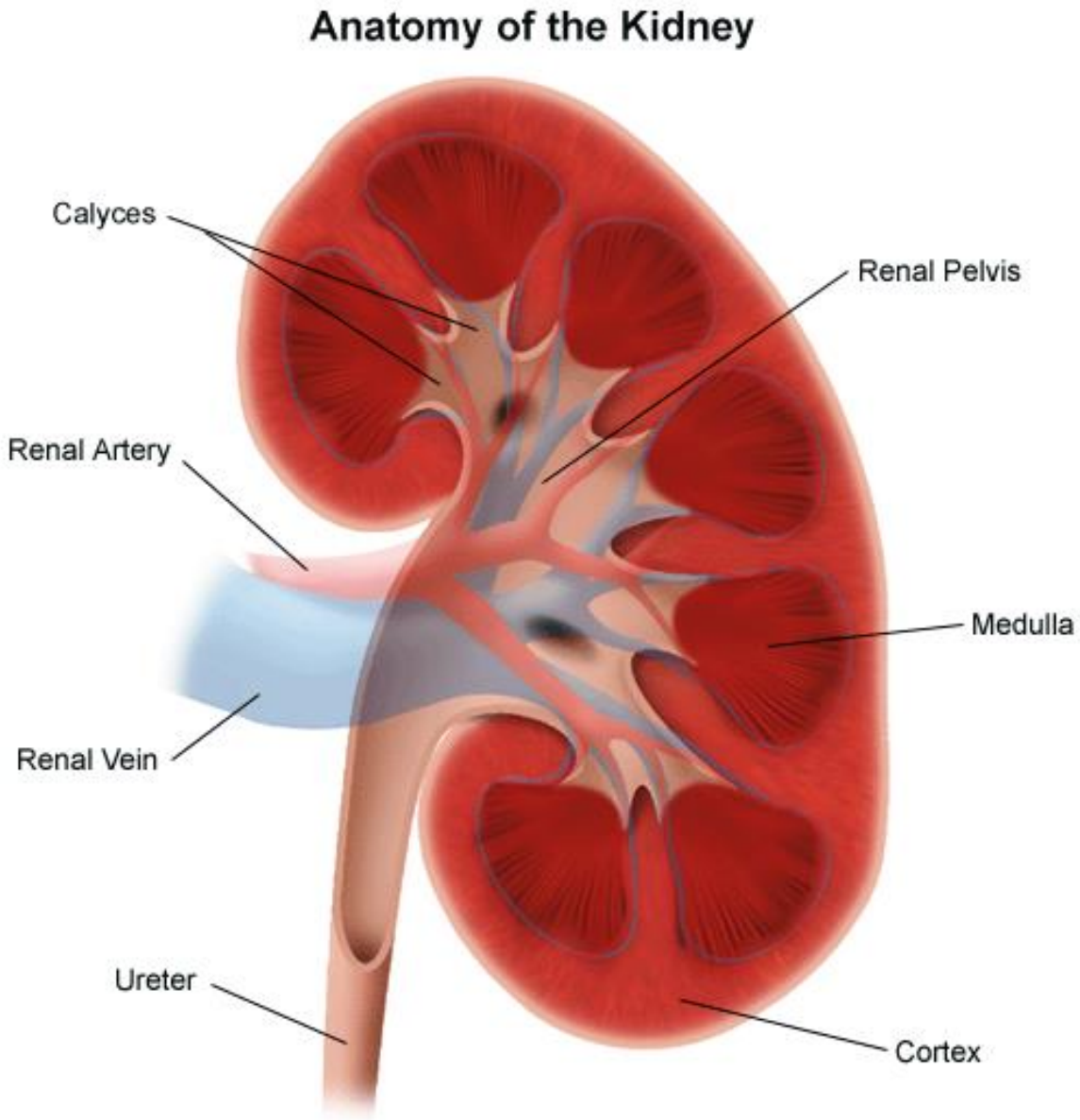
Renal Pathology 1: Glomerulus

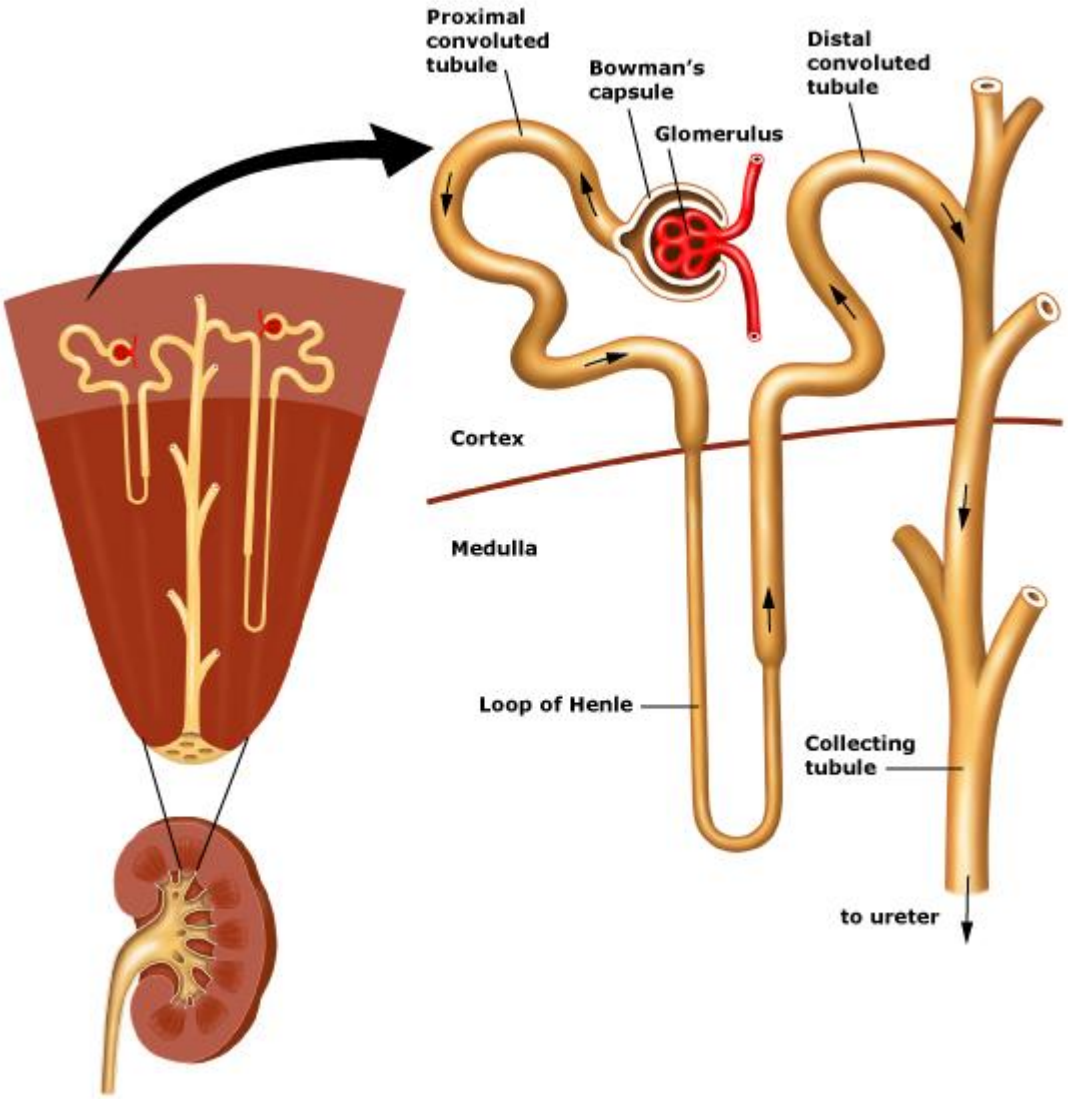
With many thanks to Elizabeth Angus PhD for EM photographs

Anatomy of the Kidney



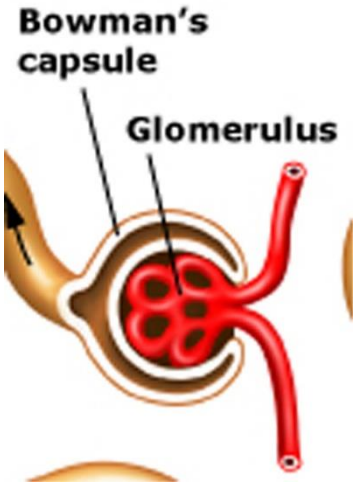
http://www.yalemedicalgroup.org/stw/Page.asp?PageID=STW028980

