Glomerulonephritides/ Glomerulopathies - 1

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Department of Pathology

Objectives

At the end of this lecture you should be able to

- Discuss the basic pathological changes occur in the glomeruli in glomerular diseases
- Describe the changes in a renal biopsy in glomerular diseases
- Classify glomerulopathies

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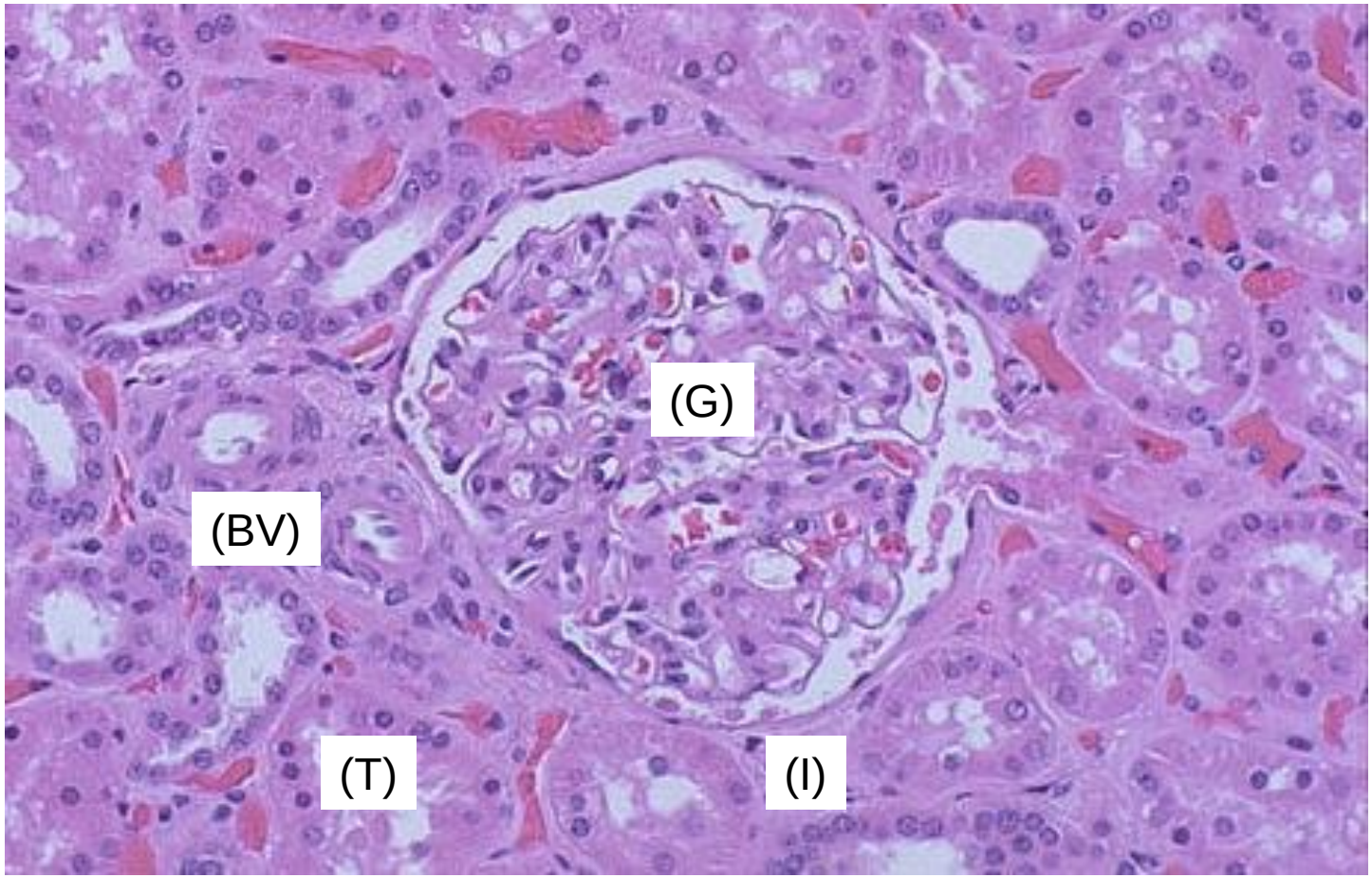
Kidney
Basic morphologic compartments



Glomerulus (G) Tubules (T)

Interstitium (I) Blood vessels (BV)

