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The Kidney and the Urinary Tract System

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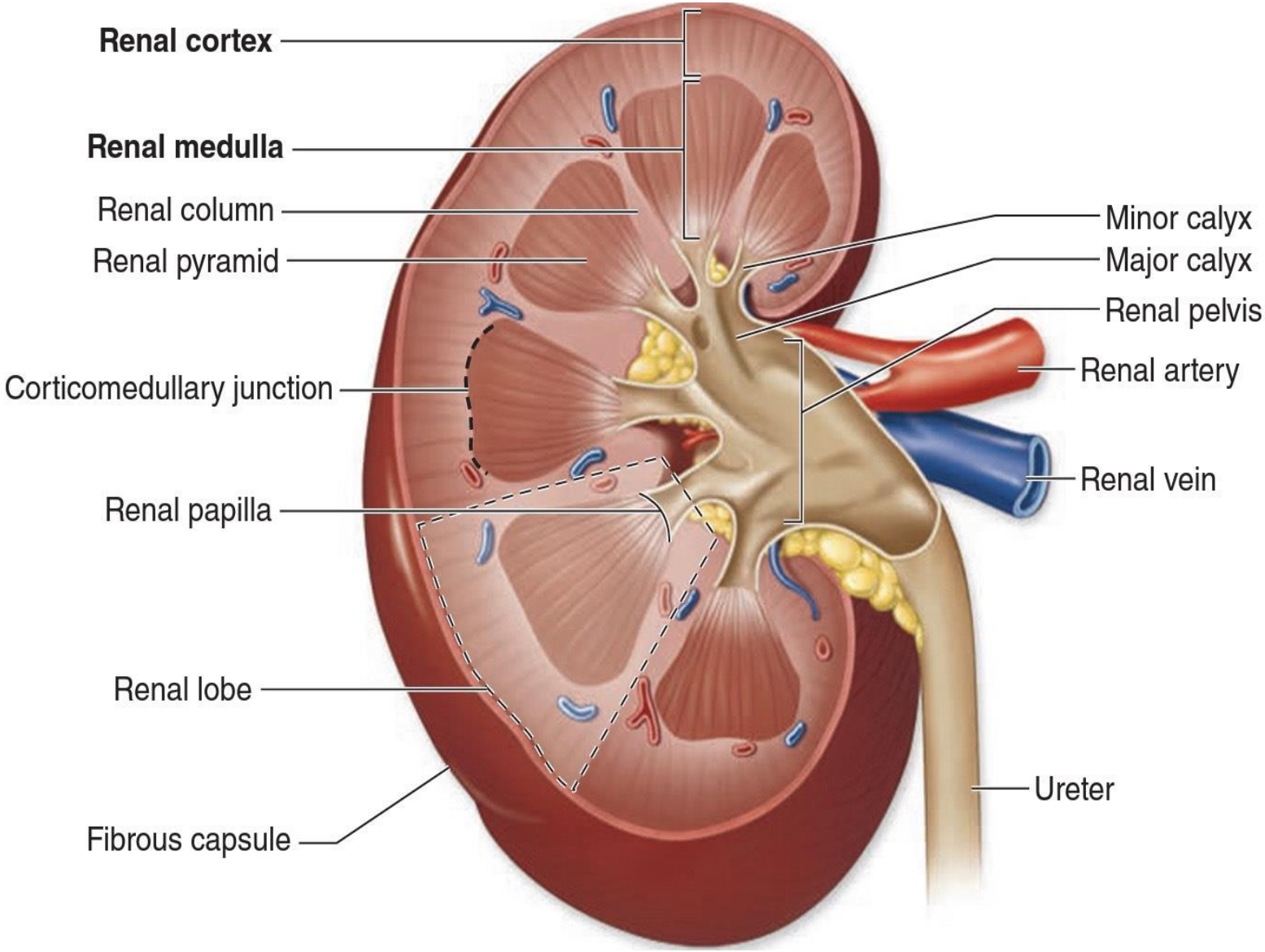
. The kidneys:

- Each kidney is a bean shaped organ that has an outer cortex, surrounding medulla that is divided into 8-12 renal pyramids
-The apex of each pyramid inserts into the minor calyx , a subdivision of two or three major calyces extending from the renal pelvis.

Structure of the kidney



Functions of the kidney

1. Excrete the metabolic waste products , and thus regulating the body concentration of water, salt, calcium, phosphorus and others.
2. Maintain acid –base balance of plasma.
3. Secreting hormones such as erythropoietin, renin , prostaglandins, and regulate vitamin D metabolism.

Clinical manifestations of Renal diseases :

1.Azotemia:

- Elevation in blood urea nitrogen(BUN) and creatinine levels with reduced glomerular filtration rate (GFR).
- It is a consequence of many renal disorders.

2. Nephritic syndrome:

.It is a clinical entity caused by glomerular disease and characterized by :

- **Hematuria**
- **Azotemia**
- **Mild to moderate proteinuria**
- **Hypertension**

. It is the classical presentation of acute poststreptococcal glomerulonephritis.

3. Nephrotic syndrome

-Characterized by

1. Heavy proteinuria (more than 3.5 g/day)

2. Hypoalbuminemia

3. Severe edema, hyperlipidemia, and lipiduria

4. Asymptomatic hematuria and/ or proteinuria:

Typically a manifestation of IgA nephropathy, alport syndrome , subtle or mild glomerular abnormalities.

5. Acute renal failure(ARF):

.Characterized by rapid decline in GFR (within hours to days), with an acute increase in serum creatinine , often associated with oliguria and anuria.
It can result from glomerular, interstitial, vascular or acute tubular injury.

