Renal Pathology (1)2021

Lect1&2

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OBJECTIVES

- DESCRIPTION OF GLOMERULI
- SYMPTOMS RELATED TO RENAL IMPAIRMENT’
- LABORATORY DIAGNODSIS
- GLOMERULAR DISEASES
- NEPHROTIC SYNDROME
- NEPHRITIS SYNDROME
- URINARY TRACT INFECTIONS
- CHILDHOOD HUS
- THROMBOTIC MICROANGIOPATHIES
- MALIGNANT H & MALIGNANT NEPHROSCLEROSIS

- Kidney diseases can be divided into those affecting the 4 basic components:

(1) glomeruli

(2) tubules

(3) Blood vessels

(4) interstitium;

because some components seem to be more vulnerable to specific forms of renal injury; **e.g. glomerular(G)** diseases are often **immunologically mediated;**

whereas **tubular & interstitial** disorders are more likely to be caused by **toxic or infectious agents,**

CLINICAL MANIFESTATIONS OF RENAL DISEASES

- Azotemia is another word that refers to high levels of urea and is used primarily when the abnormality can be measured chemically but is not yet so severe as to produce symptoms.
- Renal azotemia is produced by many renal disorders, but azotemia may also arises from extra renal disorders including:
- Prerenal azotemia is encountered when there is **hypo perfusion** of the kidneys, which decrease GFR in the absence of renal parenchymal damage.
- Postrenal azotemia can result when urine flow is **obstructed below the level of the kidney**. Relief of the obstruction is followed by correction of the azotemia.

❑**Uremia** means progression of the azotemia to clinical manifestations & systemic biochemical abnormalities

❑**Uremia** is the condition of having high levels of urea in the blood. Urea is one of the primary components of urine. It can be defined as an excess of amino acid and protein metabolism end products, such as urea and creatinine, in the blood that would be normally excreted in the urine.

❑Uremic syndrome can be defined as the terminal clinical manifestation of kidney failure (also called renal failure).[It is the signs, symptoms and results from laboratory tests which result from inadequate excretory, regulatory and endocrine function of the kidneys.

❑ Both uremia and uremic syndrome have been used interchangeably to denote a very high plasma urea concentration that is the result of renal failure.

❖Signs and symptoms

- Classical signs of uremia are: progressive weakness and easy fatigue, loss of appetite due to nausea and vomiting, muscle atrophy, tremors,, anemia, hemostasis disorders, , granulocytic, lymphocytic and platelet dysfunction , osteomalacia, β_2-microglobulin amyloidosis, bone disease (via vitamin D deficiency, secondary,hyperparathyroidism and hyperphosphatemia), itching, skin dryness, polyneuritis, restless legs, cramps, peripheral neuropathy, abnormal mental function diurnal somnolence, night insomnia, memory and concentration disorders, asthenia, headache, confusion, fatigue, seizures, coma, encephal opathy
- frequent shallow respiration and metabolic acidosis. Without intervention via dialysis or kidney transplant, uremia due to renal failure will progress and cause stupor, coma and death. Because uremia is mostly a consequence of kidney failure, its signs and symptoms often occur concomitantly with other signs and symptoms of kidney failure.

DIAGNOSIS

- A detailed and accurate history and physical will help determine if uremia is acute or chronic. In the cases of acute uremia, causes may be identified and eliminated, leading to a higher chance for recovery of normal kidney function, if treated correctly.

Blood tests

- Primary tests performed for the diagnosis of uremia are basic metabolic panel with serum calcium and phosphorus to evaluate the GFR, blood urea nitrogen and creatinine as well as serum potassium, phosphate, calcium and sodium levels.
- Principal abnormality is very low (<30) GFR. Uremia will demonstrate **elevation of both urea and creatinine,** likely elevated potassium, high phosphate and normal or slightly high sodium, as well as likely depressed calcium levels.
- As a basic work up a physician will also evaluate for anemia and thyroid and parathyroid functions. Chronic anemia may be an ominous sign of established renal failure.
- The thyroid and parathyroid panels will help work up any symptoms of fatigue, as well as determine calcium abnormalities as they relate to uremia vs longstanding or unrelated illness of calcium metabolism.

Urine tests

- A 24-hour urine collection for determination of creatinine clearance may be an alternative, although not a very accurate test due to the collection procedure.
- Urinalysis with microscopic examination for the presence of protein, casts, blood and pH.

THE CLINICAL MANIFESTATIONS OF RENAL DISEASE CAN BE GROUPED INTO 8 MAJOR SYNDROMES.

- Some are peculiar to diseases of G; others are present in diseases that affect any one of the 4 components. These are:

(1) Acute nephritic syndrome is a G syndrome characterized by acute onset of gross hematuria(RBCs in urine), mild to moderate proteinuria, edema,azotemia,& hypertension;it is the classic presentation of acute poststreptococcal GN.

