Glomerulonephritides/ glomerulopathies Lecture - II

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Objectives

At the end of this lecture you should be able to

Describe briefly the microscopic features of the kidney (LM - H&E, PAS and silver stains, IF, EM) in

- Acute diffuse proliferative glomerulonephritis
- Rapidly progressive glomerulonephritis
- Minimal change disease
- Membranous glomerulopathy
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis

Acute diffuse proliferative GN

- Typically caused by immune complexes

Exogenous antigens

eg. **Post infectious GN**

- Commonly preceded by streptococcal infection

- Other causes…..

- Pathogenesis …….(Reading assignment)

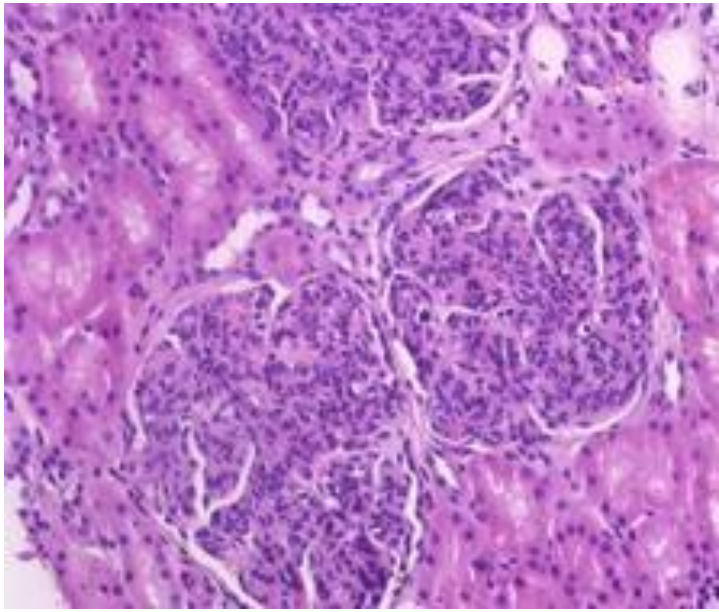
Endogenous antigen - eg. **SLE**

Macroscopy

Enlarged kidneys

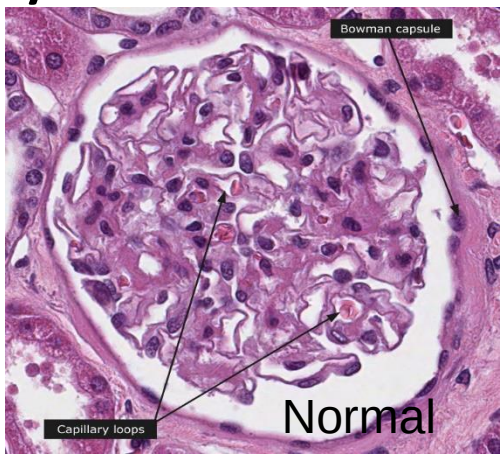
Light microscopic changes

Glomerular changes

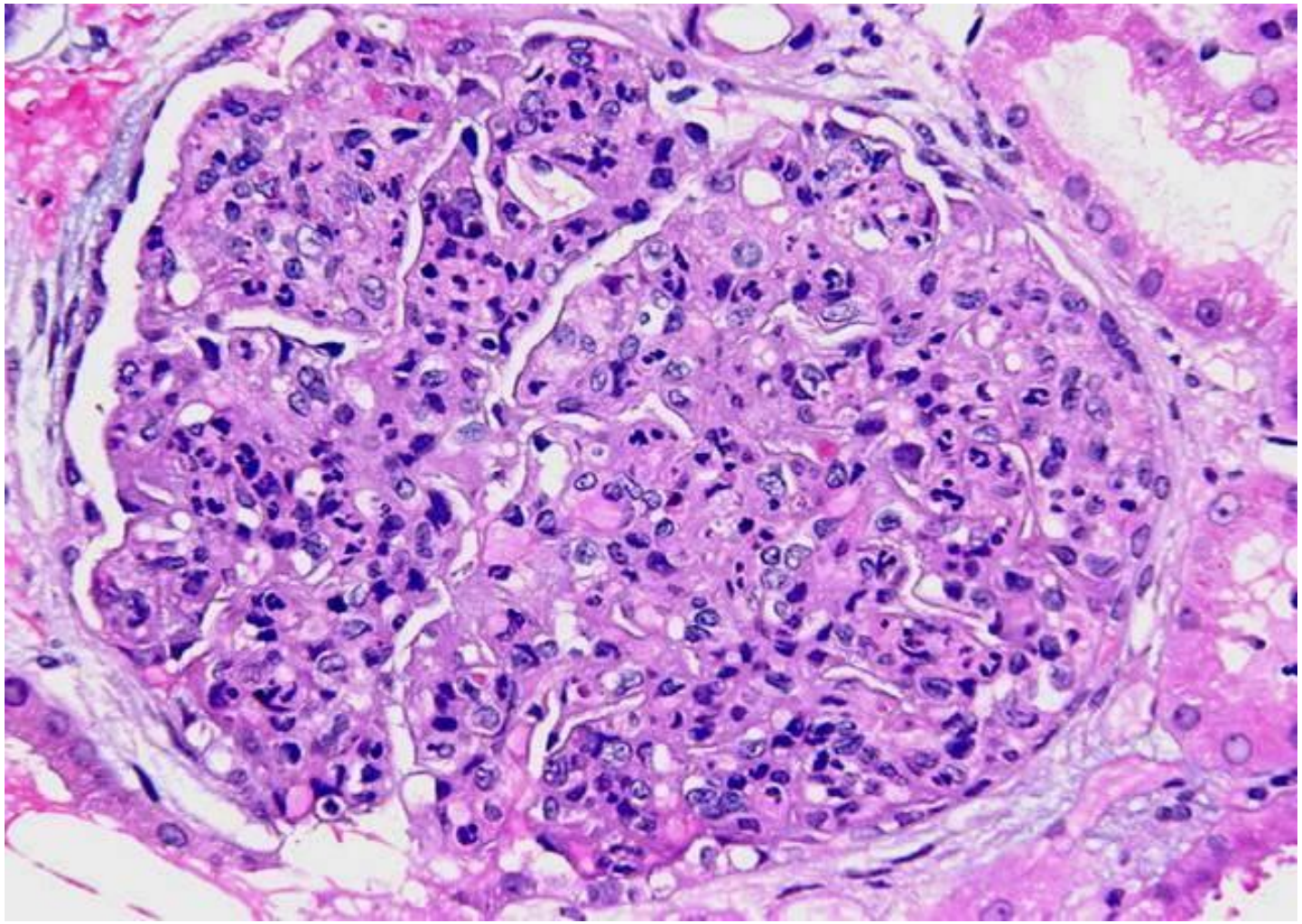


- Diffuse and global involvement

- Hypercellular glomeruli
  - Proliferation of mesangial cells and endothelial cells
  - Infiltration of neutrophils and monocytes
- Glomeruli appear “bloodless”
  - Swelling of the endothelial cells
  - Obliteration of the capillary lumina

