Immune Complex Nephritis

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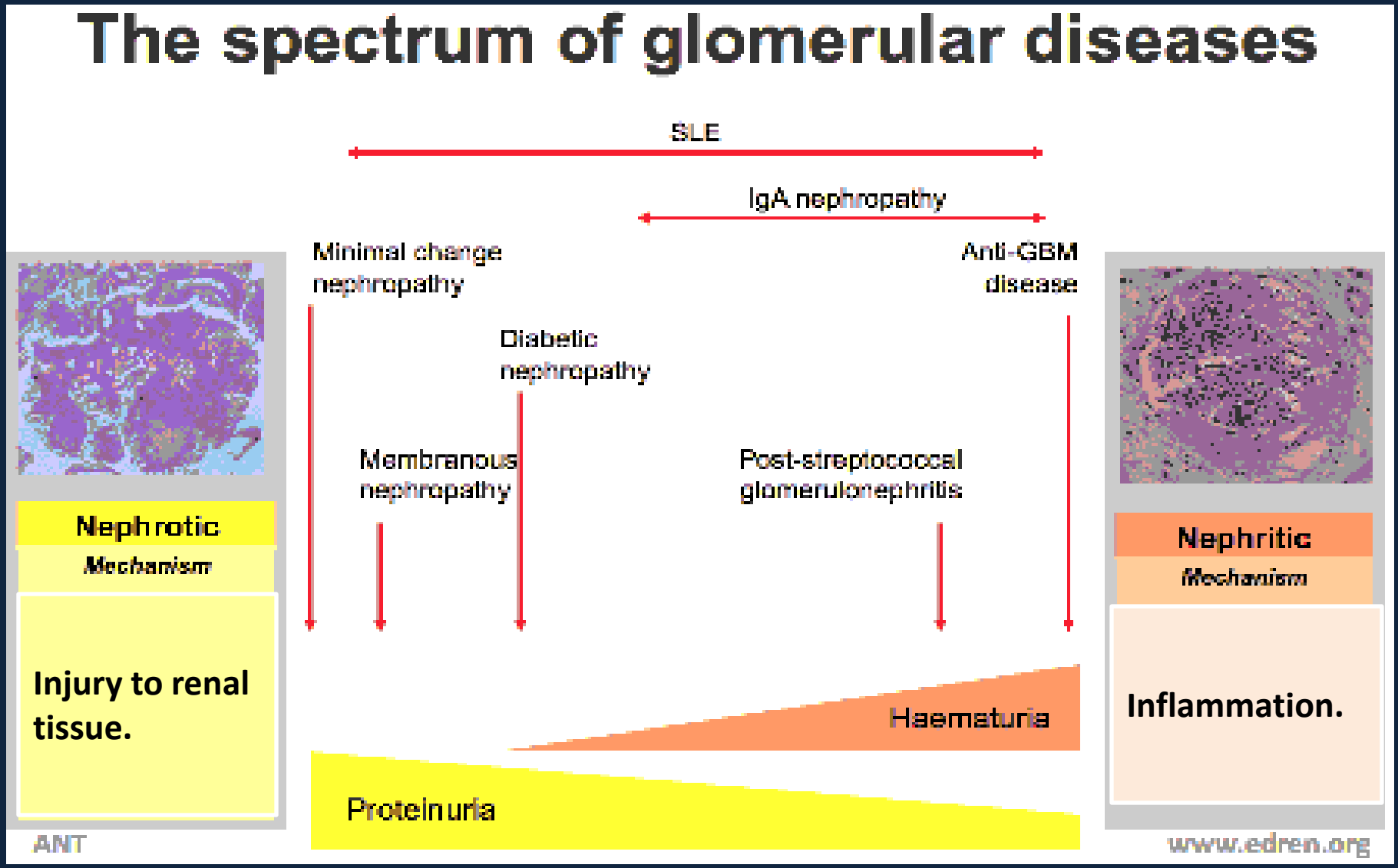
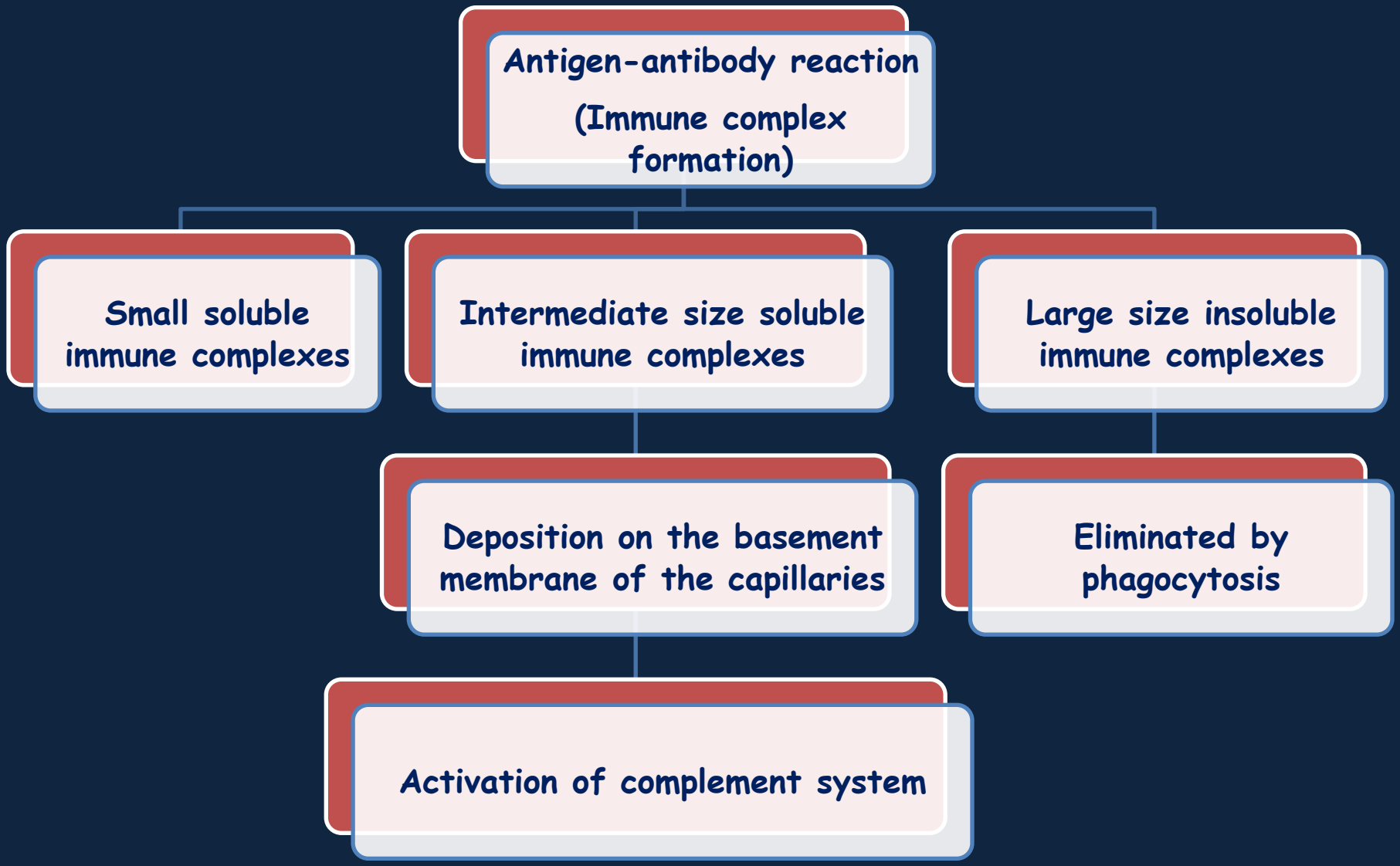
Objectives

- Understand the importance of immune complexes in the pathogenesis of renal injury.
- Learn that immune complexes form in the circulation and may deposit in different tissues.
- Understand the dynamics of deposition of complexes which depend on the size and rate .
- Identify the different types of renal disease based on the site of deposition of the immune complexes.