6. Chronic renal disease:

.The presence of a persistent diminished GFR, and various metabolic and electrolyte disturbances

It is the end result of all chronic renal parenchymal diseases.

7. End-stage renal disease (ESRD):

The GFR is less than 5% of normal; this is the terminal stage of uremia.

8.Urinary tract infection

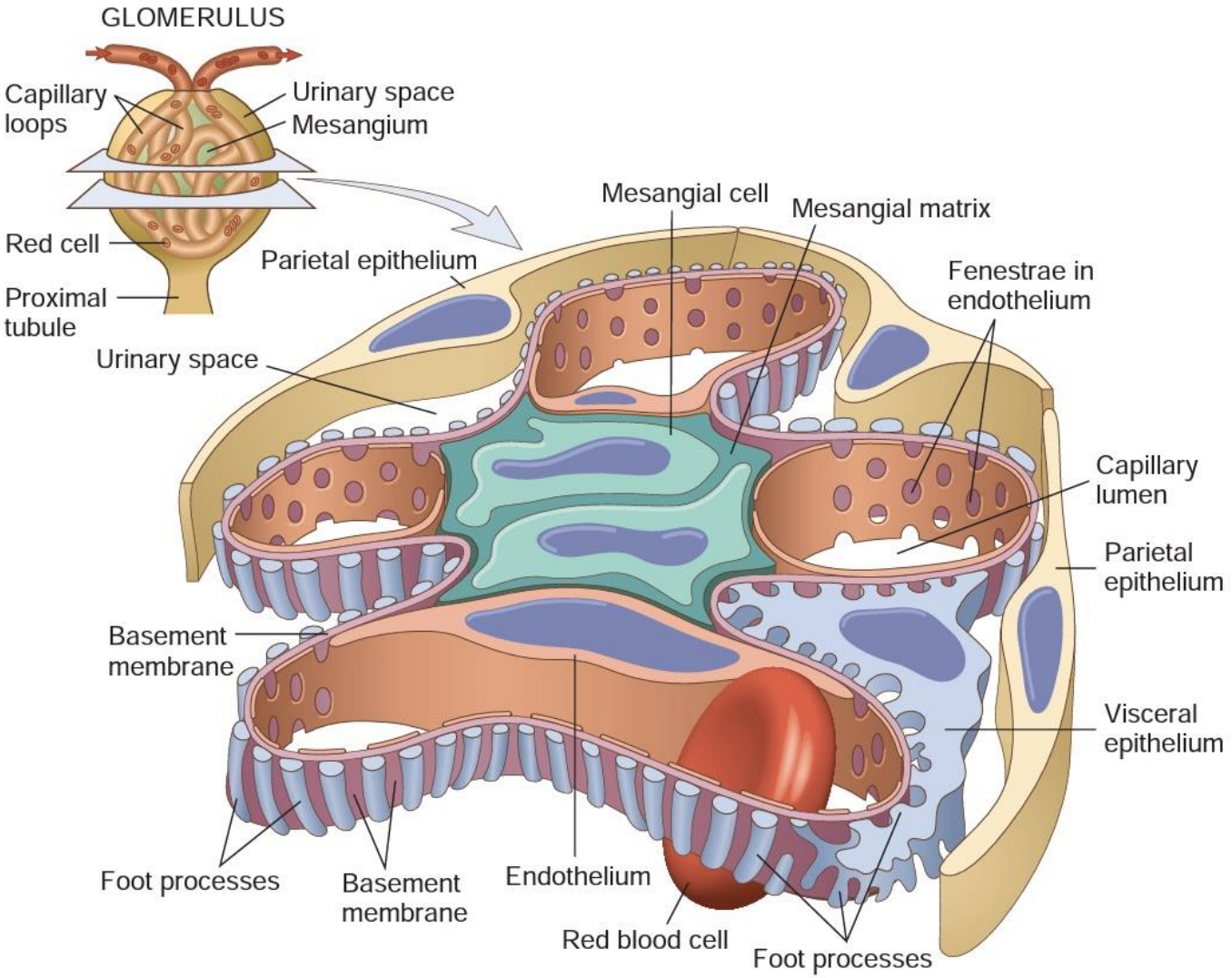
- Characterized by **bacteriuria** and **pyuria**
- It affect the kidney (pyelonephritis) or the bladder (cystitis).

9. Nephrolithiasis (renal stones)

Manifested by severe pain (renal colic) and hematuria

.The study of the kidney diseases is facilitated by dividing them into those that affect the **four basic morphologic** components : glomeruli , tubules , interstitium and blood vessels.

Glomerular Diseases



.Glomerular diseases constitute some of the major problems in nephrology.

.Glomerulonephritis is classified into two main types:

- **Primary glomerulonephritis** : in which the kidney is the only or predominant organ involved.
- **Secondary glomerulonephritis**: which the kidney is one of many organs damaged by a systemic disease.

Glomerular diseases

Primary Glomerular Diseases

Minimal-change disease
Focal segmental glomerulosclerosis
Membranous nephropathy
Acute postinfectious glomerulonephritis
Membranoproliferative glomerulonephritis
IgA nephropathy
Dense deposit disease
C3 glomerulonephritis

Glomerulopathies Secondary to Systemic Diseases

Lupus nephritis (systemic lupus erythematosus)
Diabetic nephropathy
Amyloidosis
Glomerulopathy secondary to multiple myeloma
Goodpasture syndrome
Microscopic polyangiitis
Granulomatosis with polyangiitis
Henoch-Schönlein purpura
Bacterial endocarditis–related glomerulonephritis
Thrombotic microangiopathy

Pathogenesis of glomerulonephritis

.There are two basic mechanisms of glomerular
injury:

1. Immune mediated
2. Non- immune mediated

.Immune mechanisms underlie most forms of primary glomerulopathy and many of the secondary glomerular disorders