Normal glomerulus

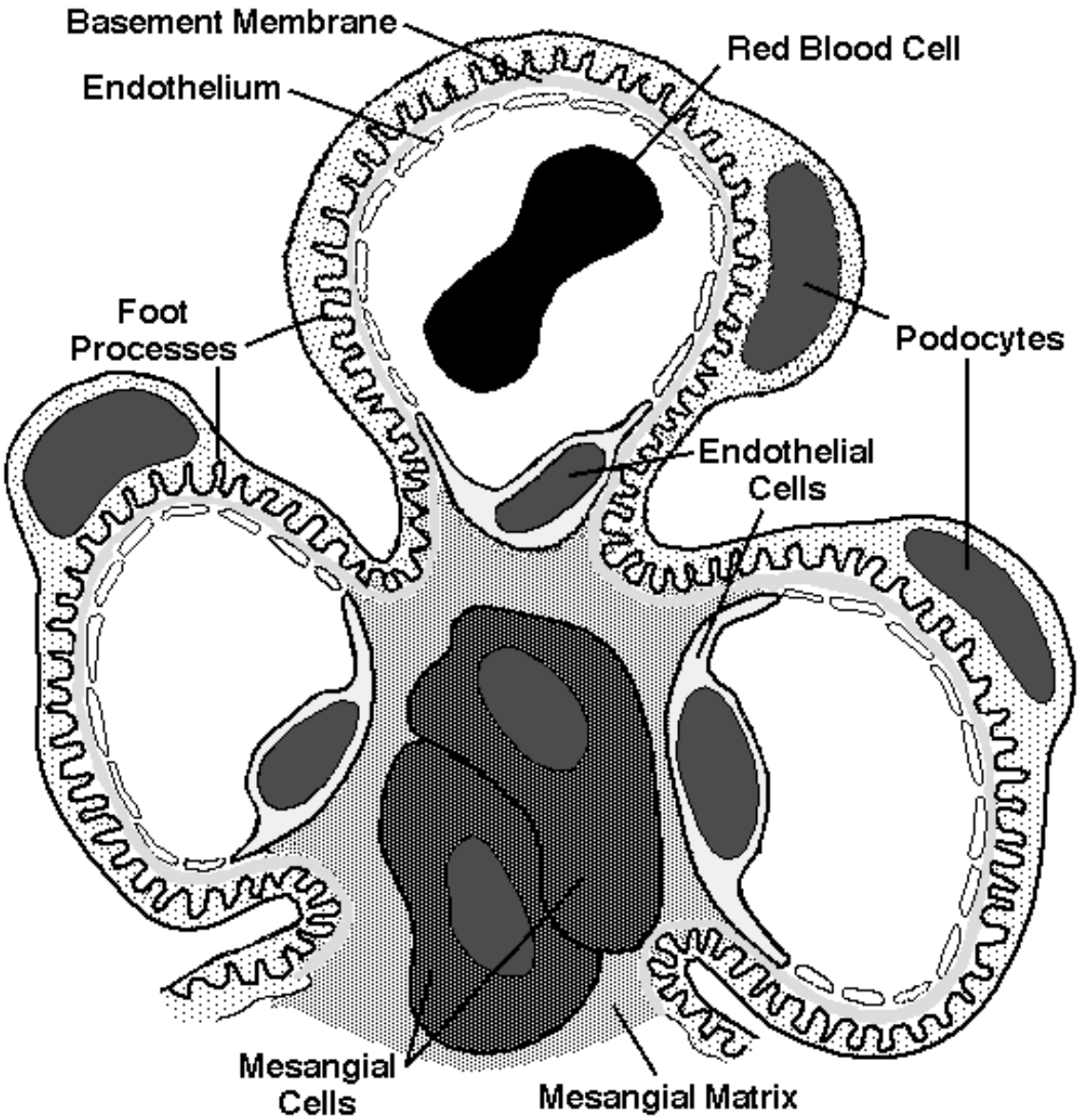
- Anastomosing network of capillaries

Endothelial cells

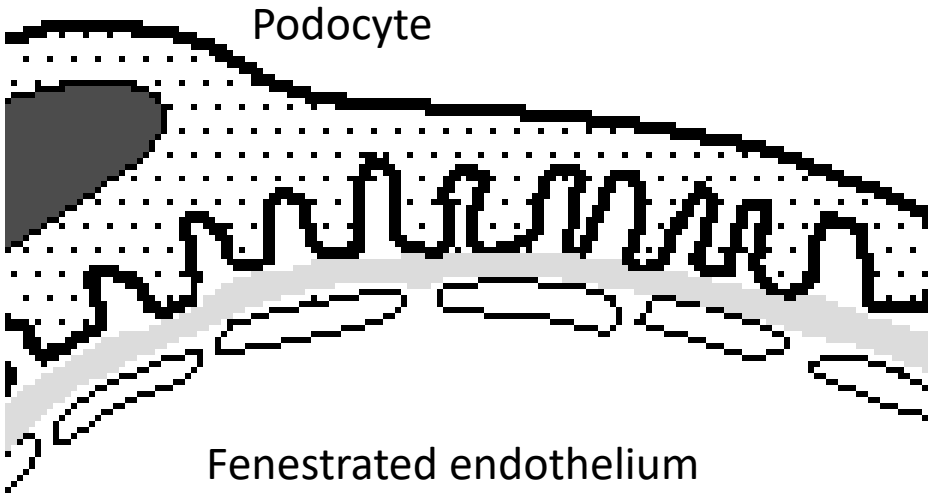
Mesangial cells

Bowman space

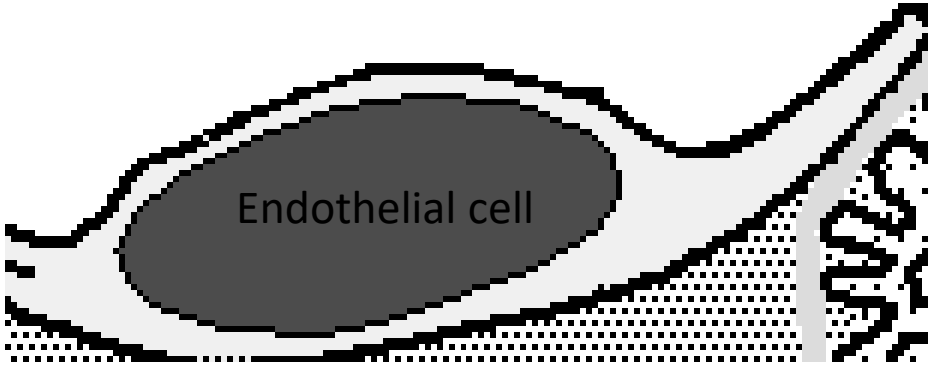
Structure of a Glomerulus



Structure of a Glomerulus



Capillary lumen



Glomerular diseases - Pathogenesis

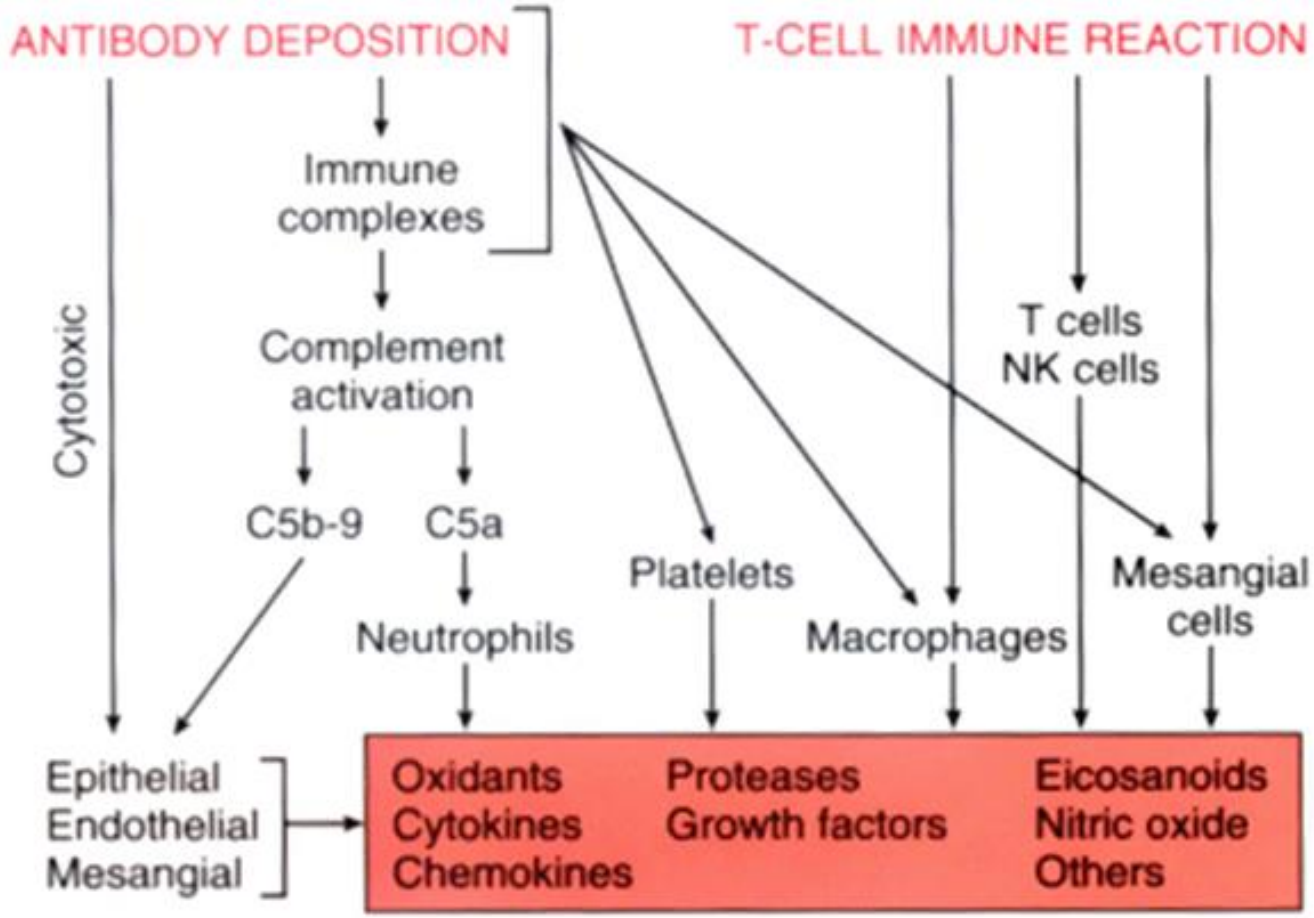
- Most are immunologically mediated

- Glomerular deposits of **immunoglobulins** and **components of complements** are found in most primary glomerulopathies and many of the glomerular diseases secondary to systemic diseases

Immune mechanisms of glomerular injury

- Antibody mediated injury
- In situ immune complex deposition
- Circulating immune complex deposition
- Cytotoxic antibodies
- Cell-mediated immune injury
- Activation of alternative complement pathway

How does the glomerular damage occur?



Mediators of immune glomerular injury including cells and soluble mediators

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Glomerular diseases
Basic pathological changes

- Hypercellularity of the glomeruli
- Thickening of the basement membrane (BM)
- Hyalinosis / sclerosis of the glomeruli