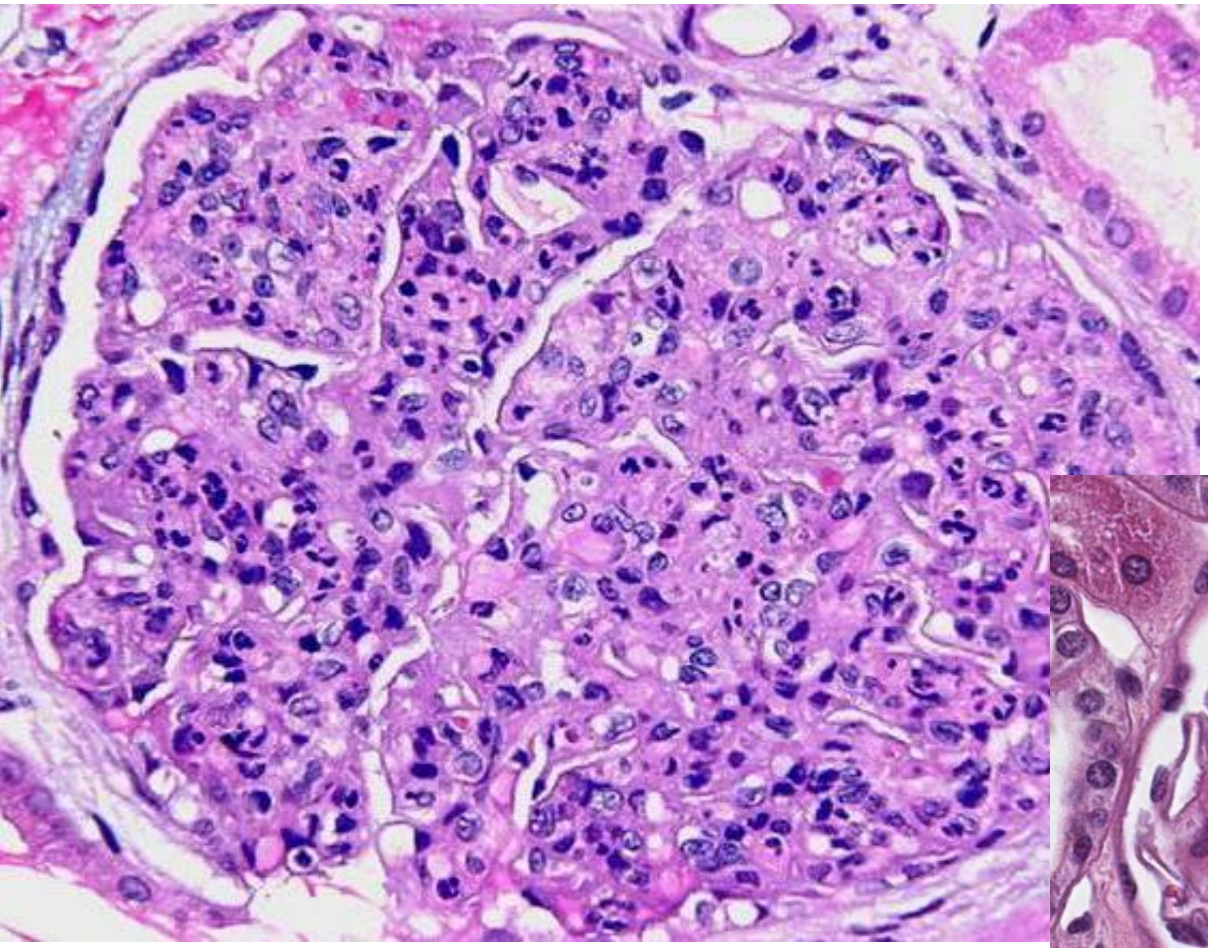


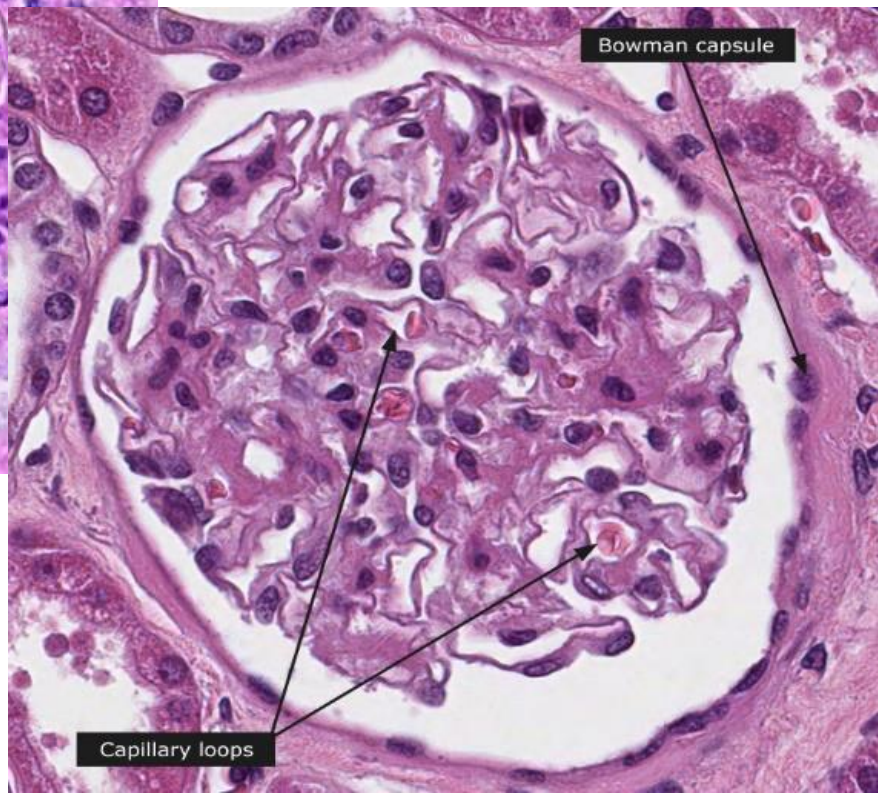
- Hypercellular glomeruli



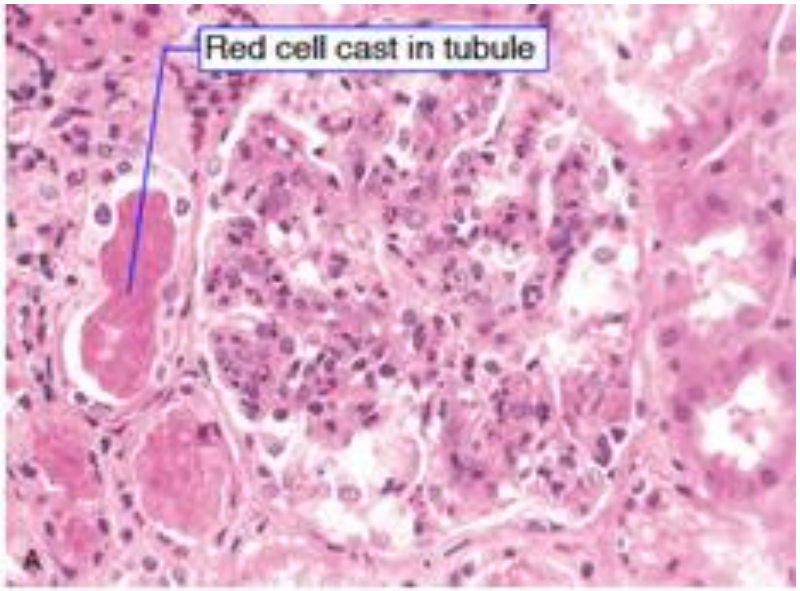
- Increased proliferation of mesangial cells and endothelial cells

- Infiltration of neutrophils and monocytes




Bowman capsule
Capillary loops

Light microscopic changes



Tubules

- Hyaline droplets in the lining epithelium of PCT
- Red cells, red cell casts
- sometimes granulocytes casts in tubular lumina

Interstitium

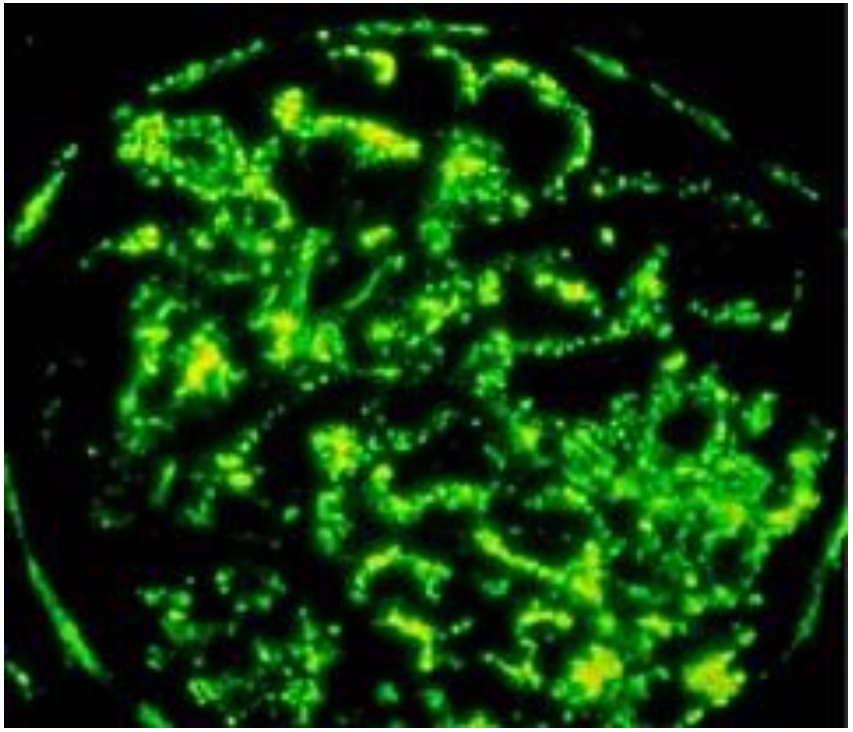
Oedema and inflammation

- Mononuclear cells and neutrophils infiltration

Blood vessels - Normal

Immunofluorescence microscopy (IF)

- **Granular deposits** in the mesangium and along the GBM
  - Immunoglobulins - IgG, IgM
  - Complement - C3



Rapidly Progressive Glomerulonephritis (RPGN)

Type I (Anti-GBM- antibody -induced disease)

Limited to kidney

Goodpasture syndrome

Type II (Immune complex deposition)

Primary

Post infectious GN

Lupus nephritis

Henoch-Schonlein purpura (IgA nephropathy)

Type III (Pauci-immune)

Primary

ANCA associated

Wegener granulomatosis

Microscopic polyangitis

RPGN

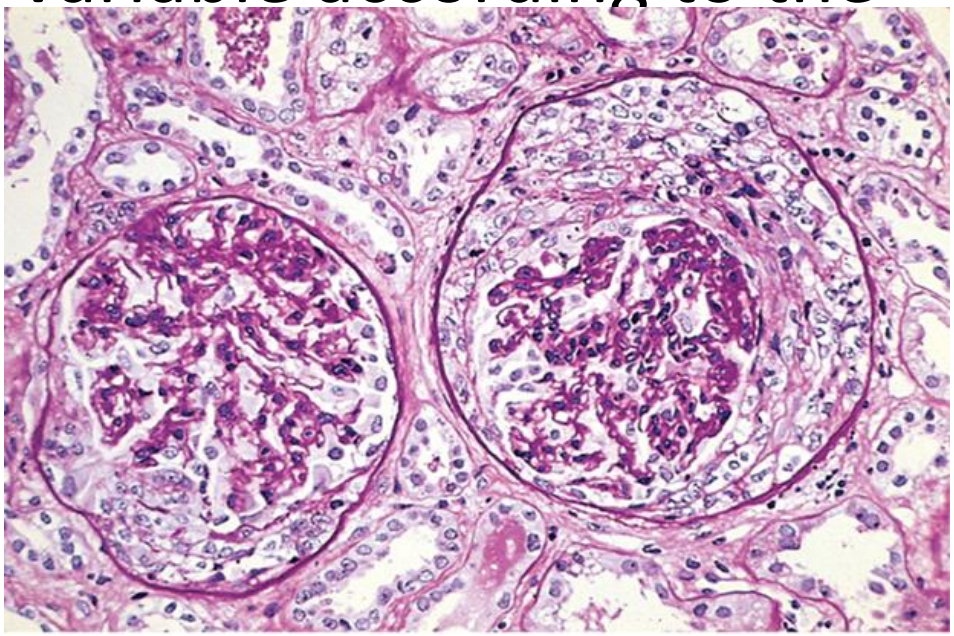
- Macroscopy

  - Kidneys are enlarged and pale

  - Petechial haemorrhages on the cortical surface

- Microscopy

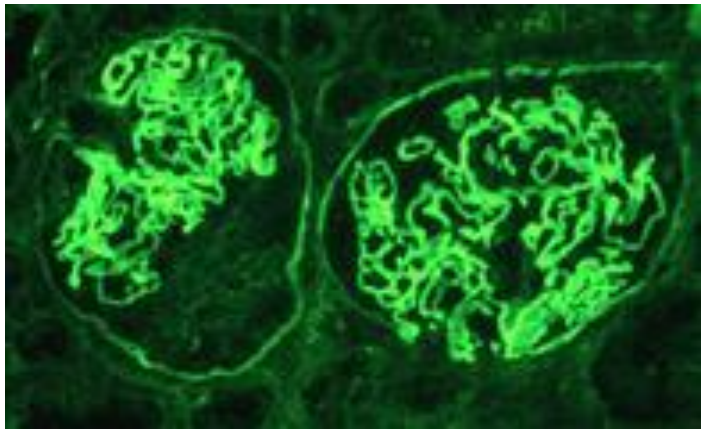
  Glomerular pathology is variable according to the underlying cause