Immune Mechanisms of Glomerular Injury

1. Antibody-Mediated Injury:

*In Situ Immune Complex Deposition:

-Fixed intrinsic tissue antigens

-planted antigens

Exogenous (infectious agents, drugs)

Endogenous (DNA, immunoglobulins, immune complexes, IgA)

*Circulating Immune Complex Deposition:

- Endogenous antigens (e.g., DNA, tumor antigens)

-Exogenous antigens (e.g., infectious products)

* autoantibody mediated GN

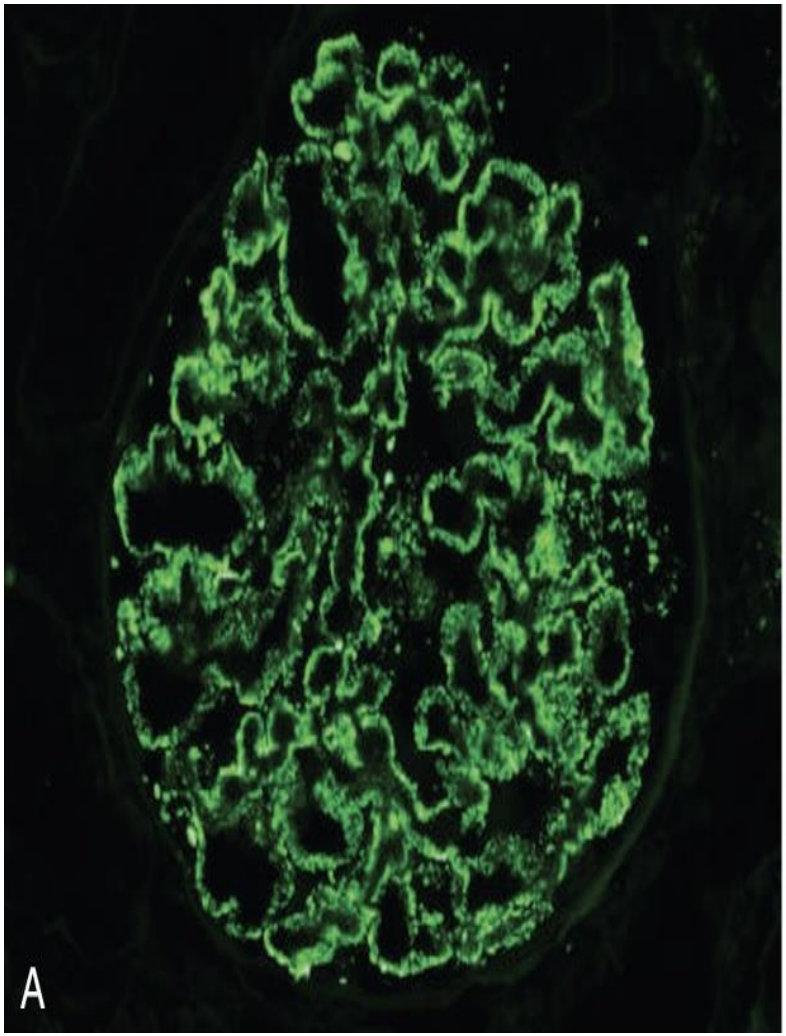
2.Cell-Mediated Immune Injury

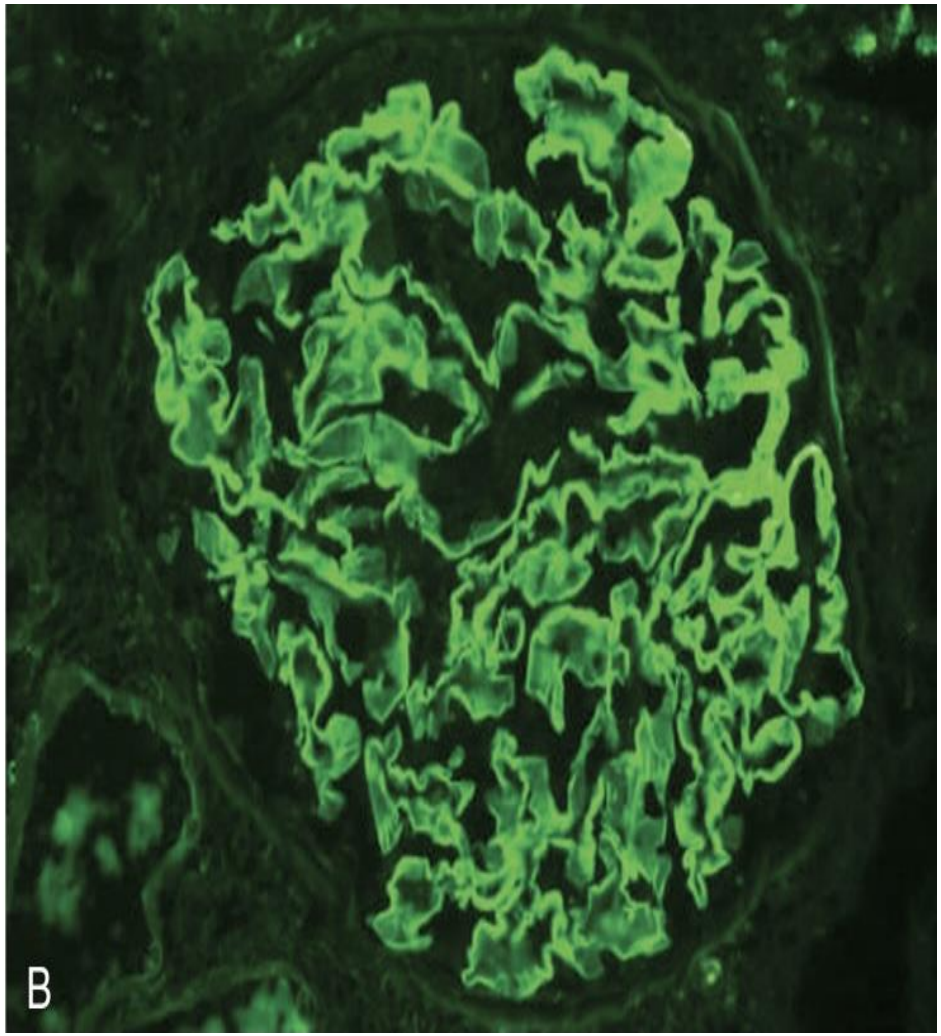
3.Activation of Alternative Complement Pathway