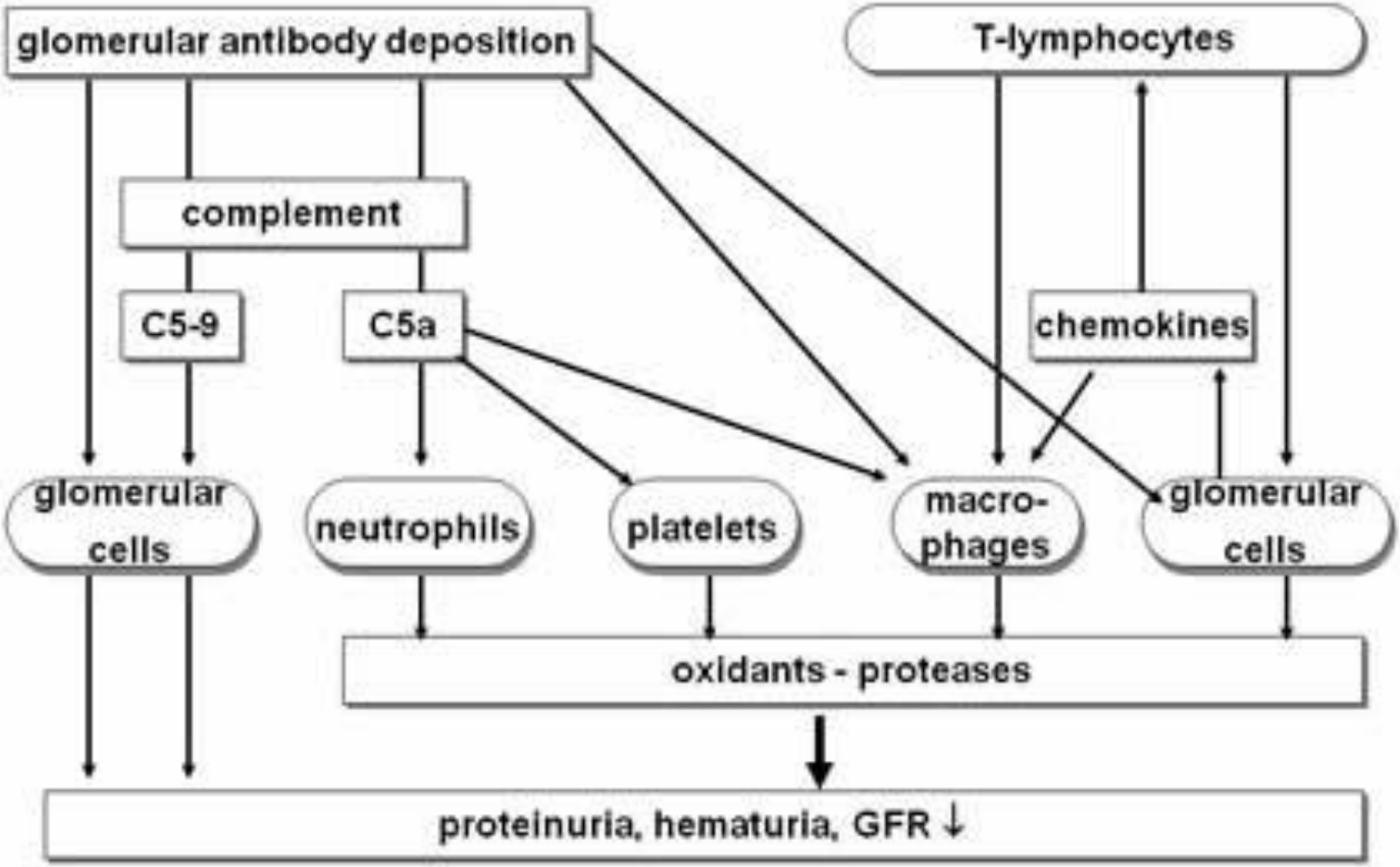
Complexes of antibody with various microbial OR self antigens induce type II or III hypersensitivity reactions in the kidney :



Pathogenesis of immune-complex nephritis (Type III hypersensitivity reactions)