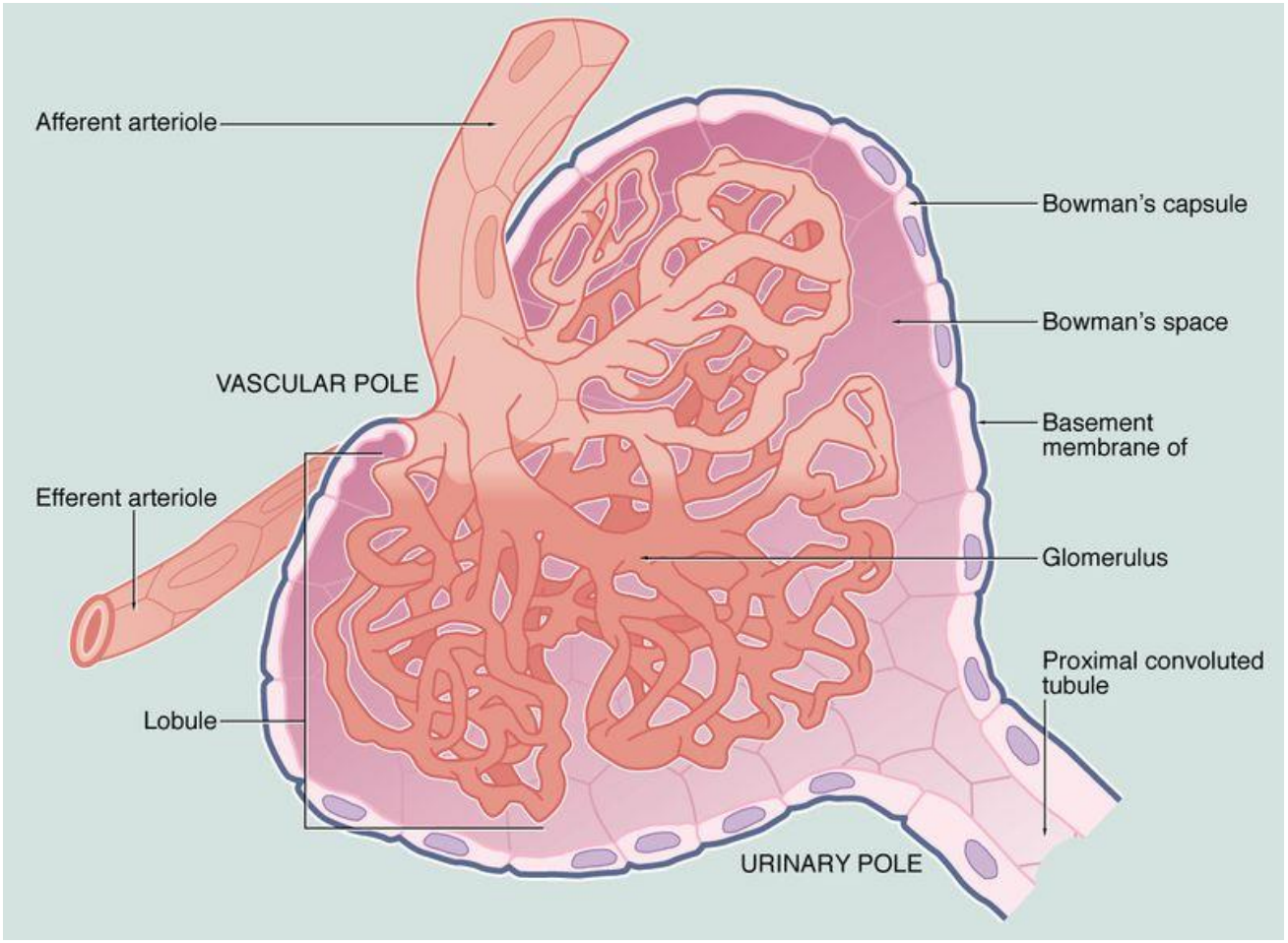
The Nephron



http://www.beltina.org/health-dictionary/nephron-function-kidney-definition.html

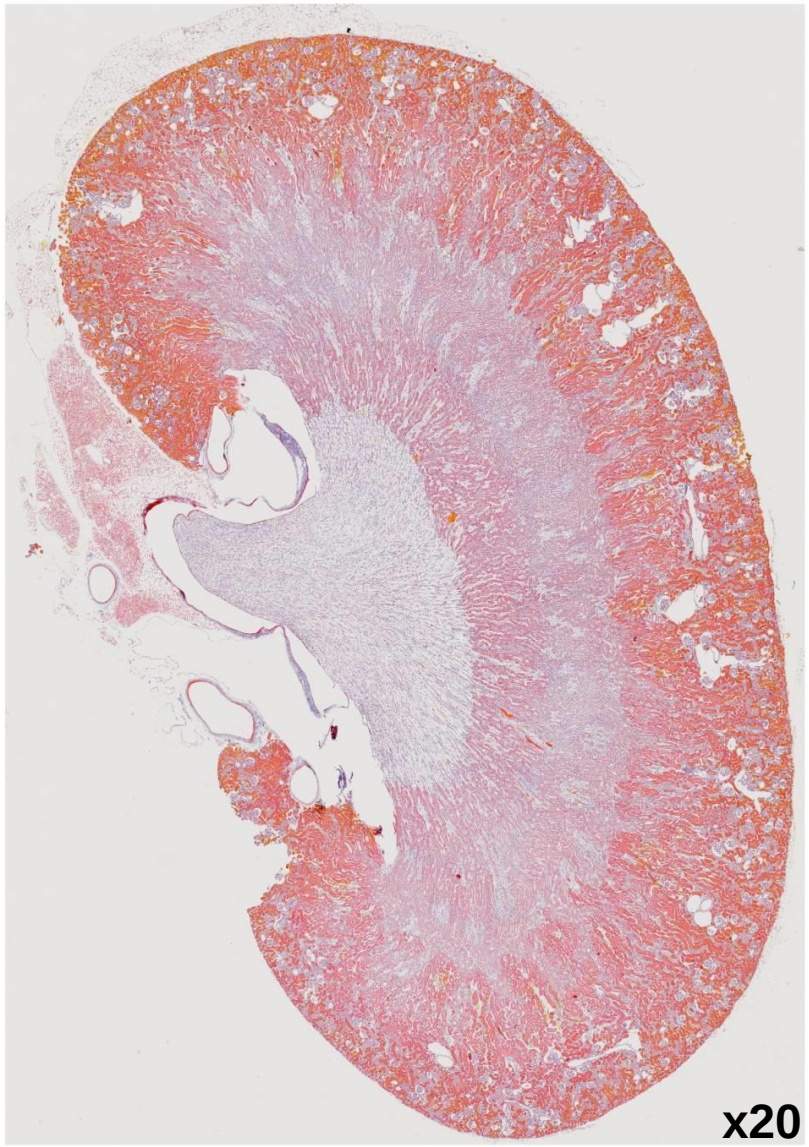
The Renal Corpuscle

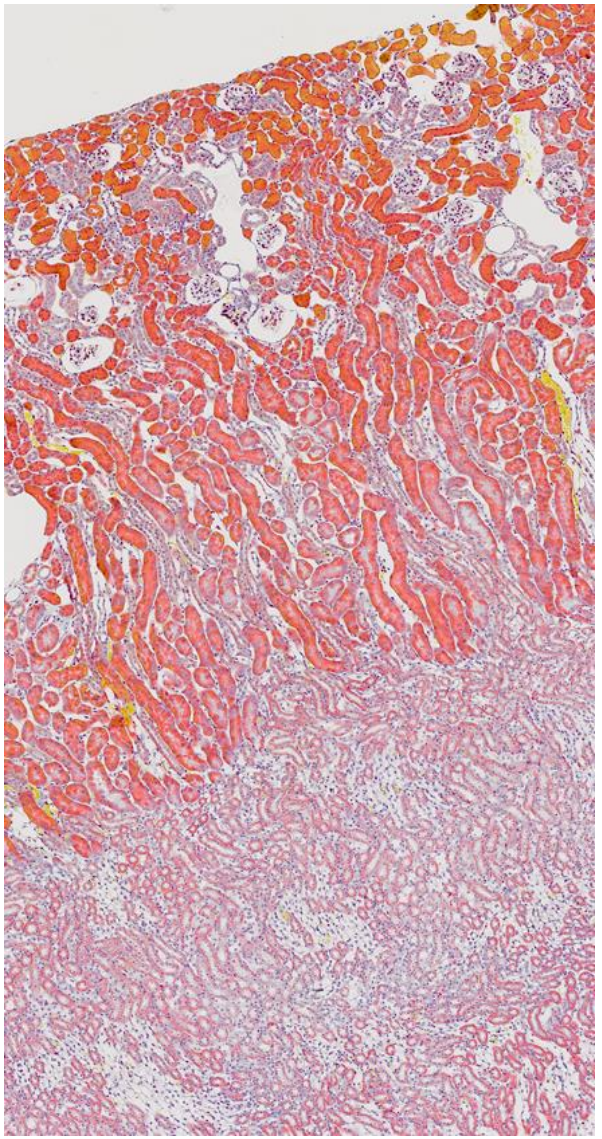




Wheater's Functional Histology A Text & Colour Atlas, 2009

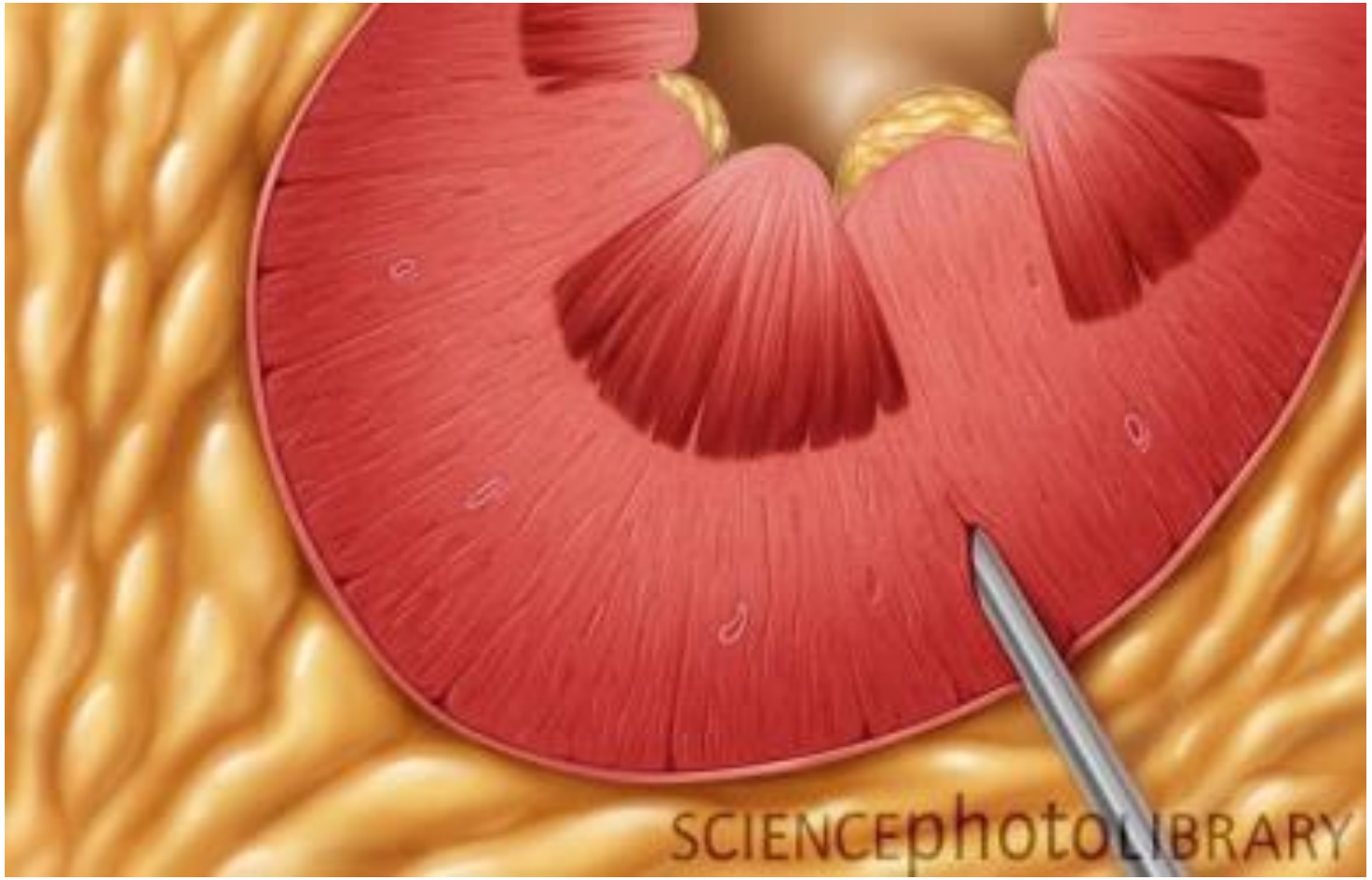
Anatomy of the Kidney



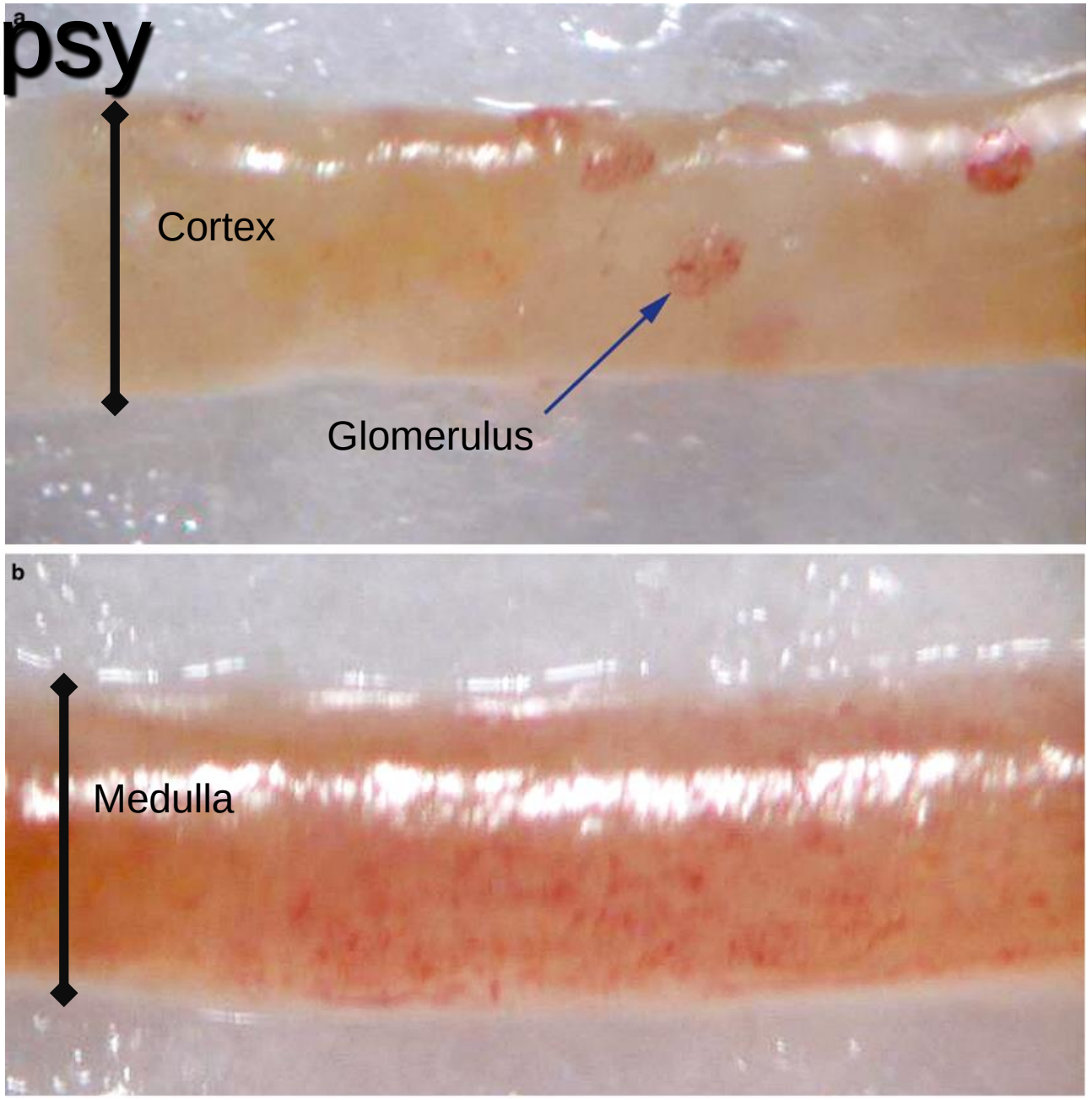


MSB mouse kidney courtesy of Matt Sharp

Needle Biopsy

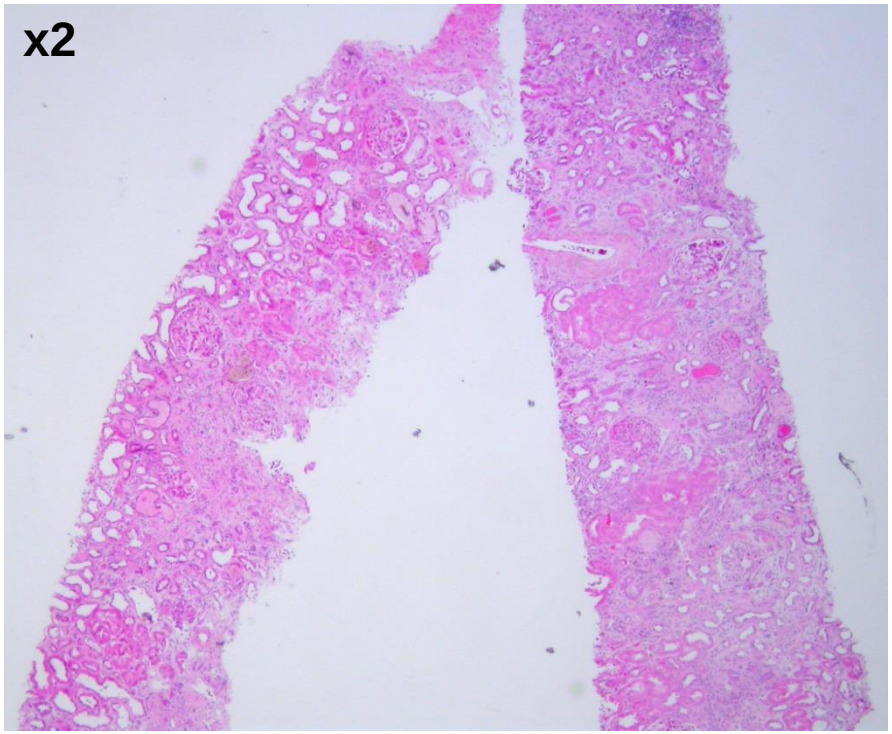


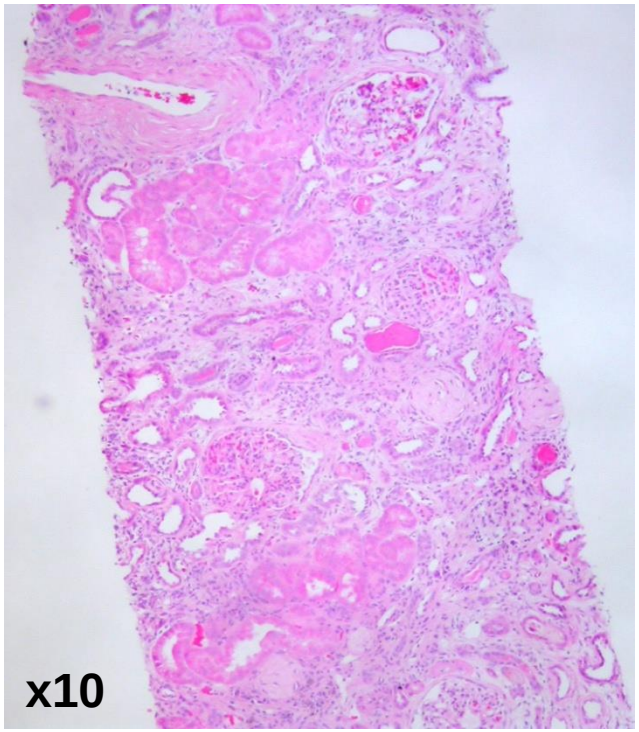