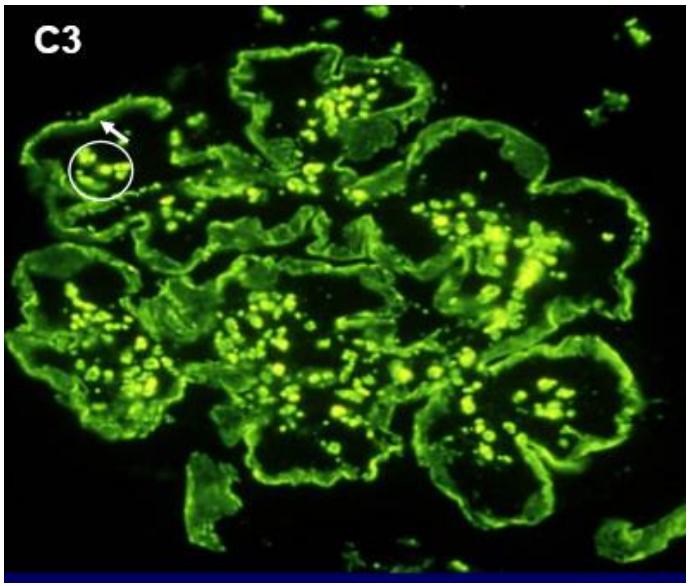


Dominant feature

- **Crescent formation**

RPGN - IF



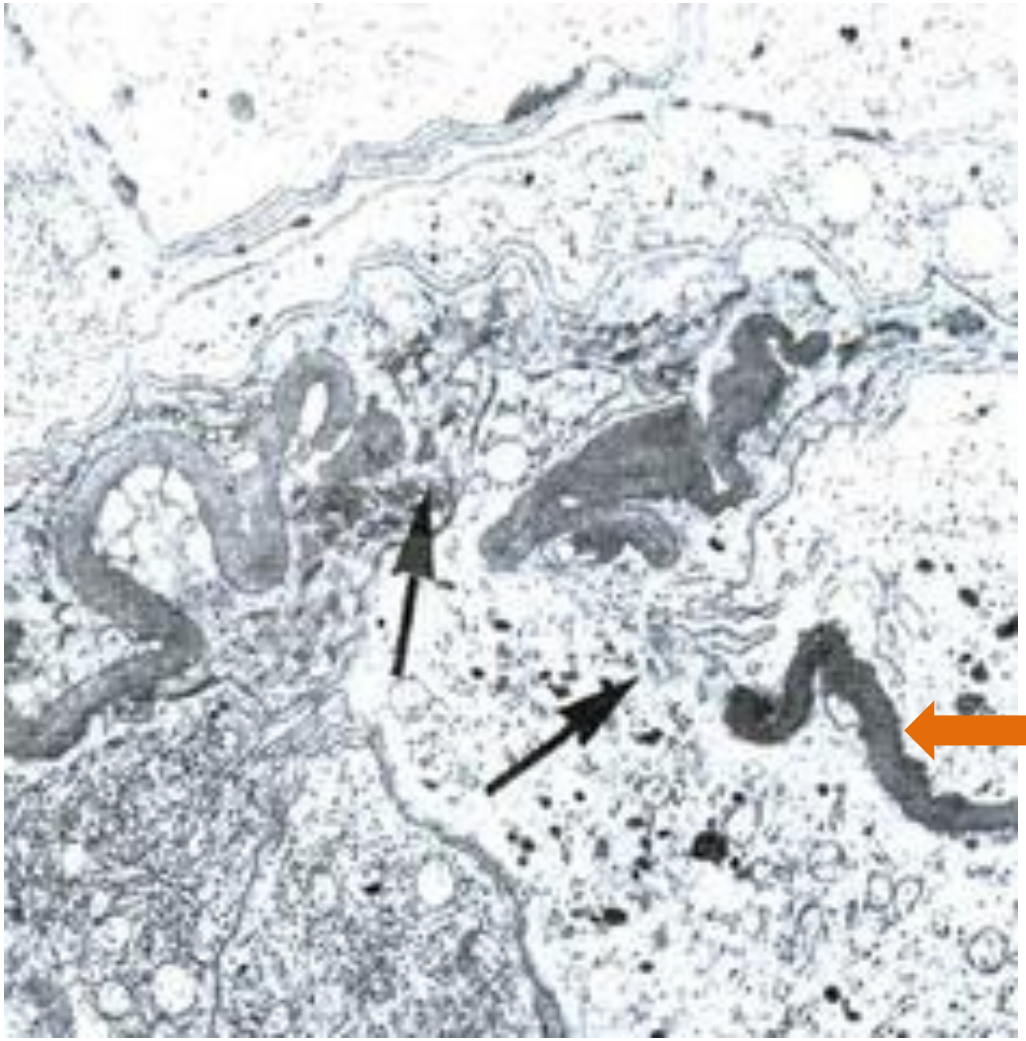


Type I RPGN
Linear deposits of IgG and C3

Type II RPGN
Granular deposits of

Type III RPGN
- No deposits

RPGN - EM



GBM

Rupture of the GBM

Minimal change disease

- Pathogenesis - Read

Minimal - Change Disease

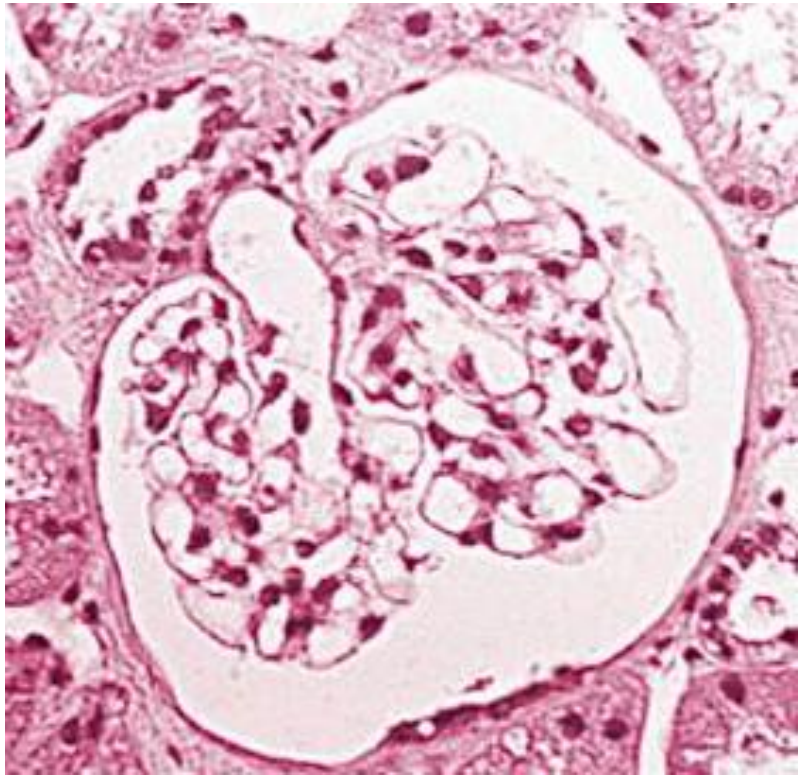
Microscopic changes

LM

- Glomeruli - Normal
- Proximal convoluted tubules

  - lipid and hyaline/ protein droplets

  - Hyaline casts



IF Microscopy

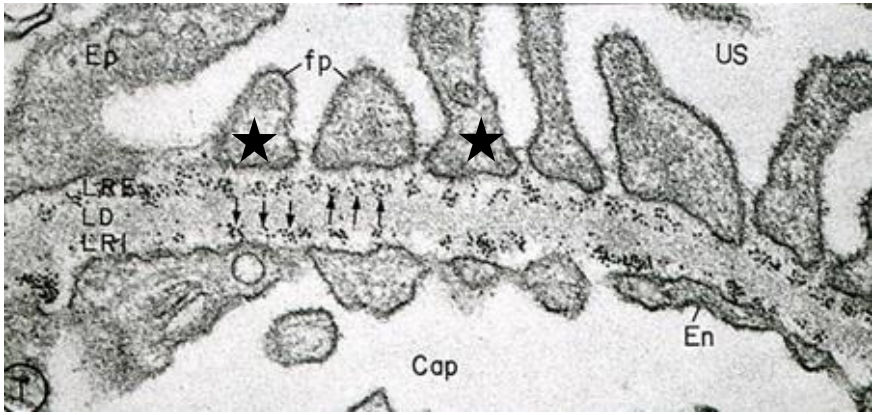
No Immunoglobulin or complement deposits

EM

- No immune complex deposits
- **Characteristic lesion is in the visceral epithelial cells**

  The foot processes are totally obliterated

  - Flattening , retraction and swelling of the foot processes



Normal foot processes (fp)