Hypercellularity of the glomeruli

- Increase number of cells in the glomerular tufts is a result of

Cellular proliferation

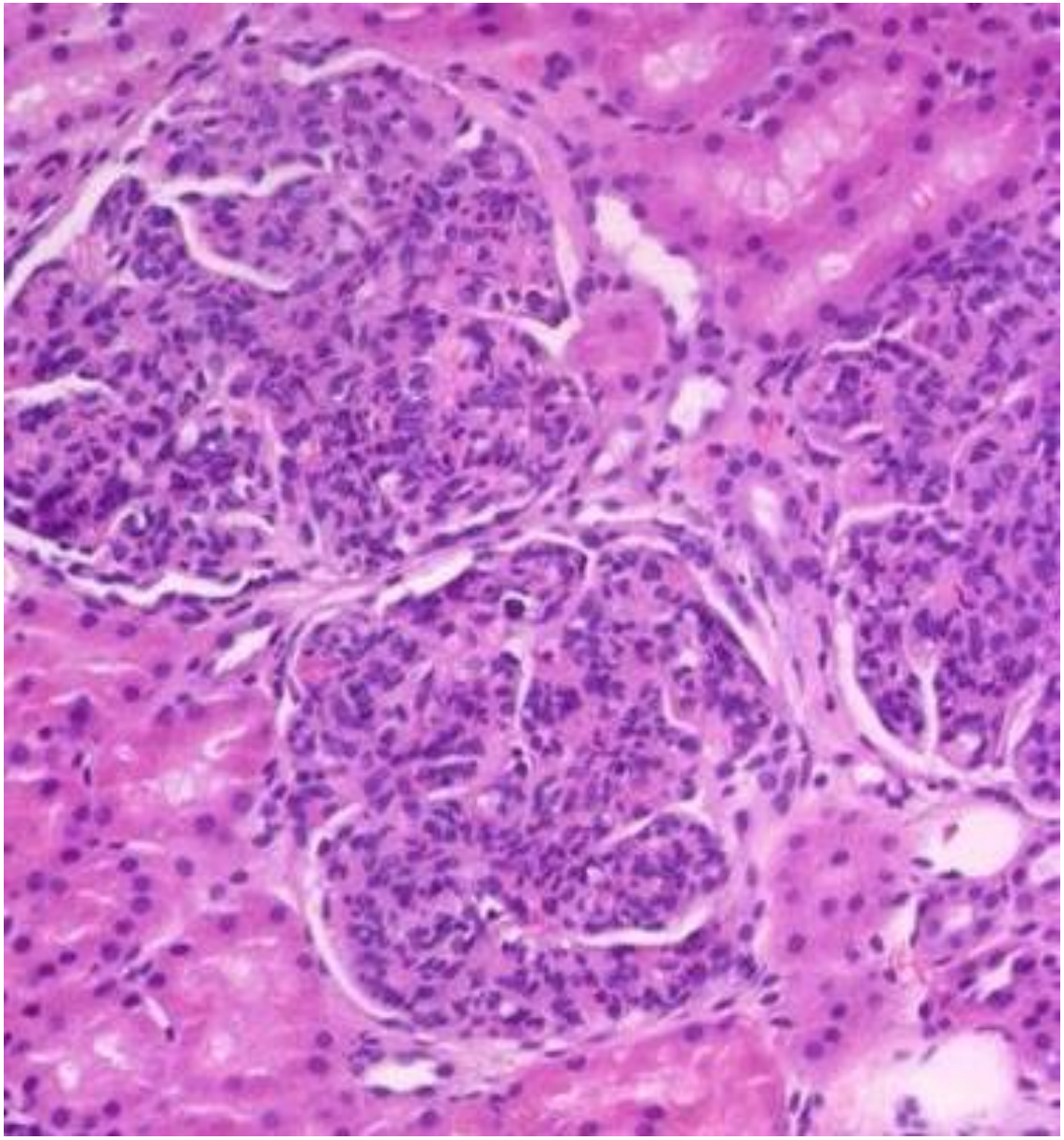
- Mesangial cells
- Endothelial cells

Leukocyte infiltration

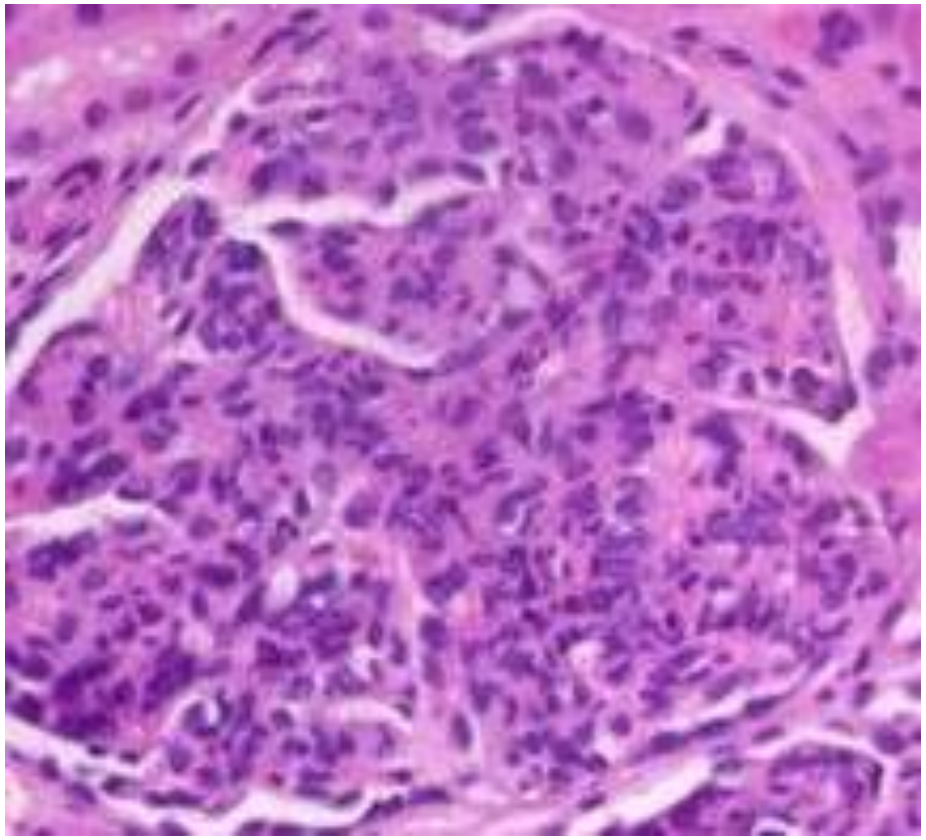
- Neutrophils, monocytes, lymphocytes

Crescent formation

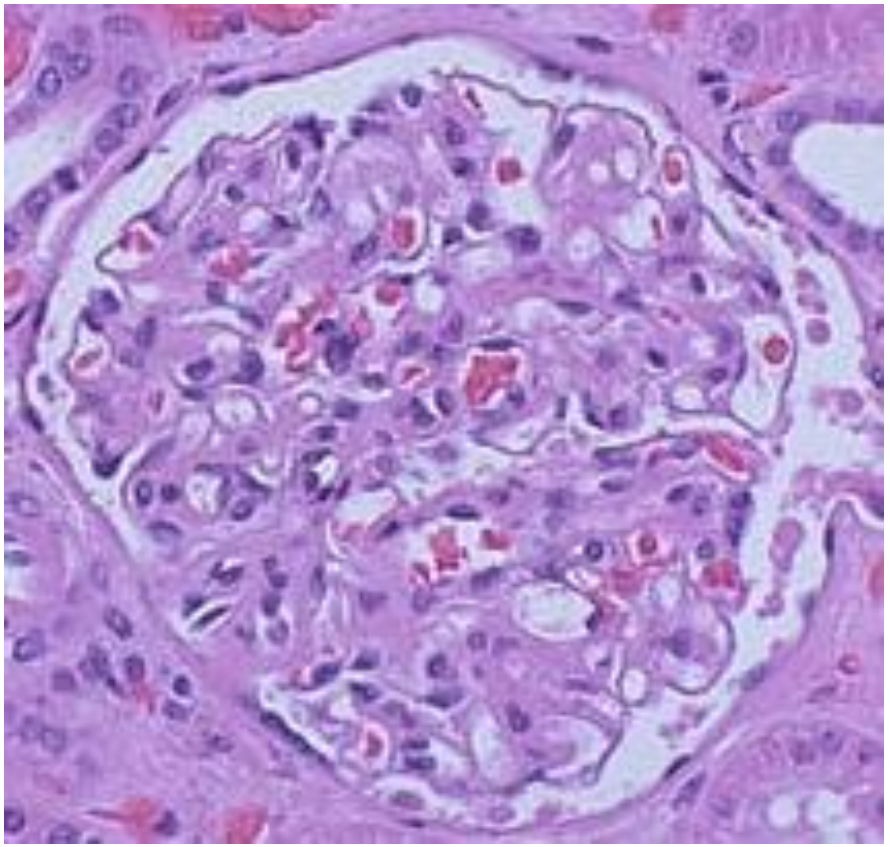
Hypercellular glmeruli



Hypercellular Glomeruli

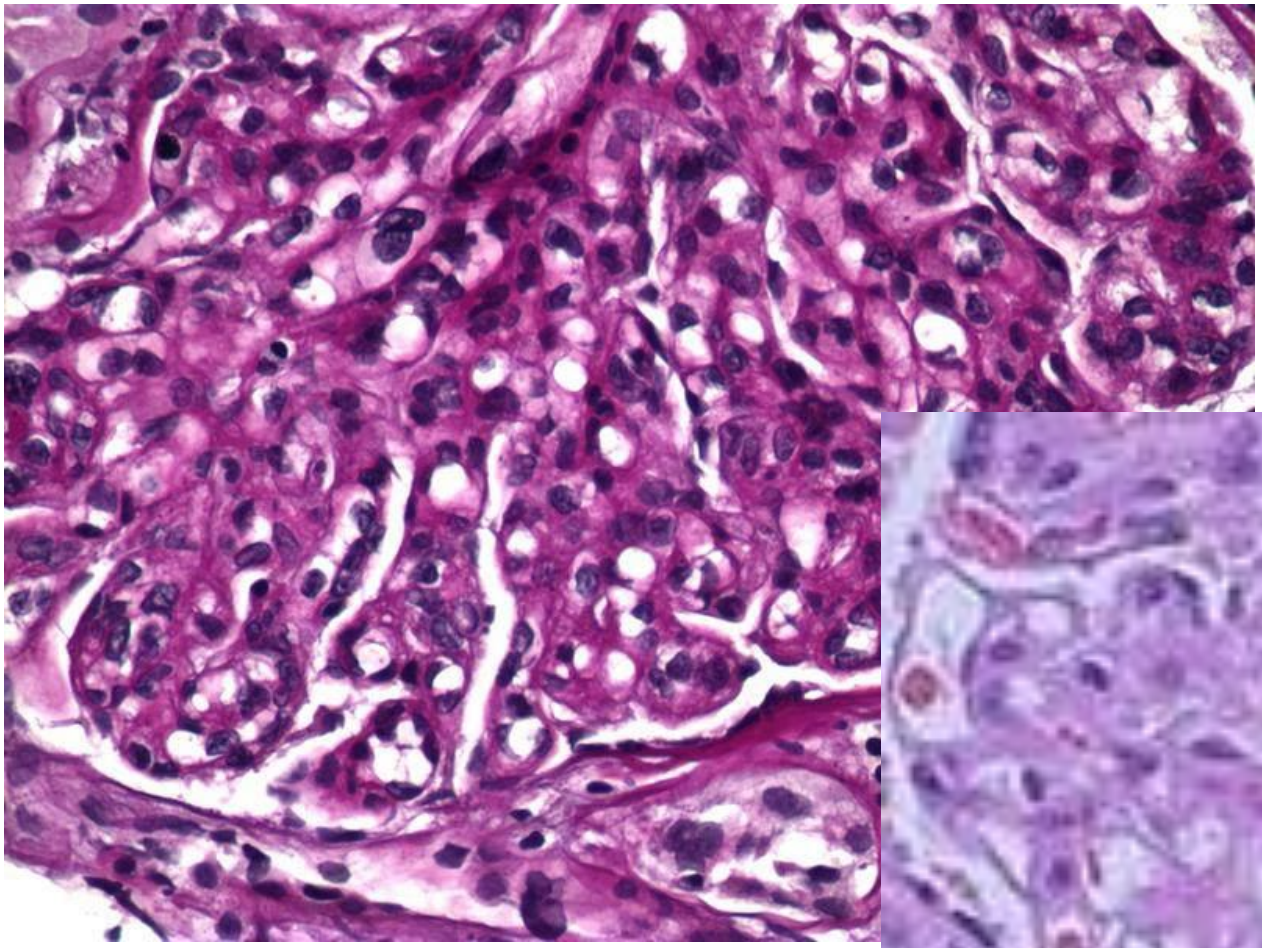


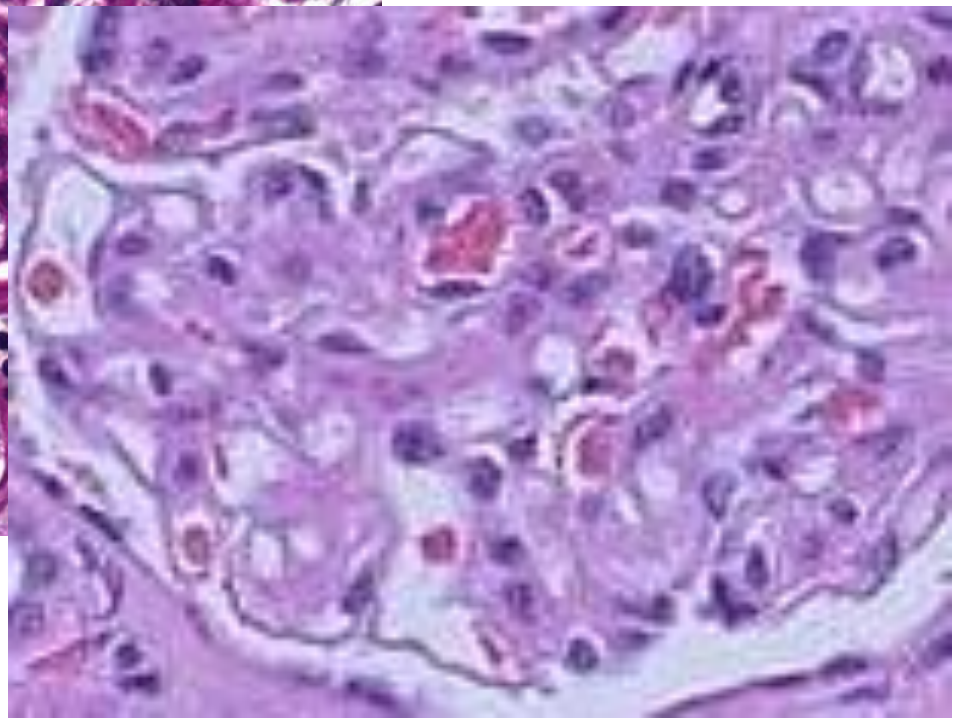
Proliferation of both mesangial cells and capillary endothelial cells