Patterns of immune complex deposition by immunoflorescence

A: Granular

B: Linear





Nephritic Syndrome

1 . Acute Diffuse Proliferative Glomerulonephritis
2 . Rapidly Progressive (Crescentic) Glomerulonephritis

1- Acute Diffuse Proliferative Glomerulonephritis (Postinfectious):

.Cluster of diseases is characterized histologically by diffuse **proliferation** of glomerular cells associated with infiltration of leukocytes.

.These lesions are typically caused by **immune complexes**.

.It usually appears **1 to 4 weeks** after a streptococcal infection of the pharynx or skin (impetigo).
Only certain strains of group A β-hemolytic streptococci are **nephritogenic**.

.**Other infections**, including those of bacterial (e.g., staphylococcal, pneumococcal and meningococcemia), viral (e.g., hepatitis B, hepatitis C, mumps, HIV), and parasitic (malaria, toxoplasmosis) can also cause similar form of GN.

.Occurs most frequently in **children** 6 to 10 years of age.

.Elevated titers of antistreptolysin O titers (**ASO**)against one or more streptococcal antigens are present.

.Serum complement (**C3**)levels are low.

MORPHOLOGY

Light microscopy (LM):

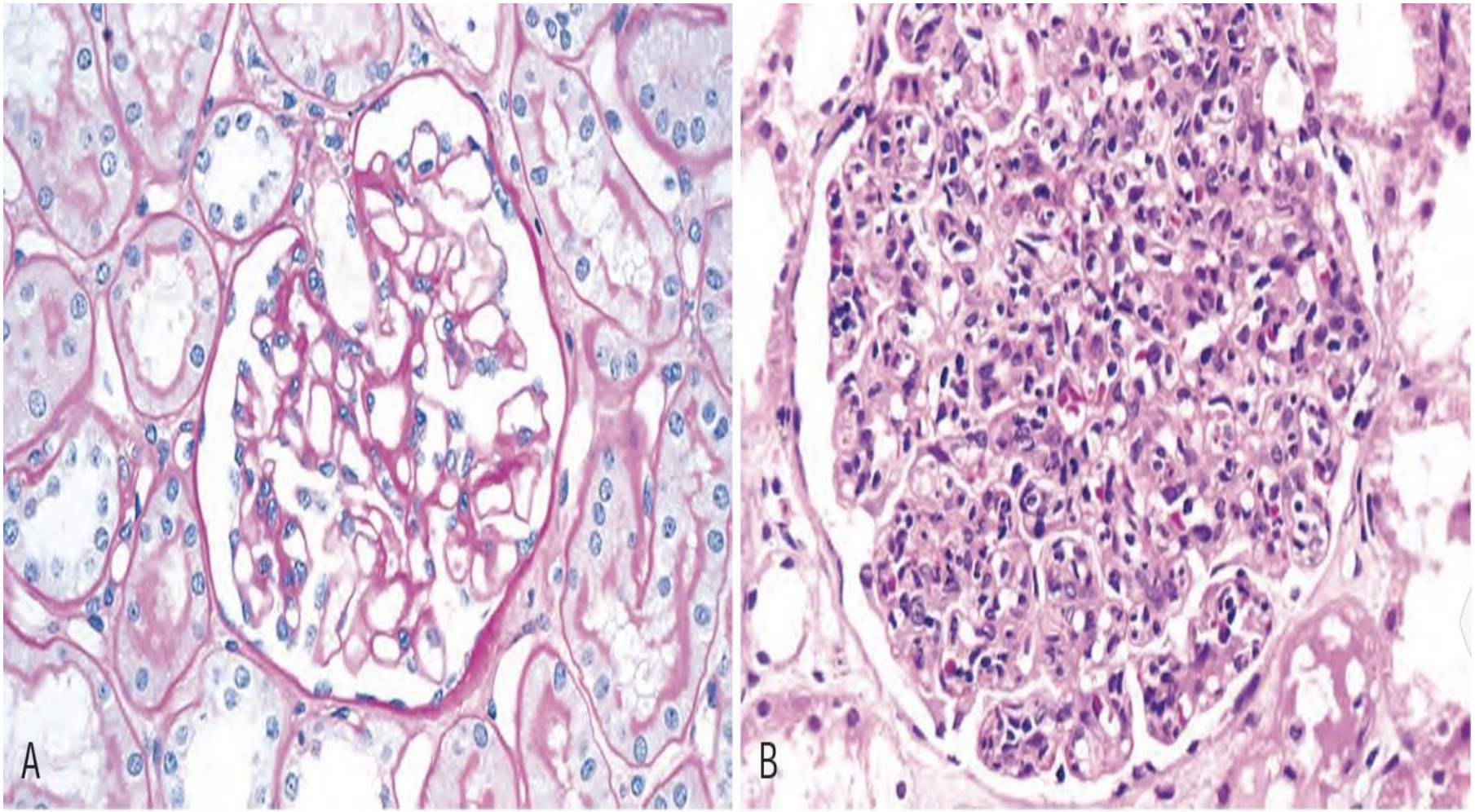
.The classic histologic picture is global and diffusely enlarged, **hypercellular** glomeruli .