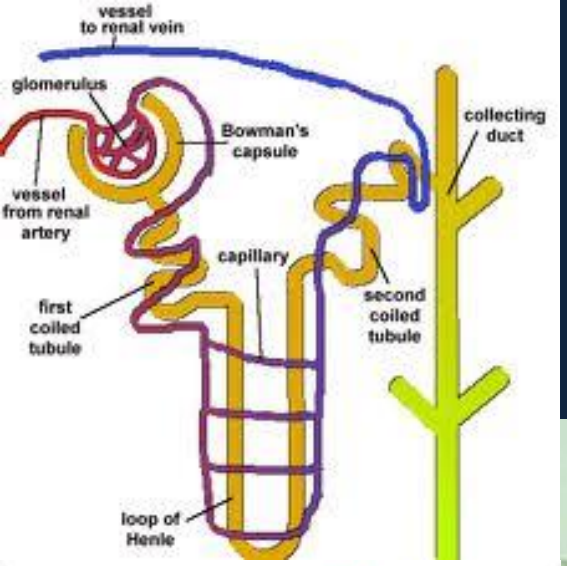
Immune-mediated glomerular injury

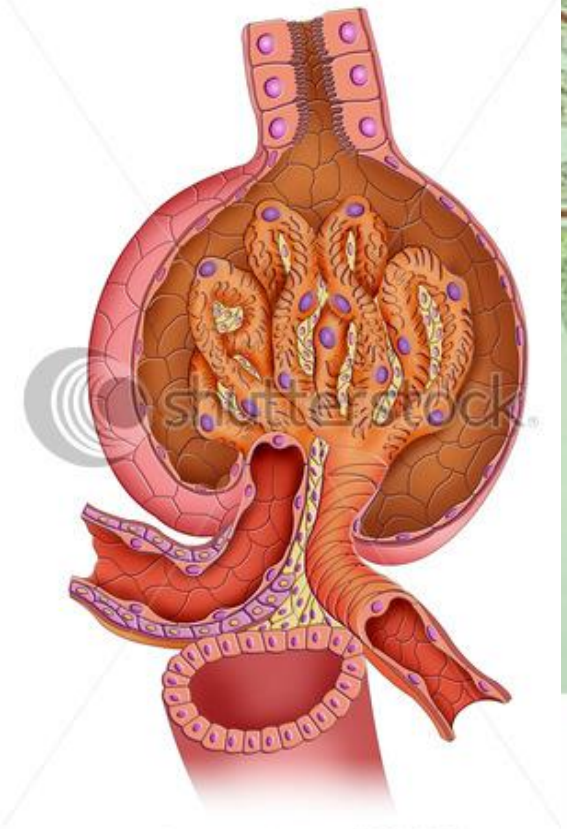


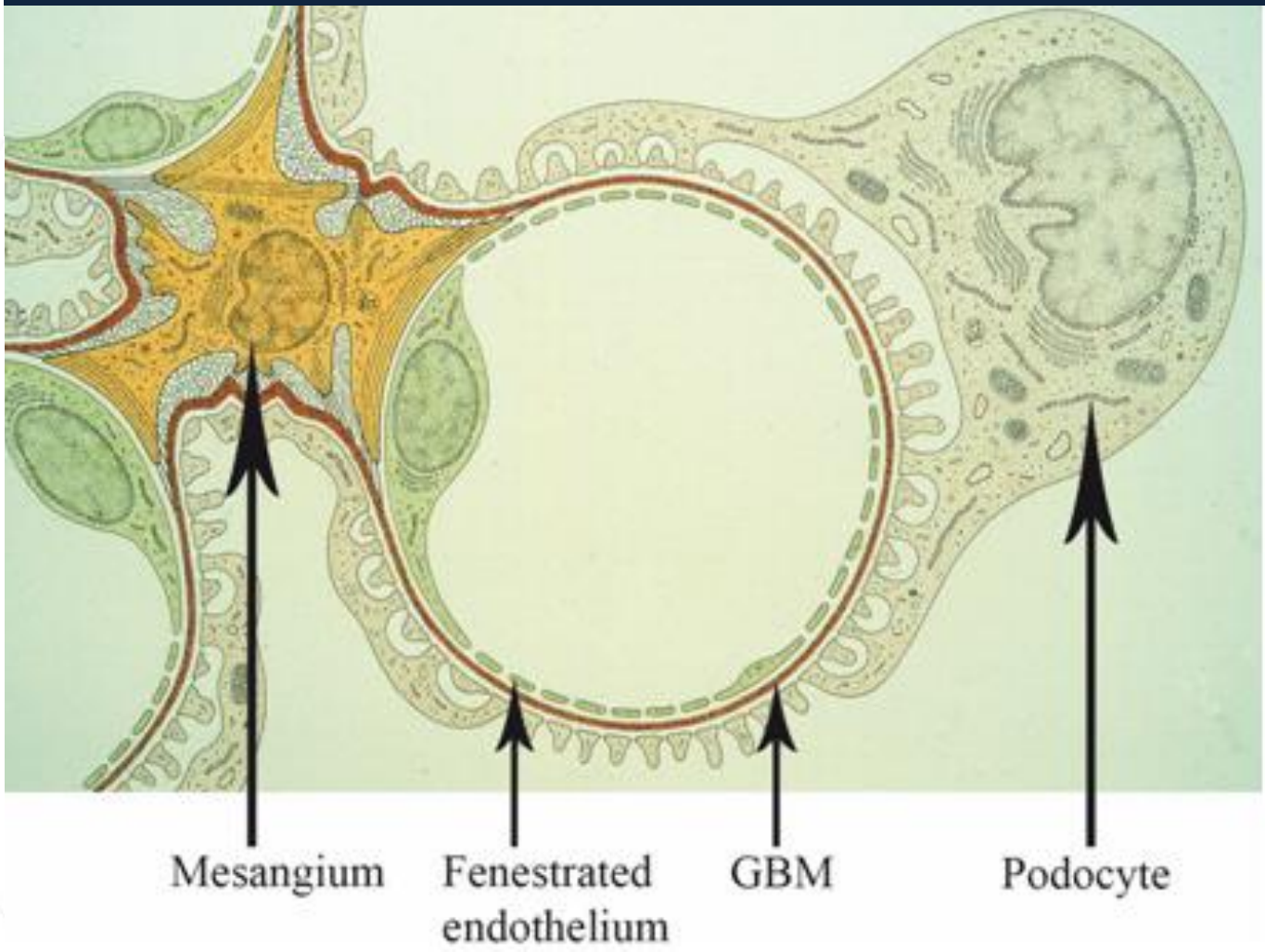
Site of deposition:

- Complexes accumulate in tissues where filtration of plasma occurs. This explains the high incidence of:
  - Glomerulonephritis (deposition in the kidney)
  - Vasculitis (deposition in the arteries)
  - Arthritis (deposition in the synovial joints)

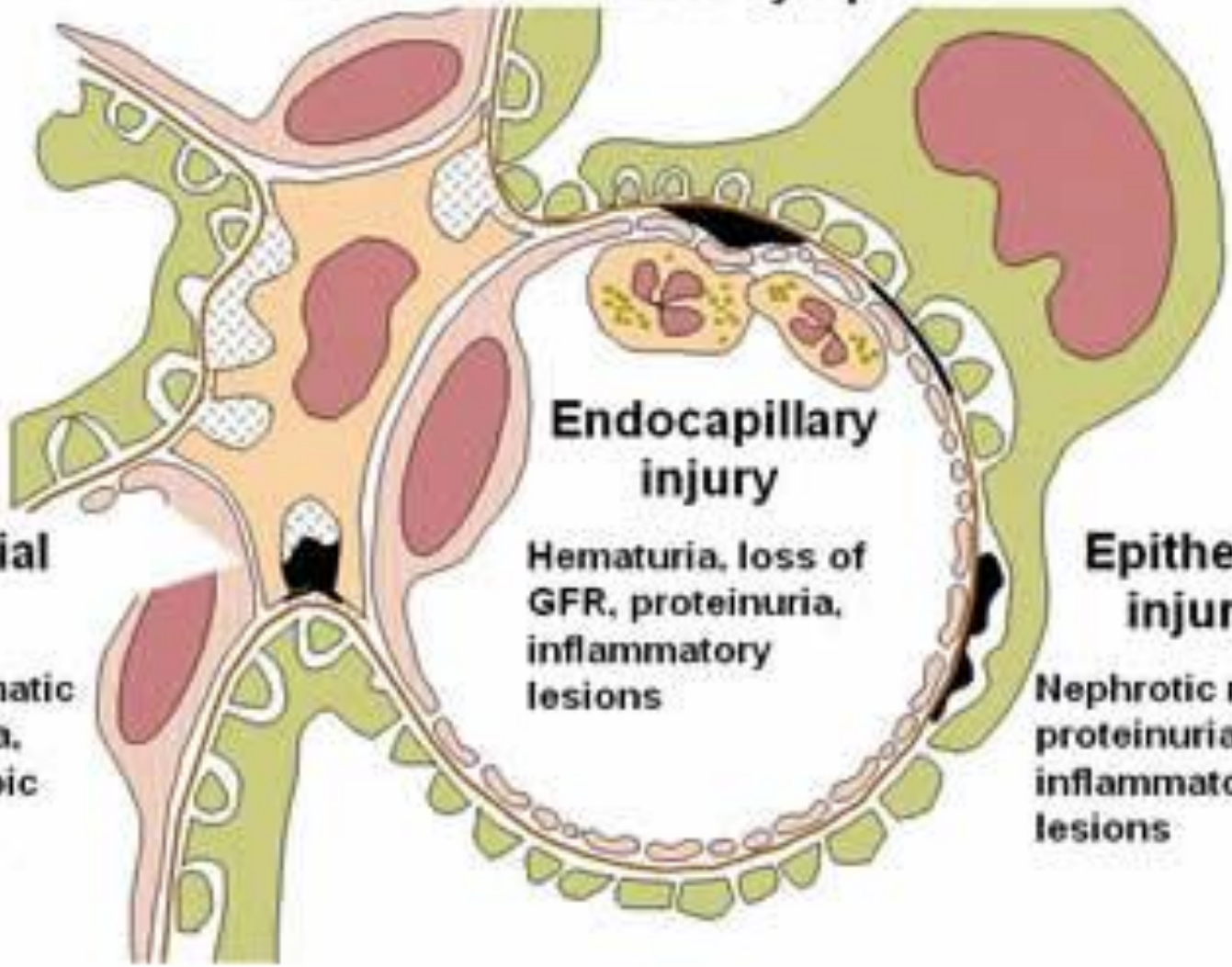
Nephron and glomerulus







Glomerular injury is determined by immune complex localization as are the clinical symptoms



Endocapillary injury

Hematuria, loss of GFR, proteinuria, inflammatory lesions

Mesangial injury

Asymptomatic proteinuria, microscopic hematuria

Epithelial injury

Nephrotic range proteinuria, non-inflammatory lesions

Types of immune-mediated renal injury:

- Antibody-mediated Injury:
  - Membranous glomerulonephritis
  - IgA nephropathy
  - Membranoproliferative glomerulonephritis
  - Post infectious glomerulonephritis
  - Antiglomerular basement membrane disease

1. Post Infectious Glomerulonephritis (GN) (Post-streptococcal)

Presentation:

- 7-14 days *after* pharyngitis.
- 14-21 days *after* (skin infection)
- Abrupt onset (Acute nephritic syndrome)

Strep antigens trigger antibodies that cross-react to glomeruli

Circulating immune complexes during filtration in the glomerulus deposit in the kidney

Immune complexes activate complement

Poststreptoccal GN

- Caused by known streptococcal types called: nephritic strains

- In most children bacterial culture will be negative
- Anti –streptolysin-O antibody(ASO) will be the only evidence

The anti-DNAse B titre is a better indicator of streptococcal skin sepsis than the ASO titre.