BM is covered by a “sheet” of epithelial cytoplasm

Membranous nephropathy

- Primary

- Secondary

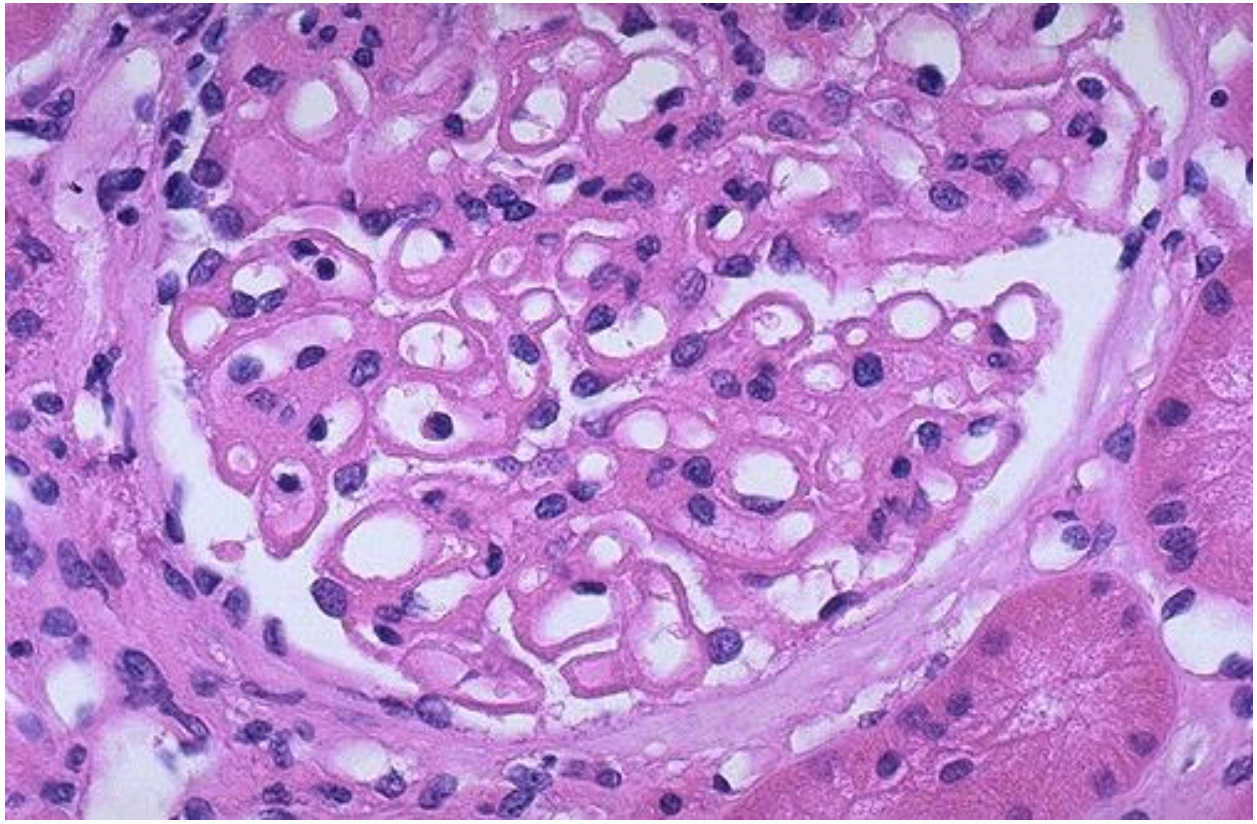
- Drugs **-** read
- Underlying malignant tumours

  (carcinoma - lung , colon, melanoma)
- SLE
- Infections(Chronic hepatitis B, C, syphilis, schistosomiasis, malaria)
- Other autoimmune diseases eg. Thyroiditis

Light microscopic changes

- Uniform , diffuse thickening of the GBM

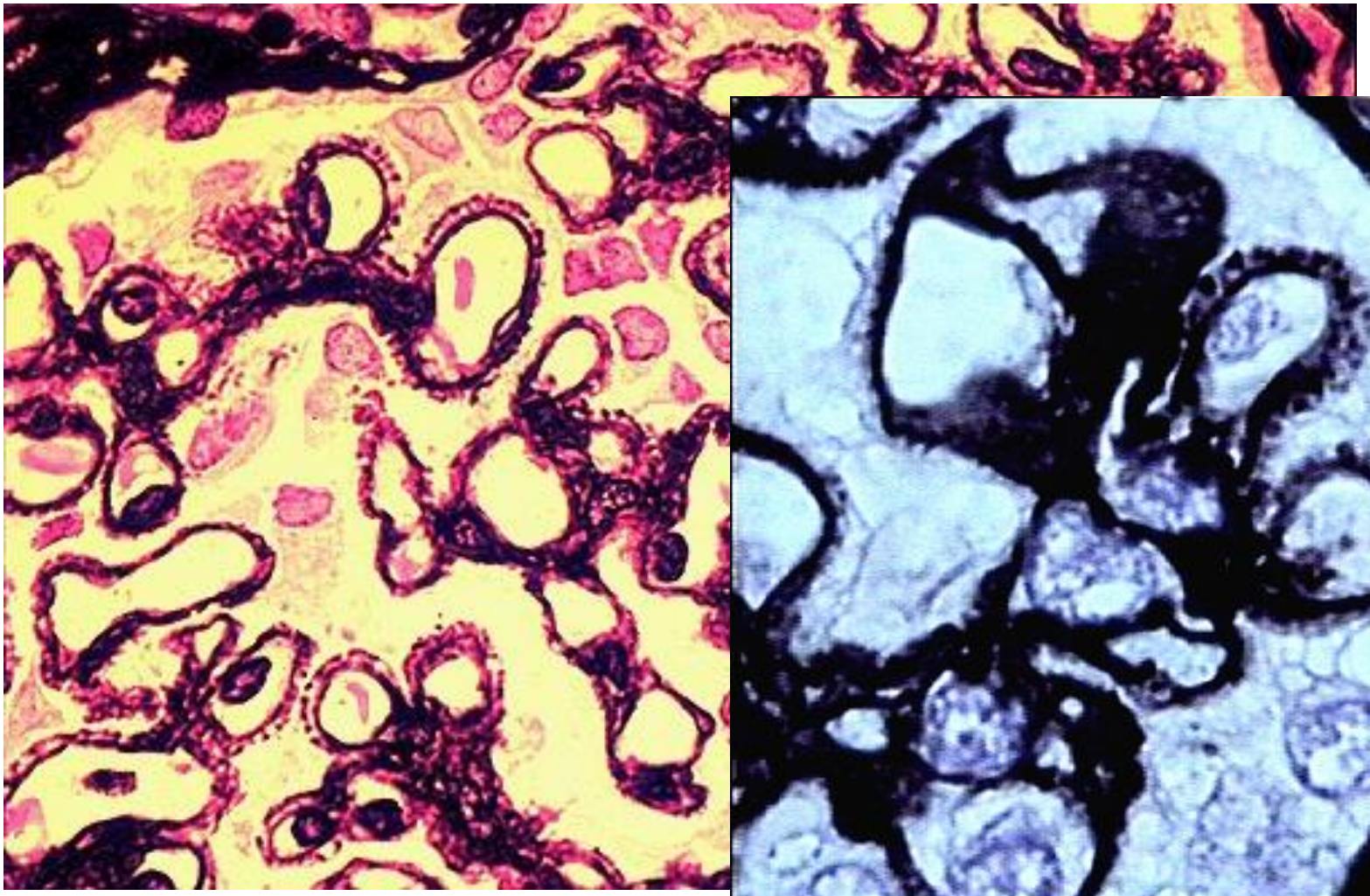
(PAS stain highlights the thickening)