.The hypercellularity is caused by :

(1) infiltration by leukocytes, both neutrophils and monocytes

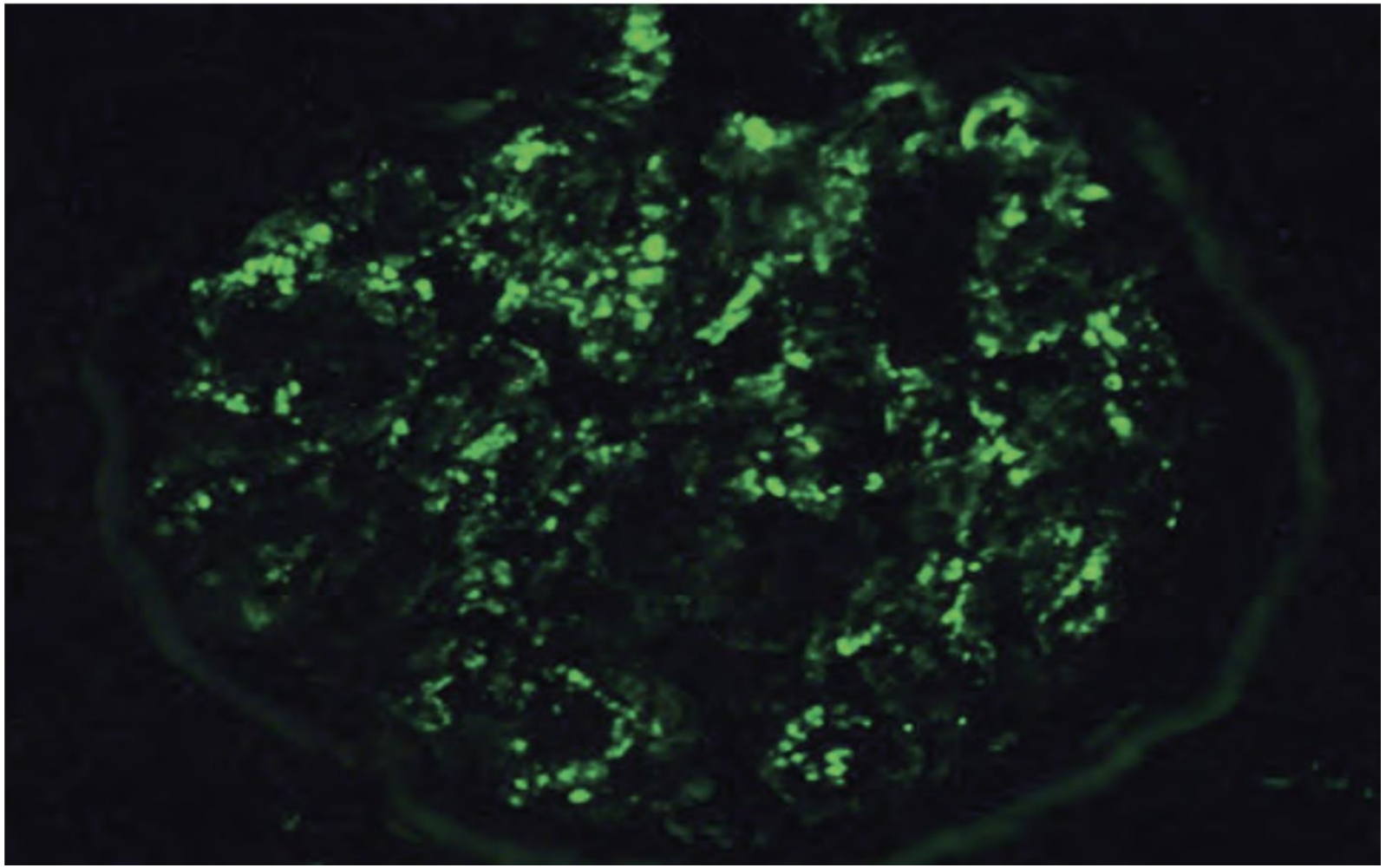
(2) proliferation of endothelial and mesangial cells

