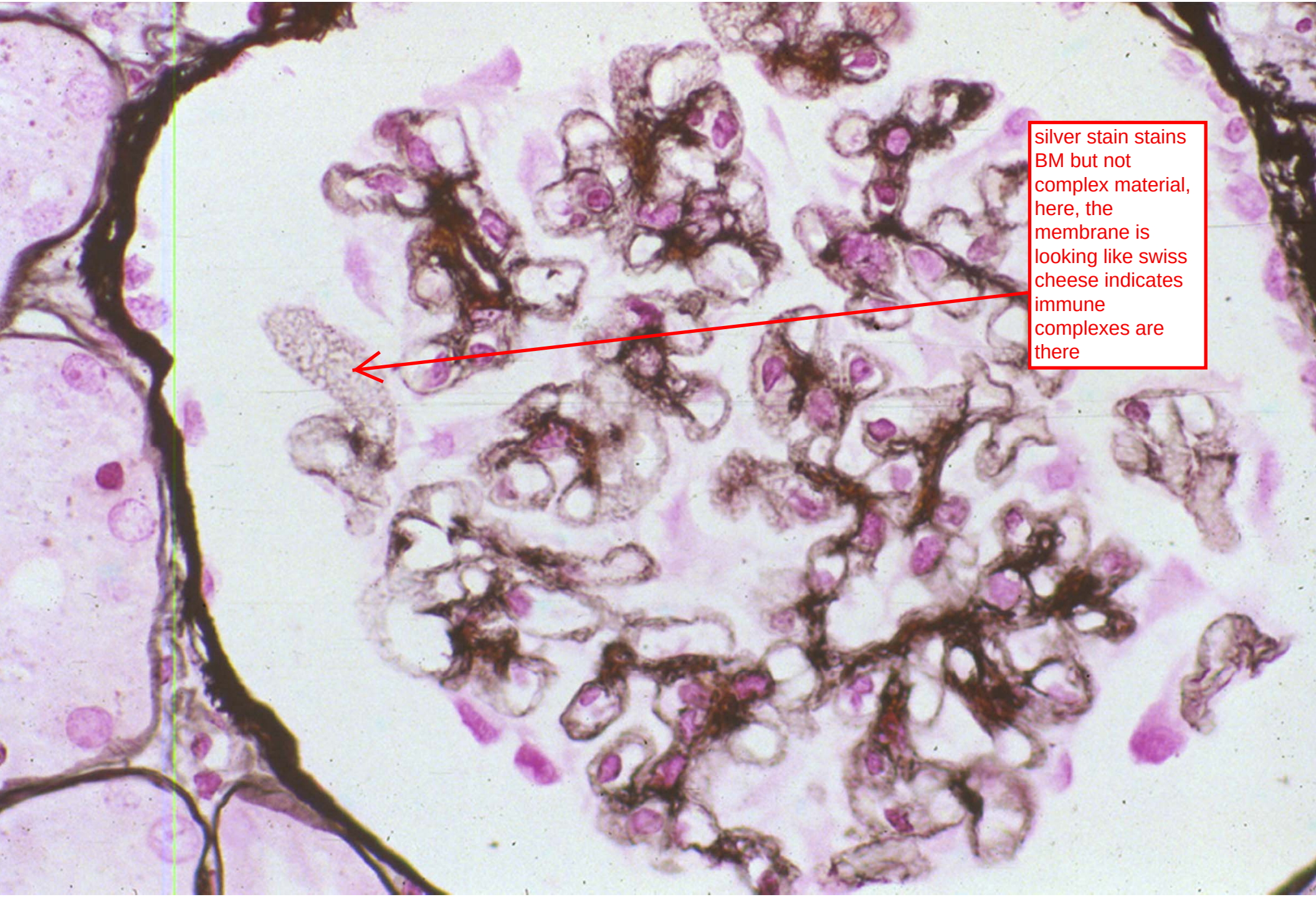
- **Pathogenesis**
  - **Antigens:**
    - **M-type phospholipase A_2 receptor (primary)**
    - **Viral antigens (hepatitis B, C) (secondary)**
  - **Immune reactants: IgG, C3**
  - **Complex location: subepithelial**
- **Histologic: Diffuse, global expansion of capillary basement membranes**
- **Clinical: Proteinuria/nephrotic syndrome; chronic course which may progress to chronic renal failure; most common in adult males**

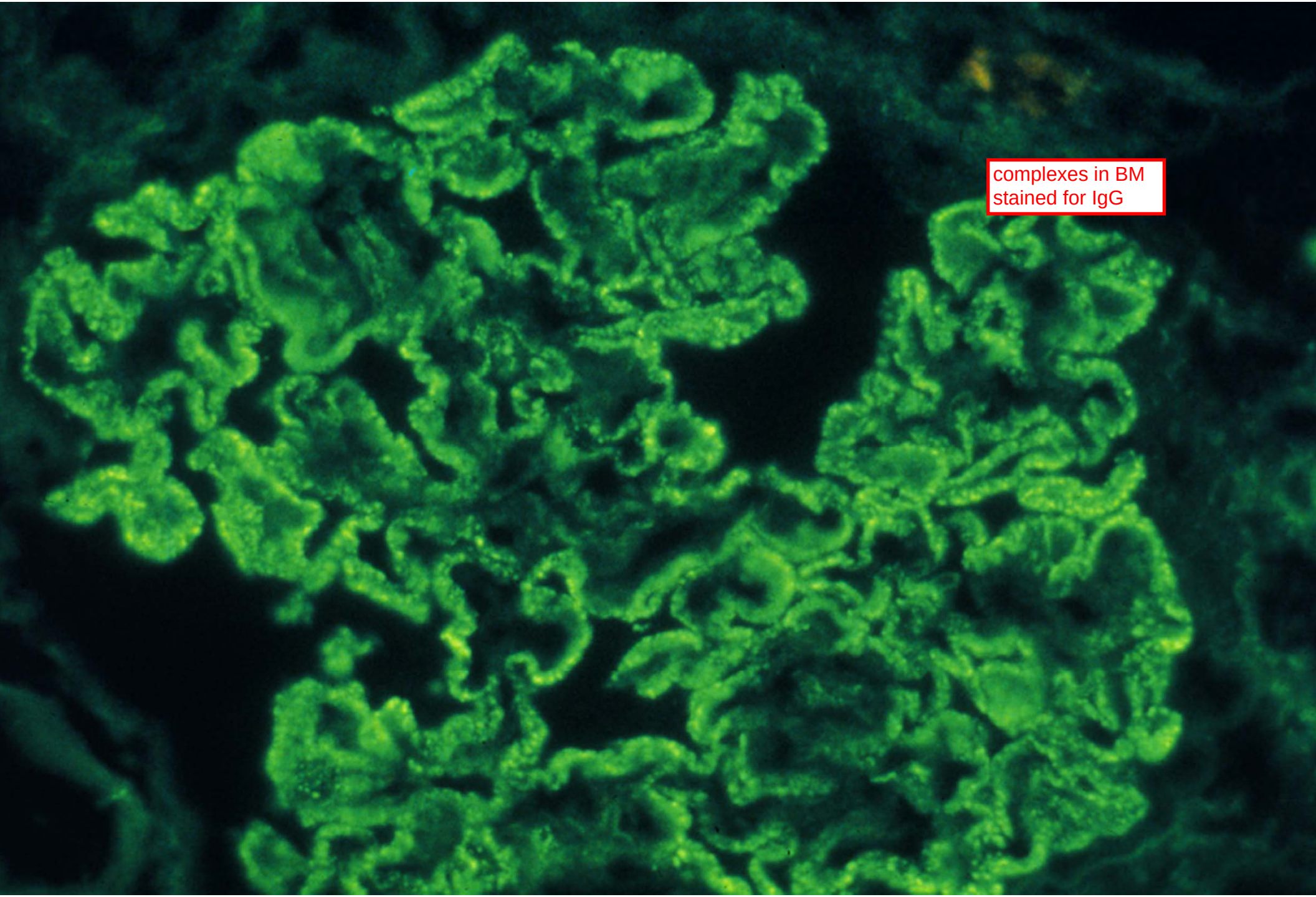
protein found on surface of visceral epithelial cell