Needle Biopsy

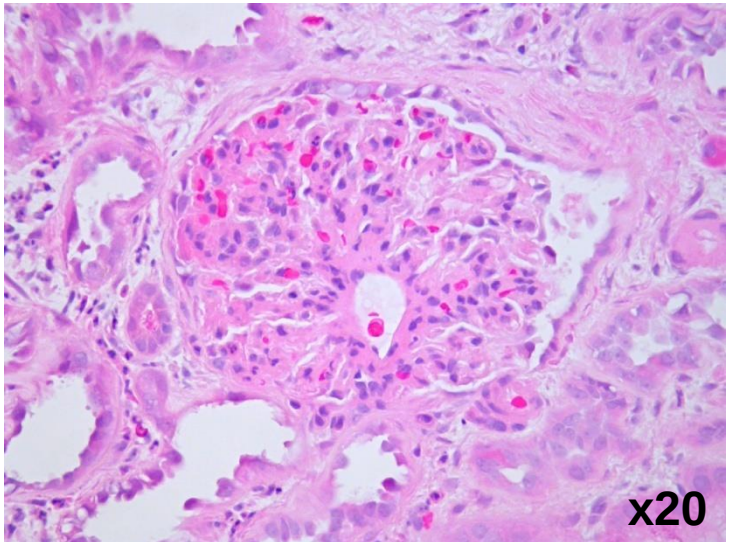


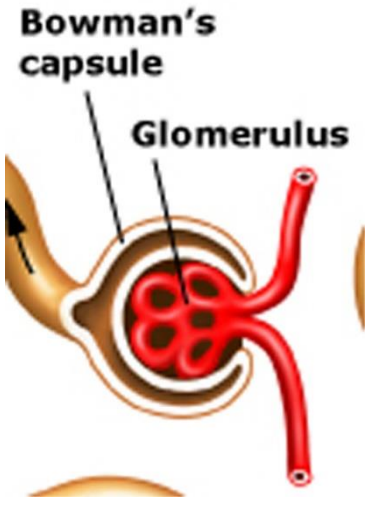
Modern Pathology (2004) 17, 1555–1563

H & E

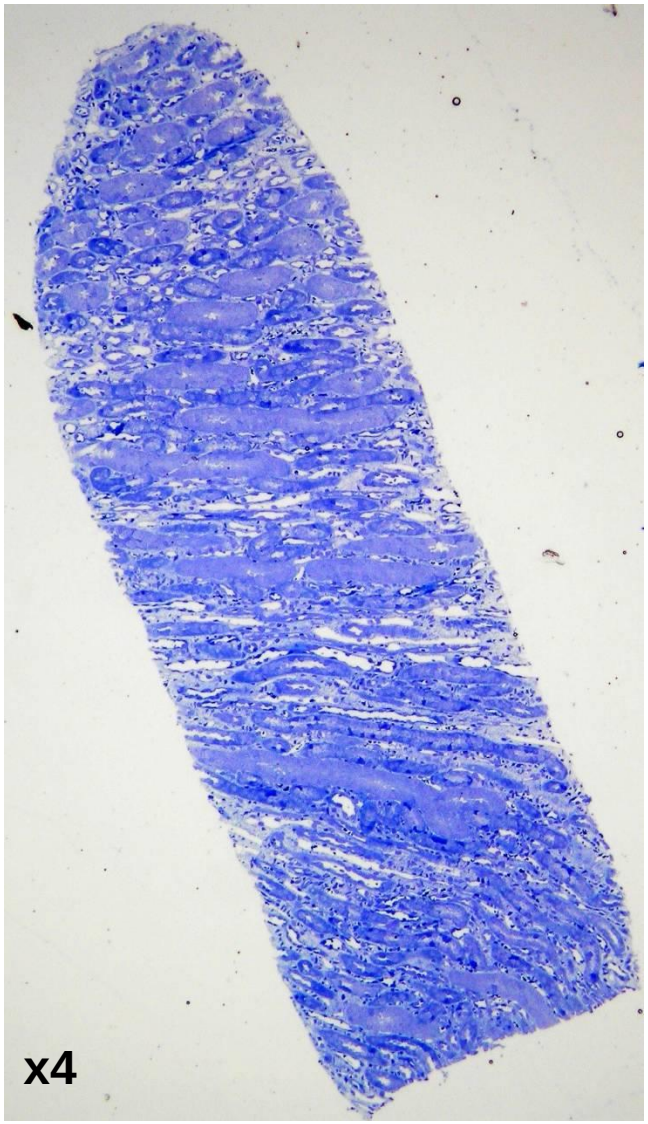


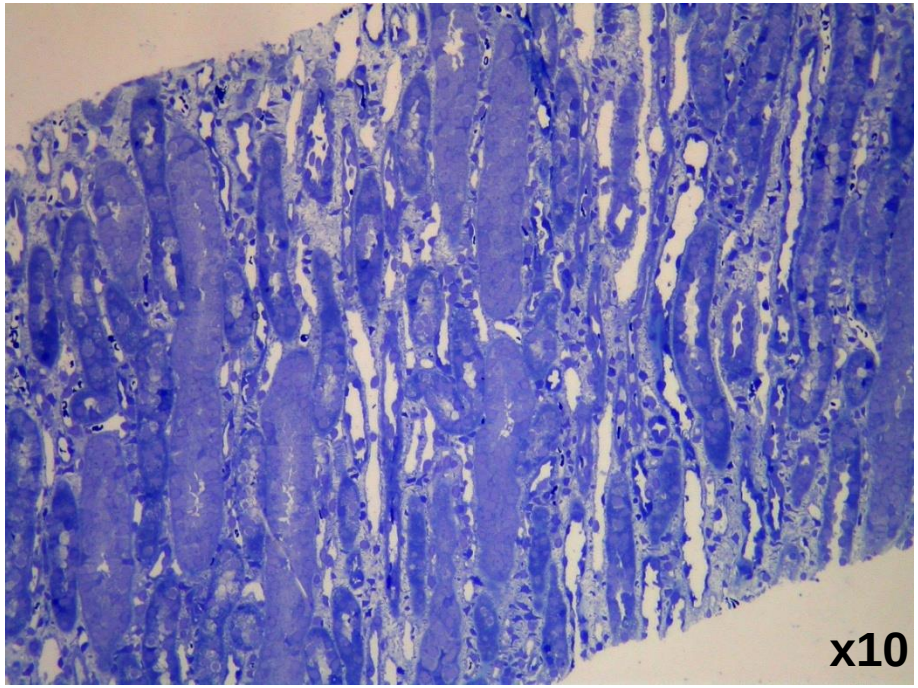




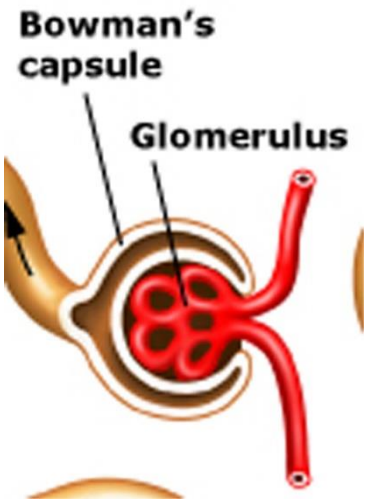


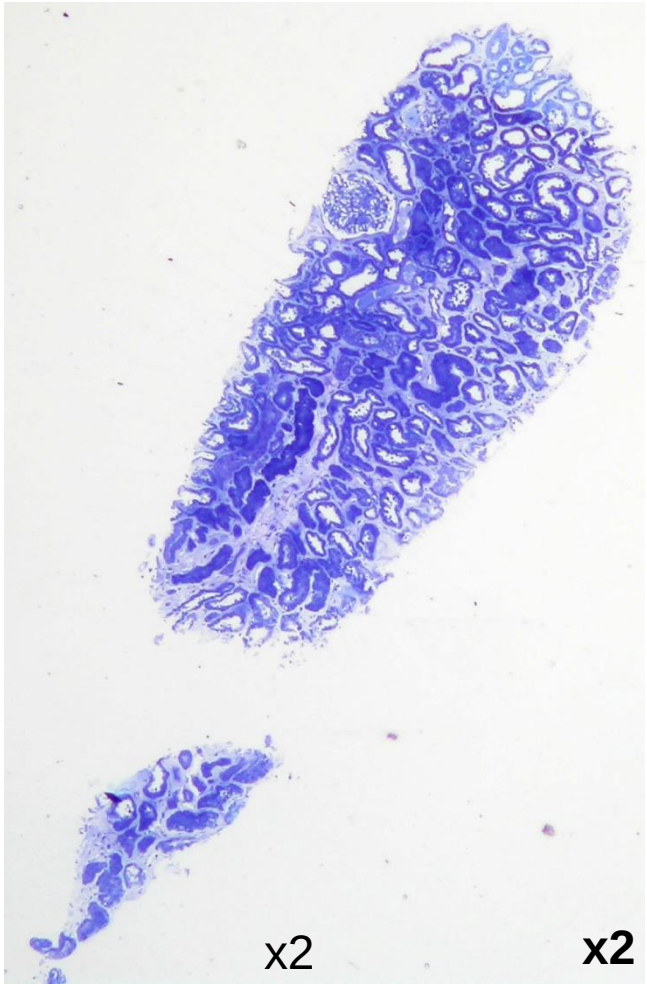
Top and Tail for EM

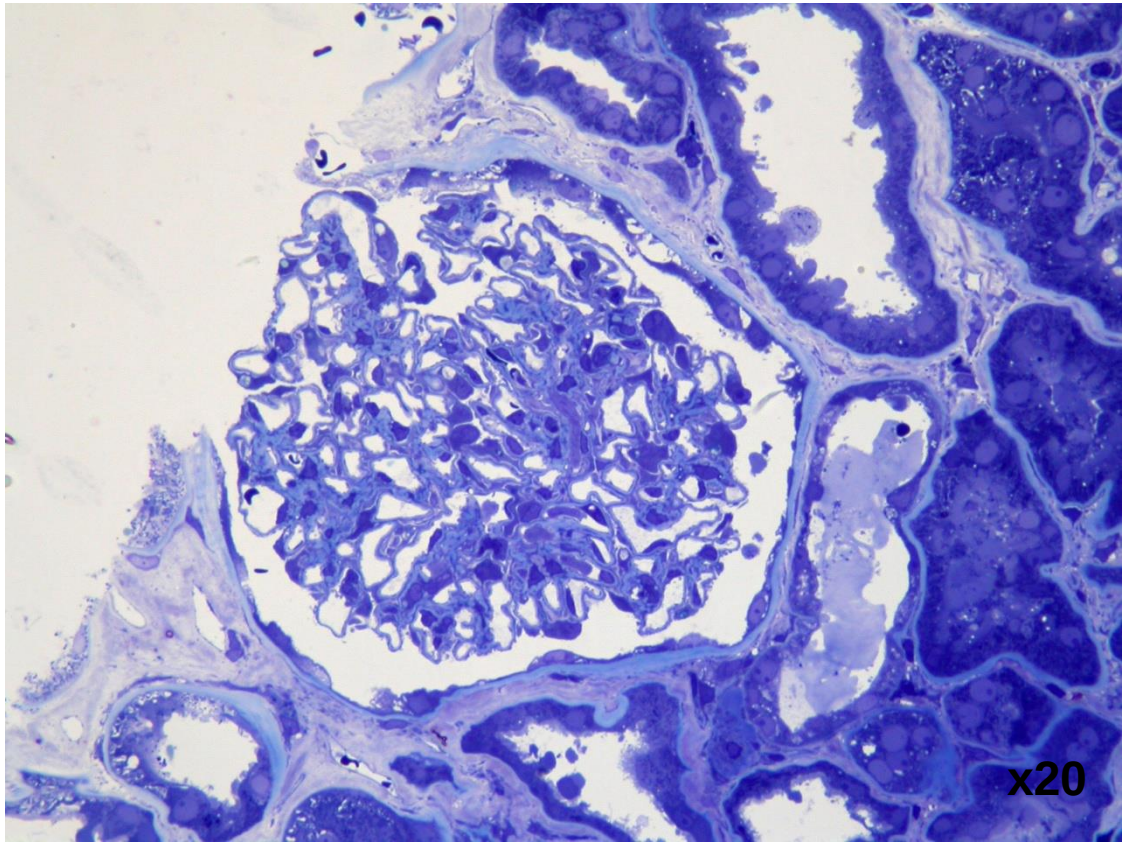




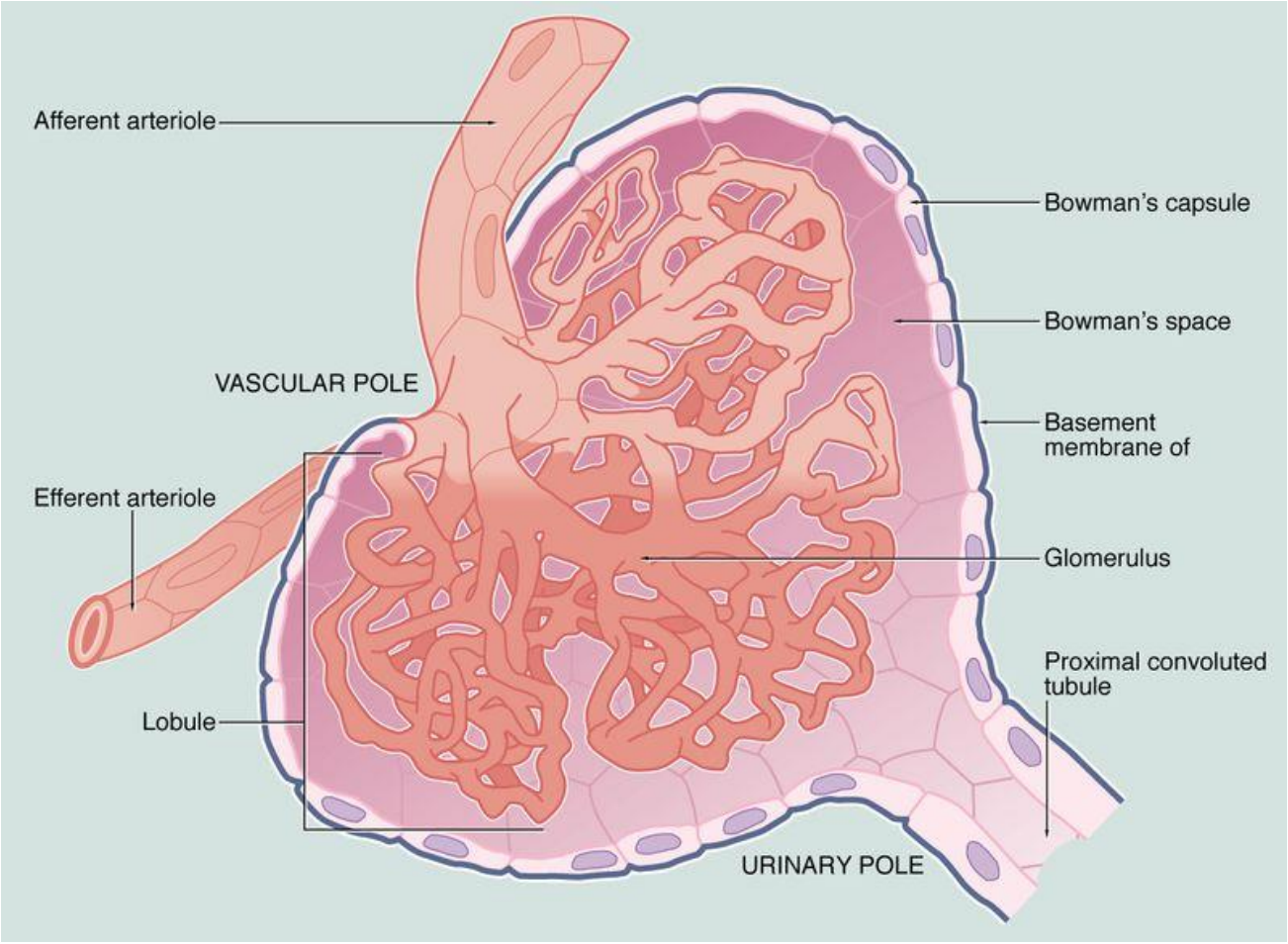
Top and Tail for EM





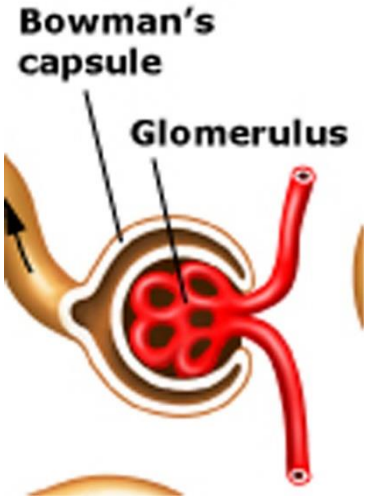


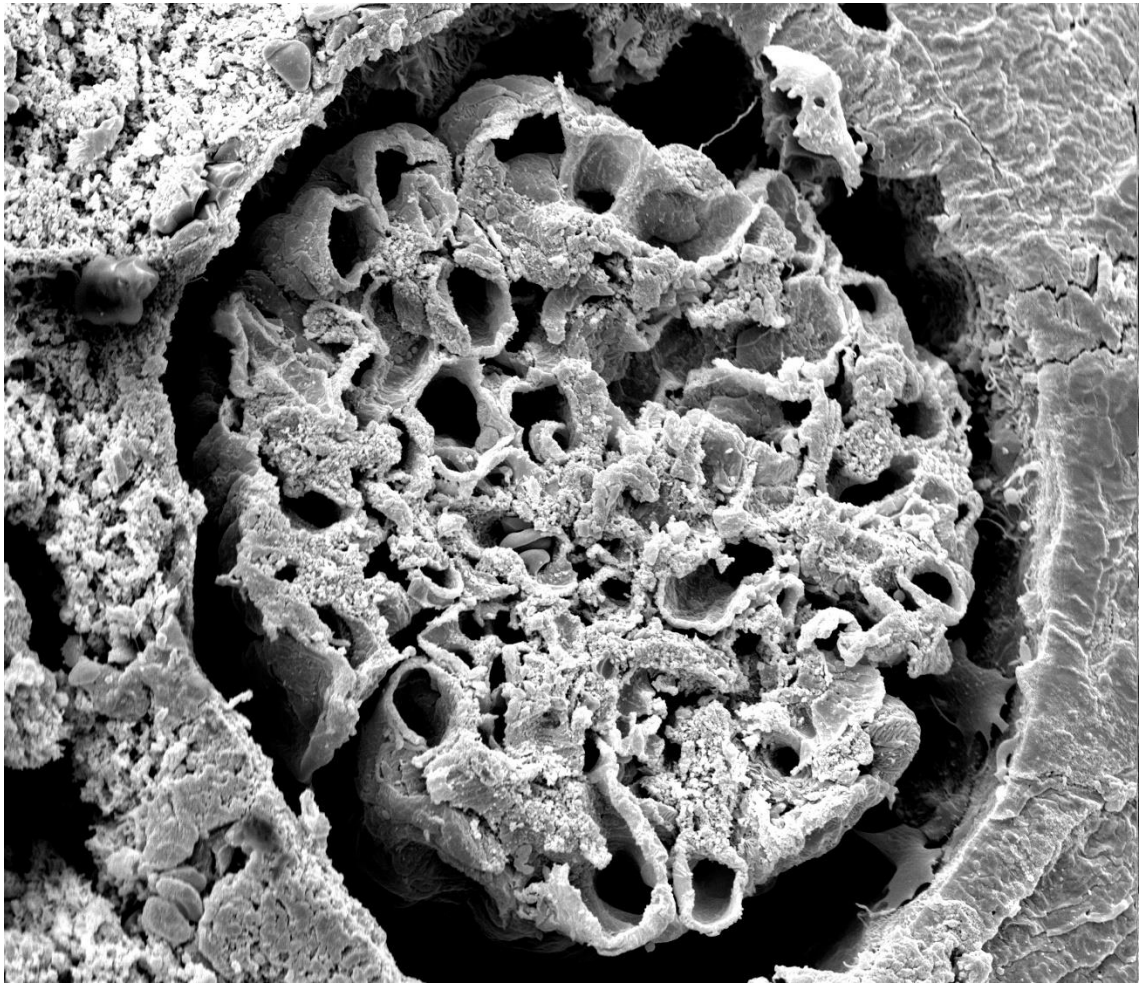