- Cholesterol and lipids in skin suppress the ASO antibody response but not the anti-DNAse B antibody titre.

Features of Acute glomerulunephritis

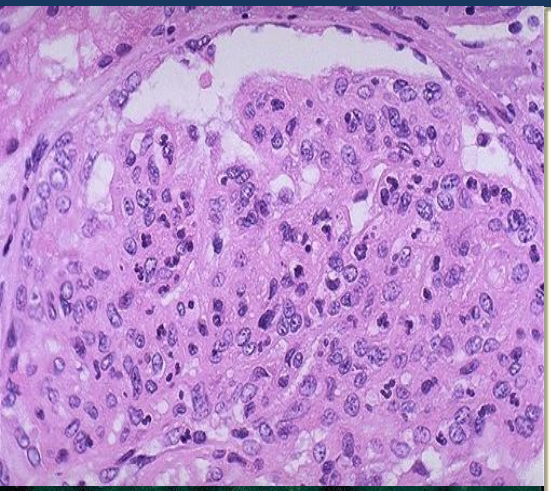
Diffuse proliferative GN (PGN)

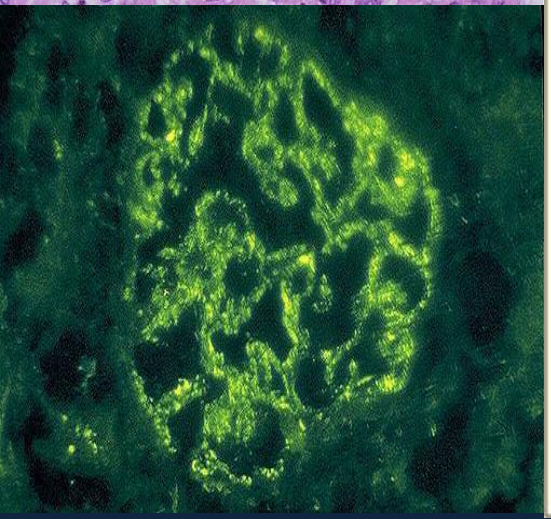
- Diffuse proliferation of glomerular cells and frequent infiltration of leukocytes (especially neutrophils)

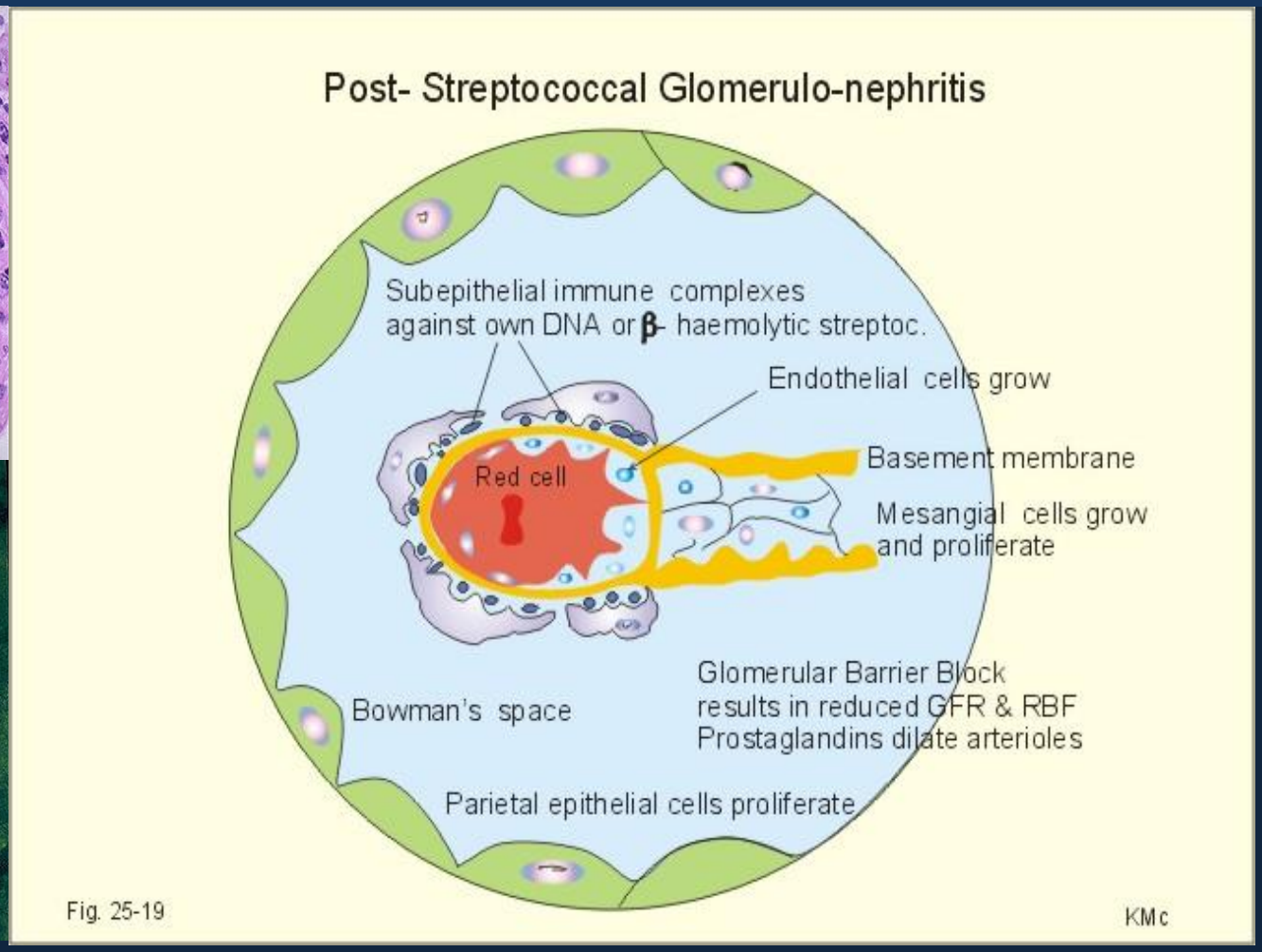
- Typical features of immune complex disease :

  - Hypocomplementemia
  - Granular deposits of IgG & complement on GBM

Post streptococcal GN. Diffuse Proliferative GN (Generalized damage to glomeruli)