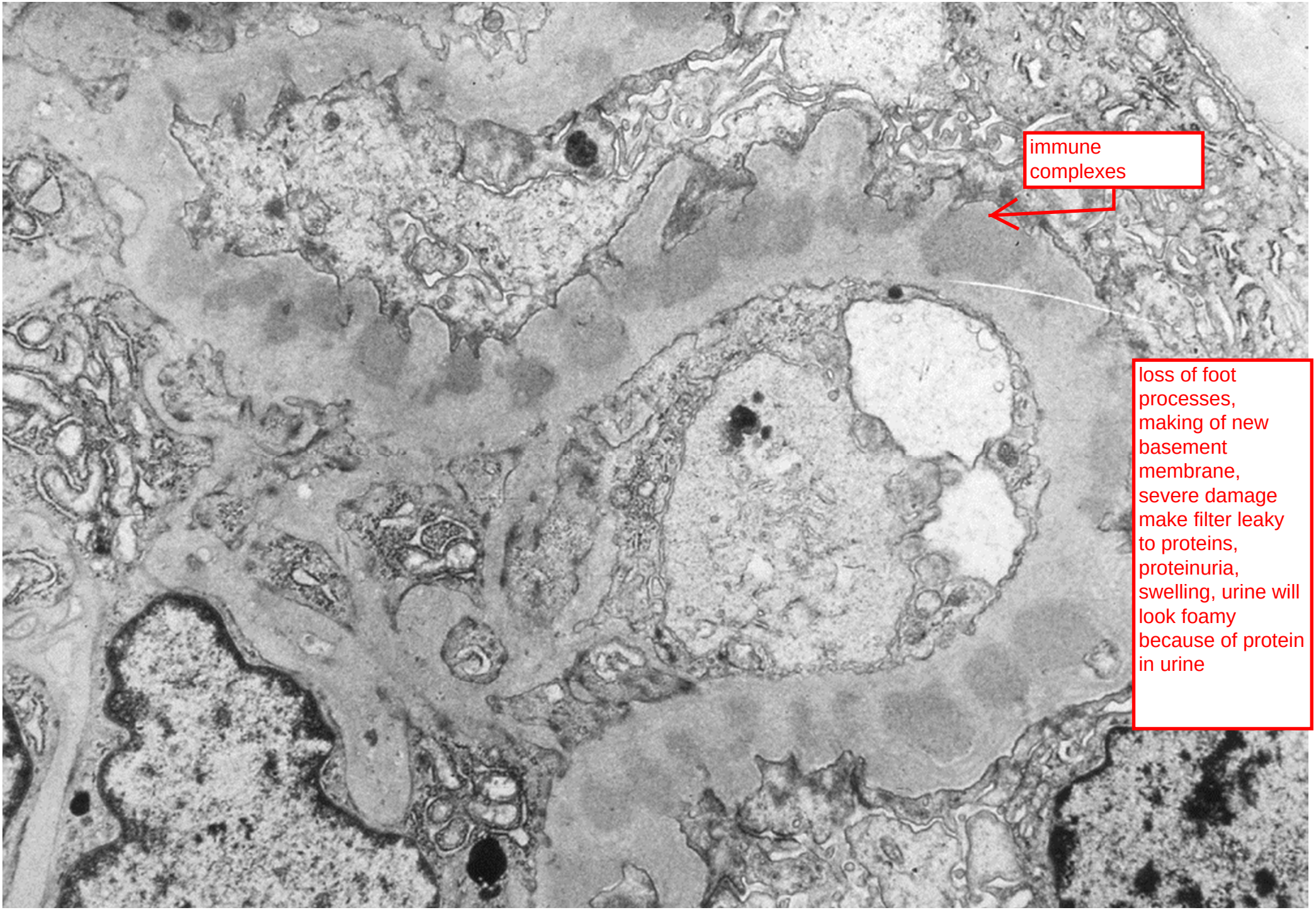
between the subepithlial cell and basement membrane, unknown how viral antigens get there but they do


normal
foot processes of podocytes are gone and allows protein to get through
abnormal
basement membrane thickened
immune complexes


later stage, complexes can be encased by basement membrane


silver stain stains BM but not complex material, here, the membrane is looking like swiss cheese indicates immune complexes are there