The Renal Corpuscle



Wheater's Functional Histology A Text & Colour Atlas, 2009

SEM – Glomerulus

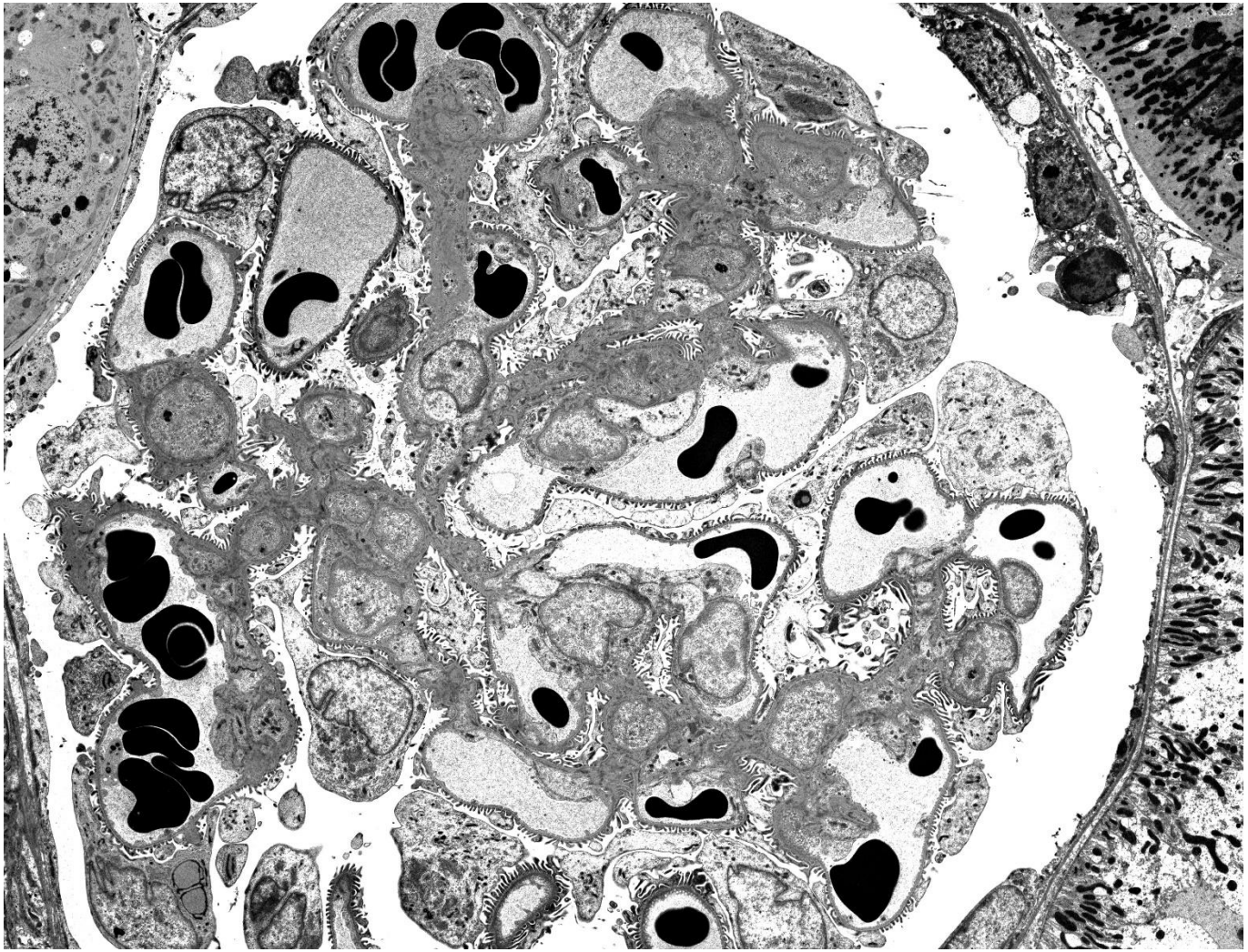




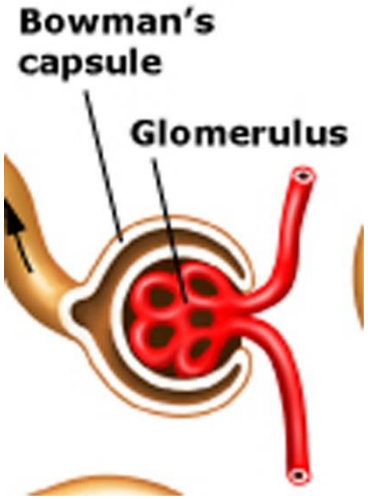
Courtesy of Anton Page

Freeze, fractured rodent glomerulus

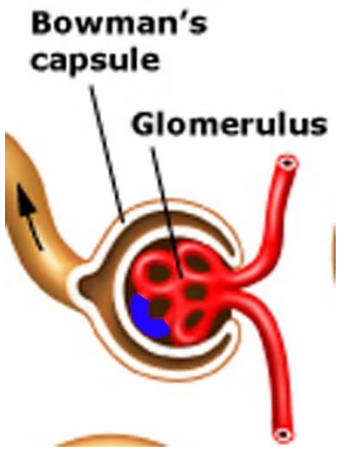
EM



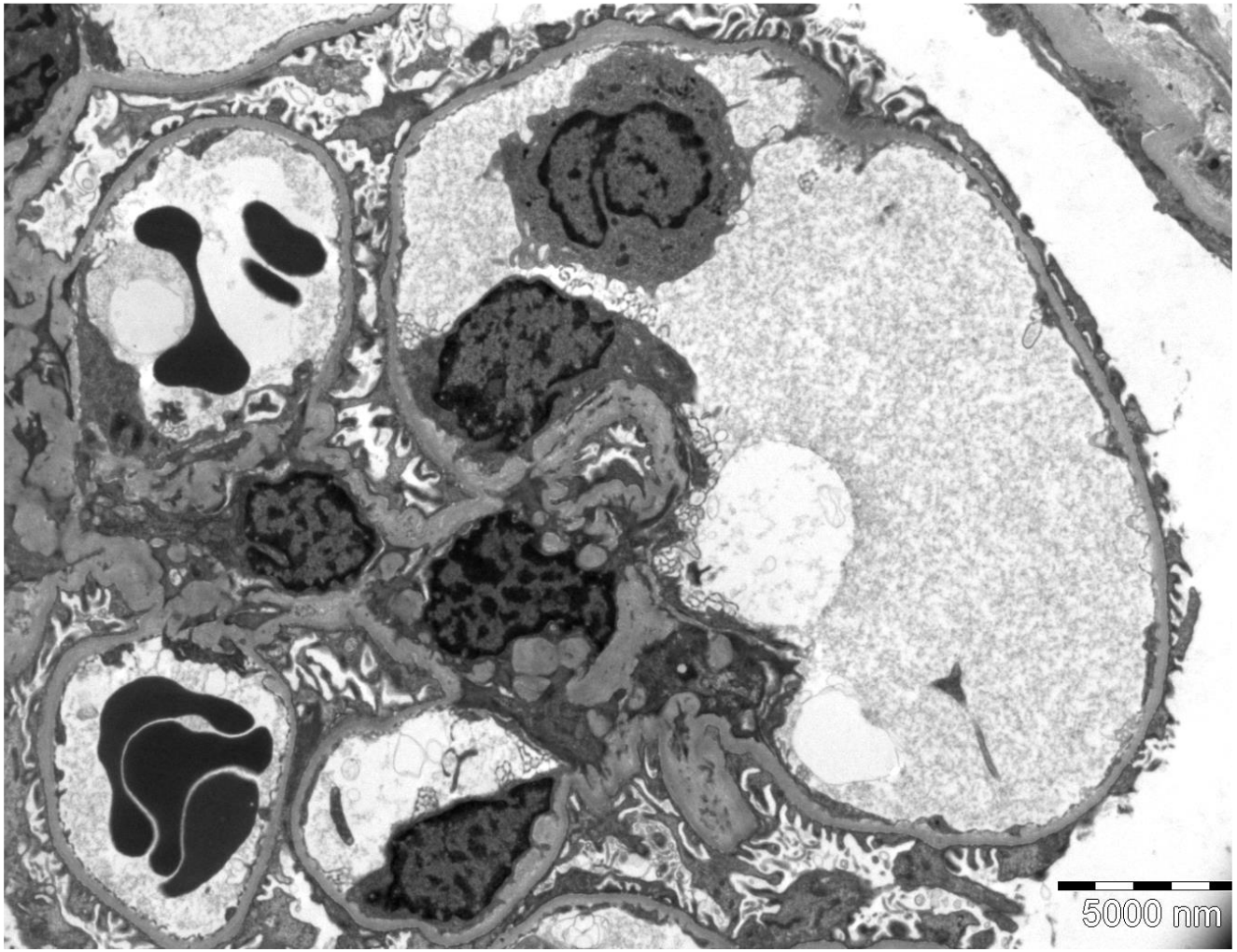
Part of a human glomerulus x 1,000



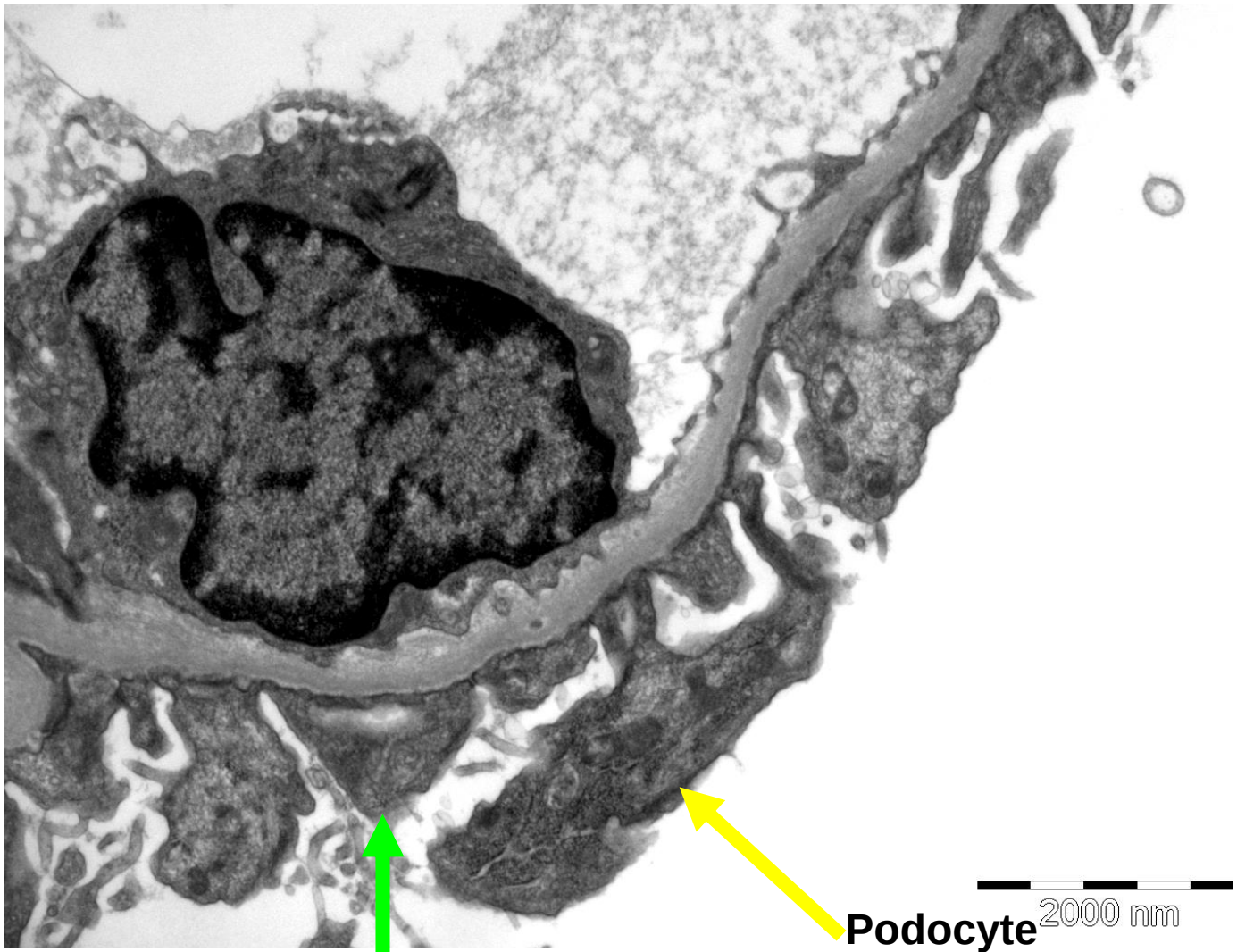
Courtesy of Anton Page

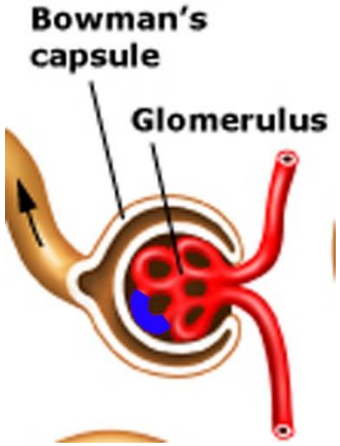


EM –Capillary loop