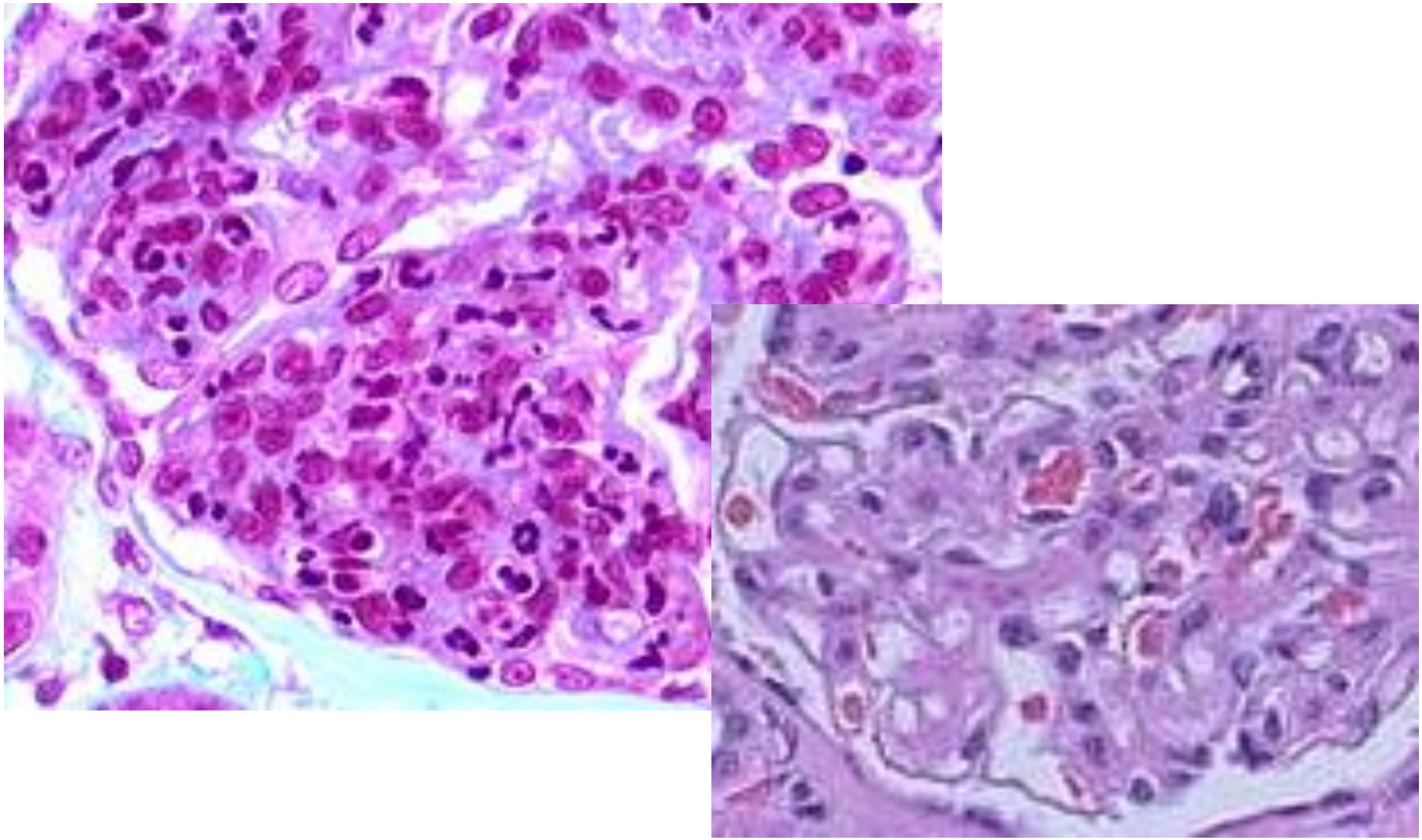
Normal glomerulus

Mesangial cell proliferation





Infiltration of leucocytes



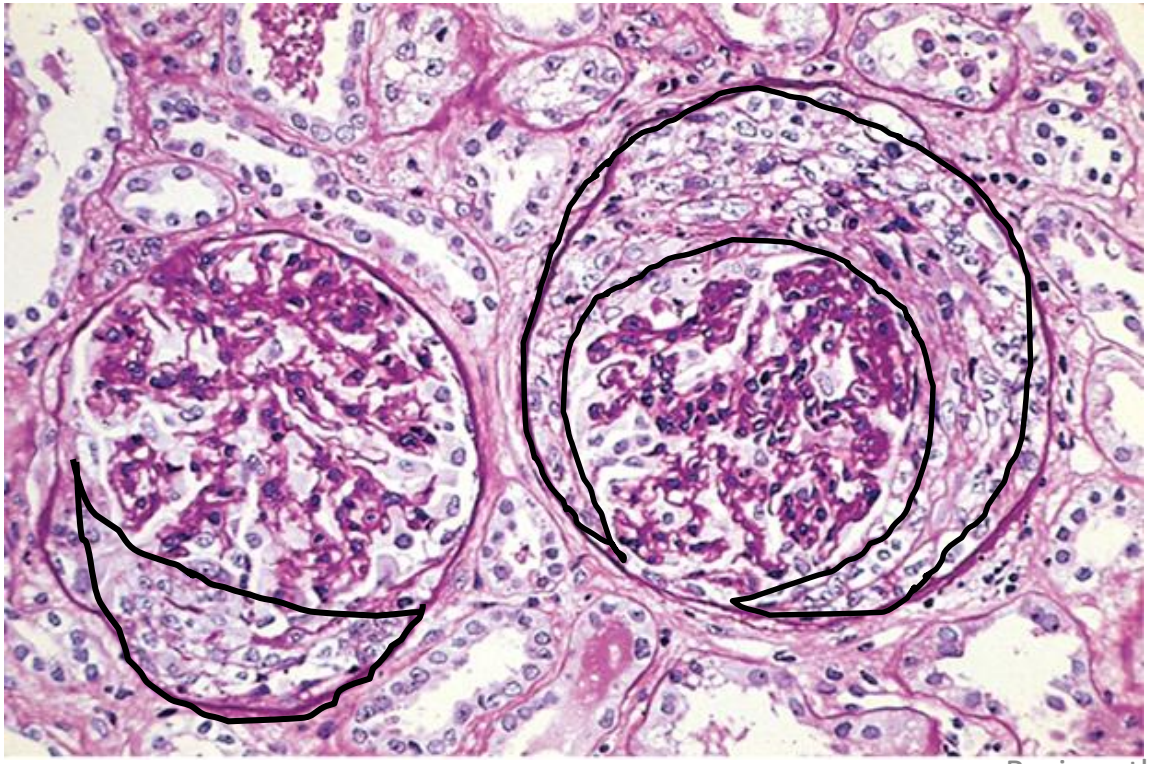
Crescent formation

- A crescent is composed of

  - proliferating parietal epithelial cells

  - infiltrating leucocytes - macrophages, monocytes

    neutrophils, lymphocytes

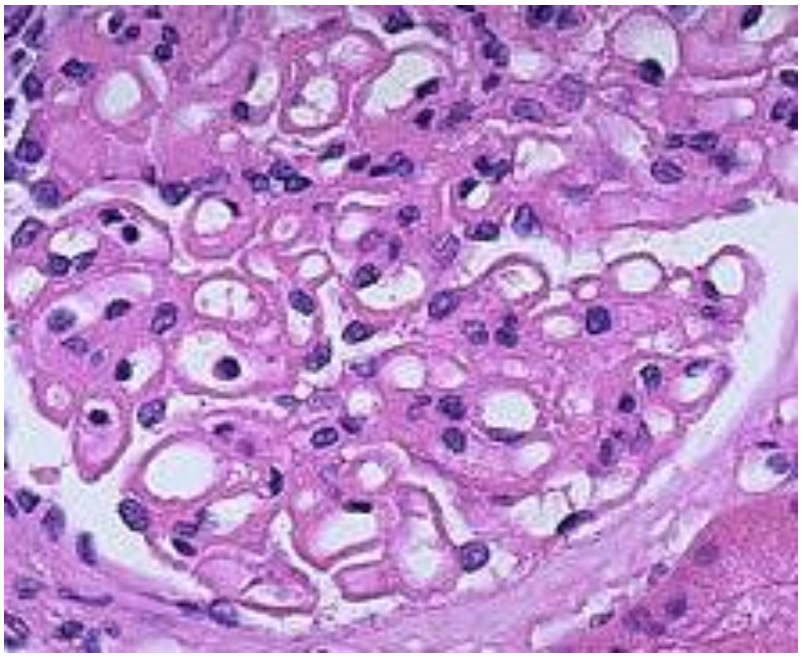


Basement membrane thickening

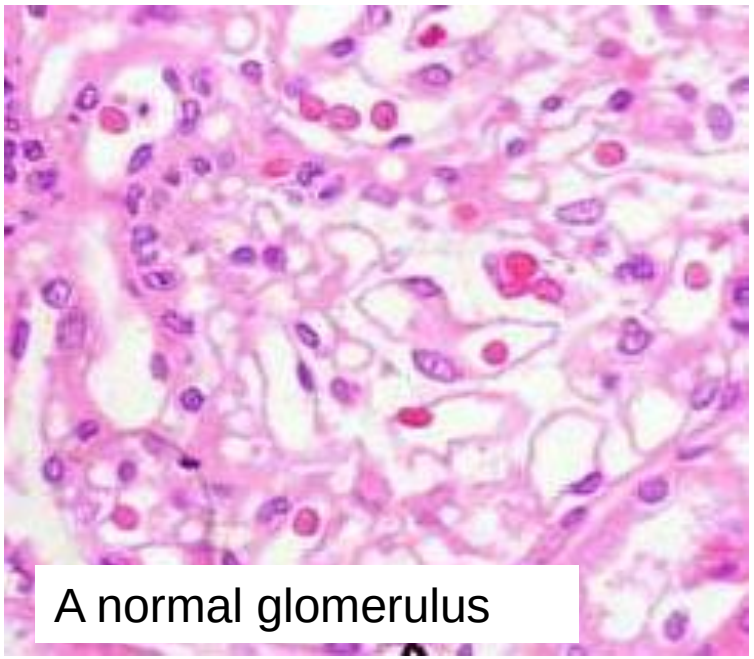
- **Deposition of material**

  - Immune complexes, fibrin, amyloid, cryoglobulins, abnormal fibrillary proteins

- **Increased synthesis of BM proteins**

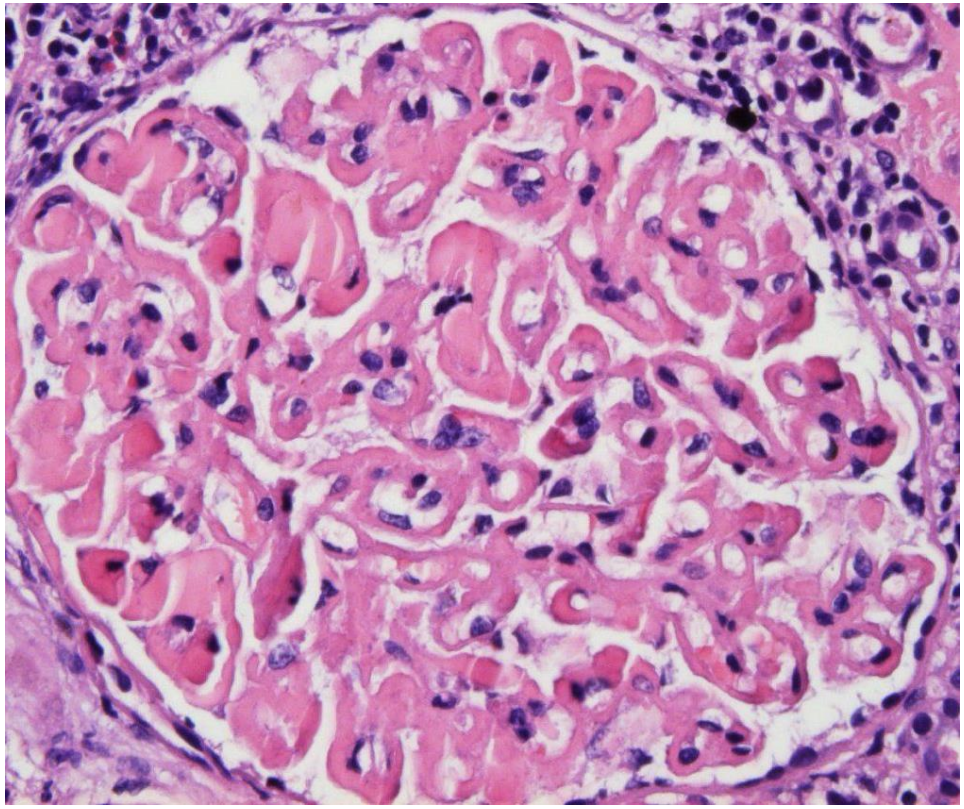


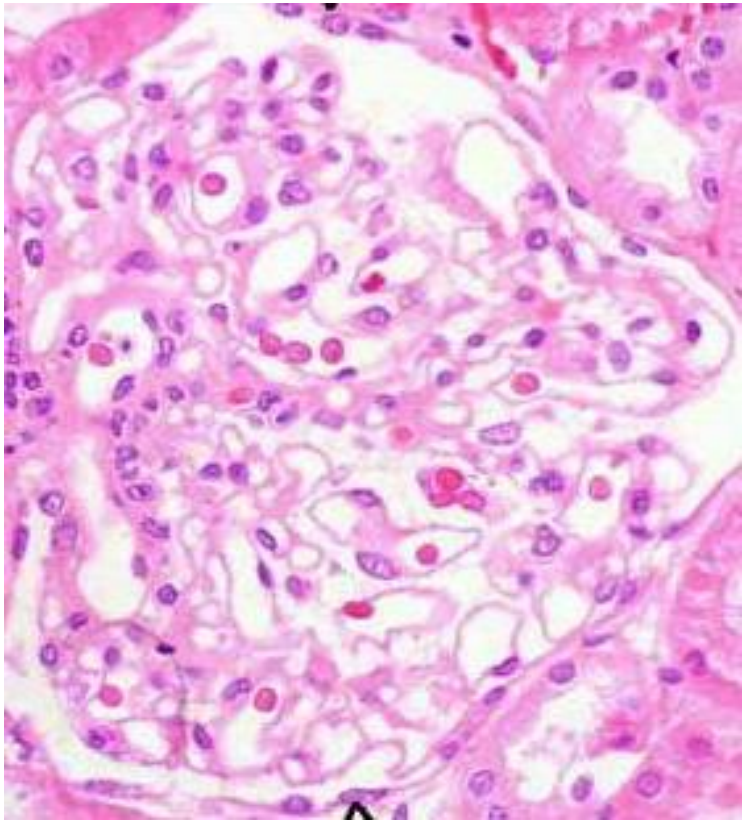
Note the thickened BM



A normal glomerulus

Basement membrane thickening





Sclerosis and Hyalinosis

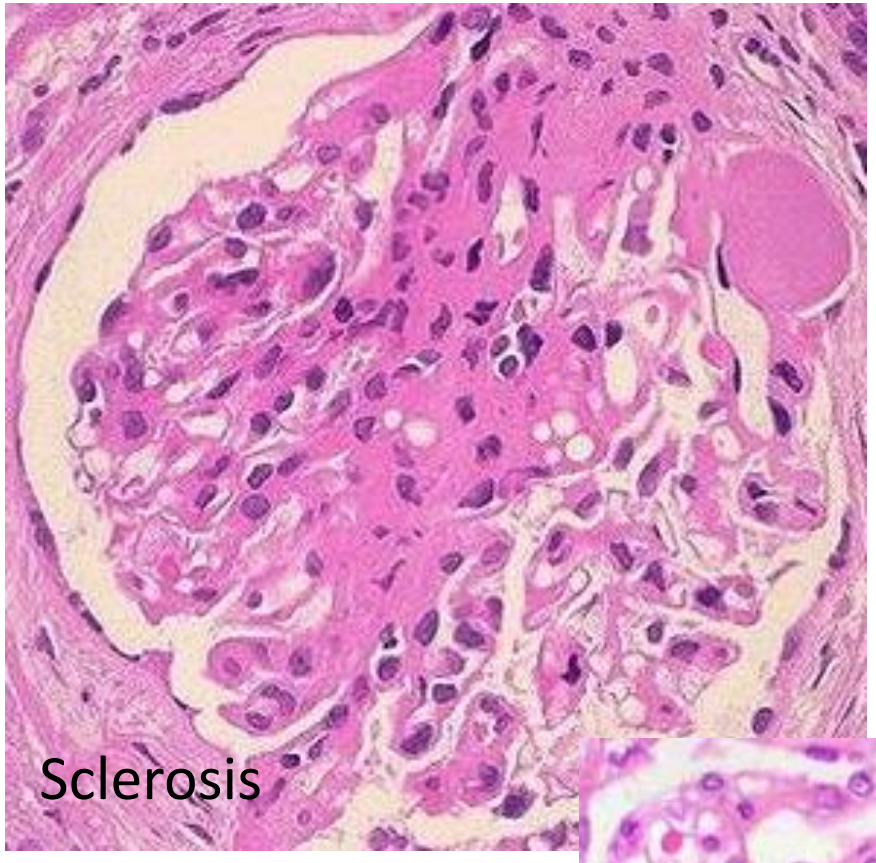
Obliterates capillary lumina