complexes in BM
stained for IgG

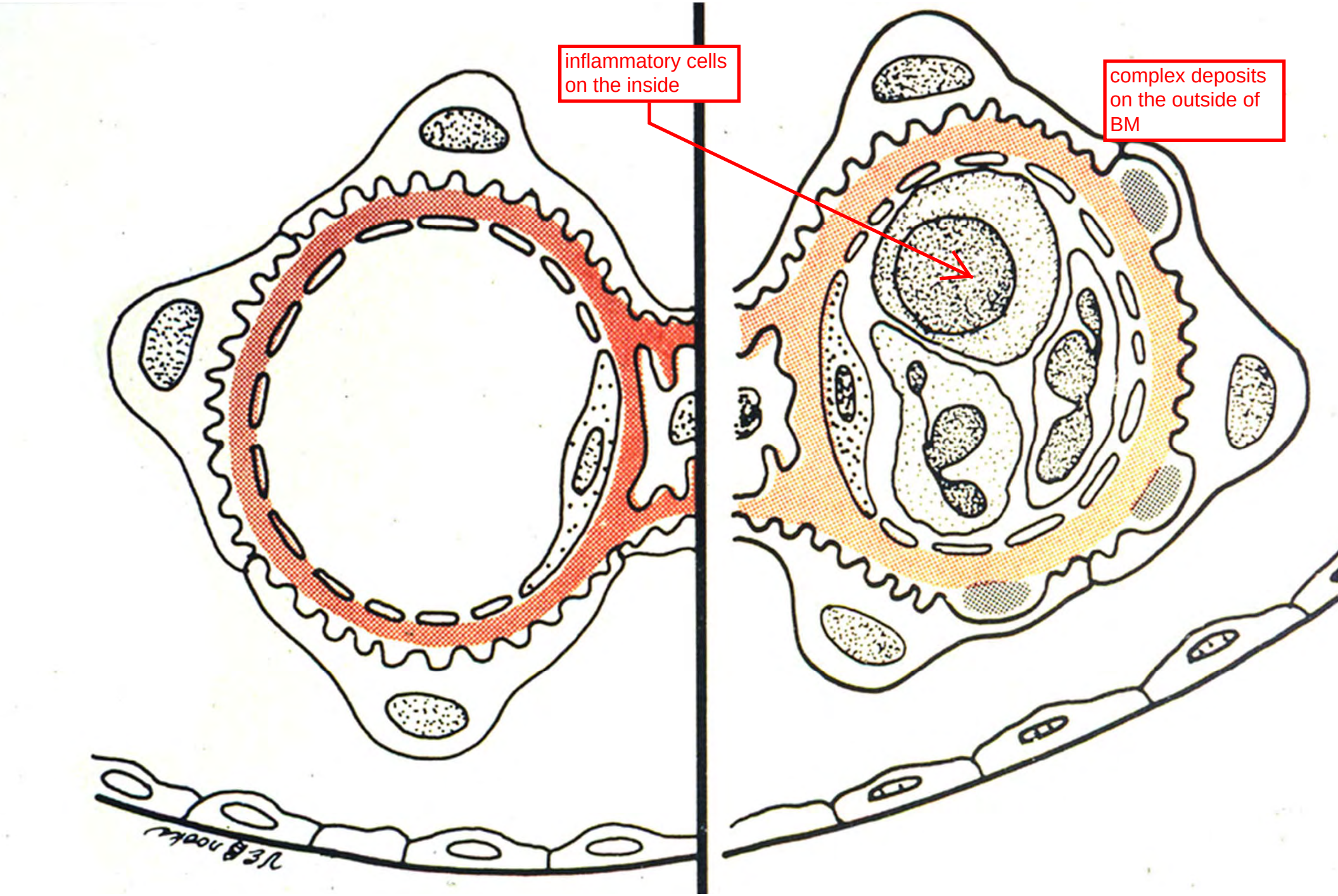

immune complexes
loss of foot processes, making of new basement membrane, severe damage make filter leaky to proteins, proteinuria, swelling, urine will look foamy because of protein in urine