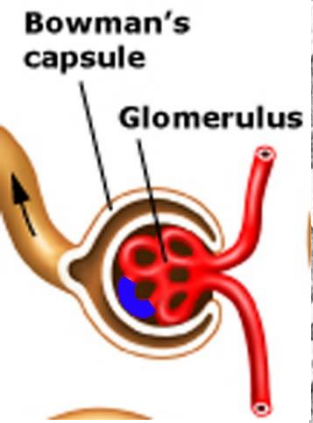


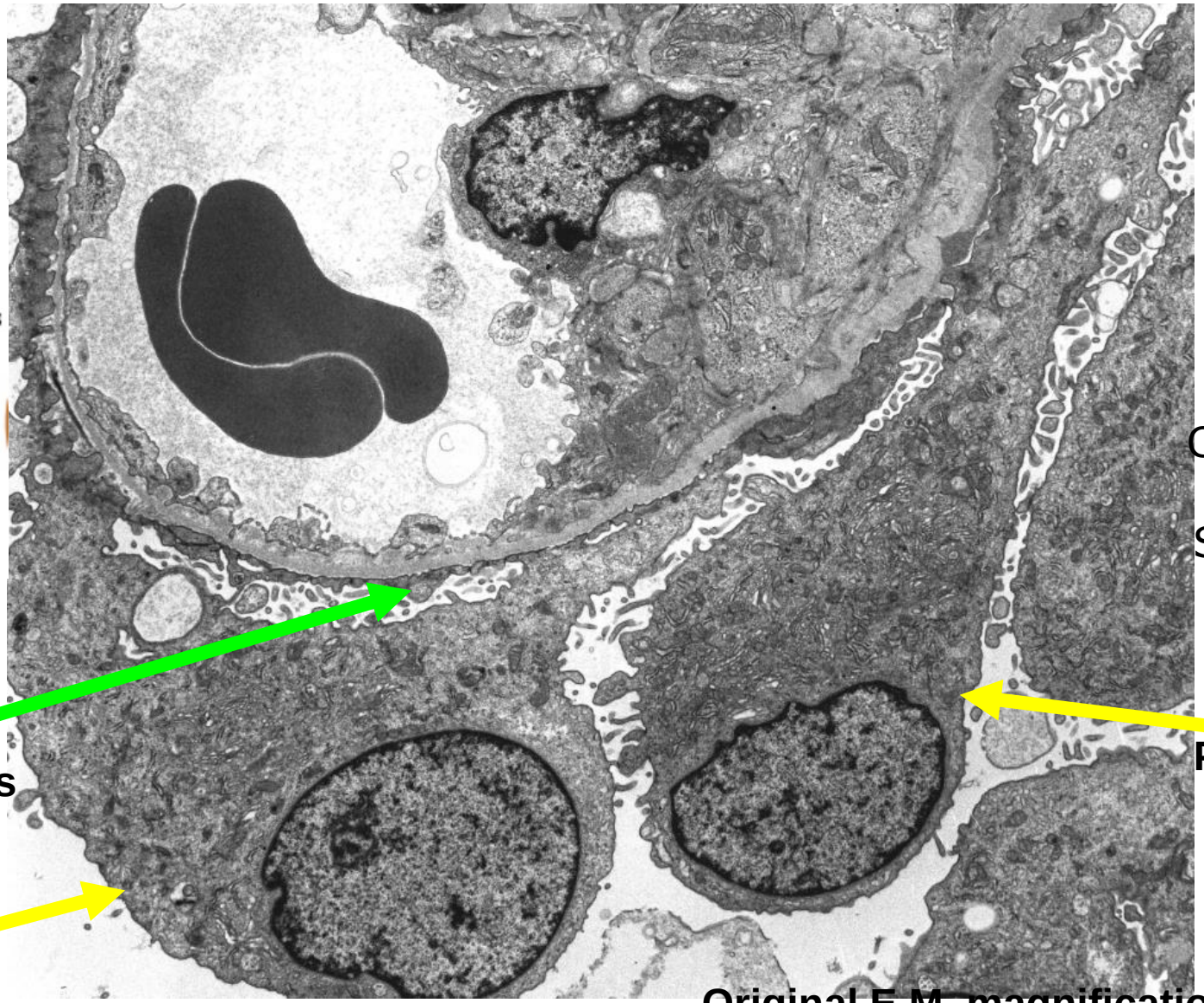
EM basement membrane





EM basement membrane





Courtesy of Sue Cox

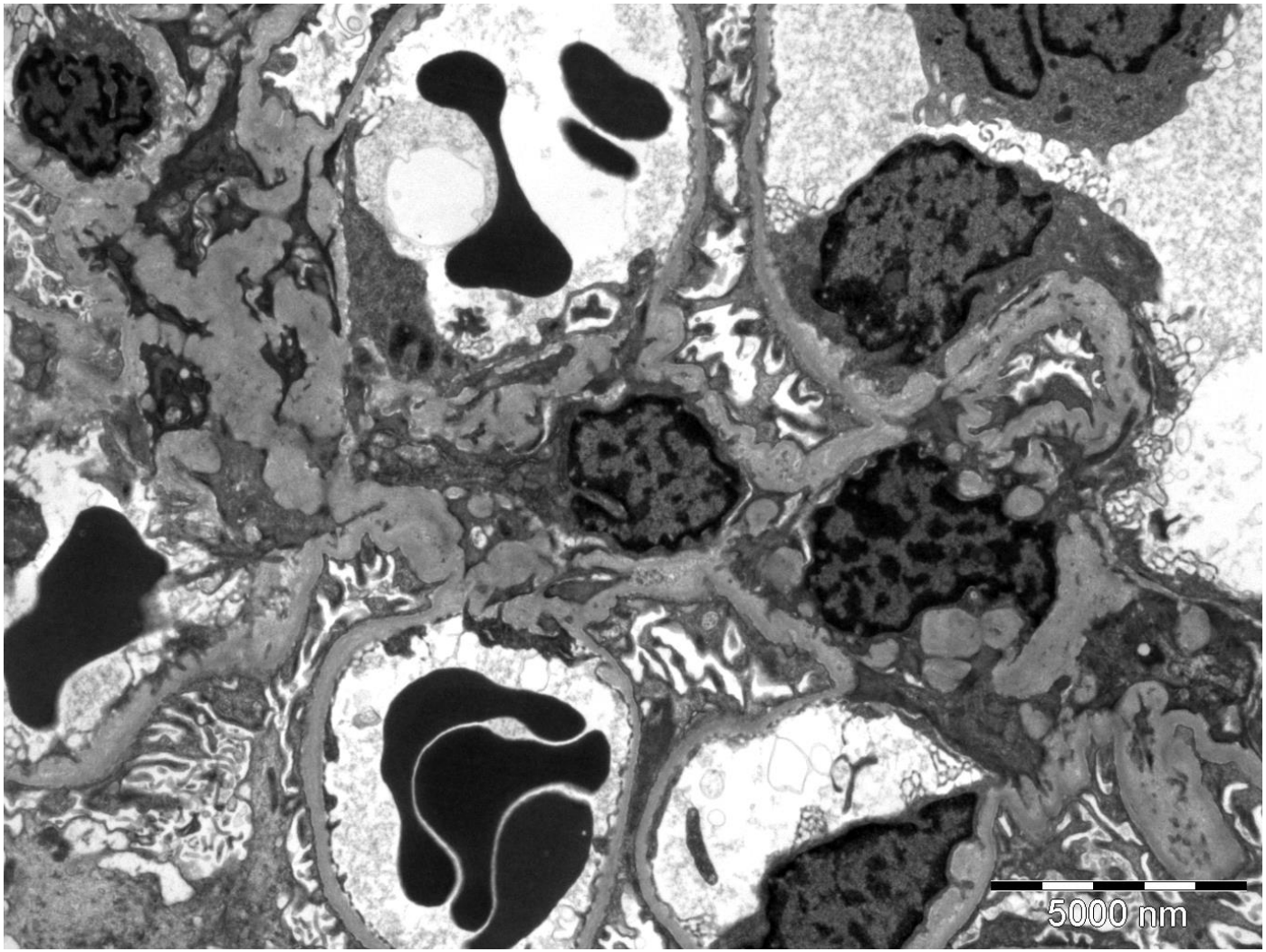
Foot process

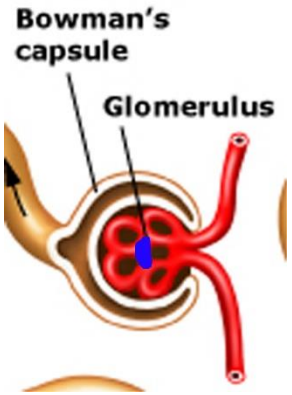
Podocyte

Podocyte

Original E.M. magnification x3,300

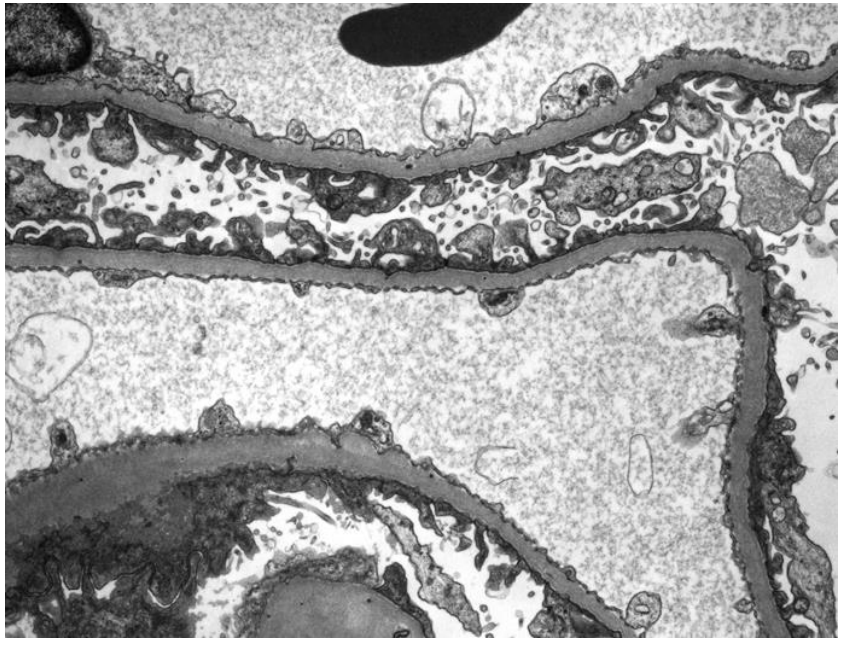
EM - mesangium

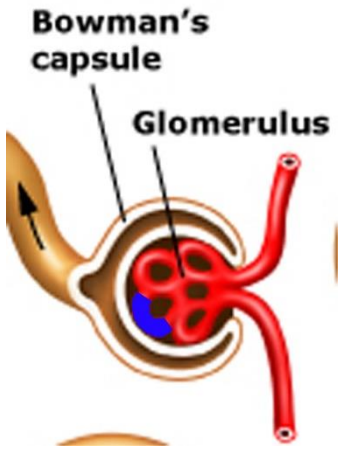




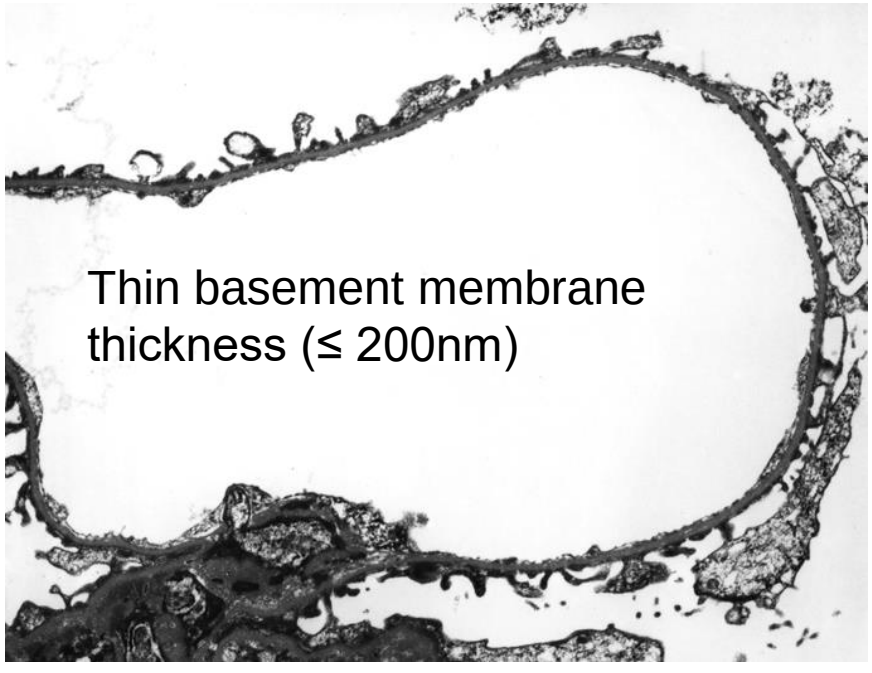
Basement Membrane

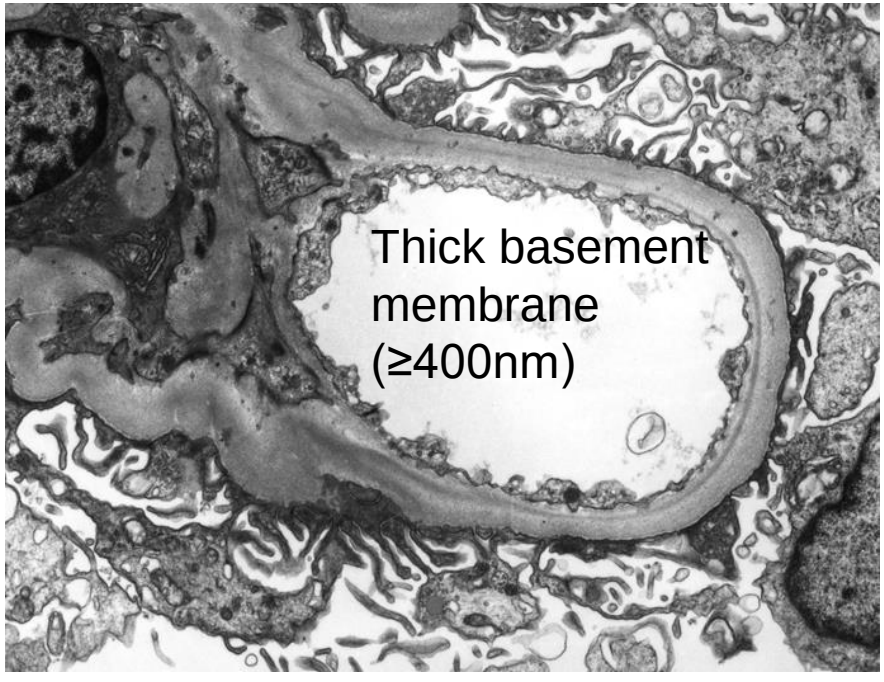
Courtesy of
Sue Cox