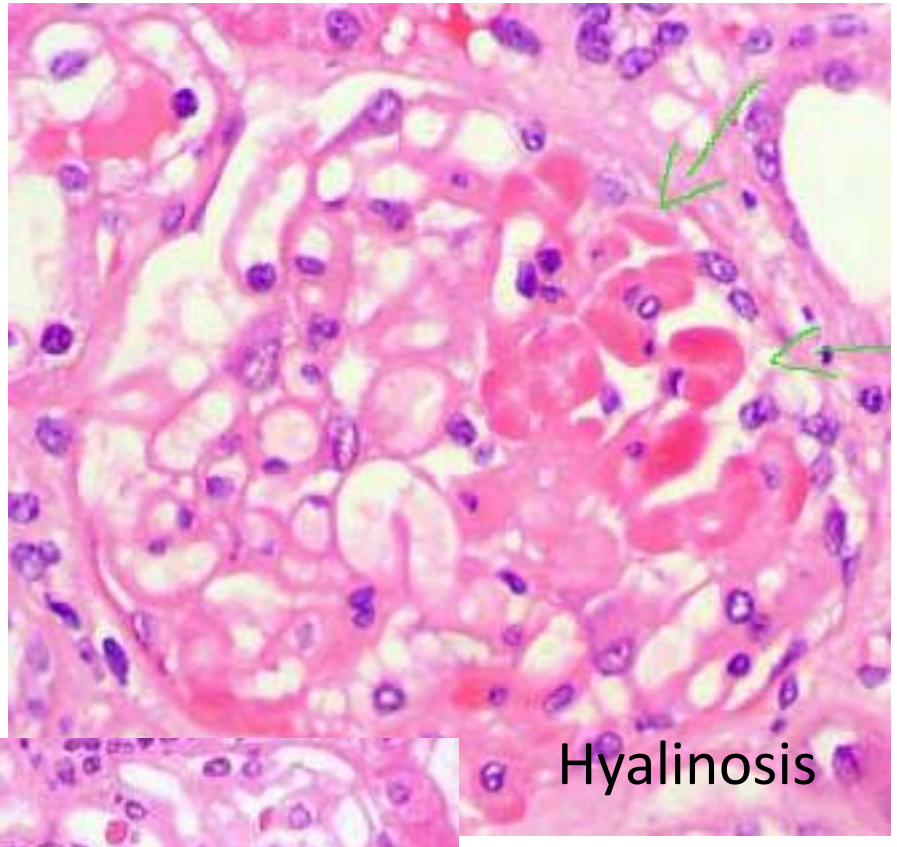
Sclerosis

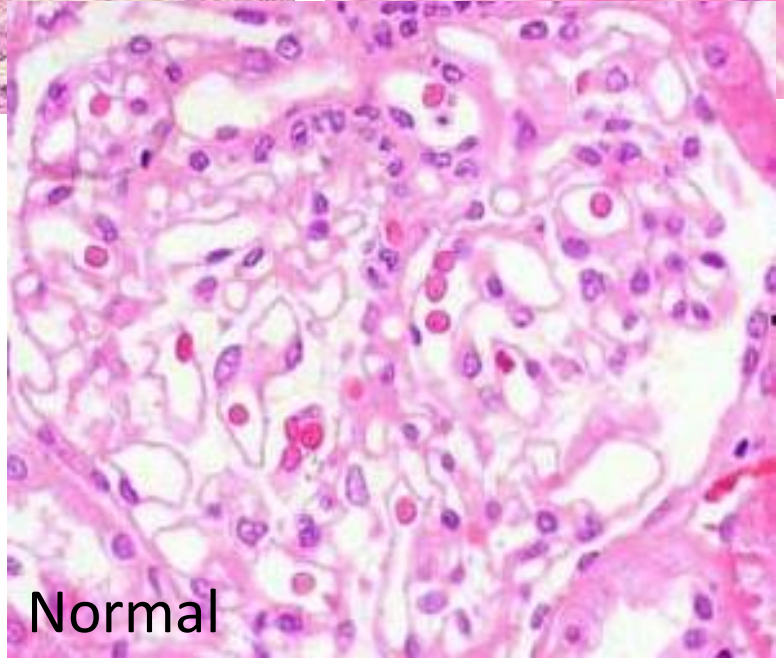
- Increase in extracellular collagenous matrix
- Confined to mesangium /involve capillary loops
- May adhere to the parietal epithelial cells and obliterates Bowman capsule

Hyalinosis/ hyaline change

- Plasma proteins release from the capillaries as the end result of various insults


Sclerosis


Hyalinosis


Normal

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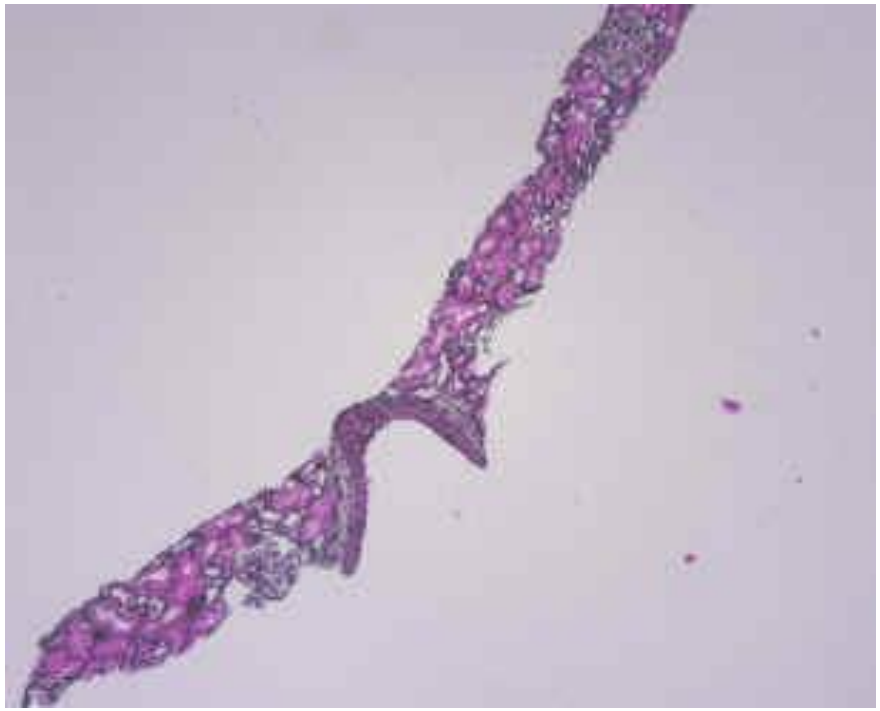
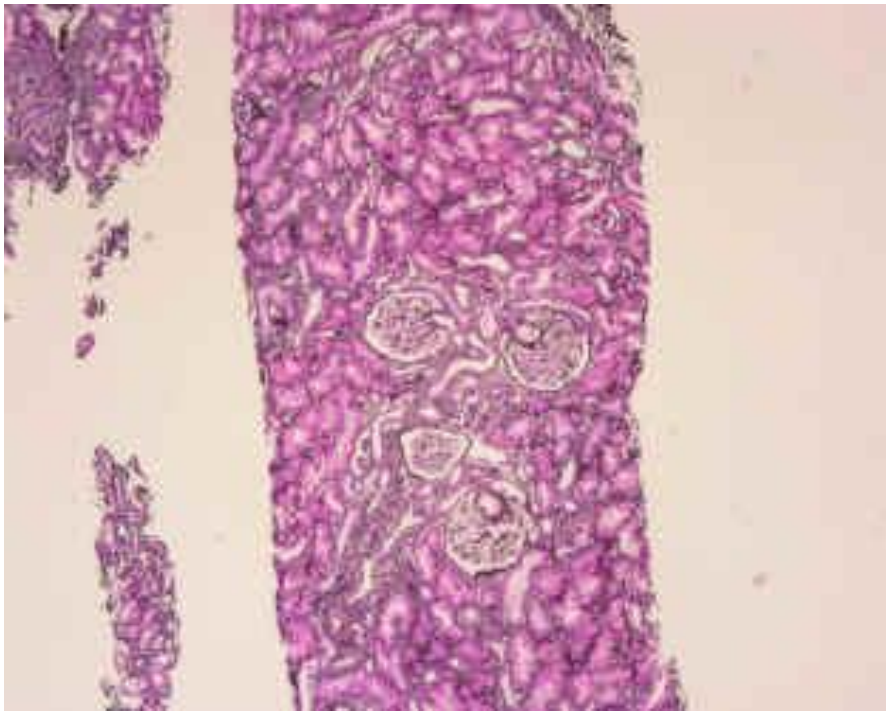




Renal core biopsy

How do we assess a renal biopsy?

- **Light microscopy**

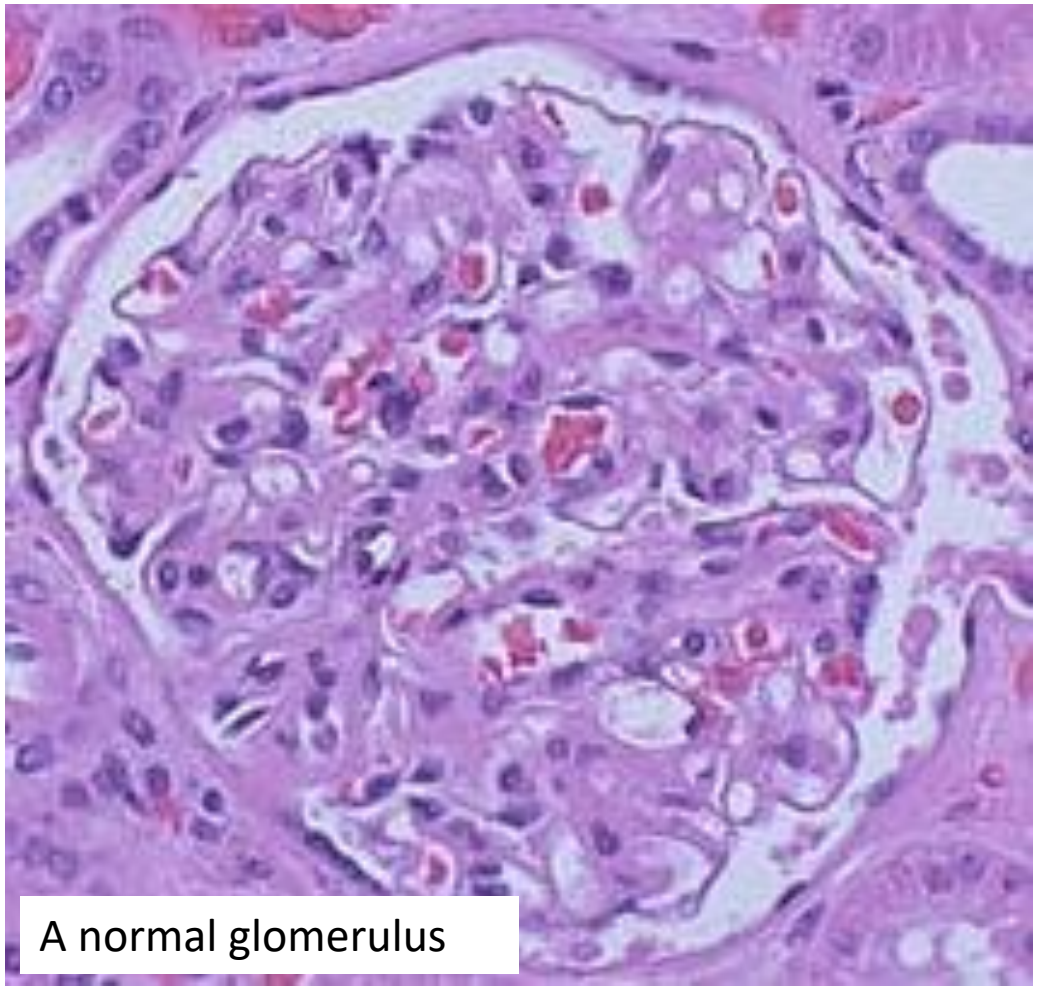
  Routine staining

  - Haematoxylin and Eosin stain (H&E)

  Special stains

  - Periodic acid stain (PAS)
  - Silver stain
- **Immunofluorescence microscopy (IF)**
- **Electron microscopy (EM)**