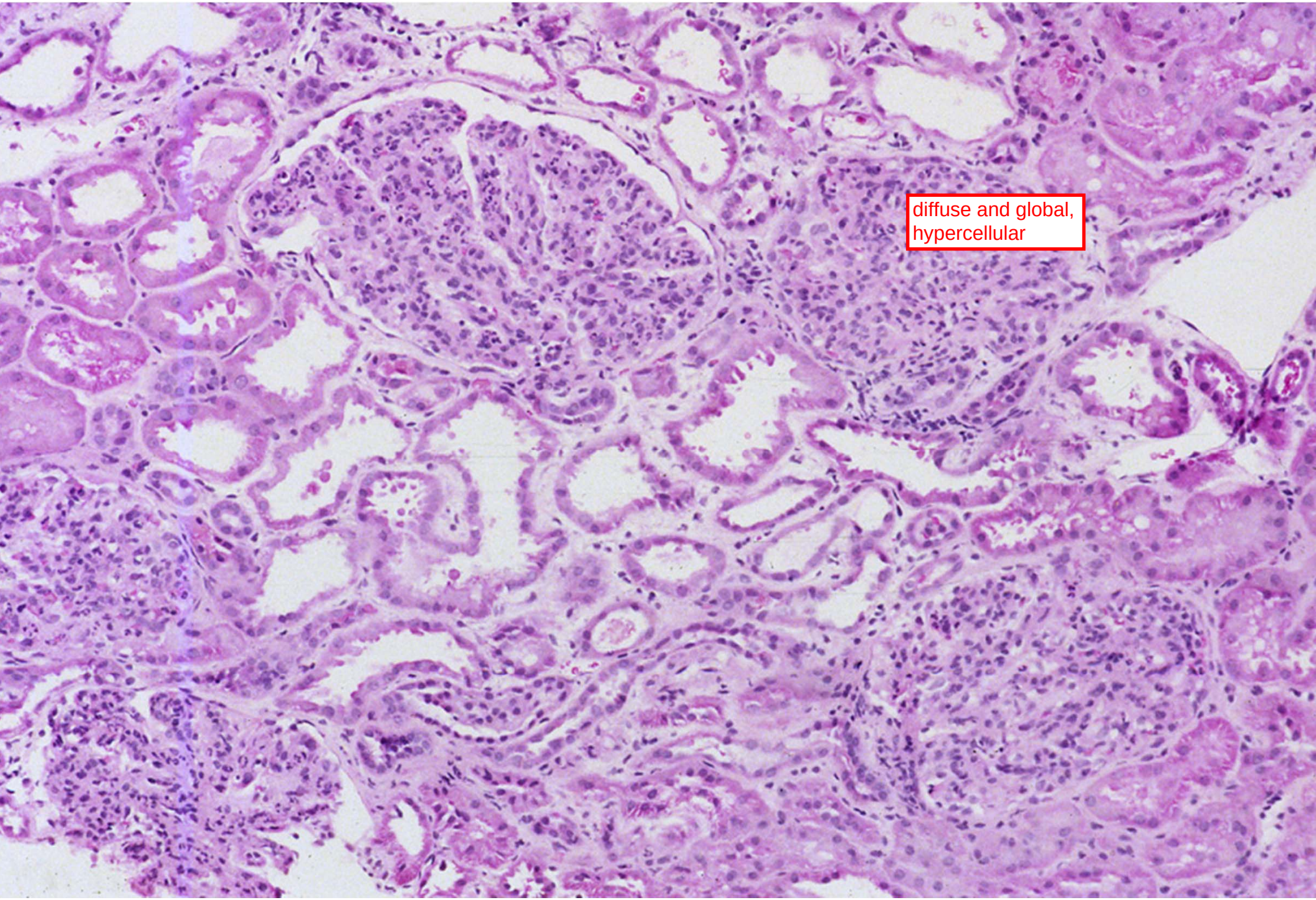
Postinfectious glomerulonephritis

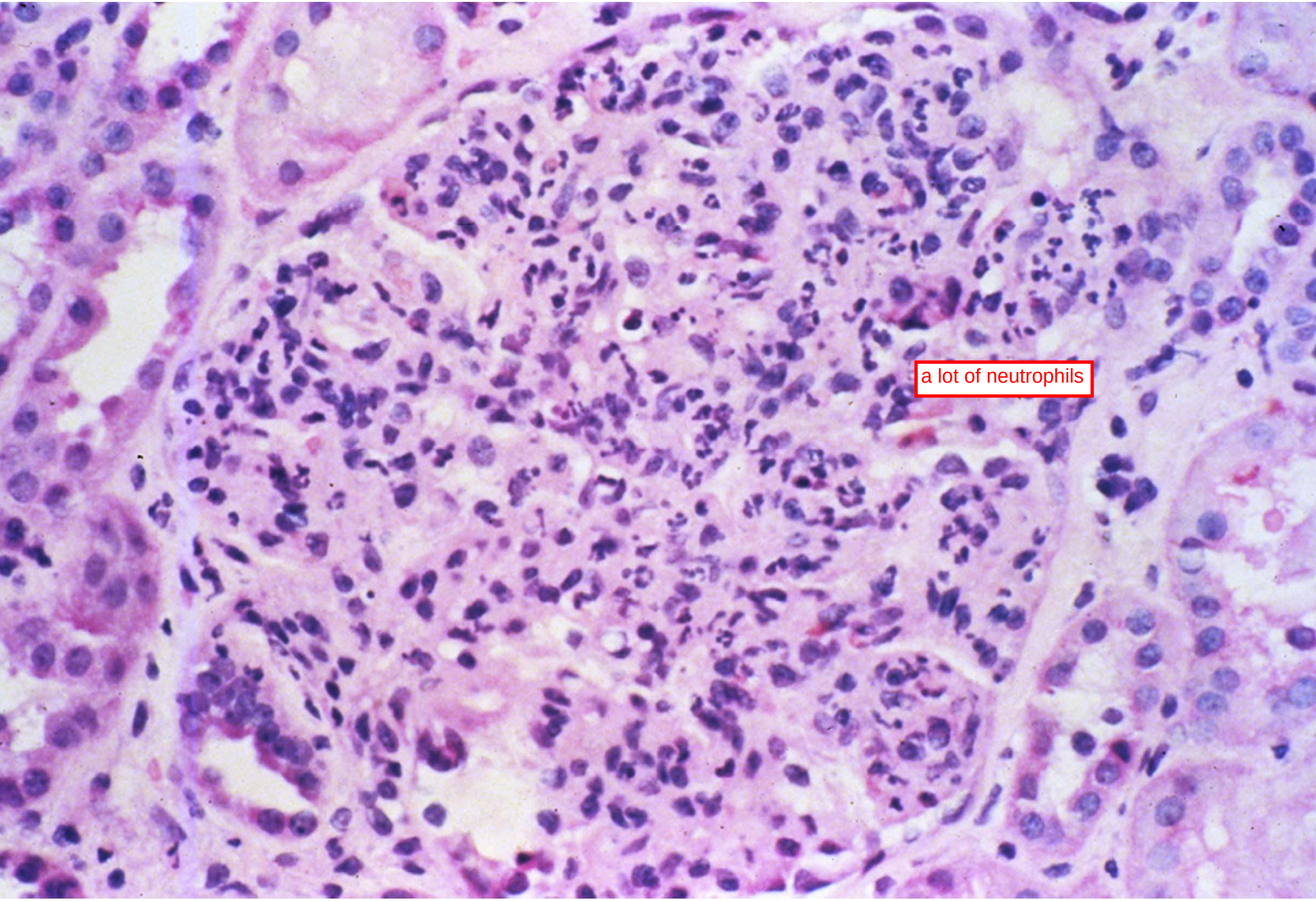
- **Pathogenesis**
  - **Antigens: bacterial components**
  - **Immune reactants: IgG, C3**
  - **Complex location: subepithelial ("humps")**
- **Histologic: Diffuse, global intrinsic cell proliferation with neutrophil infiltration**
- **Clinical: Acute onset hematuria/nephritic syndrome 1-2 weeks following infection (particularly with nephritogenic streptococci); usually resolves spontaneously; occasionally progresses to chronic renal failure; most common in children**

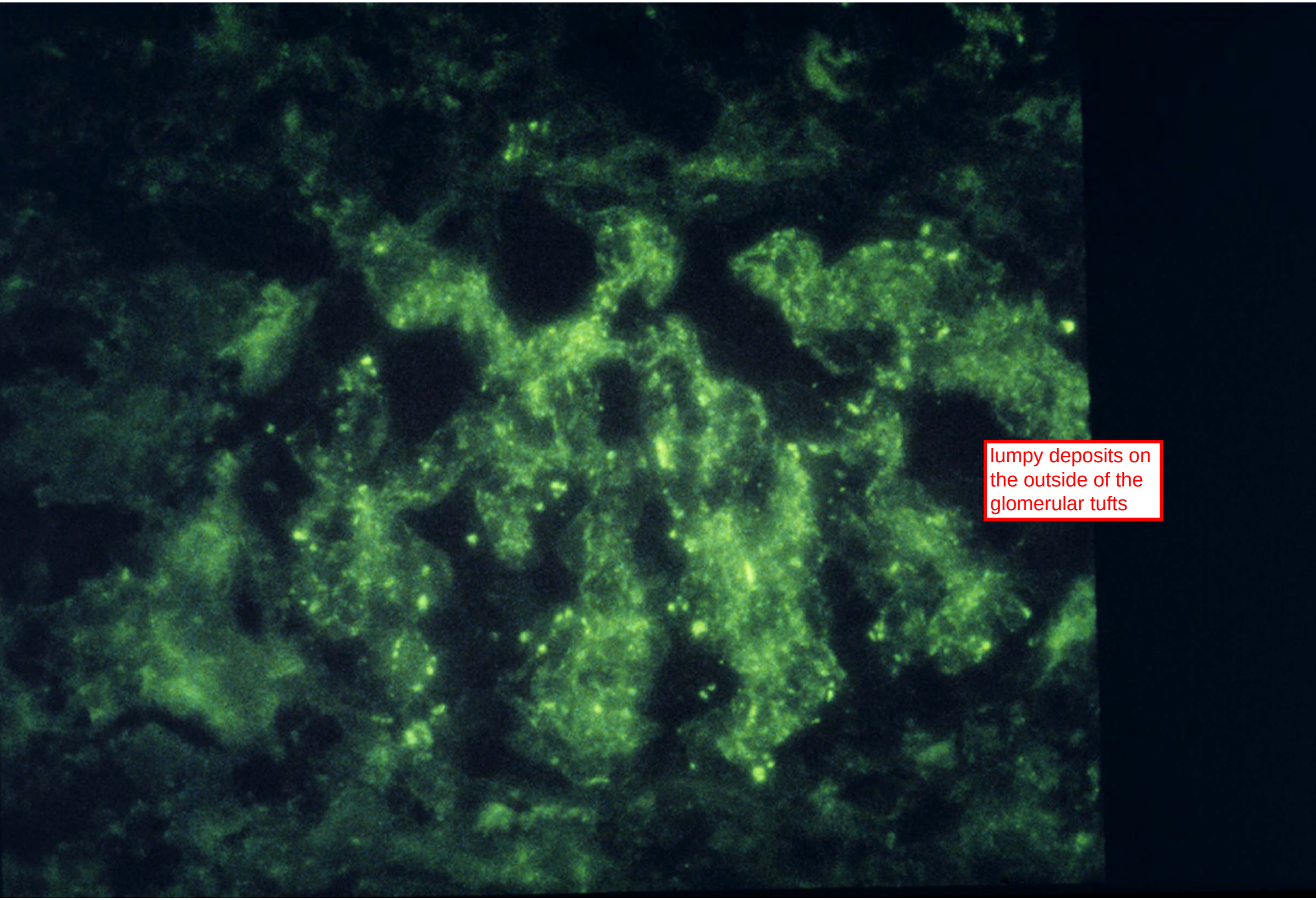
blood in urine because of damage due to inflammation