Light microscopic changes - Membranous glomerulopathy

Special stains - Silver stain

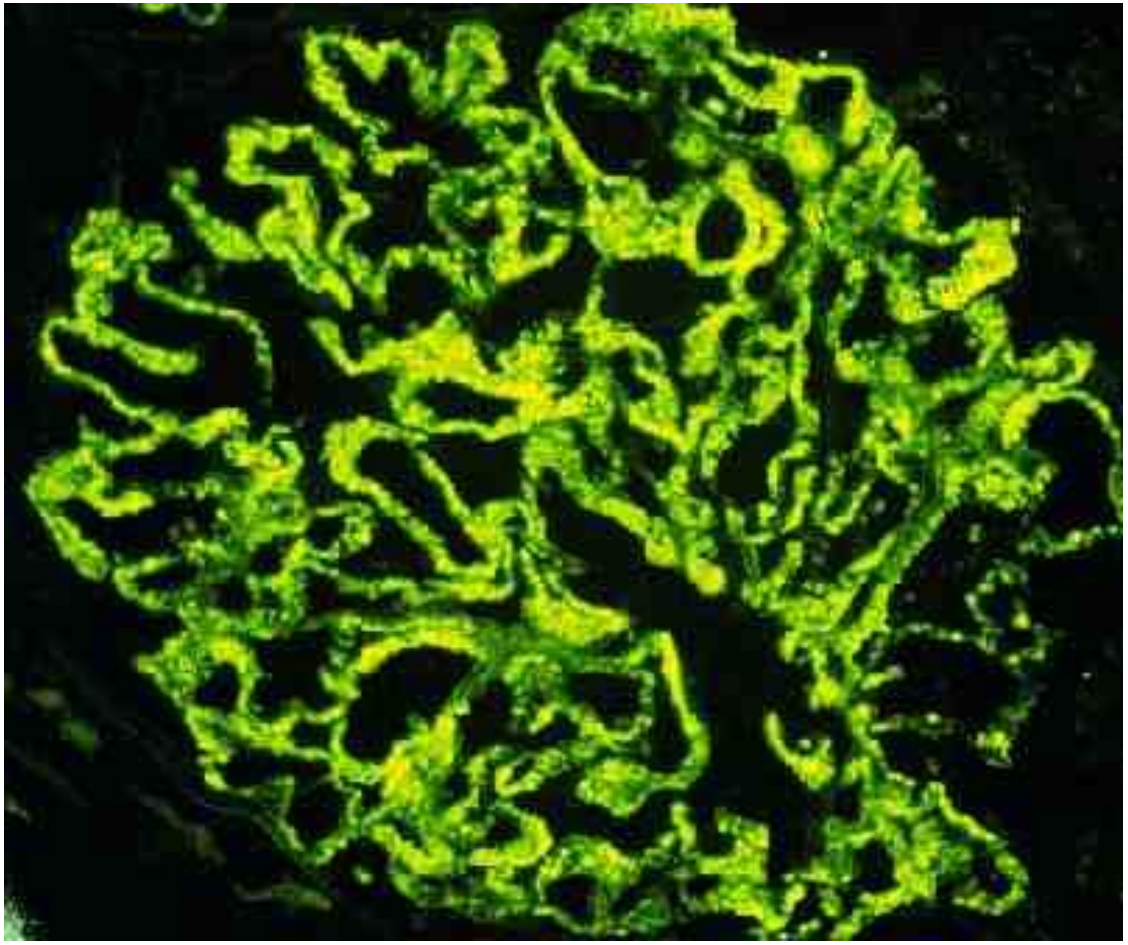
- Irregular spikes in the BM



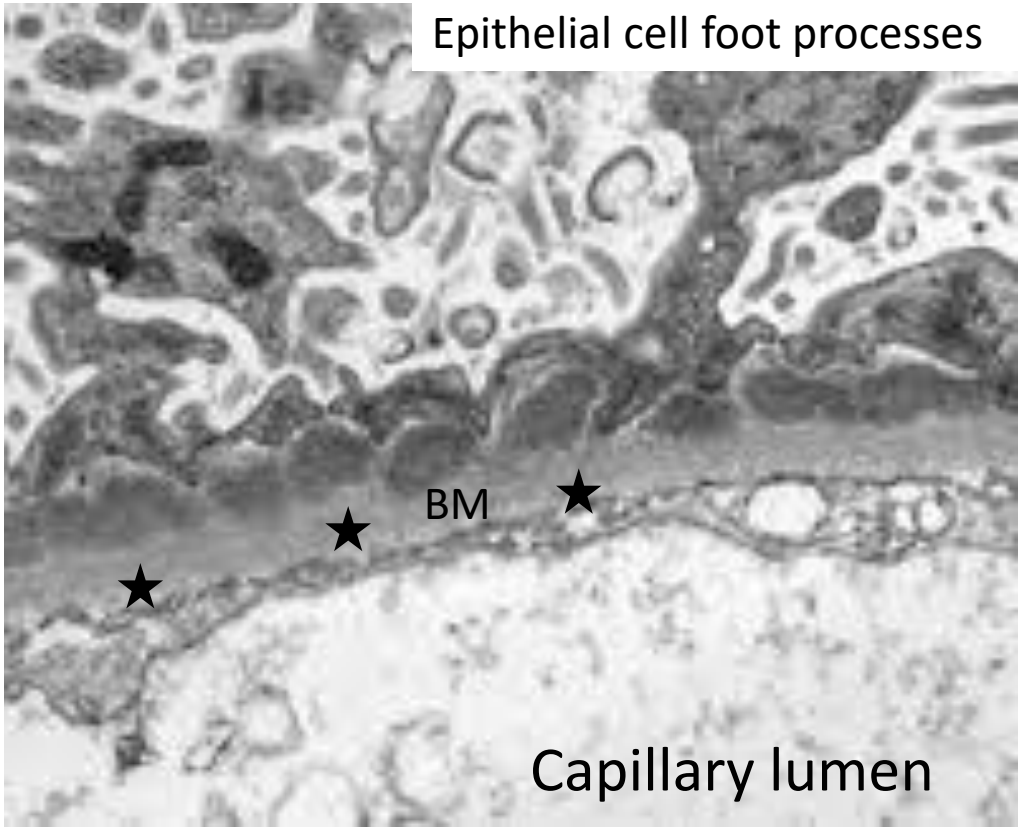
- Immunofluorescence microscopy

  Membranous glomerulopathy

  - **<u>Granular deposits</u>** containing **both immunoglobulins** and **complement components**



Electron microscopy - Membranous glomerulopathy



GBM - Thickened due to deposition of immune complexes between the BM and the epithelial cells

Subepithelial deposits (dark areas ★)

Focal segmental Glomerulosclerosis - FSGS

- Primary
- Secondary

- Associated with other known causes

HIV- associated nephropathy

Heroin nephropathy

Sickle cell disease

- Secondary to other glomerulopathies

eg. Ig A nephropathy

- Occur as an adaptation to loss of renal tissue

FSGS

- Light microscopy

Glomeruli

- Segmental sclerosing lesions
- Rest of the glomerular tuft appears normal

Tubules

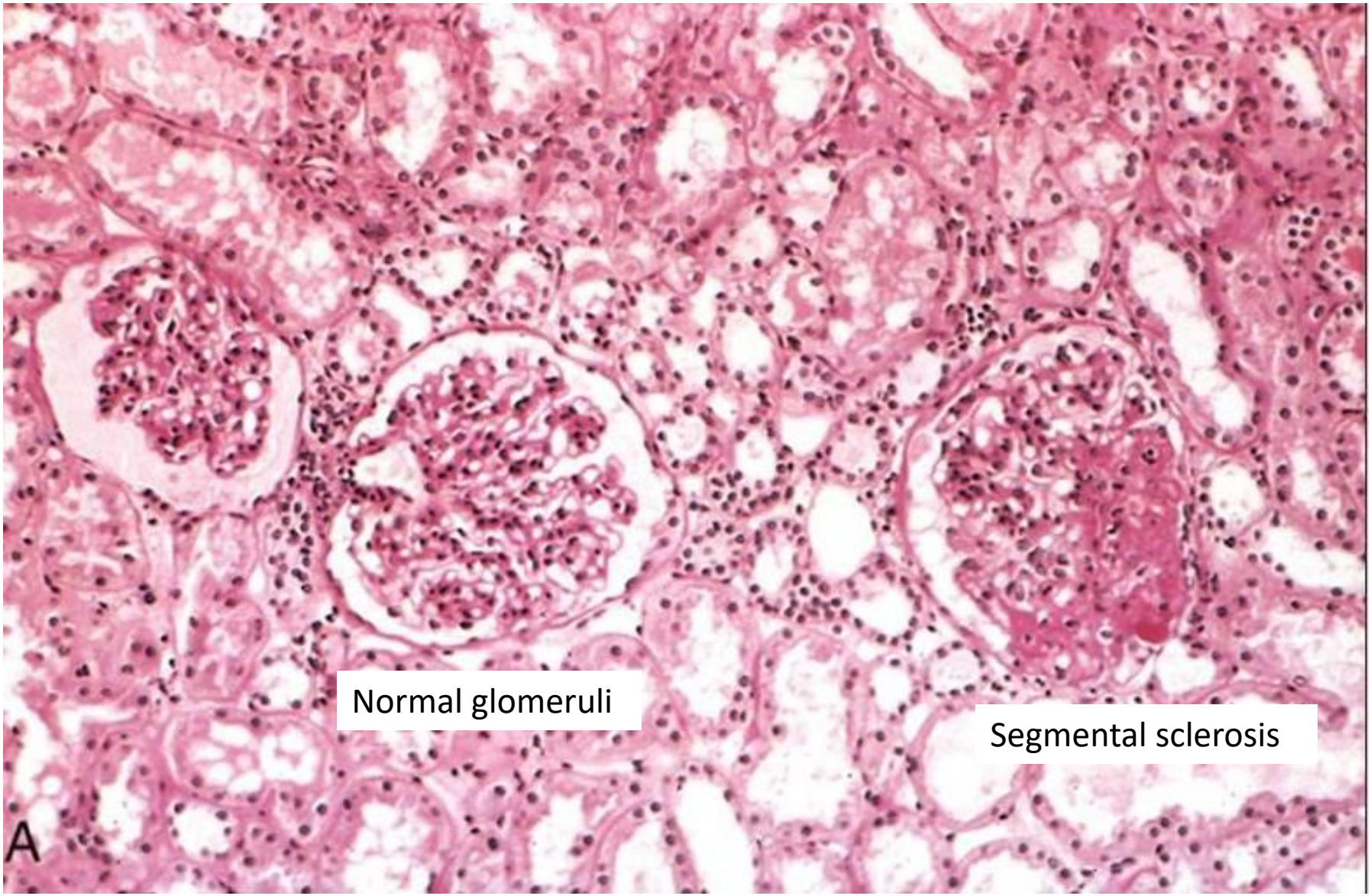
- Atrophy

Interstitium

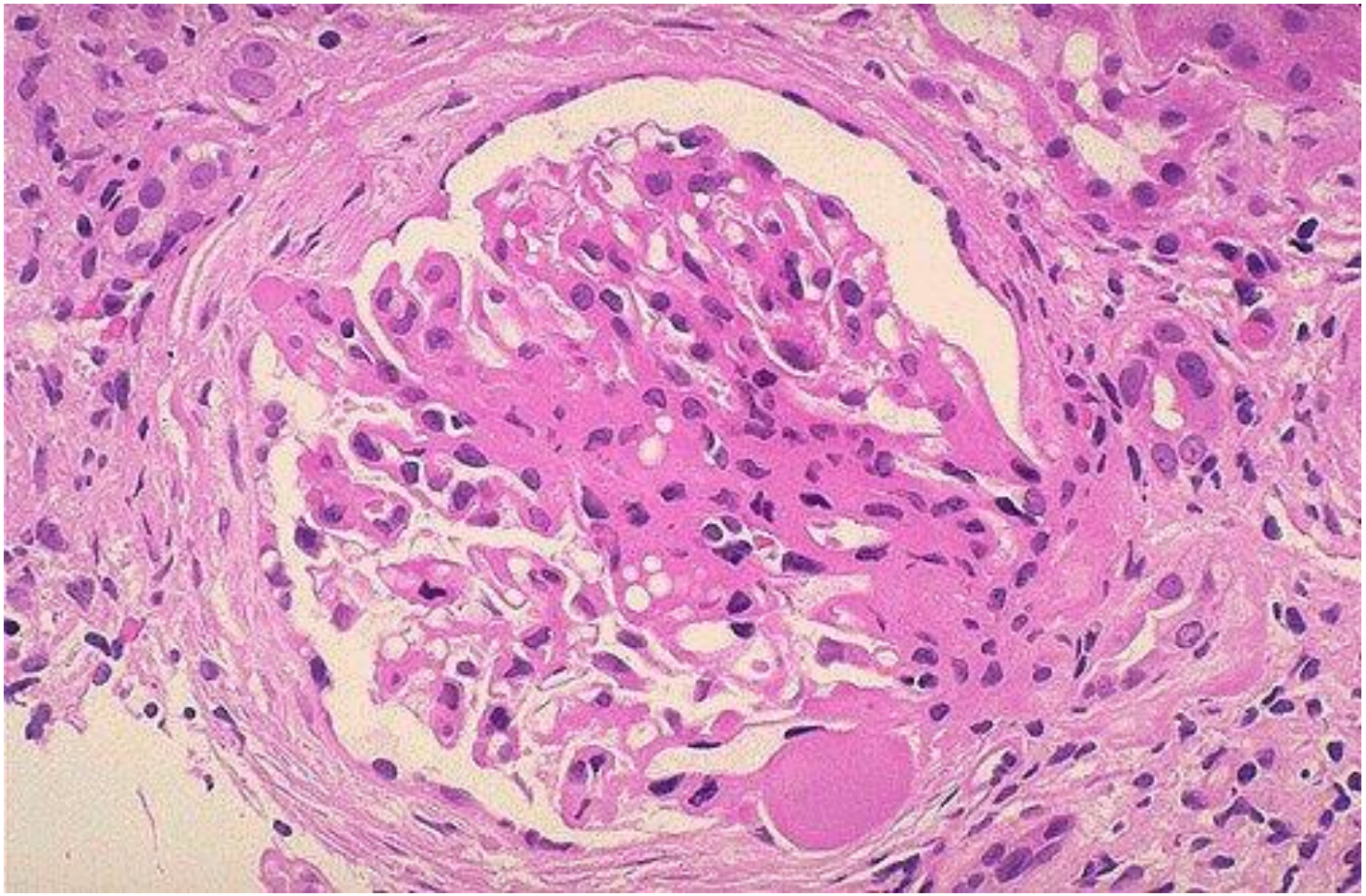
- Fibrosis

Blood vessels (afferent arterioles)