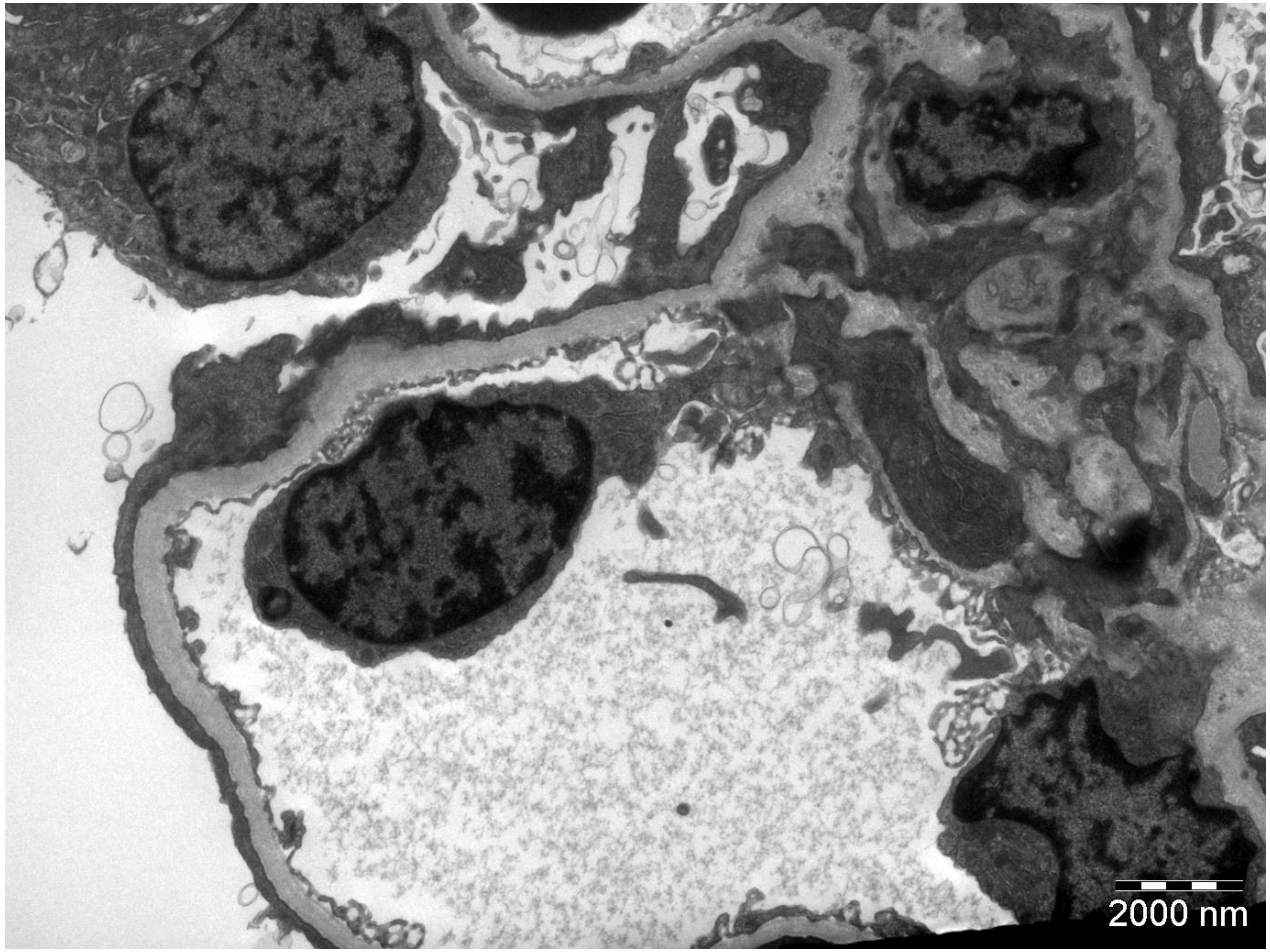


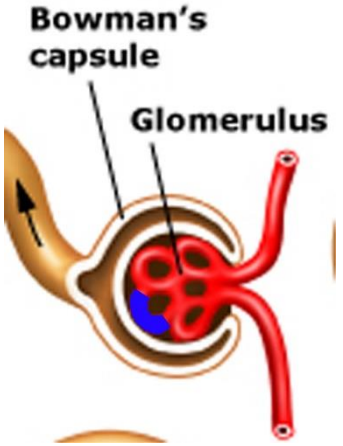
Normal basement membrane thickness (250-350nm)
x 5,000



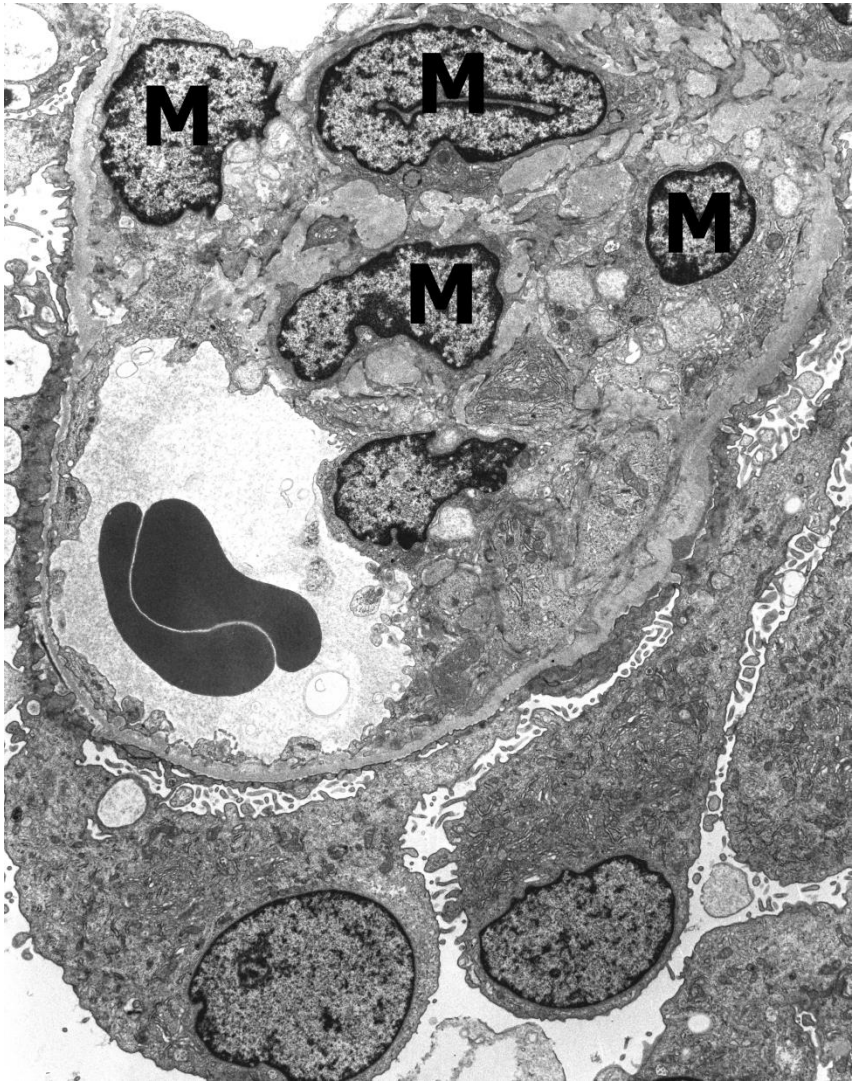


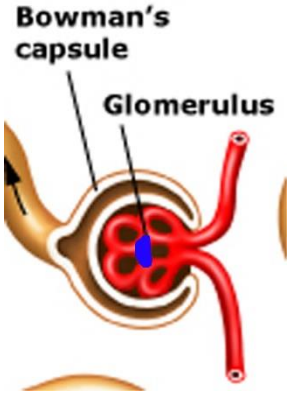
Foot Processes





Mesangial Hypercelluarity

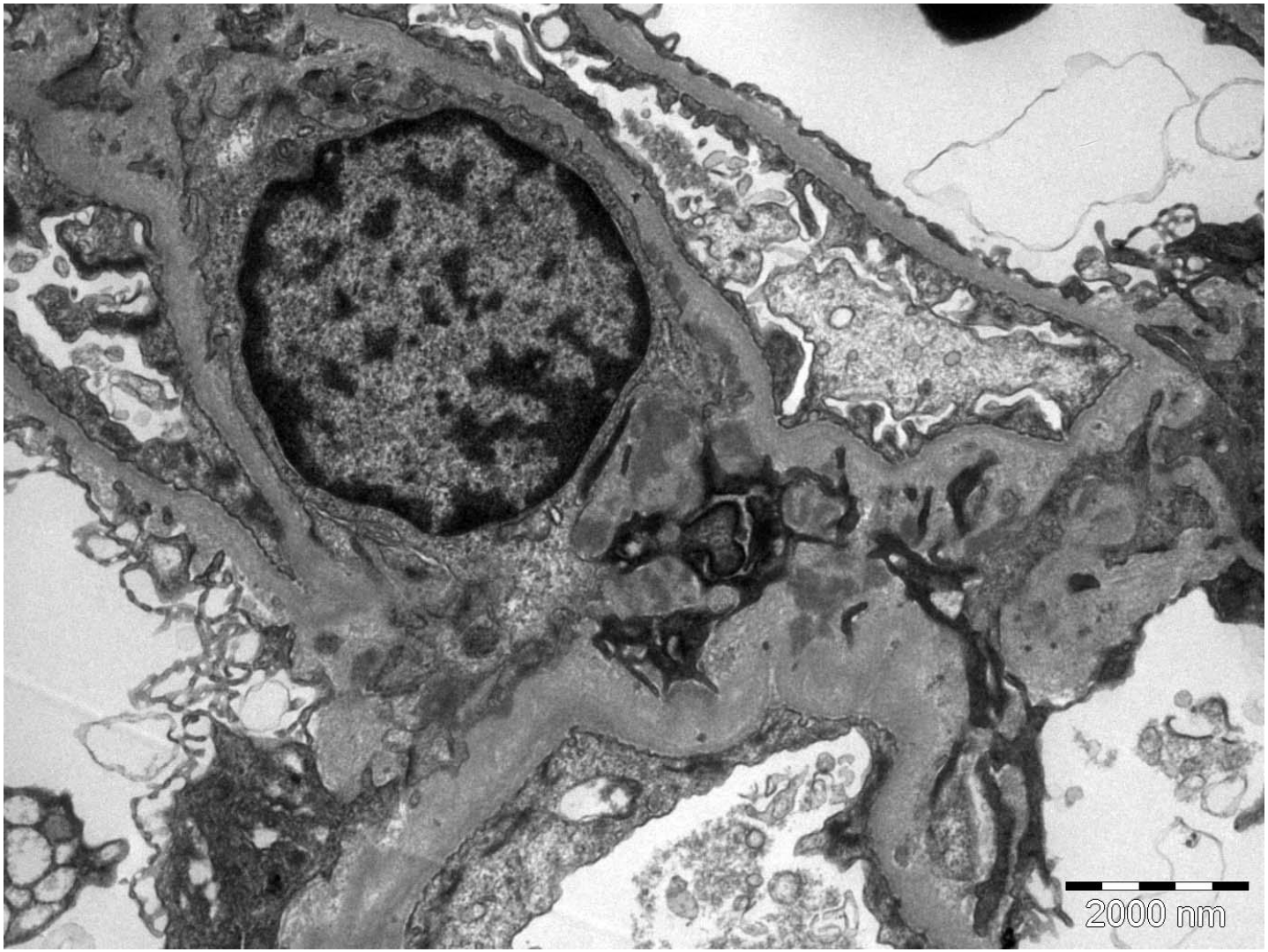


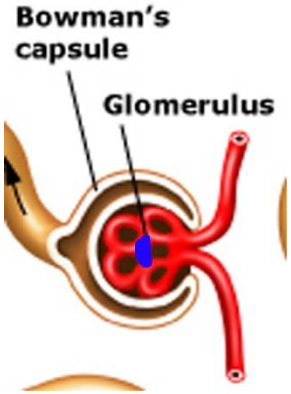


The glomerular mesangium contains increased matrix and four nuclei (**M**). The capillary is normal. There is loss of epithelial cell foot processes. Original E.M. magnification x3,300