A: Normal glomerulus.
B:Acute diffuse proliferative GN



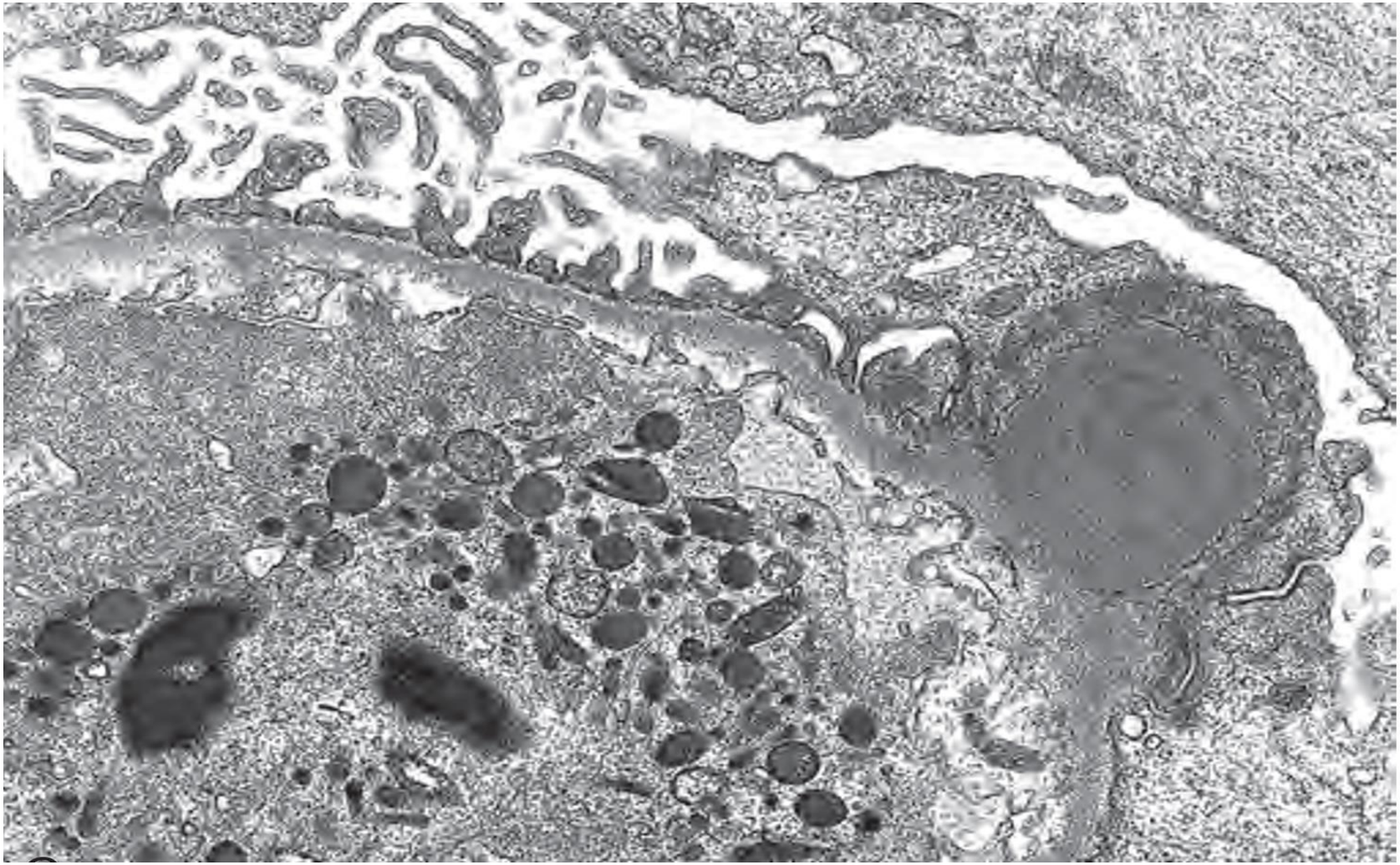
Immunofluorescence microscopy (IF)

.**Granular** deposits of **IgG, and C3**, in the mesangium and along the GBM



Electron Microscopy (EM) :

. **Subepithelial hump-like** deposits of immune complexes



Clinical course

. Malaise, fever, nausea, oliguria, and hematuria (smoky urine) 1 to 2 weeks after recovery from a sore throat.

. Mild proteinuria (usually less than 1 gm/day), periorbital edema, mild to moderate azotemia and hypertension.

Outcome

. More than **95%** of affected children eventually recover

. In adults the only about **60%** of the patients recover

2-Rapidly Progressive (Crescentic) Glomerulonephritis (RPGN)

. A syndrome associated with **severe glomerular injury**.

. Rapid and progressive **loss of renal** function associated with **severe oliguria** and signs of **nephritic syndrome**.

.The most common histologic picture is the presence of **crescents** in most of the glomeruli (crescentic glomerulonephritis)

Classification and Pathogenesis

.Mostly the glomerular injury is immunologically mediated , distinct pathogenic mechanisms have been described as follows:

1• **Anti-GBM antibody mediated disease(good pasture disease**) characterized by **linear** deposits of IgG and, C3 in the GBM.

***Goodpasture Syndrome**

Autoimmune disease consists of pulmonary hemorrhage (hemoptysis)and ARF.

. It results from Autoantibodies against the GBM (anti-GBM) and alveolar basement membrane.

. Patients are young adult male.