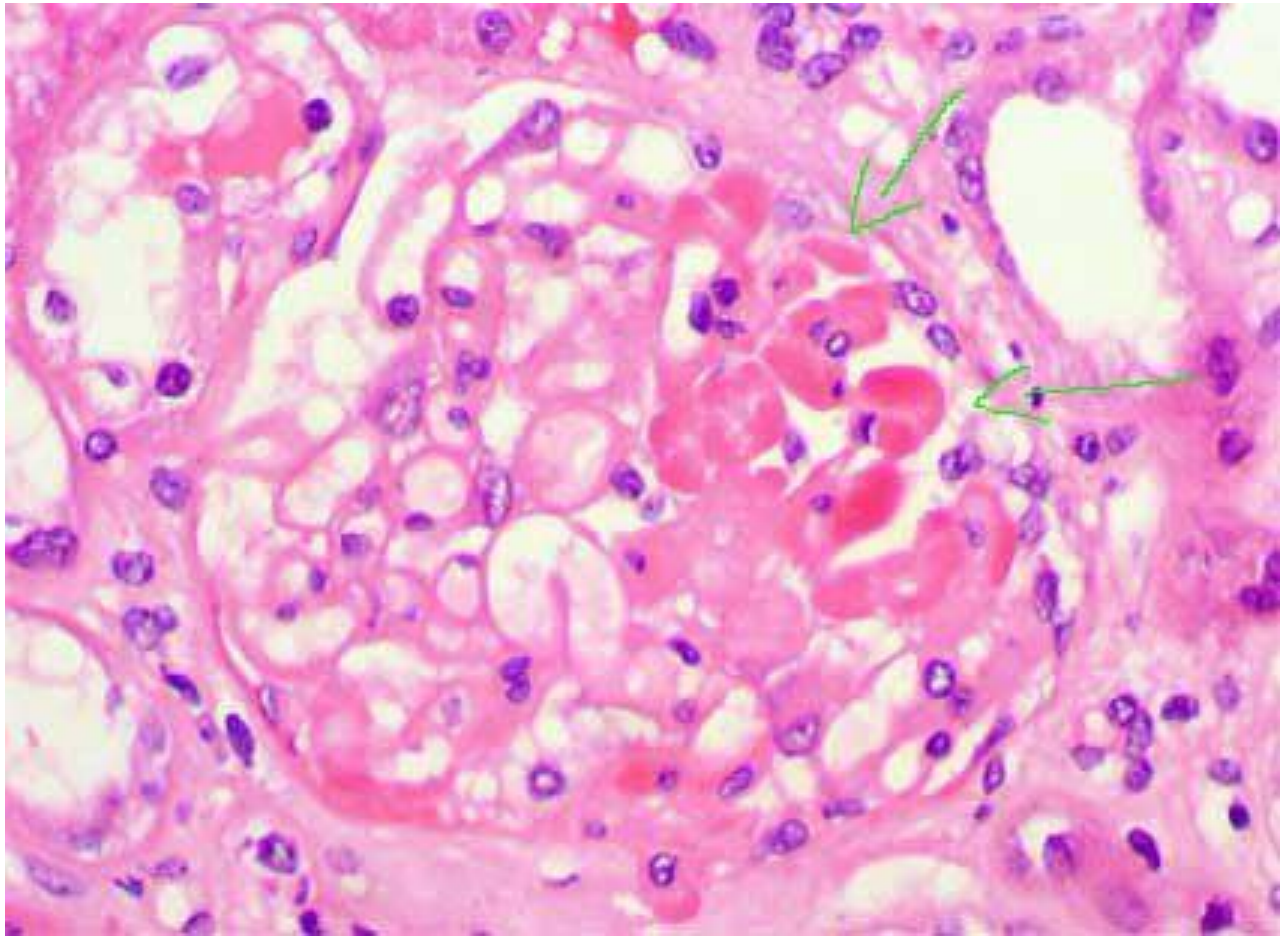
- Hyalinosis and thickening


Normal glomeruli
Segmental sclerosis
A

FSGS - Segmental sclerosis

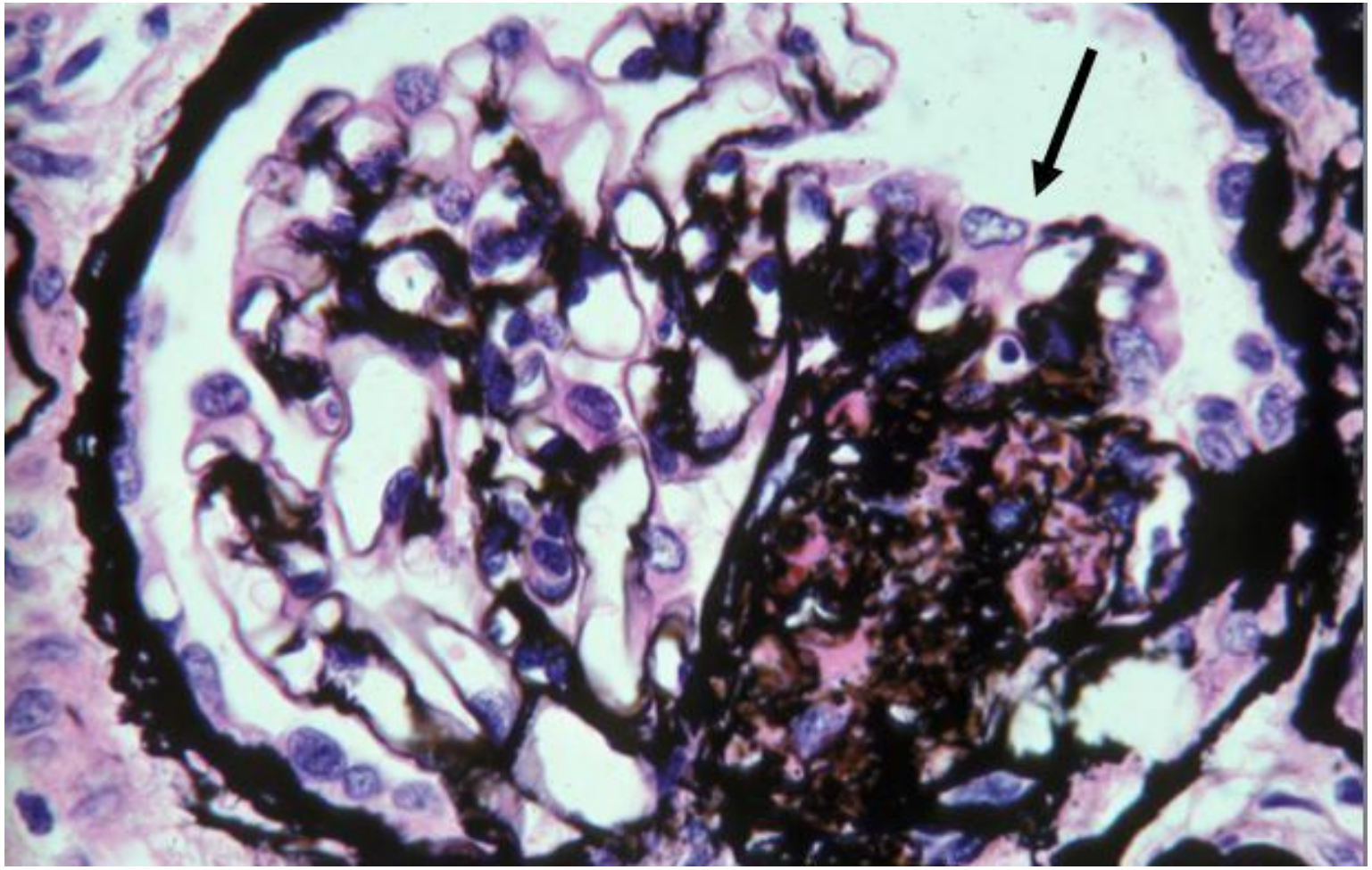


FSGS - Hyalinosis



Note - Deposition of pink colour material in the capillary walls and occluding them