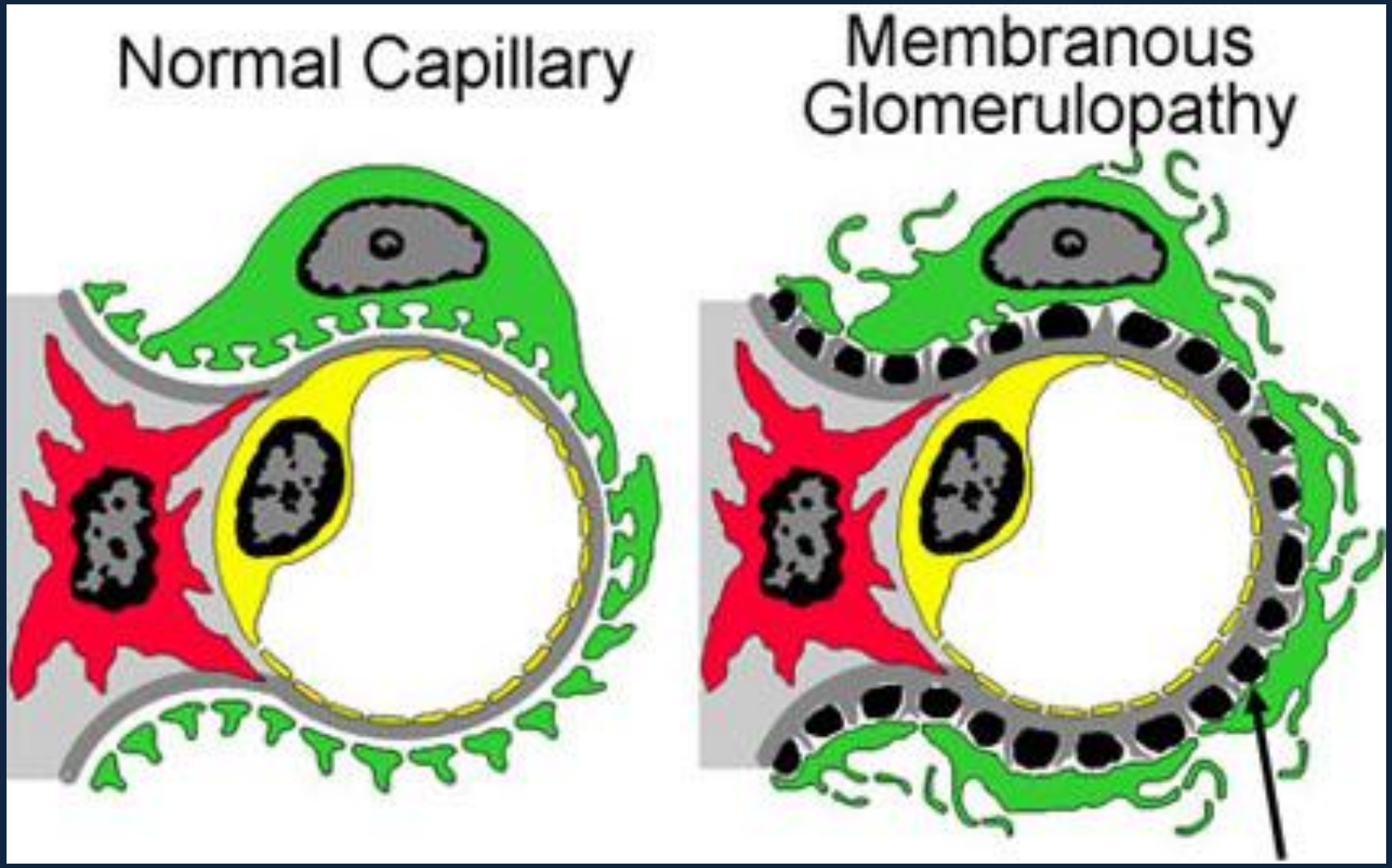
the immune deposits are distributed in the capillary loops in a granular, bumpy pattern because of the focal nature of the deposition process.

2. Membranous Glomerulonephritis (Membranous nephropathy)

- A slowly progressive disease

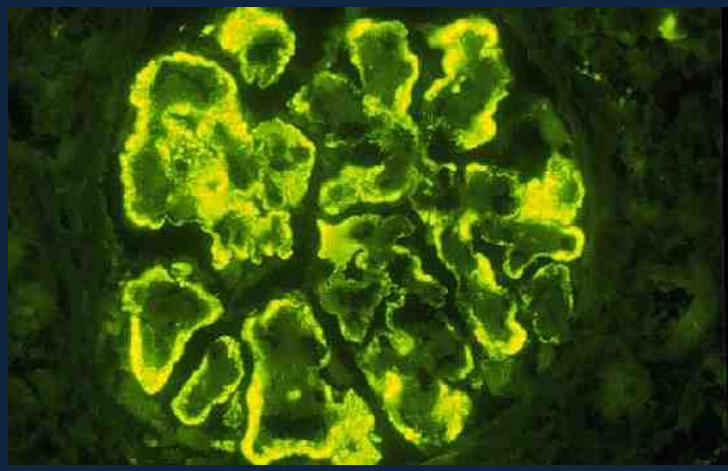
- A form of chronic immune-complex nephritis

- Most common between 30 - 50 years


Normal Capillary
Membranous Glomerulopathy

3. Membranoproliferative Glomerulonephritis (MPGN) OR Mesangiocapillary GN

It is a chronic progressive glomerulonephritis that occurs in older children and adults



2 main types :

Type I MPGN (80% of cases)

- Circulating immune complexes have been identified
- May occur in association with hepatitis B&C antigenemia, extra-renal infections or SLE
- Characterized by subendothelial and mesangial deposits

Type II MPGN

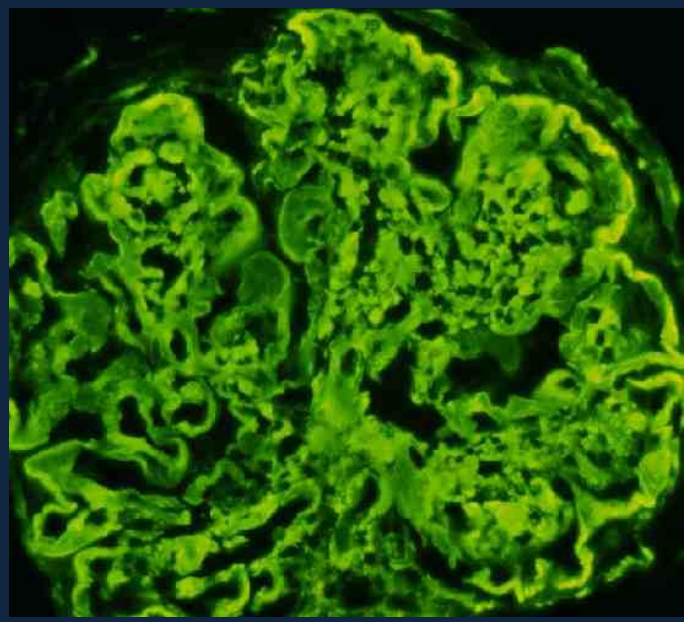
Also known as : dense deposit disease .

The fundamental abnormality is :