(2) The nephrotic syndromeis a G syndrome characterized by heavy proteinuria(excretion of >3.5 grams of protein/day in adults), hypoalbuminemia,severe edema, hyperlipidemia, & lipiduria(lipid in the urine).

(3) Asymptomatic hematuria or proteinuria,or both, is usually a manifestation of subtle (mild) G abnormalities.

(4) Rapidly progressive GN manifested by microscopic hematuria, dysmorphic RBC & RBC casts in the urine & mild-to-moderateproteinuria, resulting in loss of renal function in a few days or weeks

(5) Acute renal failure**(RF) or (Acute Kidney Injury)**is dominated by **oliguria or anuria** (no urine flow),
(6) Chronic renal failure(CRF) = Chronic Kidney Disease (CKD), is the **end result of all chronic renal diseases** It characterized by prolonged signs & symptoms of **uremia,** and in which, to maintain life,patient needs either long term 12 hours/week haemodialysis or renal transplant.

(7) Urinary tract infection**(UTI)**characterized by **bacteriuria& pyuria**(bacteria & leukocytes in the urine respectively)). The infection may be symptomatic or asymptomatic, & it may affect the kidney (pyelonephritis)or the bladder (cystitis).

(8) Nephrolithiasis(**renal stones**) is manifested by **renal colic, hematuria, & recurrent stone formation.**
★UT obstruction**&** renal tumors represent specific anatomic lesions that often have varied manifestations.

GLOMERULAR DISEASES

• One of the most common causes of chronic kidney disease and is major problems encountered in nephrology; and **chronic GN** is one of the most common causes of chronic kidney disease in humans.

• The glomerulus normally consists of an anastomosing **network of capillaries,** invested by two layers of epithelium. The visceral epithelium (**podocytes**) is an intrinsic part of the capillary wall, whereas the **parietal** epithelium lines **Bowman space**(urinary space), the cavity in which plasma ultrafiltrate first collects.

• The **G** capillary wall is the filtration unit & consists of the following structures **:**

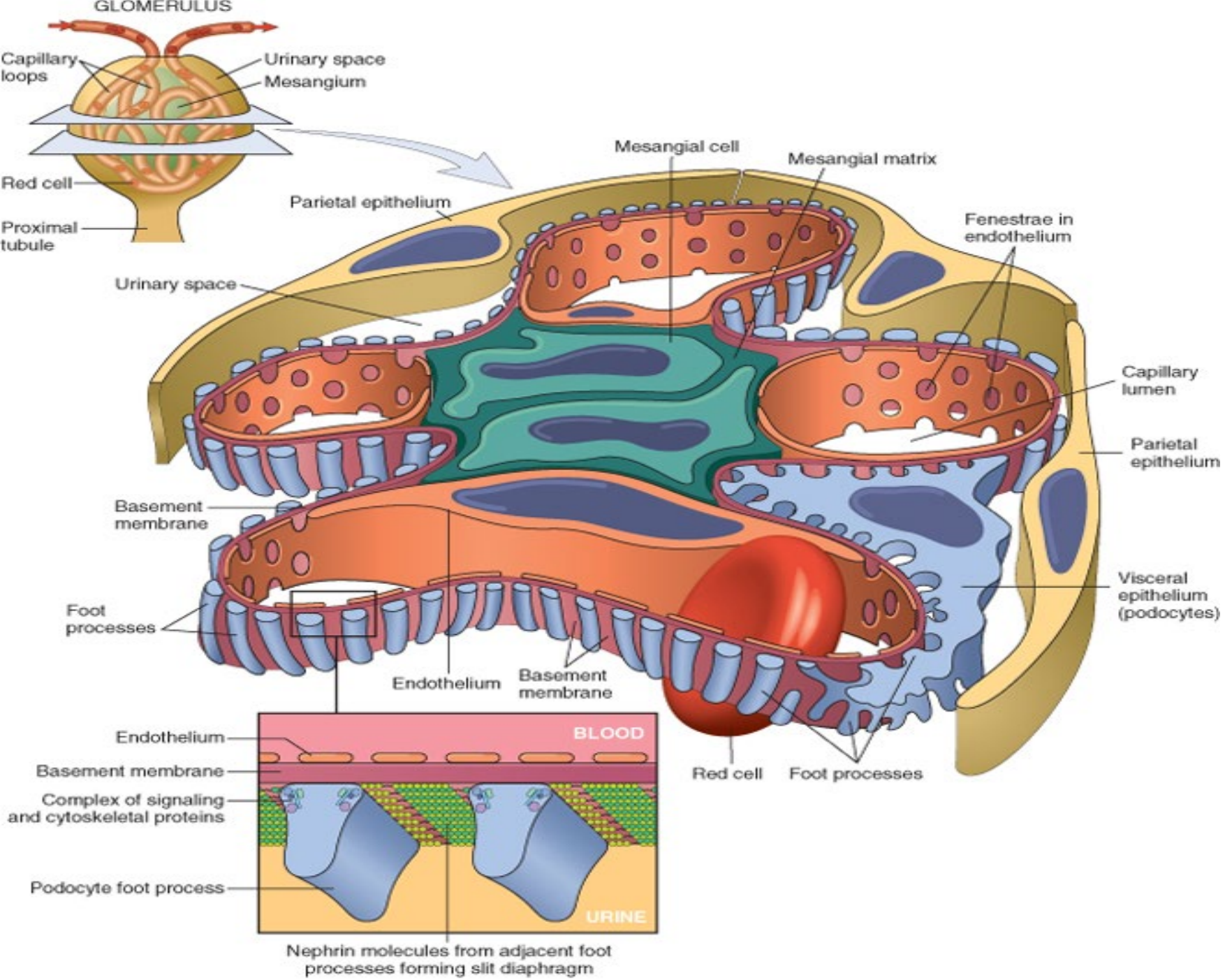
(I) A thin layer of fenestrated endothelial cells (EC).