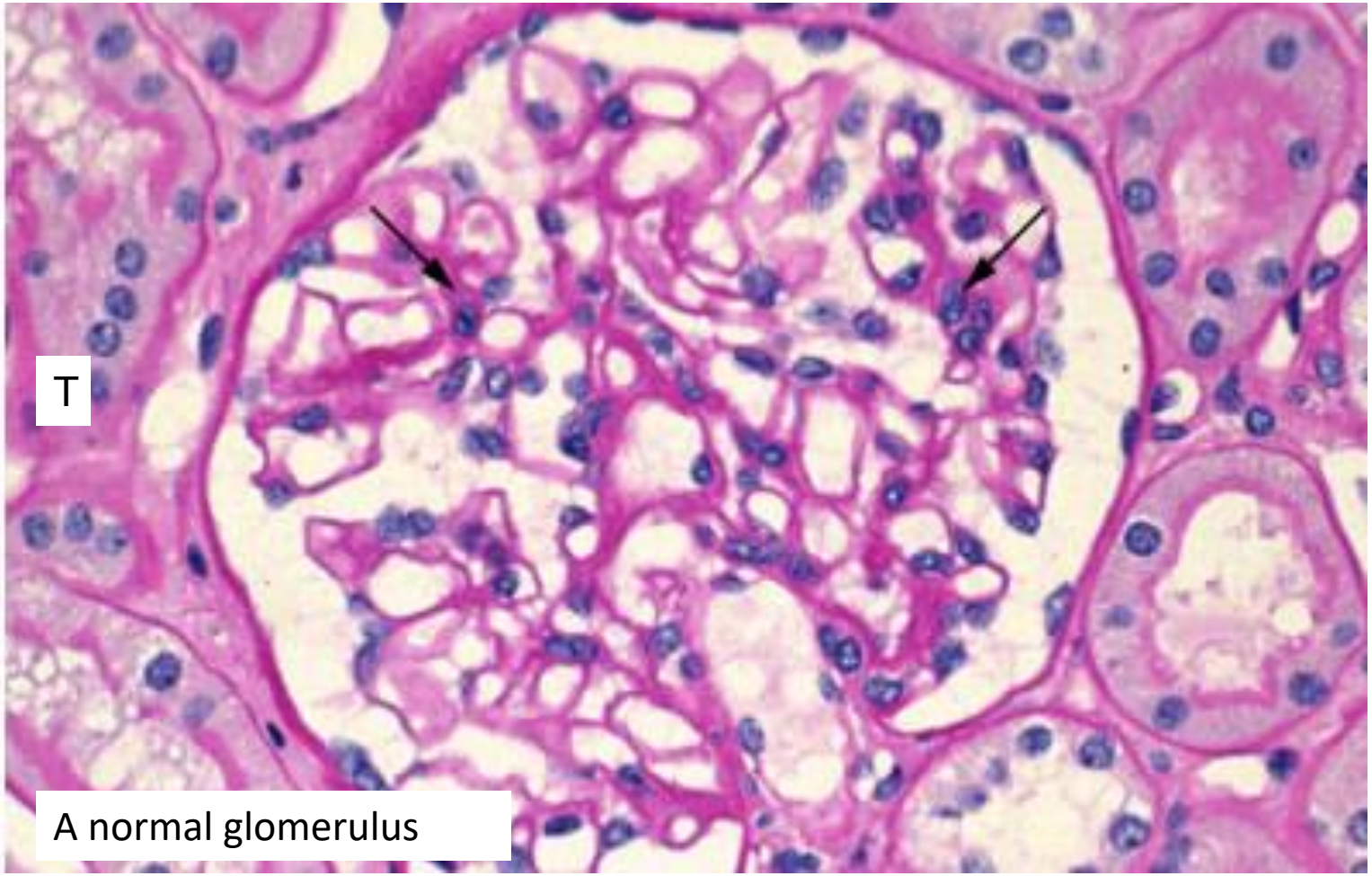
Routine H & E stain



A normal glomerulus

Note - Normal cellularity
- Patent capillaries

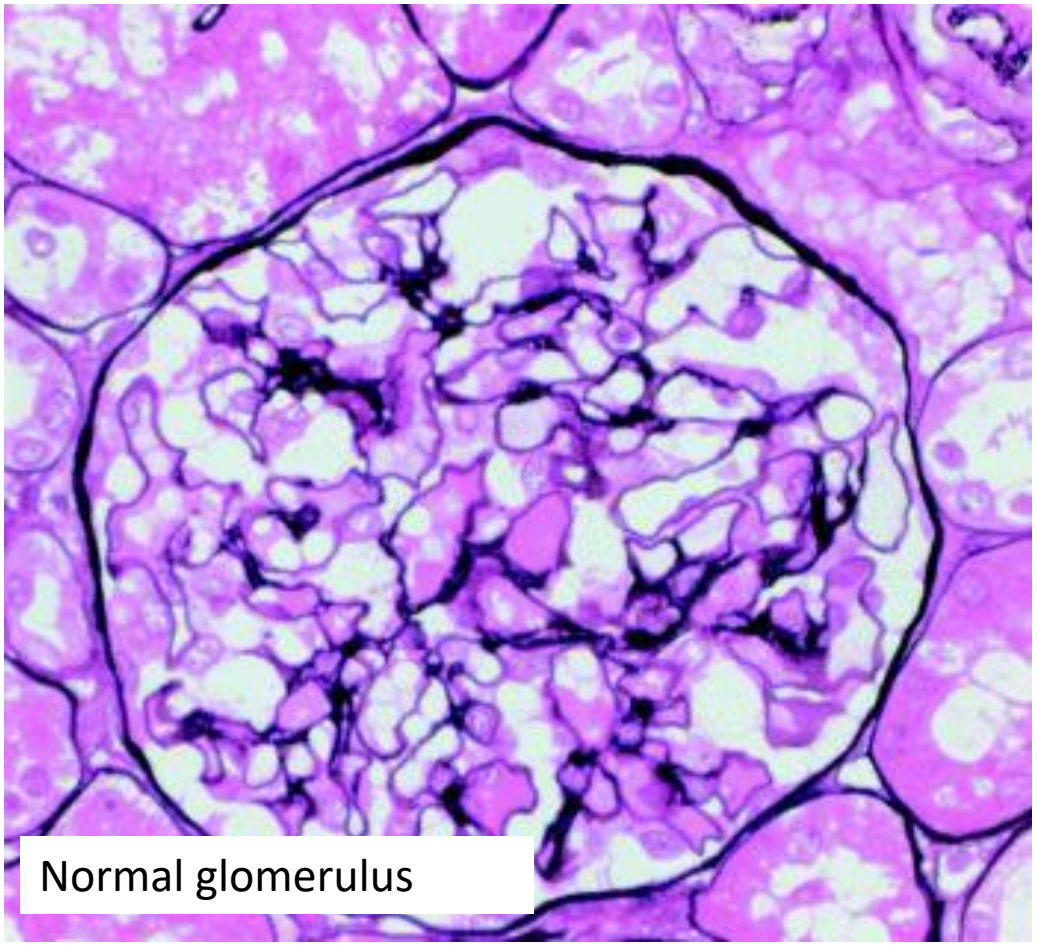
PAS stain



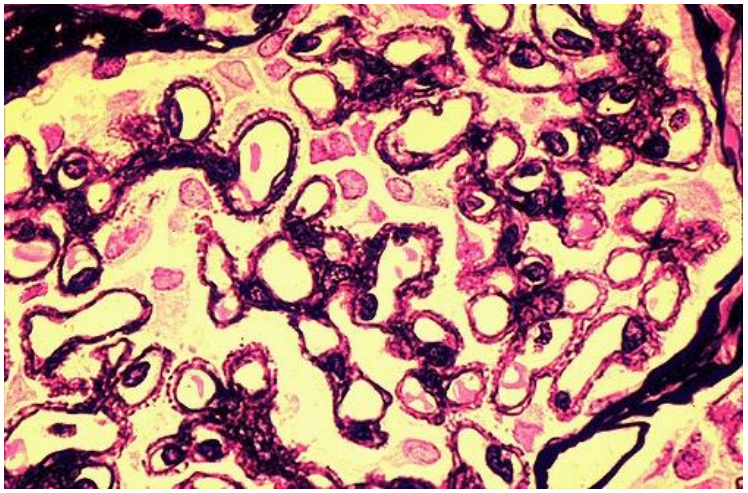
Highlights basement membranes of glomerular capillary loops and tubular epithelium

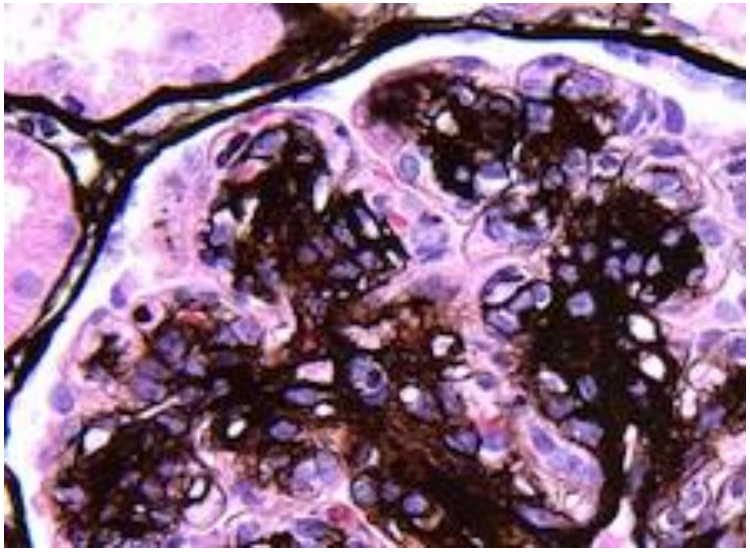
Capillary loops - Well-defined and thin with open lumina

Silver stain



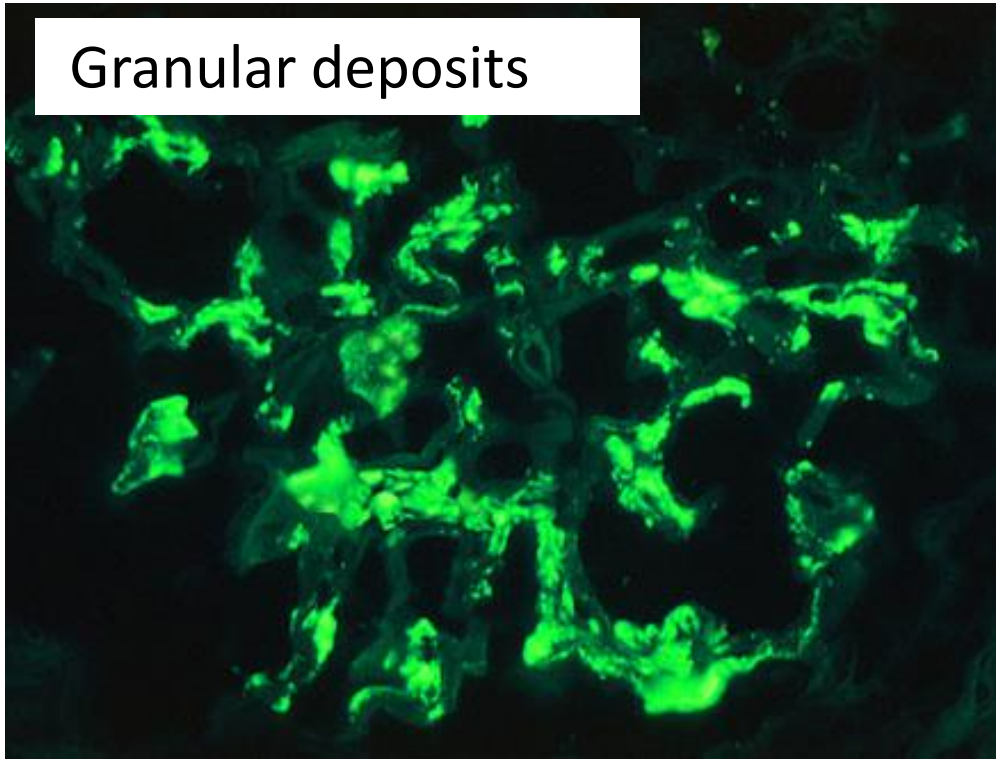
Normal glomerulus



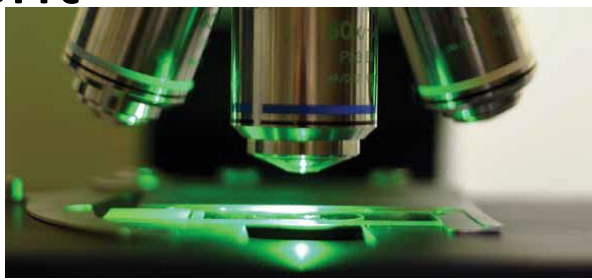


Highlights collagenous structures
(mesangial matrix and glomerular capillary basement membrane)