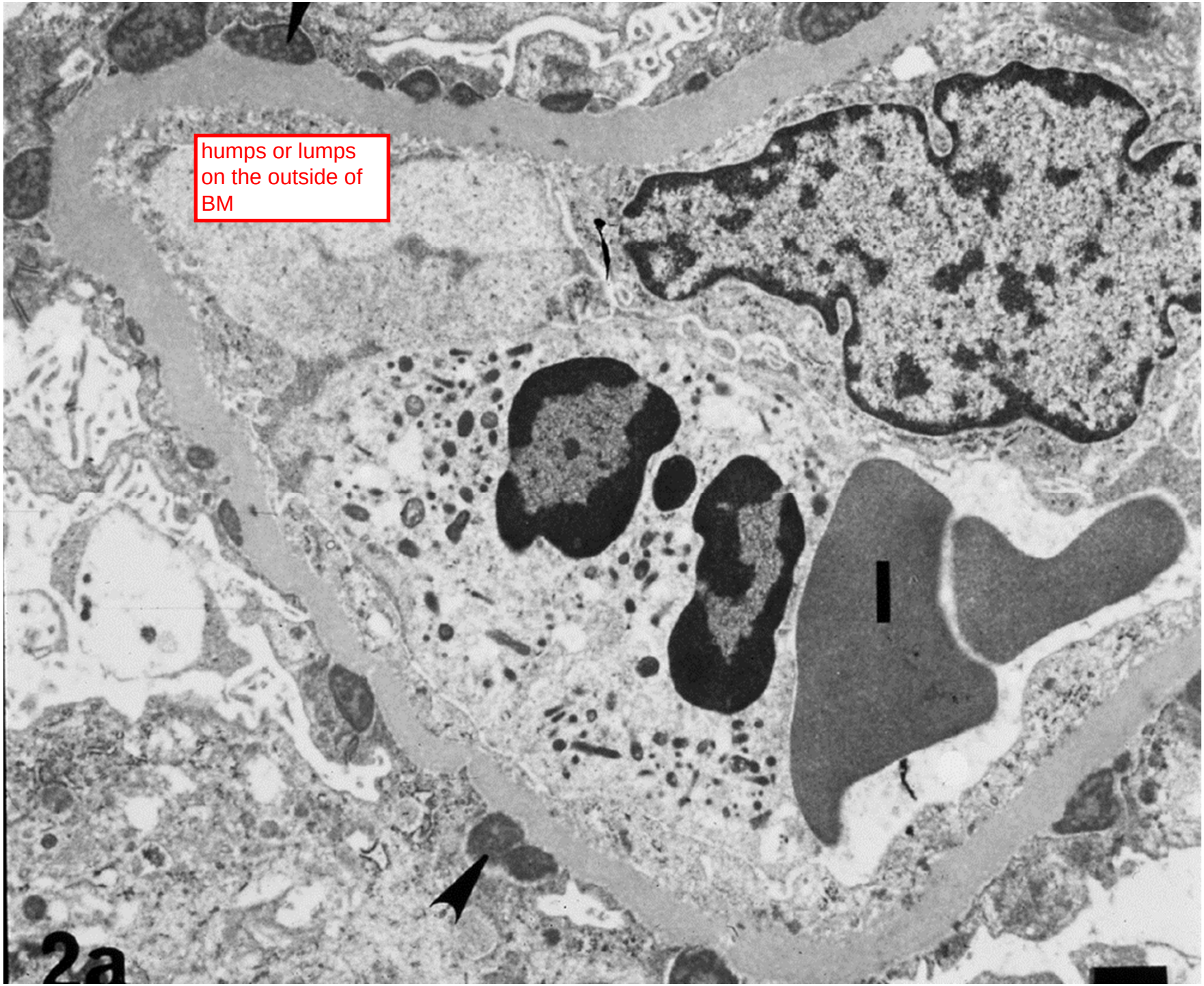
chronic renal failure in adults


inflammatory cells on the inside
complex deposits on the outside of BM


diffuse and global,
hypercellular


a lot of neutrophils


lumpy deposits on the outside of the glomerular tufts


humps or lumps on the outside of BM
2a

Mesangiocapillary (membranoproliferative) glomerulonephritis (MPGN) type I

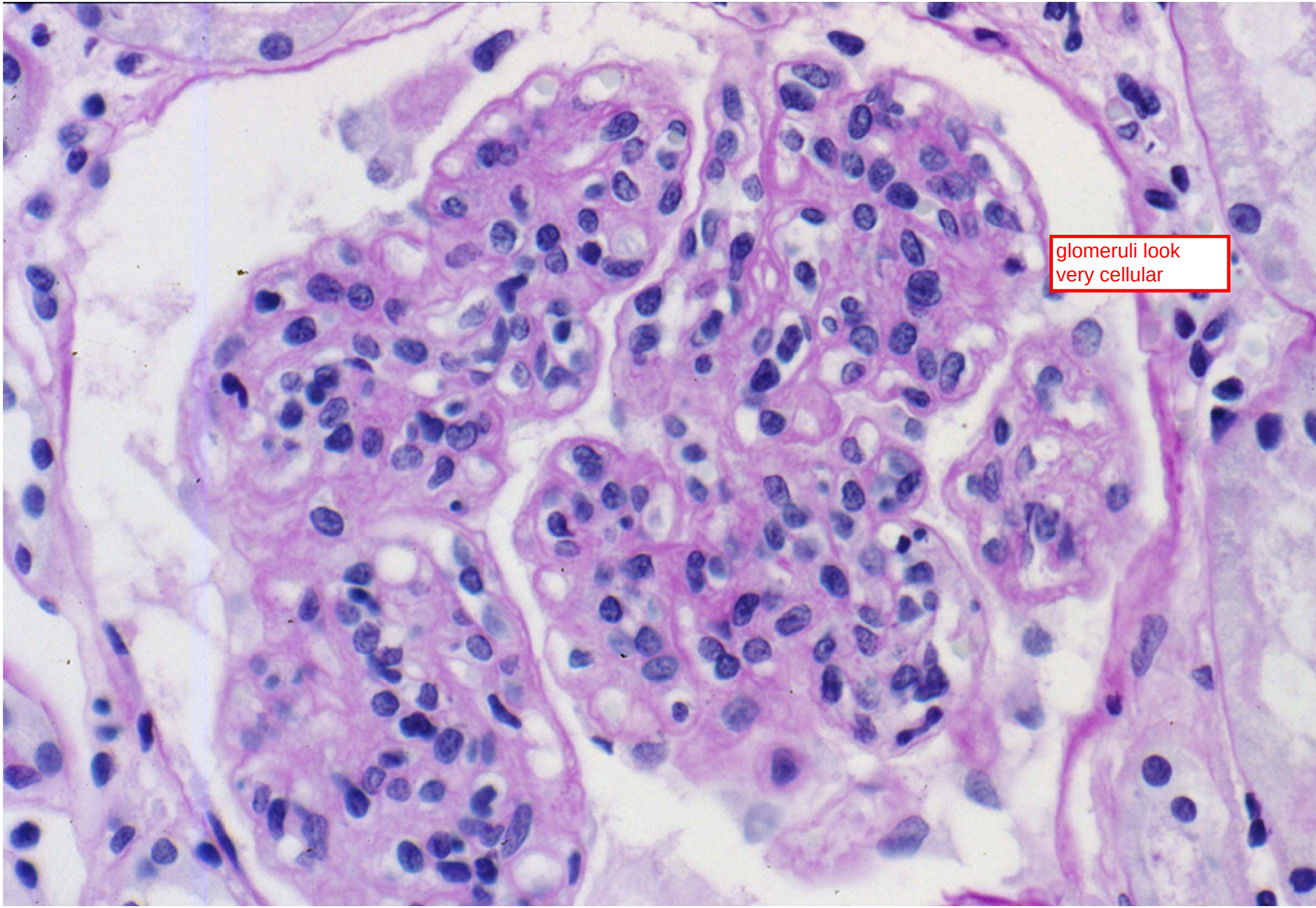
- **Pathogenesis**
  - **Antigens:**
    - **Unknown (primary)**
    - **Viral antigens (hepatitis C) (secondary)**