. Plasmapheresis may help the patients , steroids & cytotoxic drugs

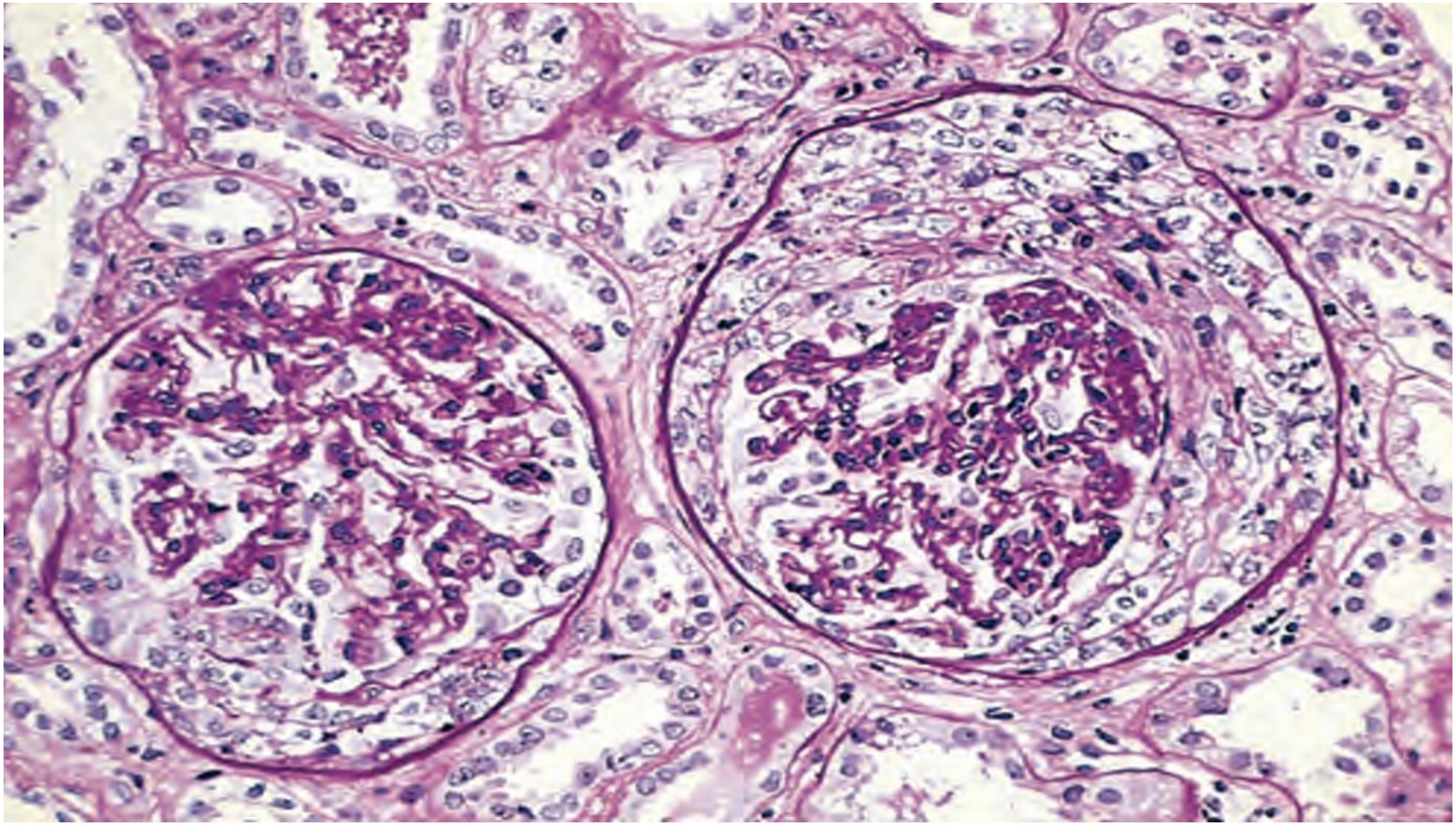
2• Diseases caused by **immune complex** deposition. can be a complication of any of the immune complex nephritides,

IF: **granular** pattern staining of immune complexes.

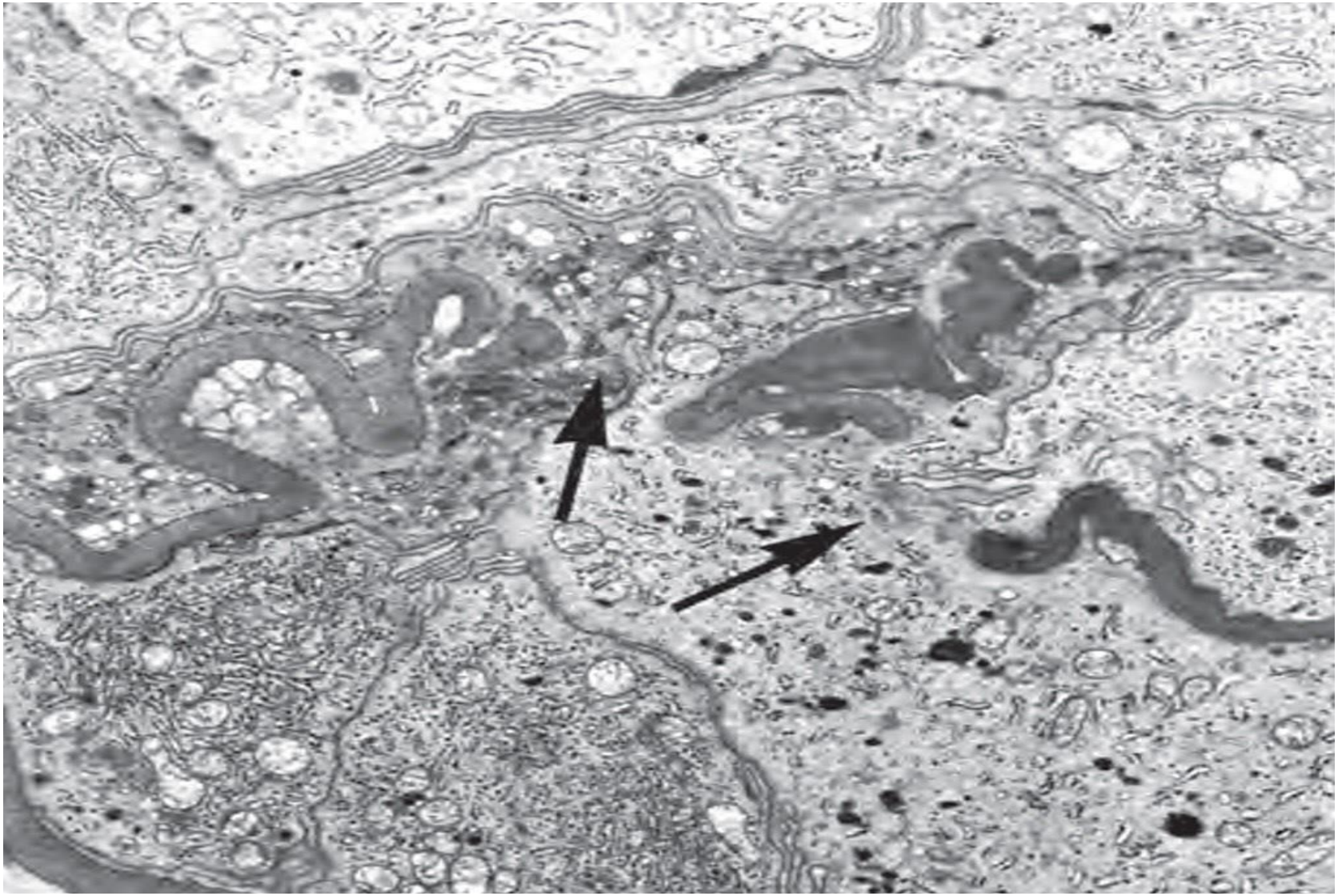
3• **Pauci-immune** RPGN, defined by the lack of detectable anti-GBM antibodies or immune complexes by immunofluorescence and electron microscopy. Most patients with this type of RPGN have circulating antineutrophil cytoplasmic antibodies (ANCAs)
This type may be a component of a systemic vasculitis such as microscopic polyangiitis , or limited to the kidneys