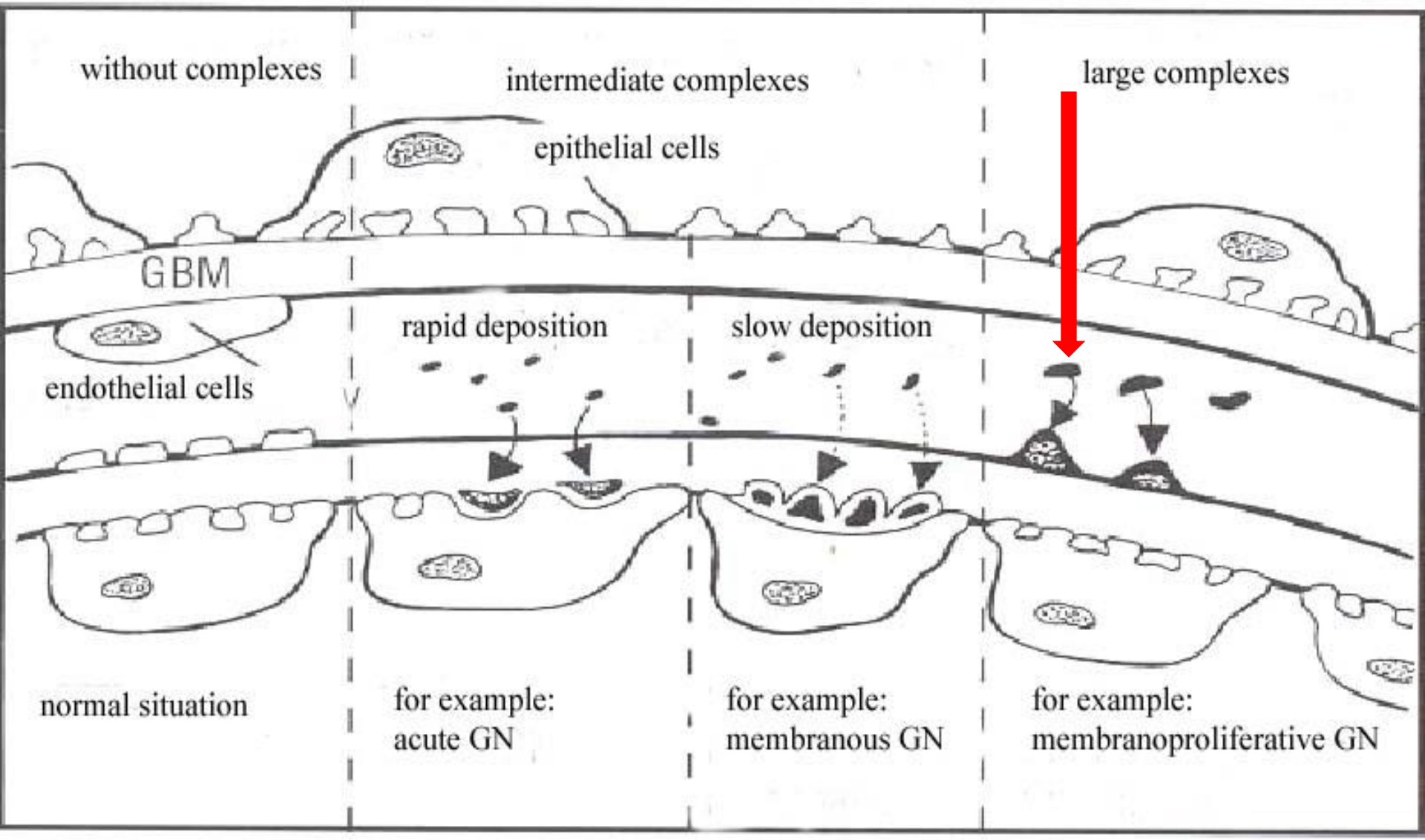
- Excessive complement activation.

- Some patients have autoantibody against C3 convertase called: C3 nephritic factor.

- Characterized by intramembranous dense deposits



Membranoproliferative GN



4. IgA Nephropathy (Berger disease)

The most common from of primary glomerulonephritis in the world

- Affects children and young adults

- Begins as an episode of gross hematuria that occurs within 1-2 days of a non specific upper respiratory tract infection

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IgA Nephropathy

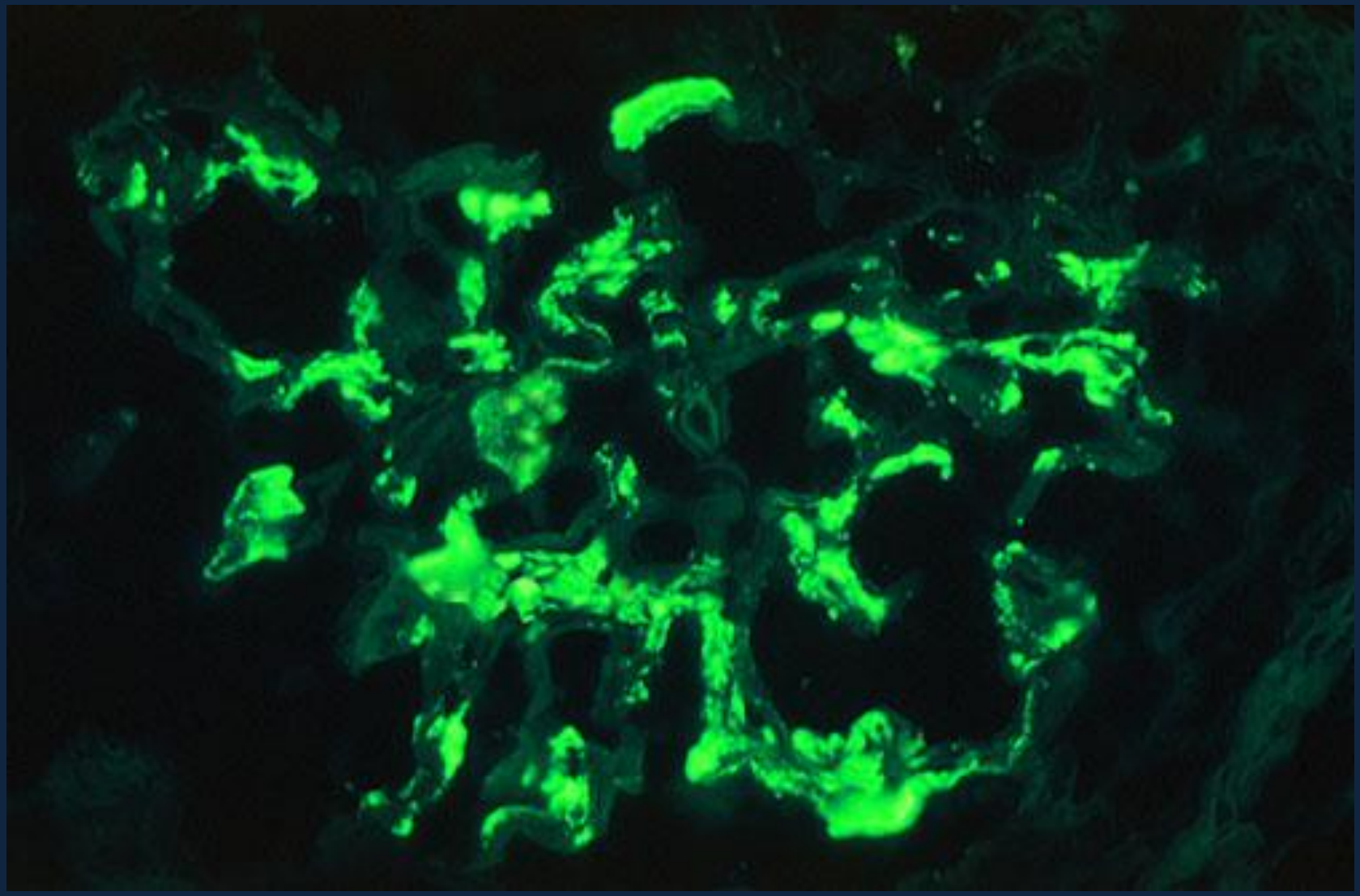
- The pathogenic hallmark is :

- Deposition of IgA & complement C3 in the mesangium

- There is evidence of :

  Activation of complement by the alternative pathway (serum complement C2 and C4 will be normal)

IgA Nephropathy



This immunofluorescence pattern demonstrates positivity with antibody to IgA. The pattern is that of mesangial deposition in the glomerulus. This is IgA nephropathy.