    - **Complement dysregulation (C3 nephritic factors)**
  - **Immune reactants: variable, usually including C3**
  - **Complex location: subendothelial**
- **Histologic: Diffuse intrinsic cell proliferation, with encroachment of mesangial cells into capillary lumens (mesangial interpositioning)**
- **Clinical: Nephrotic or nephritic syndrome with hypocomplementemia; often progresses to chronic renal failure**

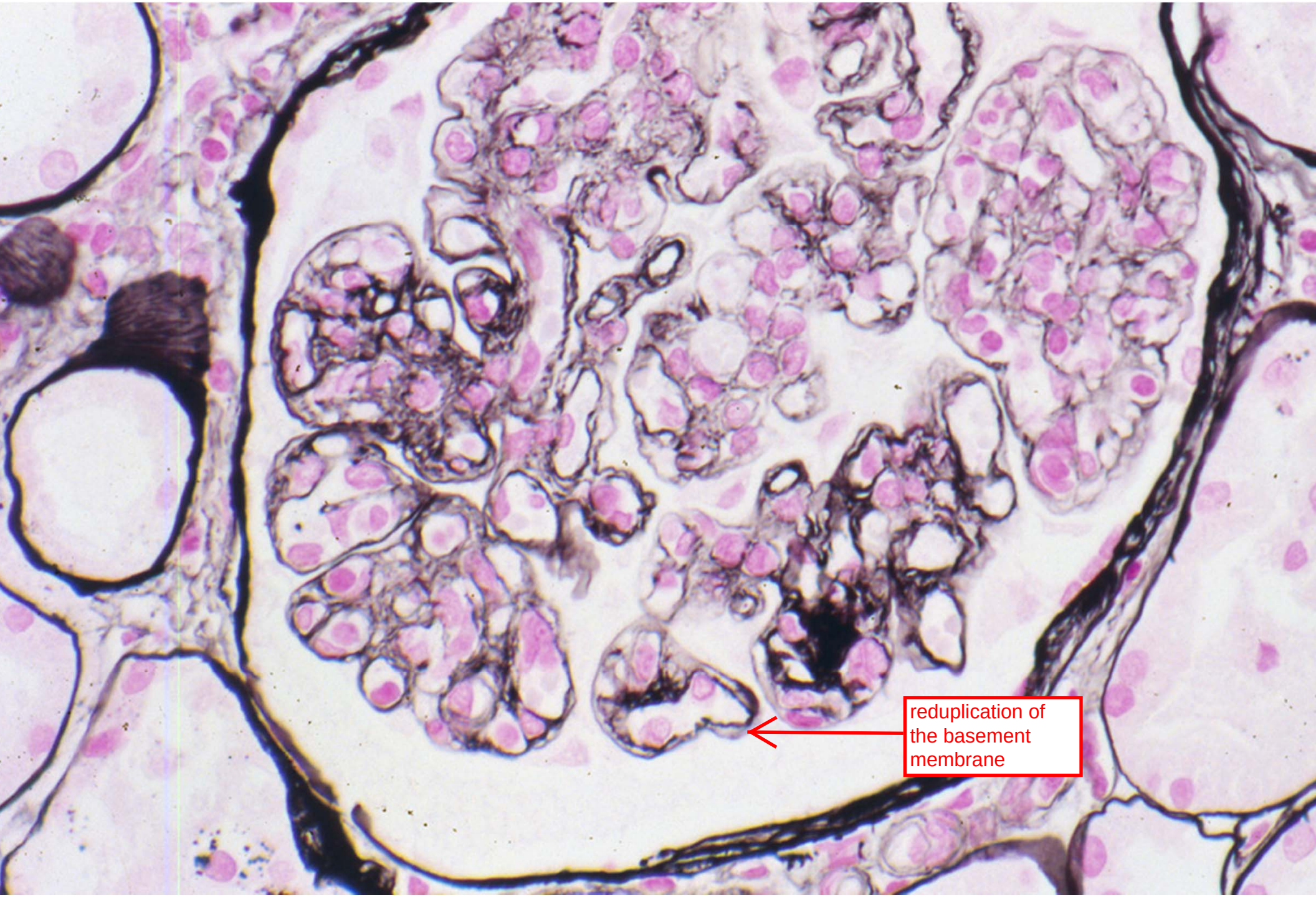
between the endothelial cell and basement membrane