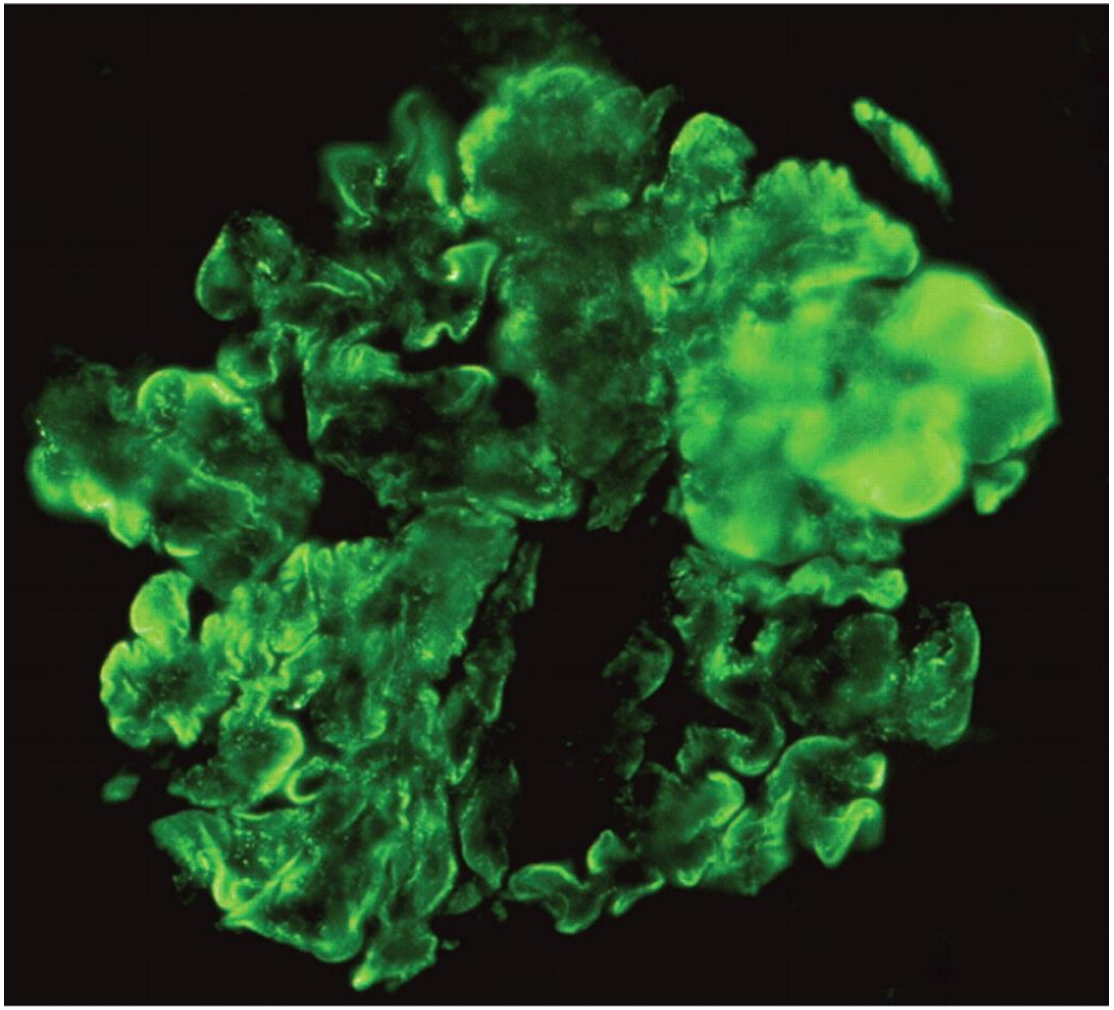
FSGS - Silver stain



Highlights the deposits

FSGS - IF

- IgM and C3 in sclerotic areas and / in the mesangium



Membranoproliferative glomerulonephritis

- Also called mesangiocapillary GN

- Primary MPGN

  Type I, Type II } LM similar; IF and ultra structural features differ

- Secondary MPGN

  Chronic immune complex disorders

  SLE, Hepatitis B infection, Hepatitis C infection, endocarditis, chronic visceral abscess, HIV infection, Schistosomiasis

  Alpha - 1 antitrypsin deficiency

  Malignant diseases – CLL, lymphoma

  Hereditary

Membranoproliferative Glomerulonephritis (MPGN)

- Characterized by
  - **Alterations in GBM**
  - **Proliferation of glomerular cells**

    Predominantly composed of mesangeal cells

    + endothelial cells
  - **Leucocyte infiltration**

Light microscopy

Glomeruli (Diffuse/ focal involvement)

- All glomeruli are enlarged

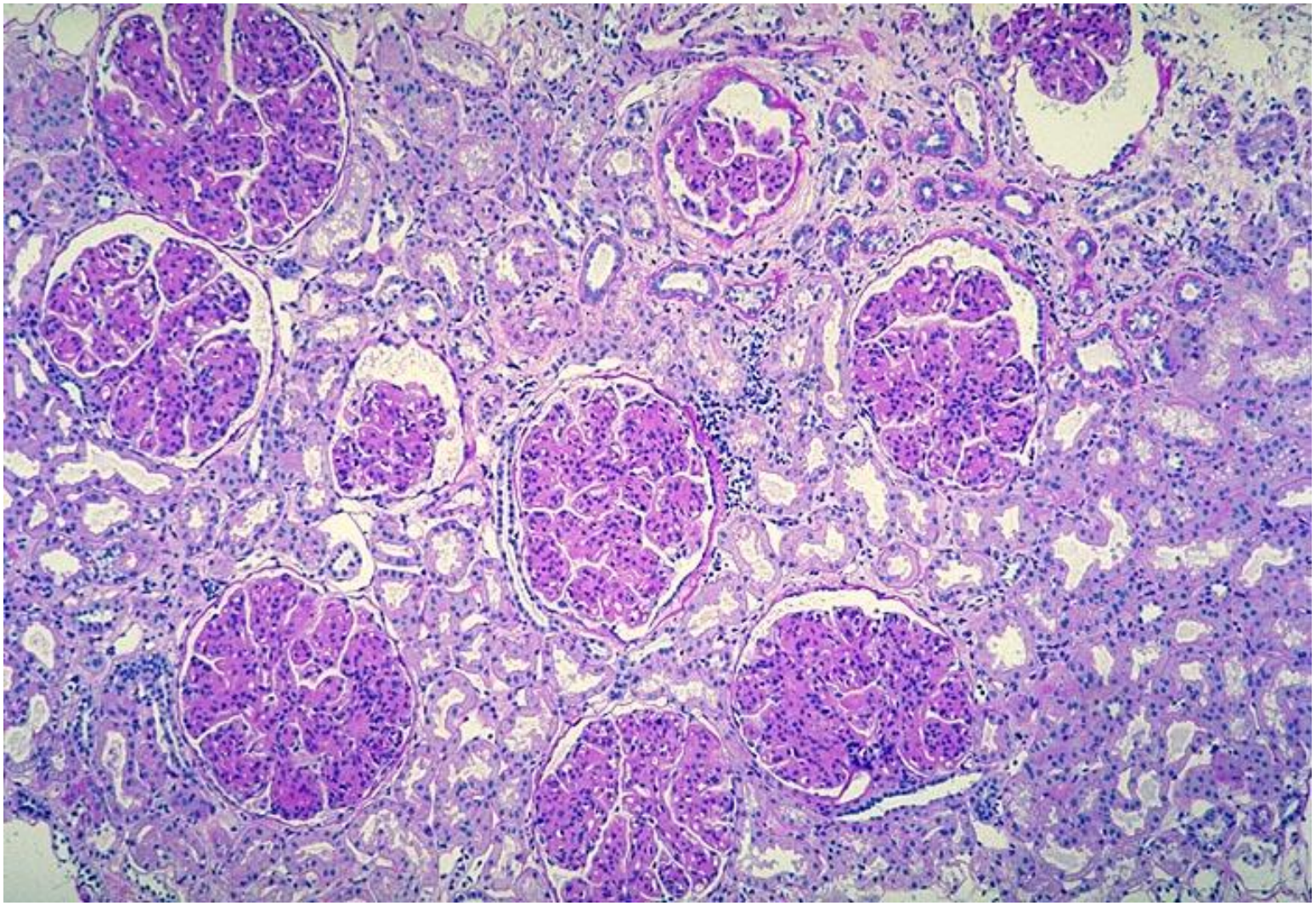
  - Lobular pattern becomes prominent

  - Hypercellular glomeruli

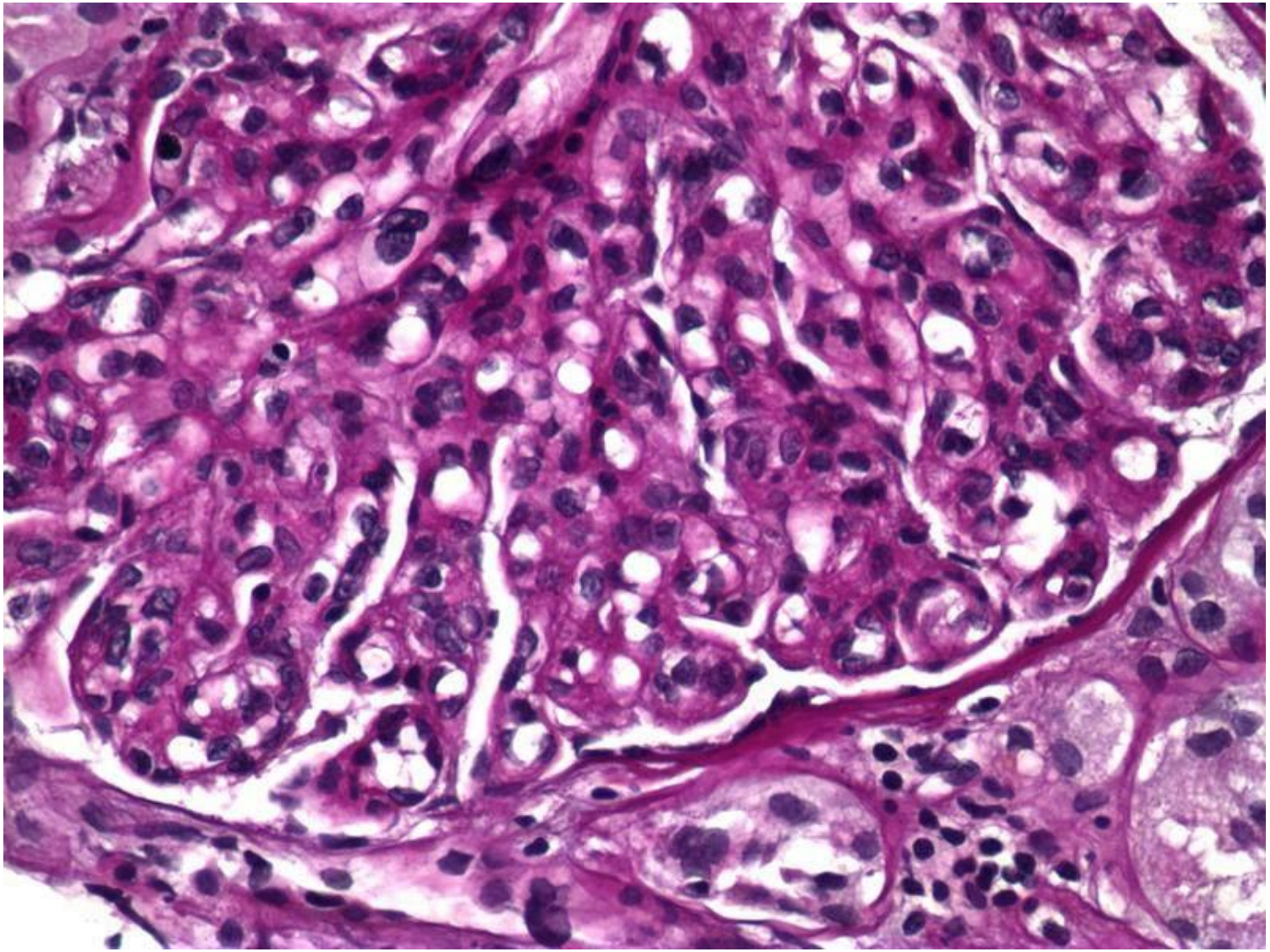
  - Proliferation of mesangial cells and capillary endothelial cells