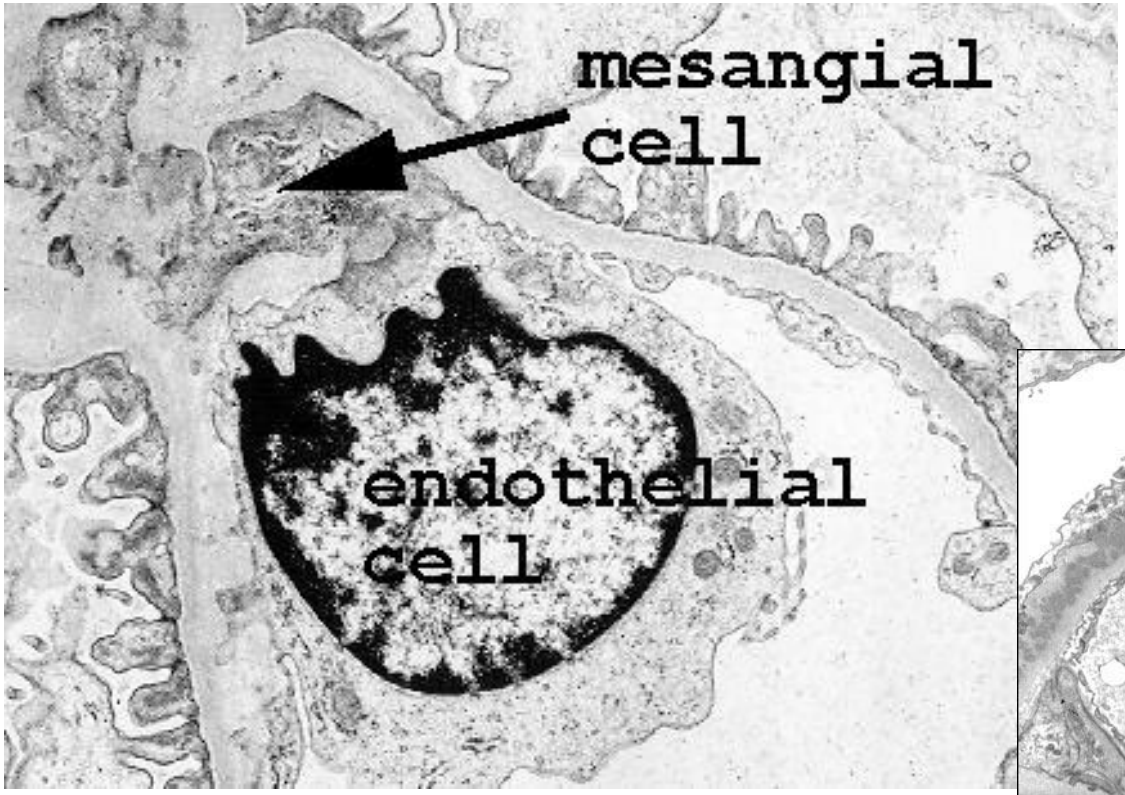
Immunofluorescence (IF)

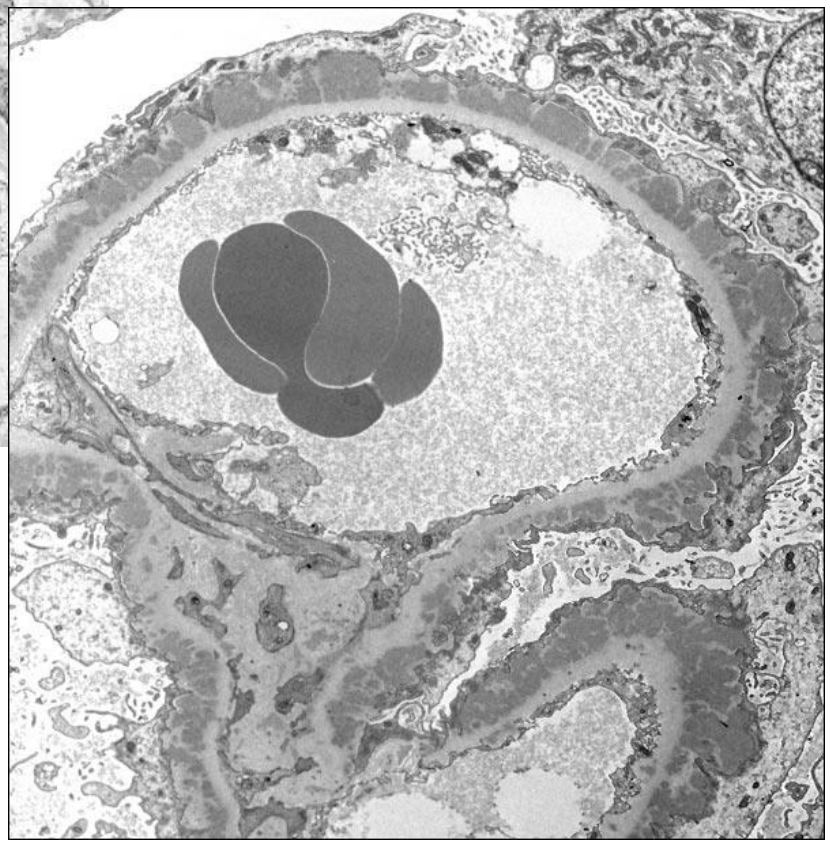


- Highlights the site and the pattern of immunoglobulin (Ig) and complement component deposition



Electron microscopy (EM)





eg. Sub epithelial deposits

How to describe the pathological changes in the glomeruli ?

In a renal biopsy

- Diffuse - All (> 80%) glomeruli are involved

  Focal - Some glomeruli are involved

  Single glomerulus

- Global - Entire glomerulus is involved

  Segmental - Part of the glomerulus is involved

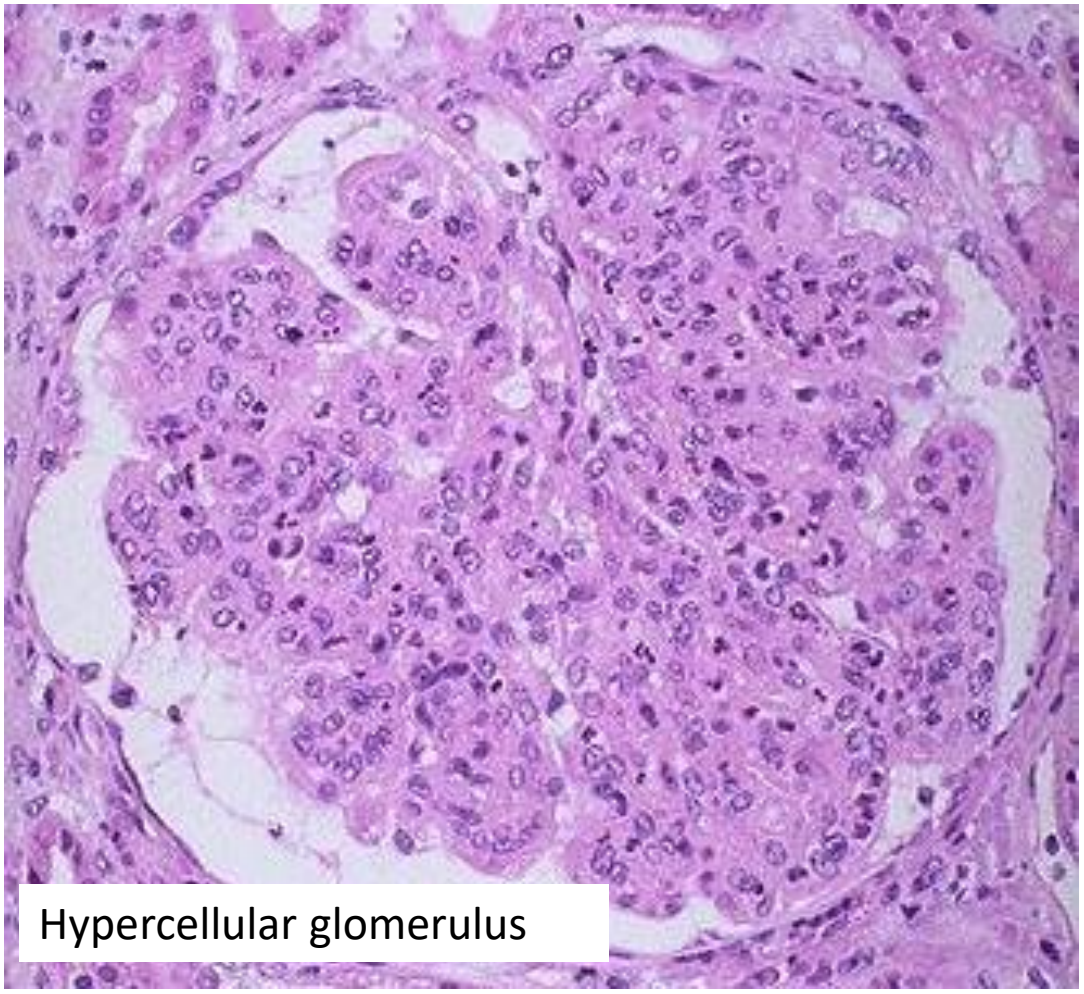
- Predominant involvement

  - **Mesangeum / capillary loops**

- Duration (in some)