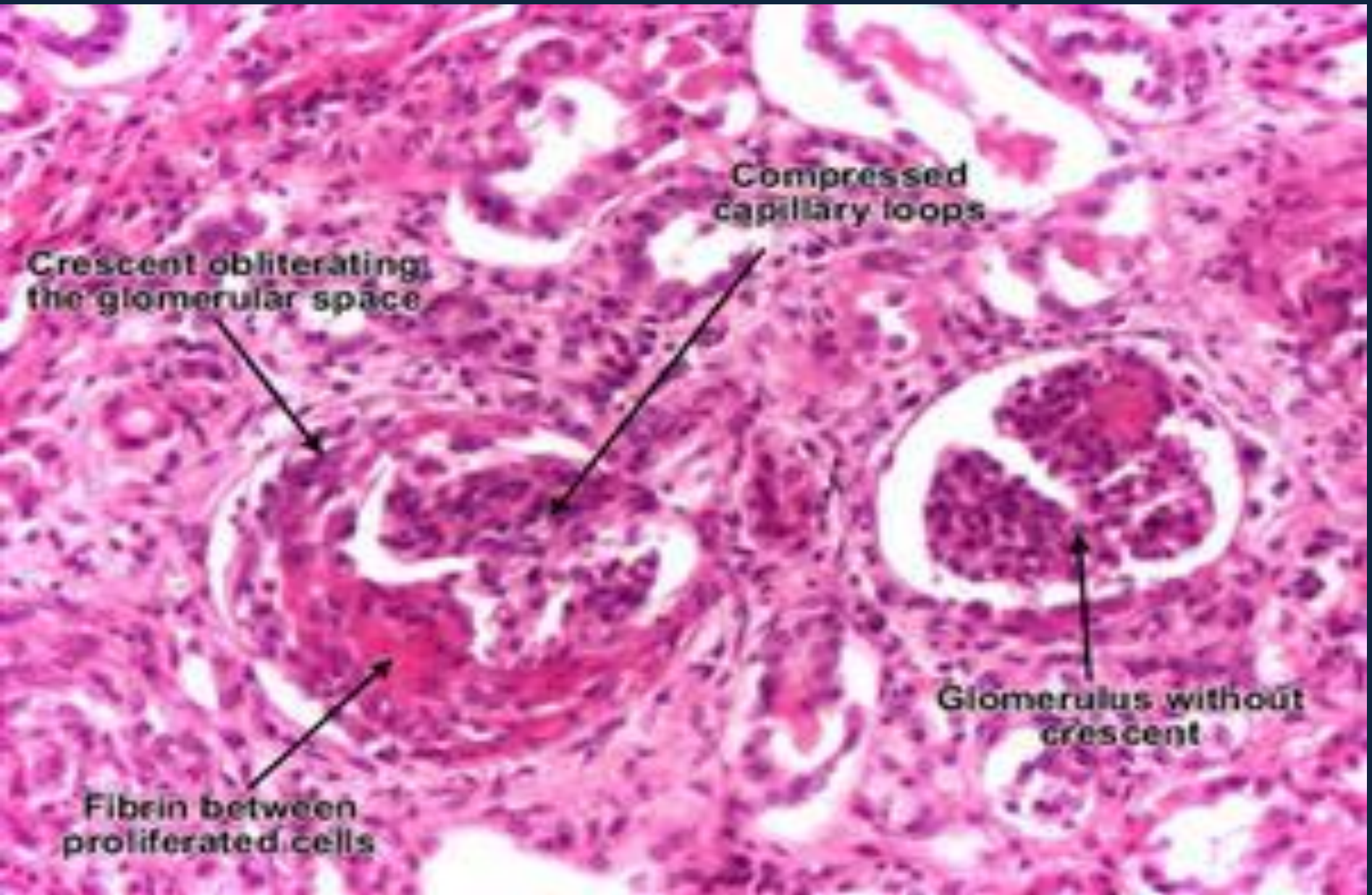
5. Rapidly Progressive (Cresentic) Glomerulonephritis (RPGN)

- RPGN is a clinical syndrome and not a specific form of GN

  In most cases the glomerular injury is immunologically mediated

  A practical classification divides CrGN into three groups on the basis of immunologic findings

Rapidly Progressive (Cresentic) Glomerulonephritis



Type I (Anti-GBM antibody) (Cresentic GN)