  - Infiltration of leucocytes

- Crescents may be present
- Increased mesangial matrix
- Thickened GBM



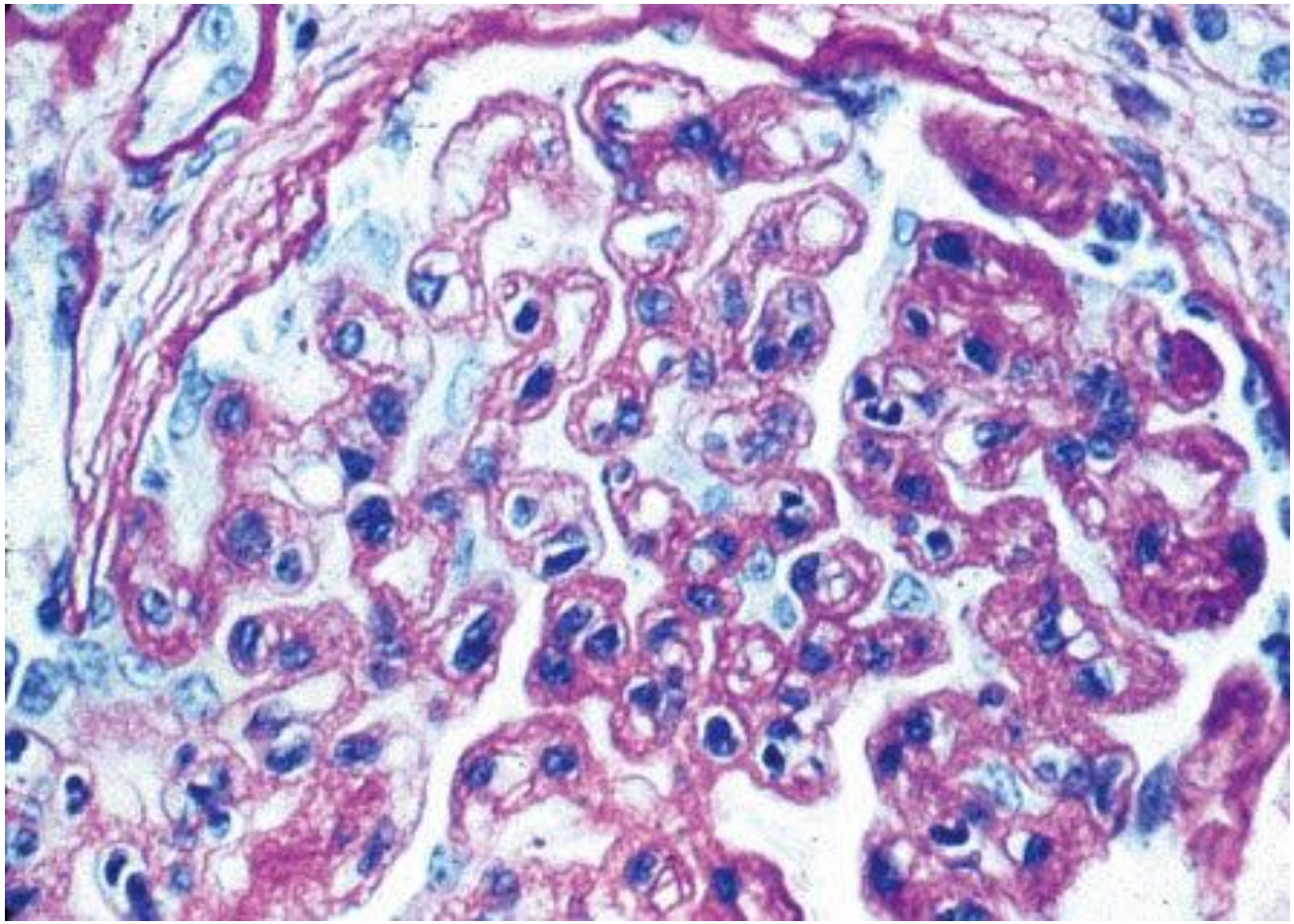
Diffuse glomerular involvement
Accentuated lobular pattern



MPGN - Increased mesangial cells and capillary endothelial cells
Thickened GBM

Membranoproliferative/ mesageocapillary glomerulonephritis

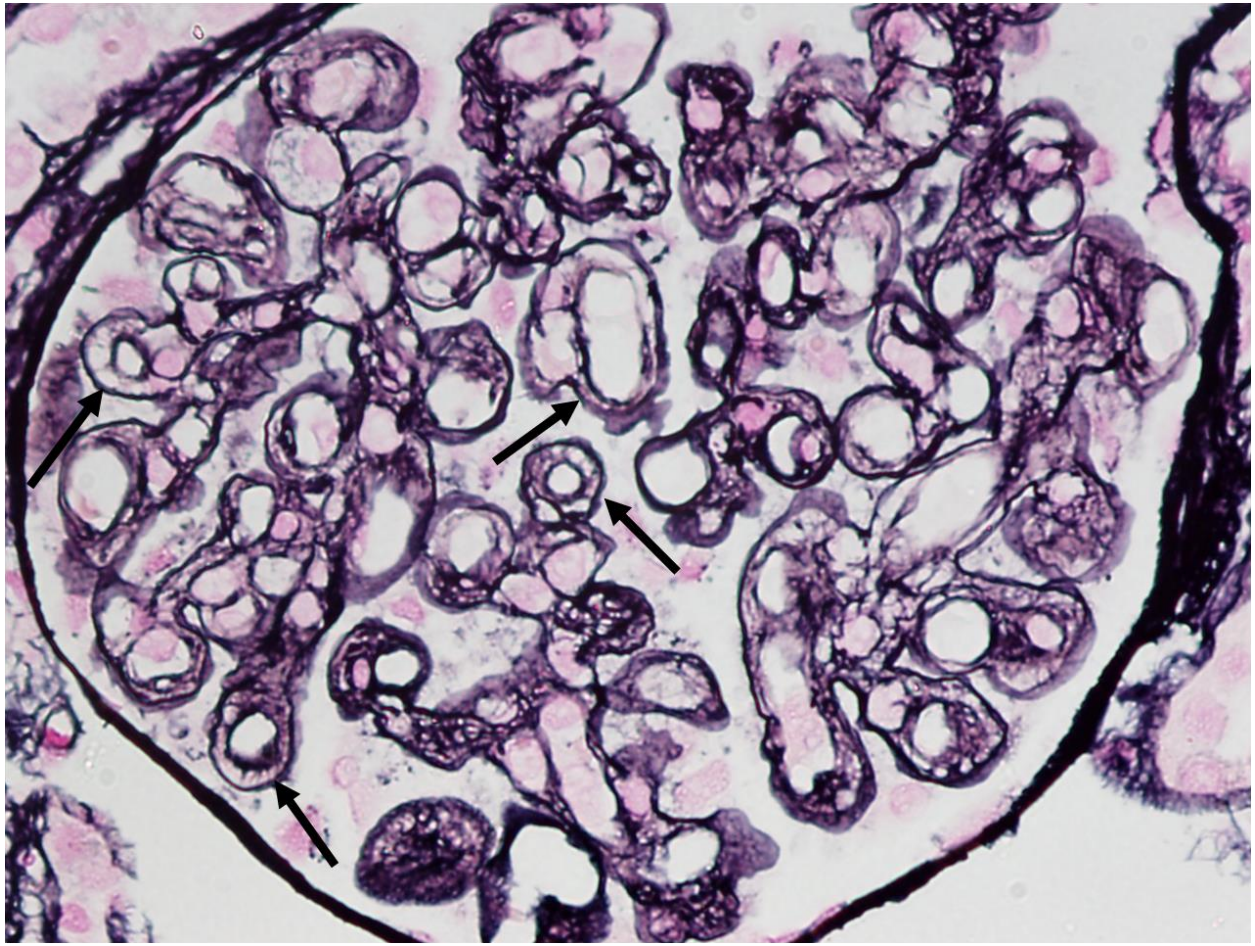
MPGN - PAS stain



Note : Thickened glomerular capillary walls

MPGN

Light microscopy - Silver stain



Glomerular capillary walls have double contours/
"Tram track" appearance

Renal biopsy

- Macroscopy : Two cores of tissue, 12 mm and 10 mm in length
- Microscopy:
- Section shows two cores of renal tissue with nine glomeruli

  All these glomeruli show thickening of the glomerular capillary basement membrane .

  There is no mesangial cell proliferation or infiltration of neutrophils.

  PAS stain highlights the global thickening of the basement membrane

  The tubules show eosinophilic hyaline deposits.

  There is no significant pathology in the Interstitium or the blood vessels

Summary

Now you should be able to

Describe briefly the microscopic features of the kidney (LM - H&E, PAS and silver stains, IF, EM) in

- Acute diffuse proliferative glomerulonephritis
- Rapidly progressive glomerulonephritis
- Minimal change disease
- Membranous glomerulopathy
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis

Reading assignment

- List the secondary causes for each of the glomerulopathy discussed above
- Pathogenesis of acute post streptococcal glomerulonephritis
- Pathogenesis of minimal change disease