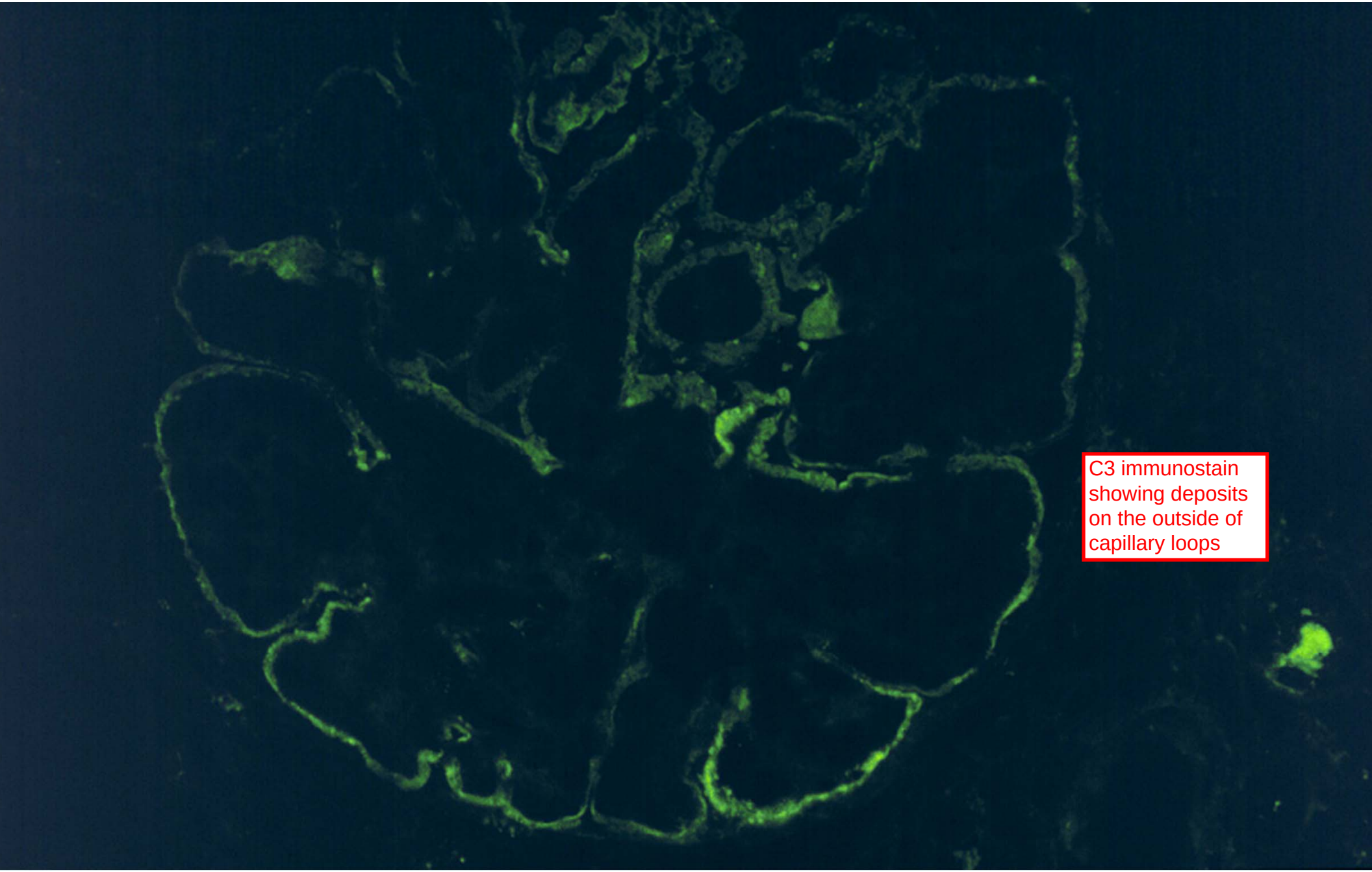
mesangial cells try to get to the deposits