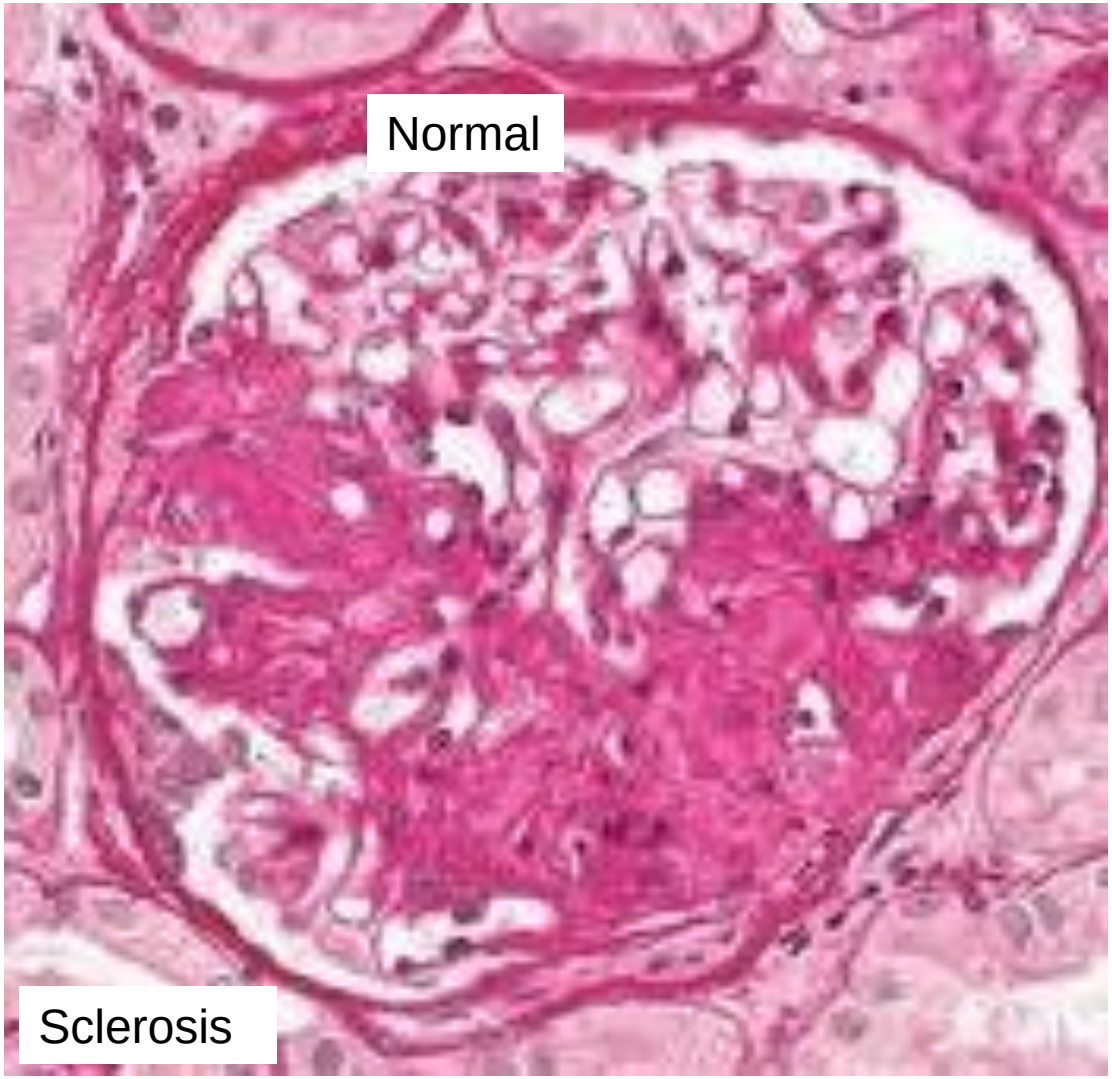
  - **Acute/ chronic**

Global involvement of a glomerulus

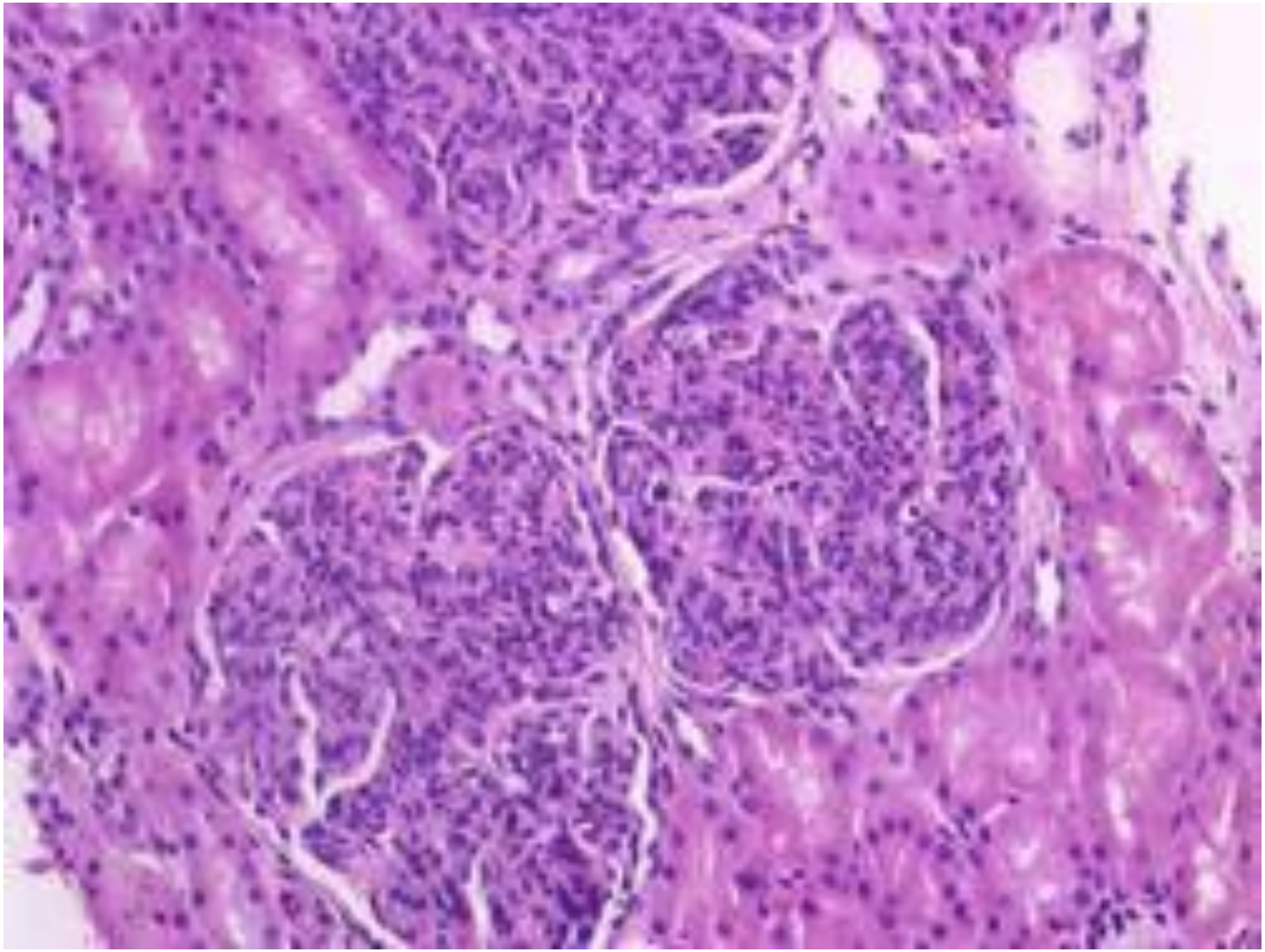


Hypercellular glomerulus

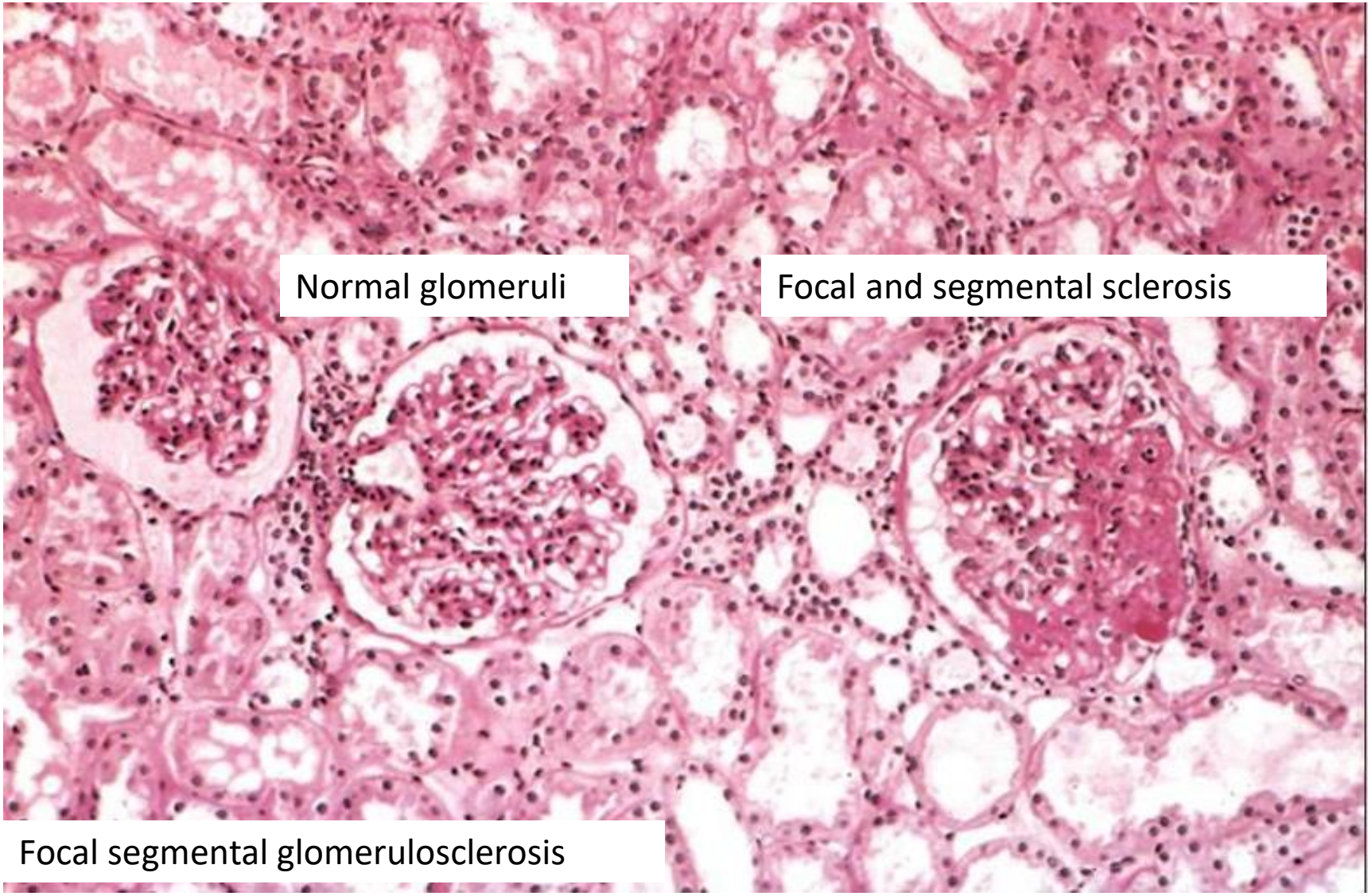
Segmental involvement of a glomerulus



Diffuse and global involvement



Focal and segmental involvement



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Glomerular diaseases

Primary glomerulopathies

- Acute diffuse proliferative GN
- Rapidly progressive GN
- Membranous glomerulopathy
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranoproliferative GN
- Ig A nephropathy
- Chronic glomerulonephritis

Systemic diseases with glomerular involvement

- Systemic lupus erythematosus
- Diabetes mellitus
- Amyloidosis
- Goodpasture syndrome
- Microscopic polyarteritis/polyangitis
- Wegener granulomatosis
- Henoch-Schonlein purpura
- Bacterial endocarditis

Hereditory disorders

- Alport syndrome
- Thin basement membrane disease
- Fabry disease

Clinical manifestations of glomerular diseases

- **Nephritic syndrome** - Haematuria, azotemia, variable proteinuria, oliguria, oedema and hypertension
- **Rapidly progressive glomerulonephritis**
  - Acute nephritis, proteinuria, acute renal failure
- **Nephrotic syndrome** – proteinuria (>3.5g/day), hypoalbuninaemia, hyperlipidaemia, lipiduria
- **Chronic kidney disease**
  - Azotemia → uraemia progressing for months to years
- Isolated urinary abnormalities
  - Haematuria and / subnephrotic proteinuria

Clinical manifestations of glomerular diseases

- Both primary glomerulopathies and systemic diseases affecting kidneys can result in these syndromes

Nephritic syndrome

- Acute diffuse proliferative glomerulonephritis (post infectious GN/ poststreptococcal GN)
- Rapidly progressive glomerulonephritis (crescentic GN)

Nephrotic syndrome

- Minimal change disease
- Membranous glomerulopathy
- Focal segmental glomerulosclerosis

- Membranoproliferative glomerulonephritis

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Classification of glomerular diseases

- Classify according to the morphological pattern
- Do not represent individual disease entities
- Provide a guide to the
  - degree of tissue damage
  - likelihood of reversibility
- Usefulness to the nephrologist
  - **Clinical data + Morphological diagnosis** + **immunological findings**

    gives a useful framework for determining the therapy and prognosis

Summary

Now you should be able to

- Discuss the basic pathological changes occur in the glomeruli in glomerular diseases
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Next lecture…..

- Discuss briefly the microscopic changes of the glomeruli in different glomerulopathies

Reading assignment

- What is nephritic syndrome?
- What is nephrotic syndrome?

Reading assignment

- Discuss the pathophysiological basis of

  proteinuria

  hypoalbuminaemia

  oedema and hyperlipidaemia in

  nephrotic syndrome
- Why patients with nephrotic syndrome are prone to infections?
- Why do they prone to develop thrombotic and thromboembolic complications?