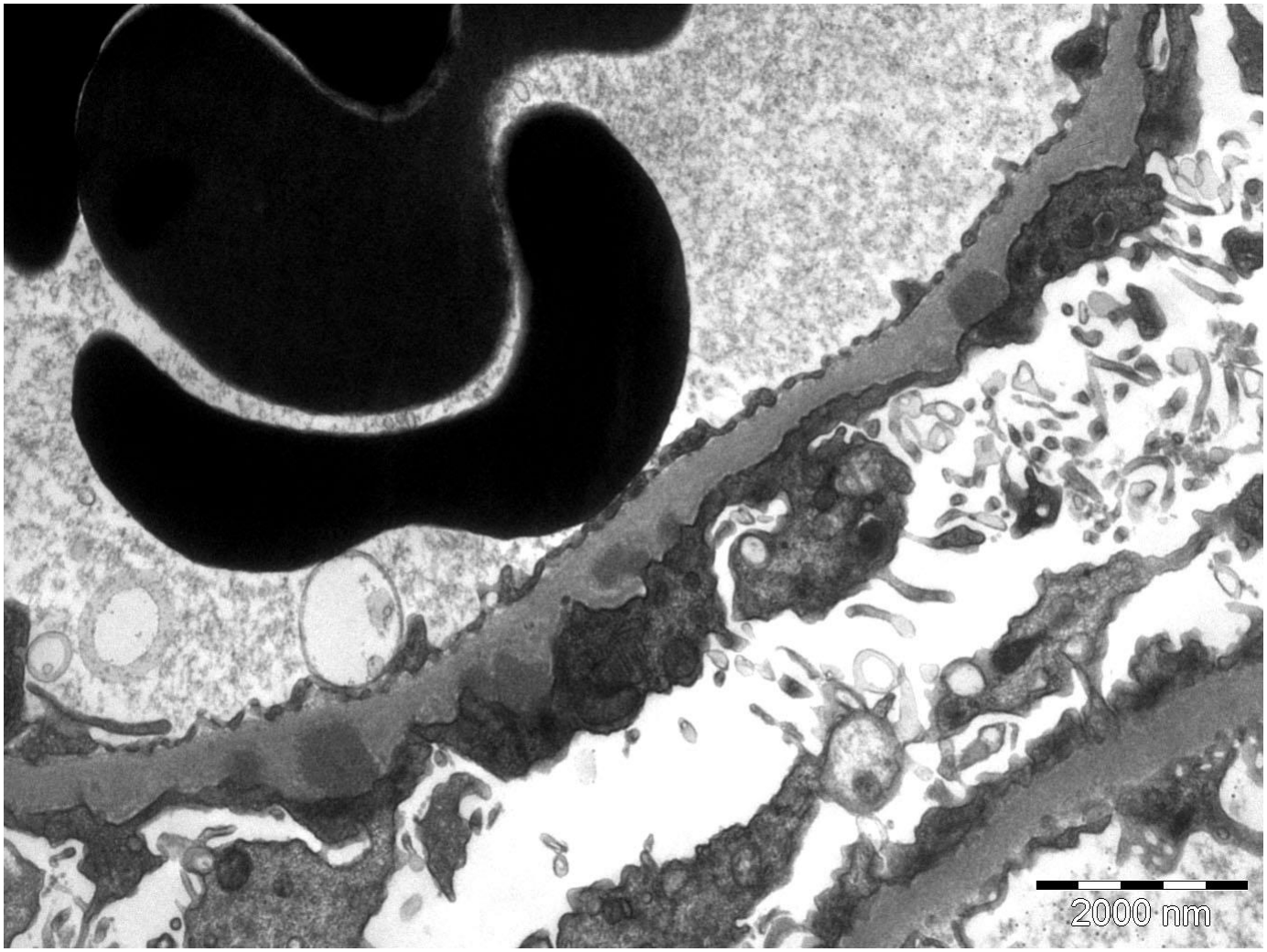
Courtesy of Sue Cox

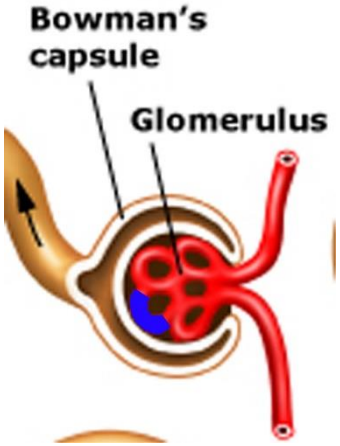
Electron Dense Deposits



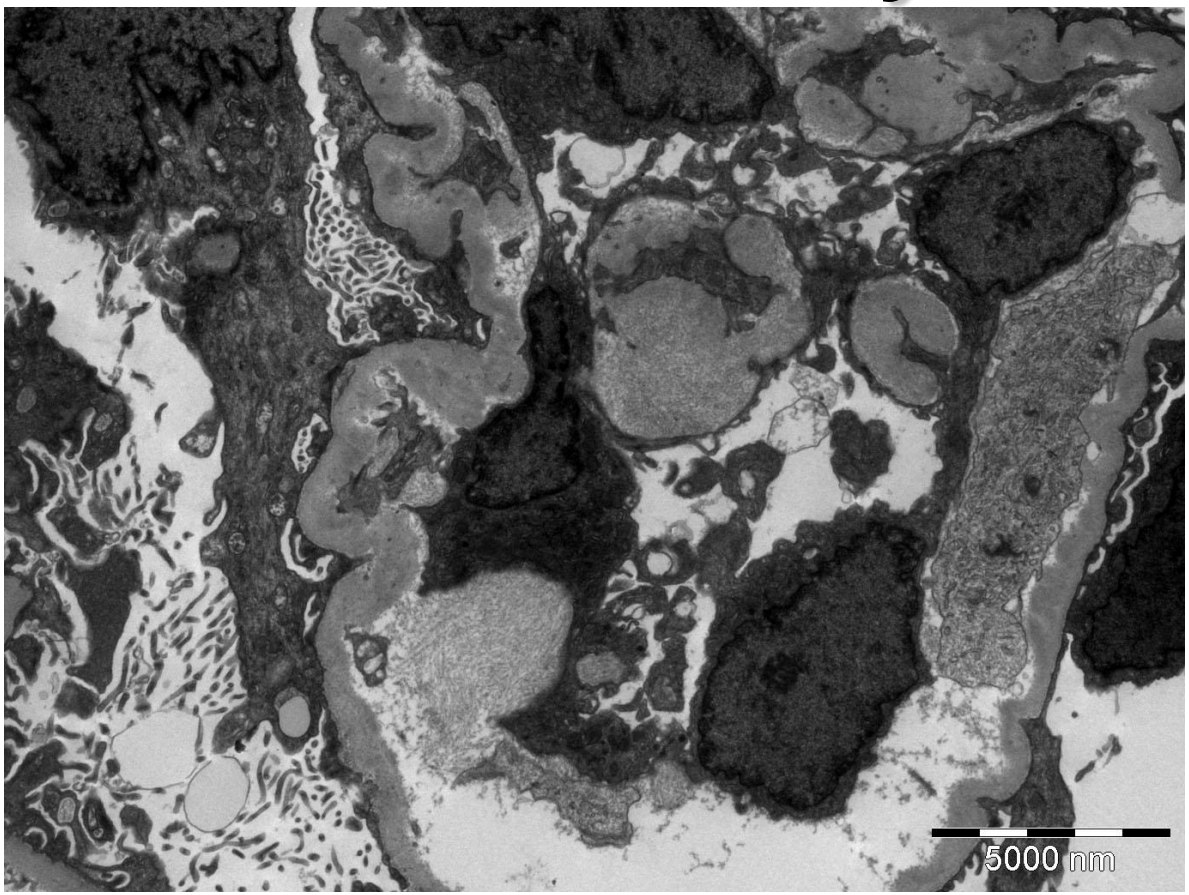


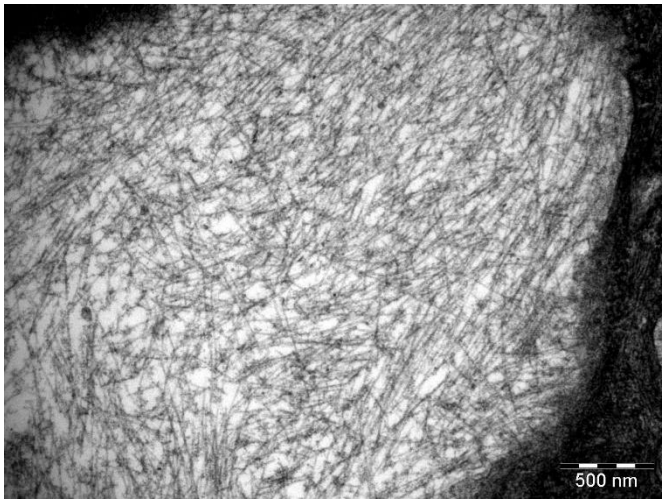
Electron Dense Deposits

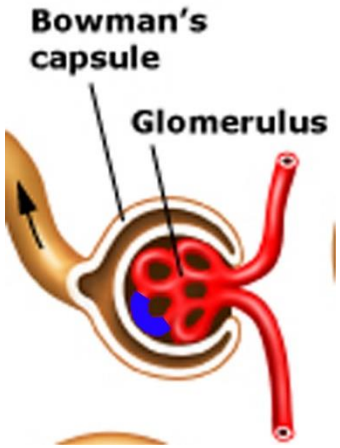




Amyloid







Glomerulonephritis (GN) patterns

- “Primary”
- (minimal change disease)
- Mesangial proliferative GN
- Focal segmental glomerulosclerosis
- Membranous GN
- Post infectious GN
- Crescentic GN
- Membranoproliferative GN

- “Secondary” lupus diabetes, amyloid, light chain disease, cryoglobulinemia,

terms

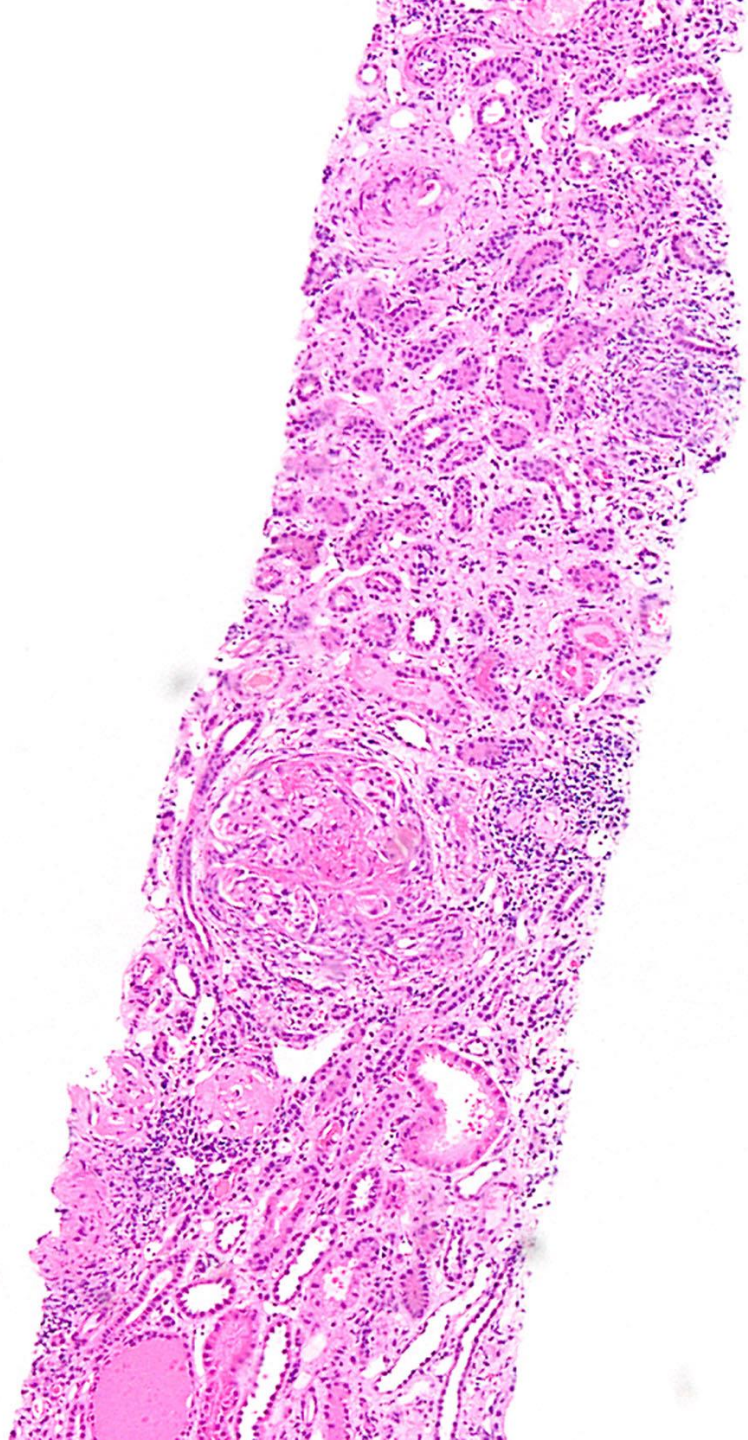
- Diffuse: involves whole glomerulus (vs focal)
- Global: involves whole glomerulus (vs segmental)