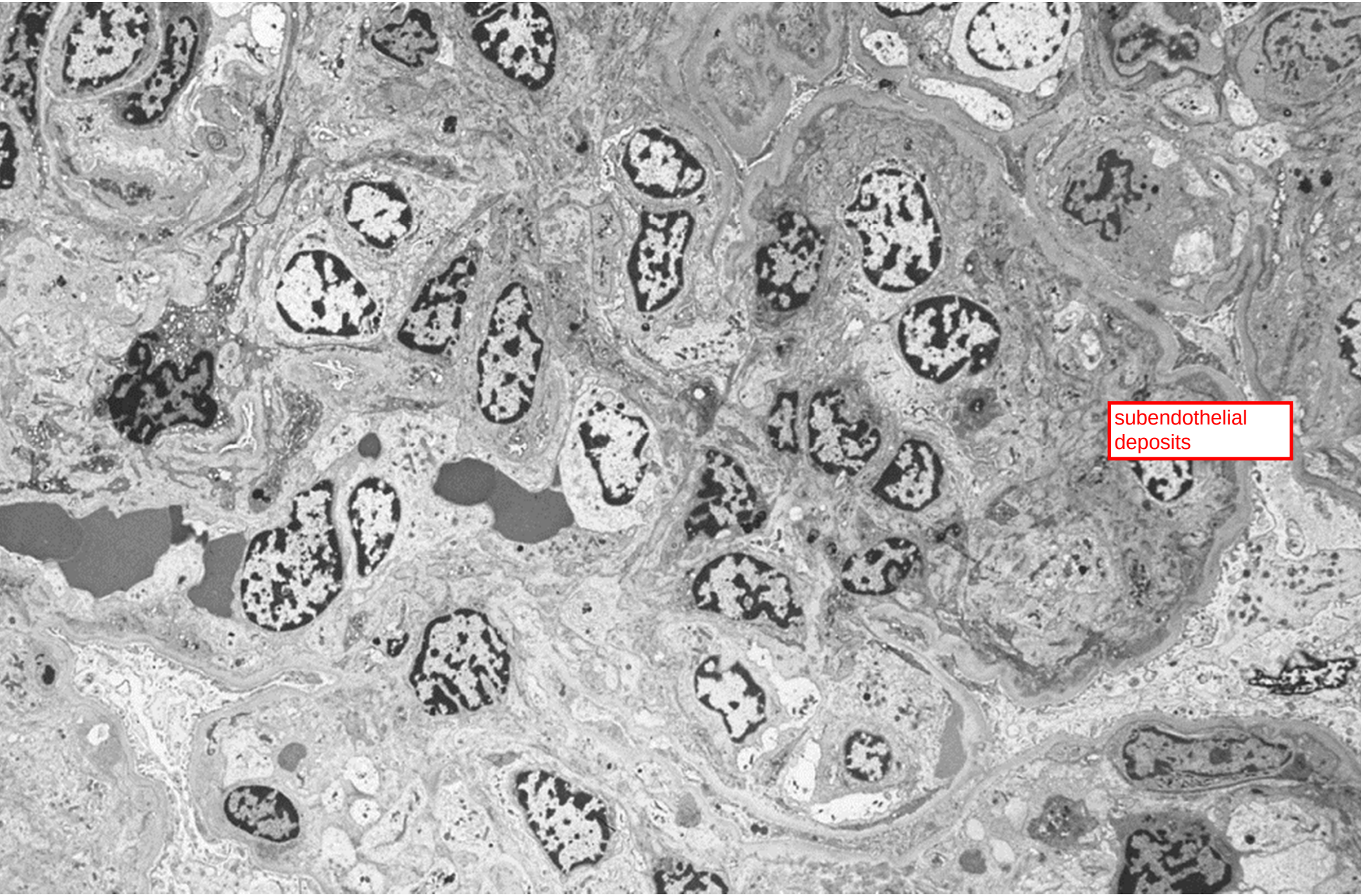
MEMBRANO-PROLIFERATIVE GN

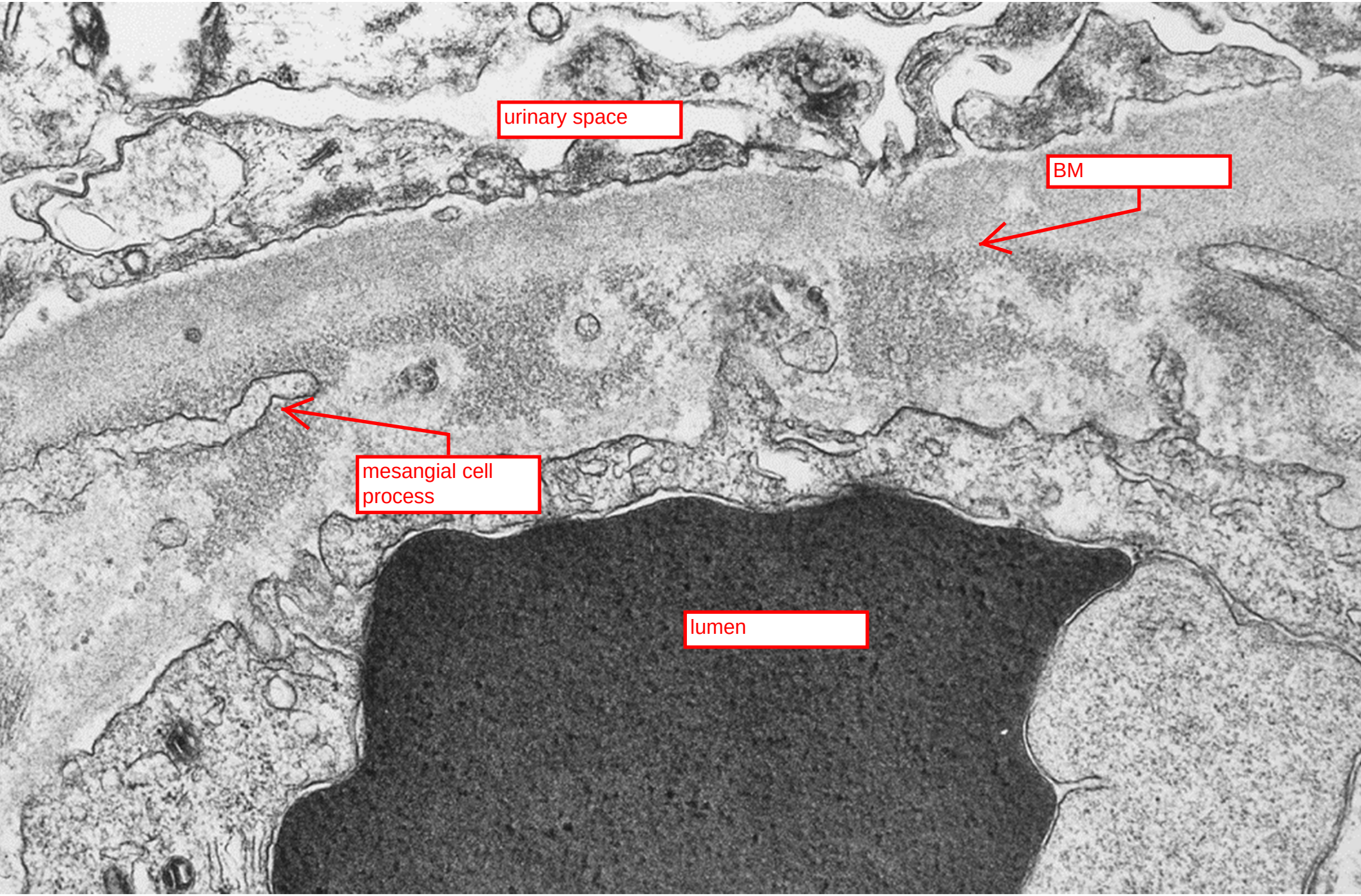
lumen, subendothelial deposits, mesangial cell crawls out on the capillary loop, lays down a basement membrane layer viceral epithelial cell looks pretty good so damaging inside and not ouside of the loop


glomeruli look
very cellular


reduplication of
the basement
membrane


C3 immunostain showing deposits on the outside of capillary loops


subendothelial
deposits


urinary space
BM
mesangial cell process
lumen

MPGN Type II (Dense Deposit Disease)