Characterized by linear deposition of IgG and C3 on the GBM

- Goodpasture syndrome

Antibodies bind also in the pulmonary alveolar capillary basement membranes

Anti - Gbm Glomerulo - Nephritis

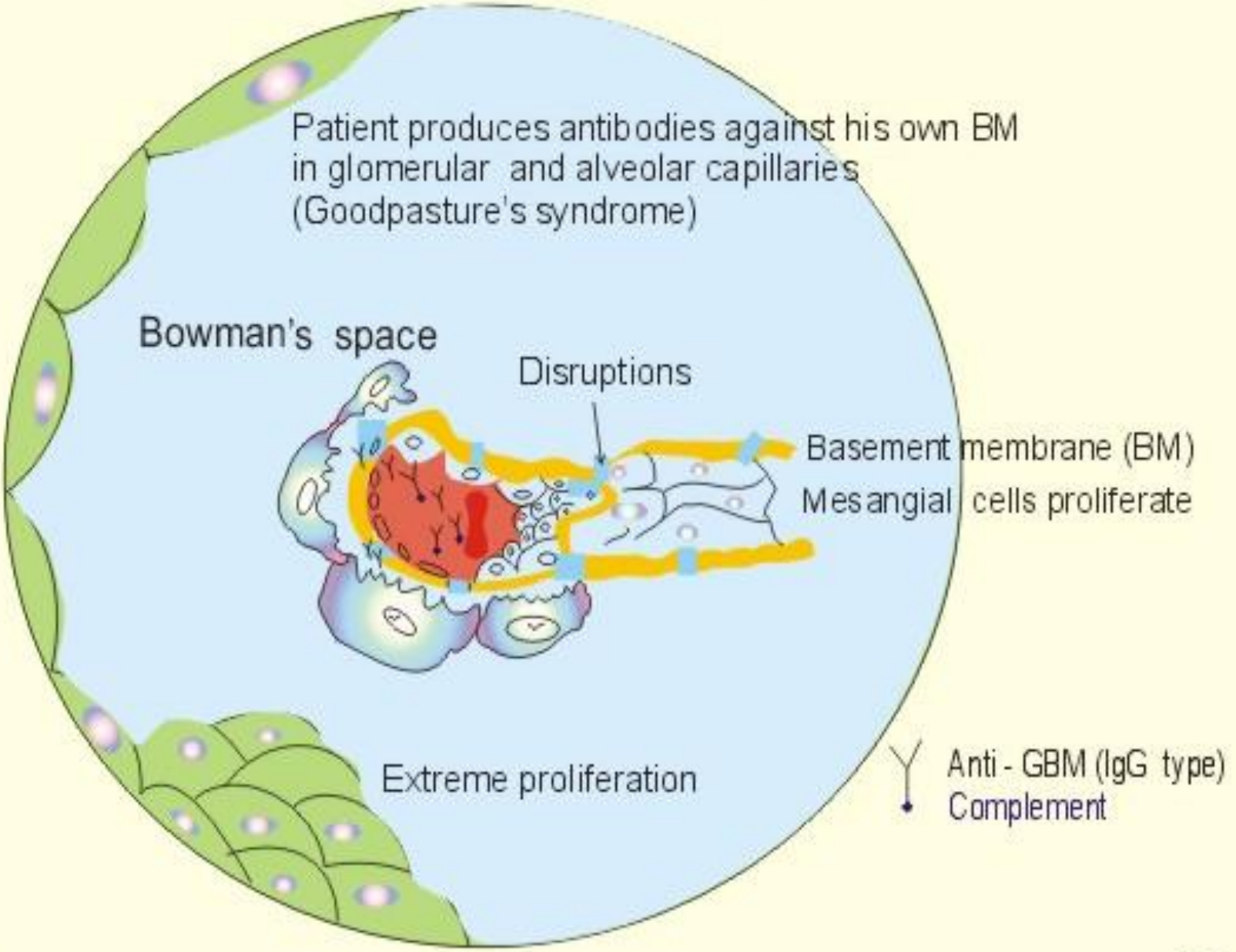


Fig. 25-20

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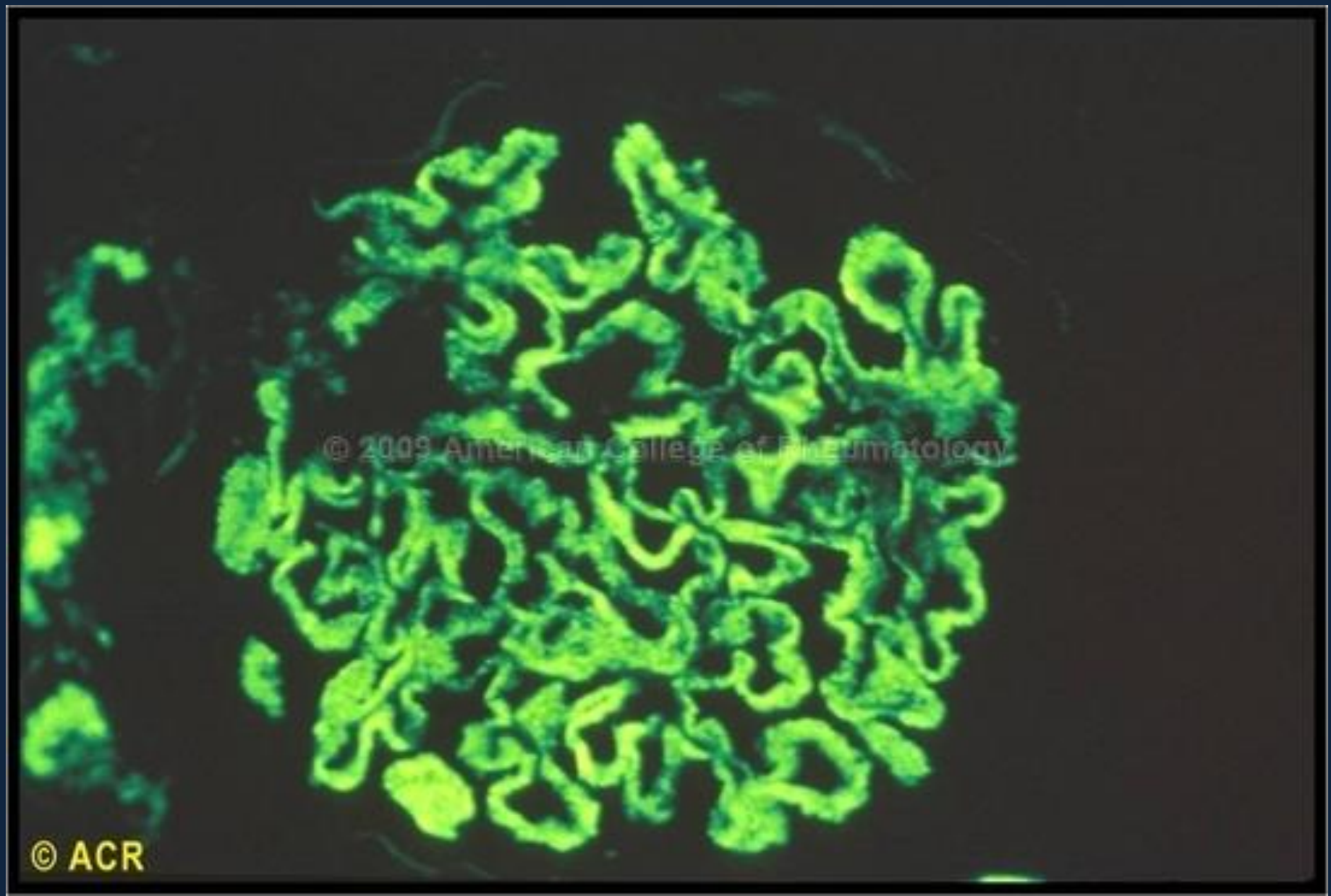
Type II
(Immune complex - mediated Cresentic GN)

- May occur as a complication of any of the immune complex nephritides

  - Post infectious.
  - SLE
  - IgA nephropathy

Characteristic granular (lumpy-bumpy) pattern of staining of the GBM for immunoglobulin & complement.

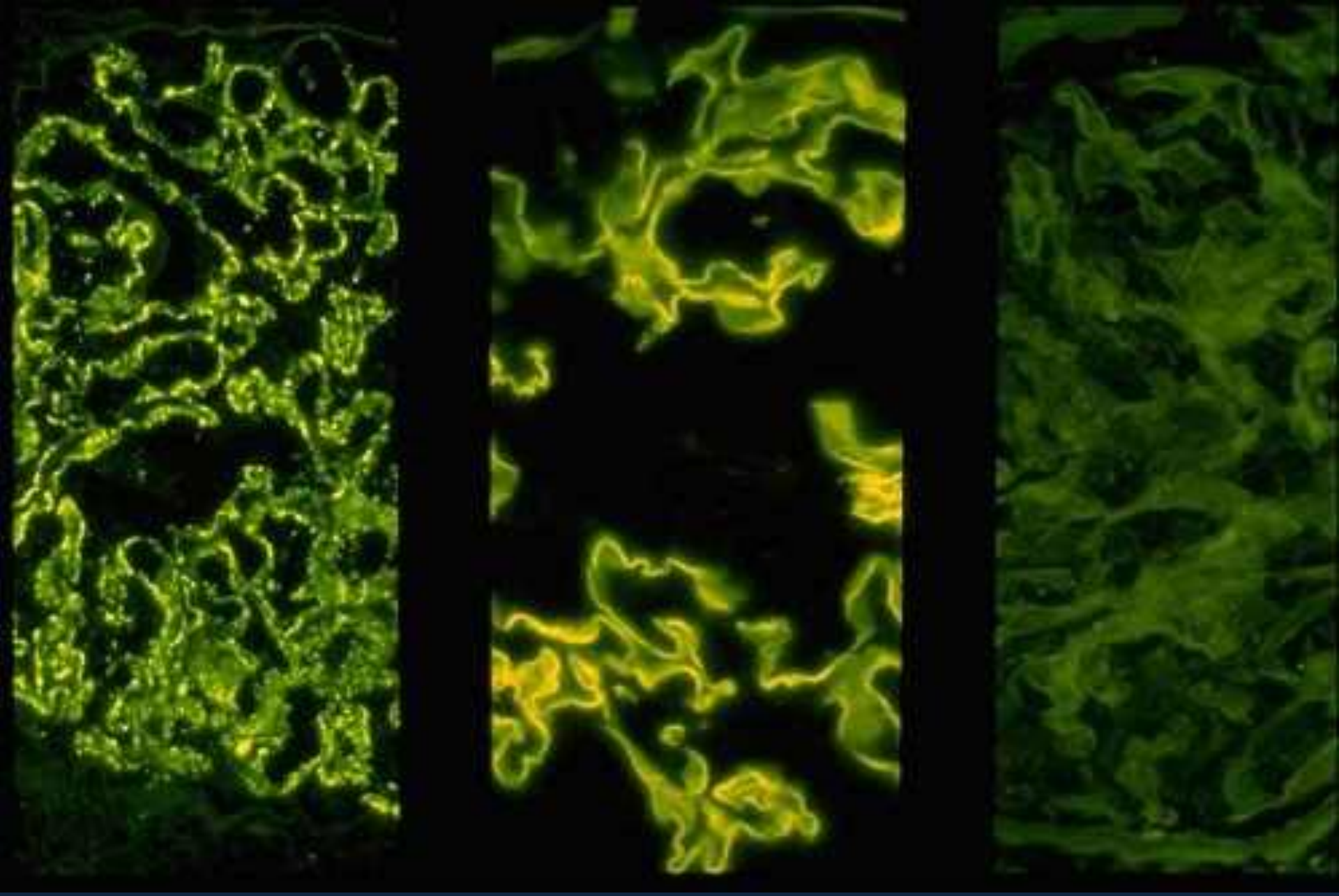
A lumpy-bumpy pattern of staining of the GBM



Type III (Pauci-immune) Cresentic GN

- Defined by the lack of anti-GBM antibodies.

- Most cases are associated with:
  Anti-neutrophil cytoplasmic antibodies in serum (ANCA) and systemic vasculitis



Granular staining
(Immune complex)

Linear staining
(Anti-GBM)

No antibody staining
(Pauci associated with vasculitis)

Take home message

- Immune complexes underly the pathogenesis of many of the glomerulo-nephritides.
- Activation of the complement system is an integral part of the process, and measurement of the complement proteins help in diagnosis and follow-up of patients.
- Immunofluoresence of renal biopsy demonstrate the presence of immune complexes and confirm the diagnosis.