MORPHOLOGY

Characterized by distinctive **Crescents**, which are formed by proliferation of parietal cells and by migration of leukocytes into the urinary space



EM: GBM focal disruption



Diseases presented mostly with asymptomatic hematuria:

1. IgA Nephropathy
2. Hereditary nephritis

IgA Nephropathy (Berger Disease)

. The most common type of glomerulonephritis worldwide.

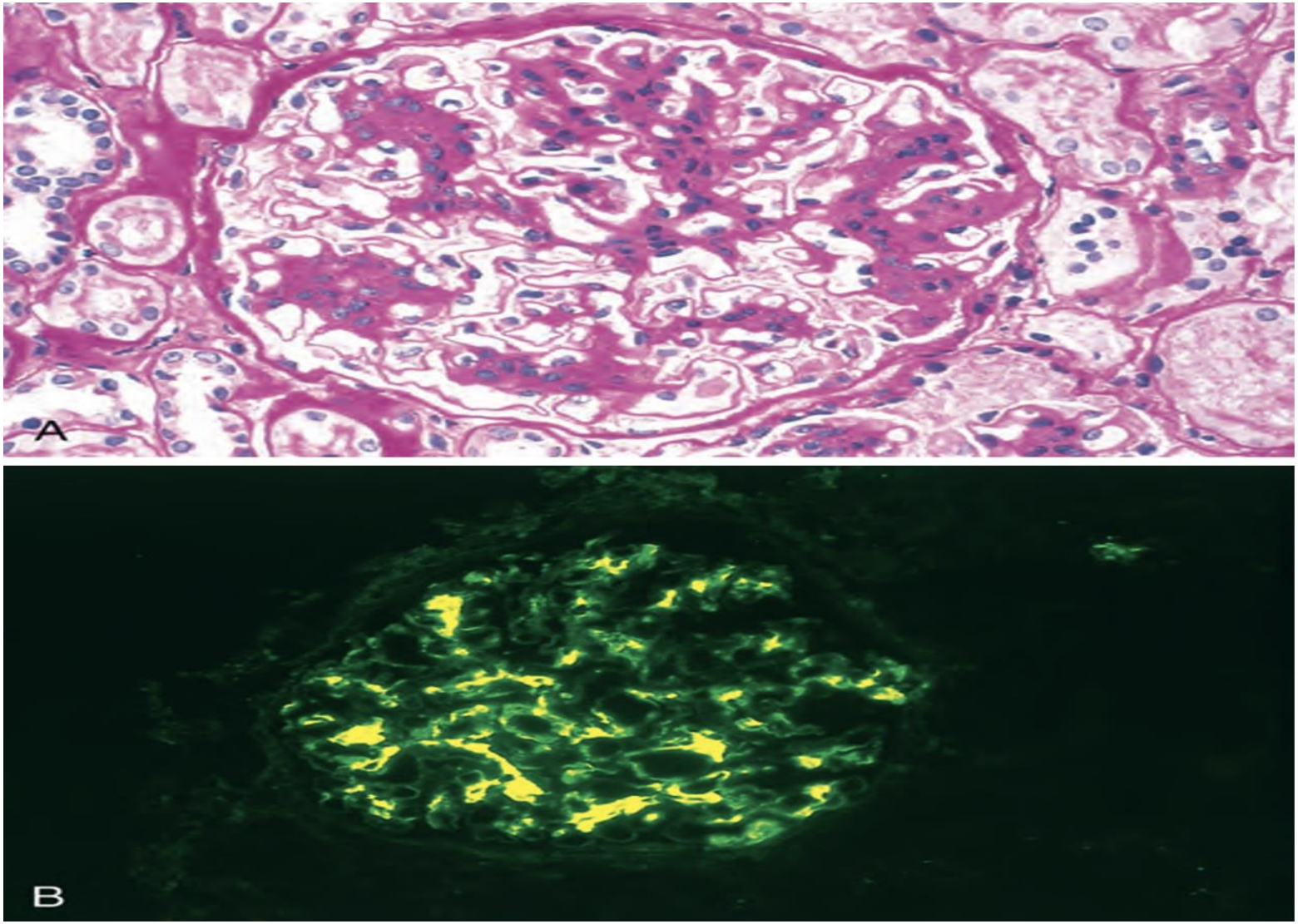
.Characterized by the presence of prominent IgA deposits in the mesangial regions and recurrent hematuria.

. The diagnosis is made only by the detection of glomerular IgA deposition

. Mild proteinuria is usually present

IgA nephropathy A: Mesangial expansion

B: Mesangial deposition of IgA



Hereditary nephritis

1. Alport syndrome : is caused by mutations in genes encoding GBM collagen.

It manifests as hematuria and slowly declining renal function.

2. Thin basement membrane disease : is also caused by mutations encoding the GBM collagen, however, unlike Alport syndrome, this is usually a benign nonprogressive disorder