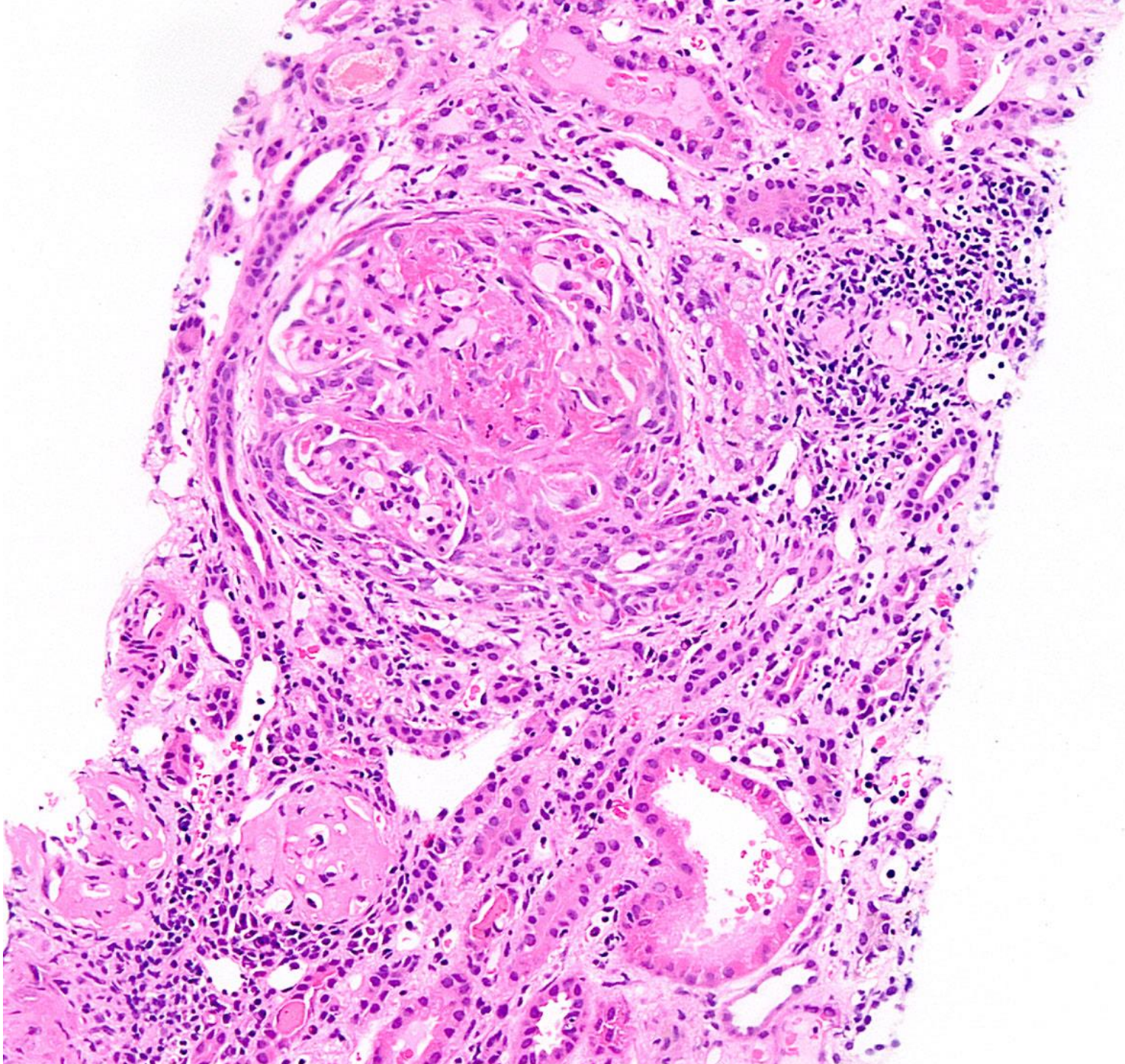
Nephrotic vs nephritic

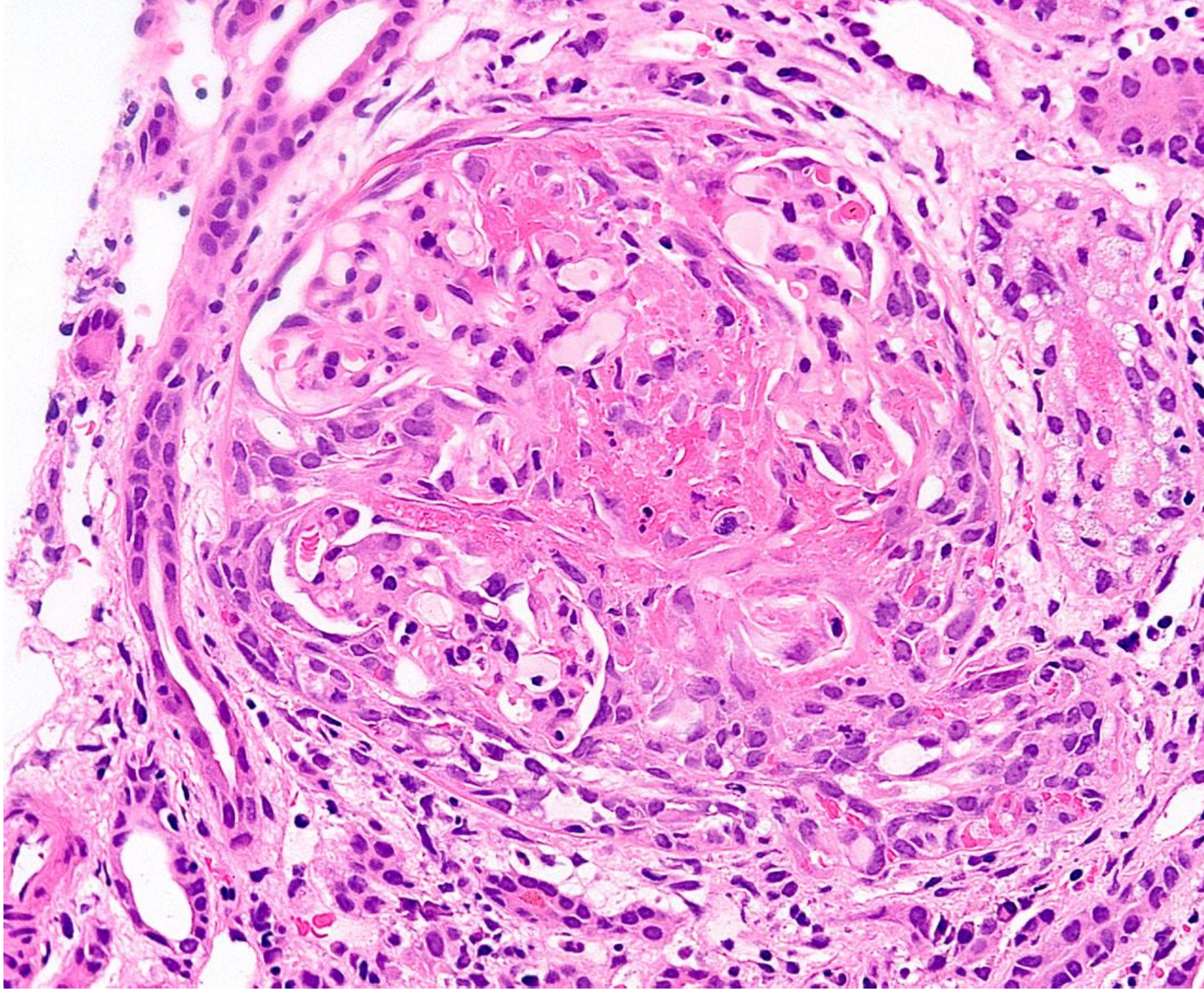
- Nephrotic
- minimal change disease, mesangial proliferative (eg. IgA disease/HSP), focal and segmental, membranous
- Nephritic
- Post-infectious (eg post-Streptococcal), membranoproliferative)

Clinical Stories

- 1-month history of malaise. renal failure, weight loss, fevers, ?cause.
- additional information: creat 300s, MCV 60
- Complement C3 and C4 within normal range
- Perinuclear ANCA (IgG) Weak positive
- Cytoplasmic ANCA (IgG) Negative
- Connective tissue ANA screen Borderline







Crescentic glomerulonephritis

- Glomeruli:There are 22 glomeruli, all of which are abnormal showing varying degrees of sclerosis and active proliferative changes. At least 9 glomeruli are globally sclerosed. Numerous fresh crescents are identified with proliferating epithelial cells seen in the urinary space. There are neutrophils present. There is periglomerular fibrosis around several glomeruli.

- Tubules / interstitium: focal tubular atrophy around damaged glomeruli.
- mixed inflammatory infiltrate: occ eosinophils, plasma cells, lymphocytes
- Vessels: no vasculitis.

- Immunohistochemistry: IgA, IgG, IgM, C1q and C3 stains are negative.

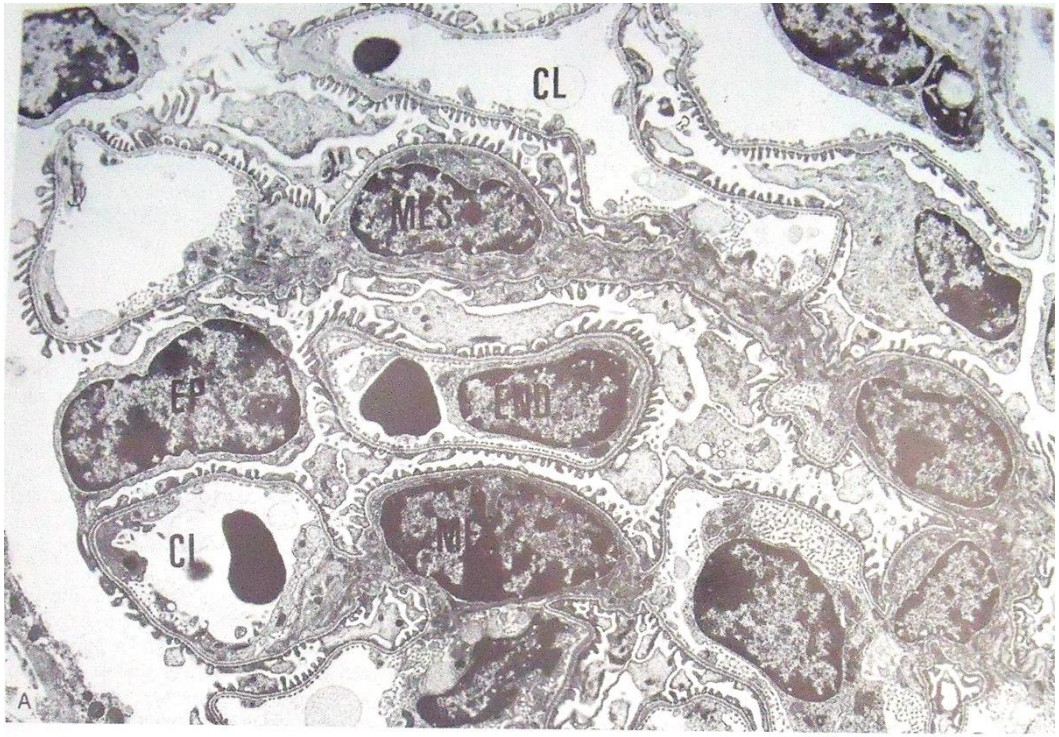
- EM: No electron dense deposits are identified.

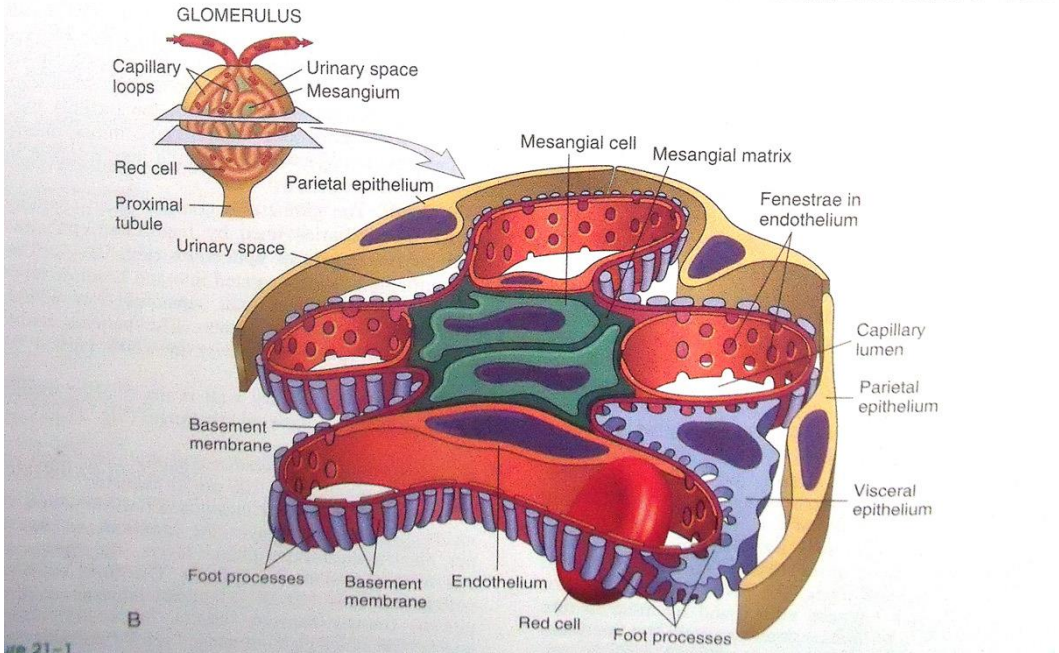
- Comment: the crescentic glomerulonephritis, negative immunohistochemistry and absence of electron dense deposits are highly suggestive of pauci immune glomerulonephritis.

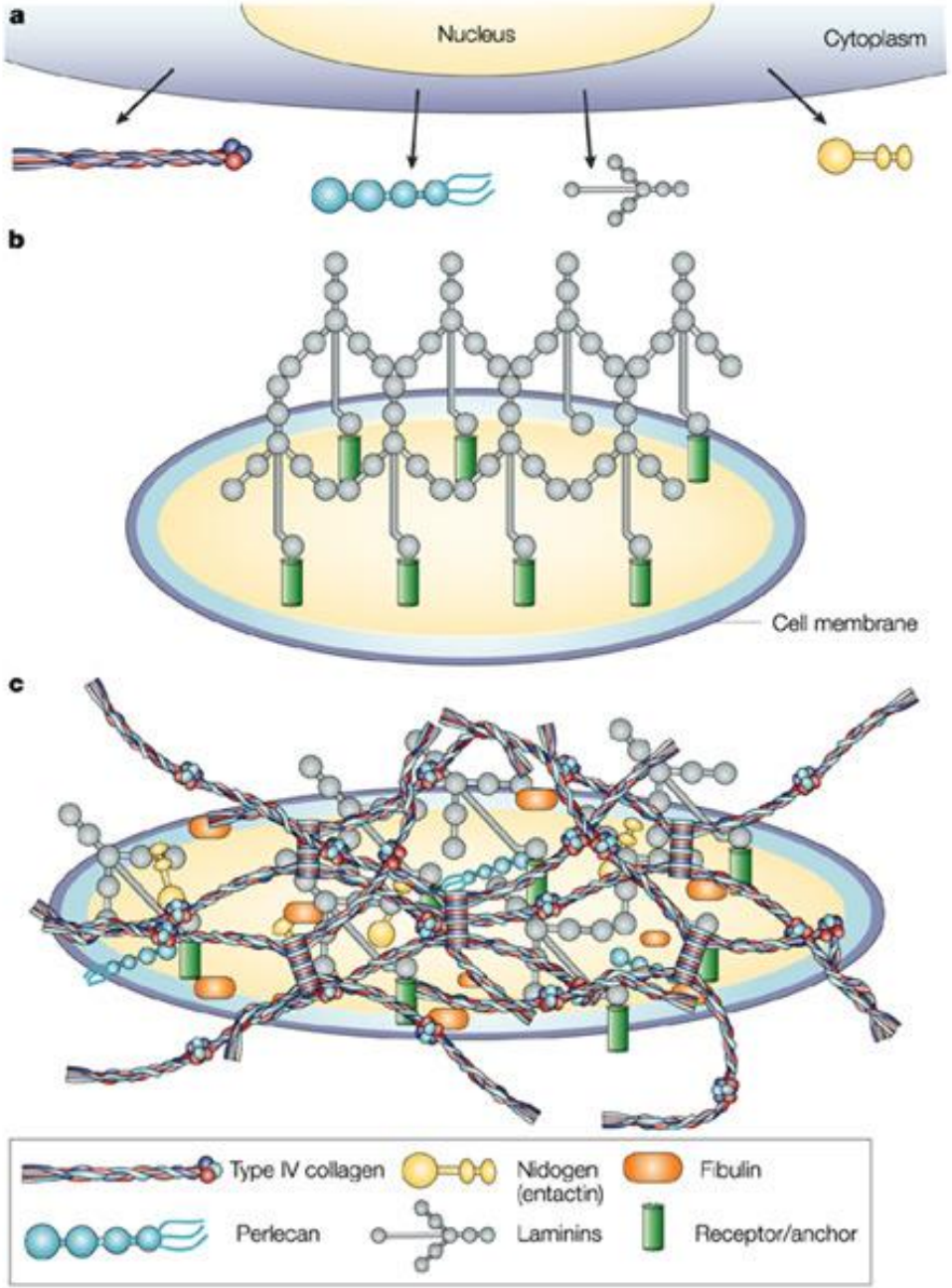
- Ddx=pauci-immune GN, postinfectious GN

seronegative pauci immune crescentic GN

- Working diagnosis is seronegative pauci immune crescentic GN. Her creatinine has significantly dropped from approx 450 to 100 (following
- steroids, plasma exchange, cyclophosphamide). Plan is to recheck ANCA in 3 months


CL
MES
EP
END
CL
A


GLOMERULUS
Capillary loops
Urinary space
Mesangium
Red cell
Proximal tubule
Parietal epithelium
Urinary space
Mesangial cell
Mesangial matrix
Fenestrae in endothelium
Capillary lumen
Parietal epithelium
Basement membrane
Visceral epithelium
Foot processes
Basement membrane
Endothelium
Red cell
Foot processes
B


a
Nucleus
Cytoplasm
b
Cell membrane
c
Type IV collagen
Nidogen (entactin)
Fibulin
Perlecan
Laminins
Receptor/anchor

Nephrotic syndrome

- 11-year old boy
- Nephrotic syndrome, partial response to steroids
- 40 glomeruli are present, none of which are globally sclerosed. Some of the glomeruli show mesangial cell hypercellularity with an increase in mesangial matrix and lobularity. There are focal, segmental sclerotic lesions. No crescents are present.
- working histological diagnosis=primary FSGS