(II) **A** glomerular basement membrane**(GBM**) with a thick, electron-dense central layer, the lamina densa,& thinner, electron-lucent peripheral layers, the lamina rara interna& lamina rara externa.The GBM consists of collagen (mostly type IV), laminin, proteoglycans, fibronectin, & several other glycoproteins.

(III) The visceral epithelial cells(podocytes),structurally complex cells that possess interdigitating foot processes embedded in & adherent to the lamina rara externa of the GBM.

- The entire G tuft is supported by mesangial cells (of mesenchymal origin) lying between the capillaries
- The major characteristics of GF are an extraordinarily **high permeability to water & small solutes**& an almost **complete impermeability to molecules of the size & molecular charge of albumin**(size: 3.6 nm.)
- This **selective permeability**, called **glomerular barrier function**, discriminates among protein molecules depending on their size (the larger, the less permeable), their charge (the more cationic (+), the more permeable), & their configuration.

Schematic diagram of a lobe of a normal glomerulus



❑ Glomeruli may be injured by diverse mechanisms, which are either a:

★Primary G diseases, those in which the kidney is the only or predominant organ involved, which we shall discuss below, or

★Secondary G diseases in which the G may be injured in the course of a number of systemic diseases (see Table number 1below); these are discussed elsewhere in this book.

❖ Glomerular Diseases Table number 1

(I) Primary Glomerular Diseases

- Minimal-change disease (MCD)
- Focal and segmental glomerulosclerosis (FSGS)
- Membranous GN = Membranous nephropathy (MN)
- Membranoproliferative GN (MPGN) Acute postinfectious GN
- IgA nephropathy
- Chronic GN

(II) Glomerulopathies Secondary to Systemic Diseases

•Lupus (SLE) nephritis •Diabetic nephropathy
•Goodpasture syndrome •Microscopic polyangiitis
•Wegener's granulomatosis •Henoch-Schönlein purpura
•Thrombotic microangiopathy •Amyloidosis
•Bacterial endocarditis-related GN •GN secondary to extrarenal infection •GN secondary to lymphoplasmacytic disorders

❖ Pathogenesis of Glomerular disease

-usually immune mediated via antibody deposition, cell mediated injury or activation of alternative complement pathway

-Antibodies deposited are either to in situ antigen (intrinsic or planted) or are circulating immune complexes

•**Intrinsic:** Goodpasture disease antigens are in basement membrane; Heymann nephritis antigens are on visceral epithelial cells; produce linear immunofluorescence patterns

•**Planted antigens** are deposited in basement membrane; may be exogenous (drugs, infectious agents) or endogenous (DNA, immunoglobulin, immune complexes); their cationic proteins bind to glomerular anionic sites and produce granular lumpy staining by immunofluorescence

•**Circulating immune complexes** may be endogenous (DNA, tumors) or exogenous (infectious products); they usually localize within glomeruli and activate complement; deposits are usually mesangial or subendothelial and resolve by macrophage phagocytosis, unless there are repeated cycles of formation (Hepatitis B / C, lupus)

•**Cell mediated immune injury** is by sensitized nephritogenic T cells

•**Progression** to end stage renal disease occurs when the glomerular filtration rate (GFR) is 30 - 50% of normal, due to compensatory hypertrophy of remaining glomeruli and systemic hypertension (inhibited by angiotensin converting enzyme inhibitors), eventually causing glomerulosclerosis

❖ The Nephrotic Syndrome

- a clinical complex resulting from glomerular disease & includes the following:
- (1) massive proteinuria (3.5 gm /day in adults).
- (2) hypoalbuminemia (≤ 3 gm/dL).
- (3) generalized edema
- (4) hyperlipidemia and lipiduria.
- (5) little or no azotemia, hematuria, or hypertension.

Causes of Nephrotic Syndrome

- **1-Primary Glomerular Diseases**
- **2-Secondary (Systemic Diseases with Renal Manifestations)**

- **Primary Diseases that Present Mostly with Nephrotic Syndrome**
- **1-Minimal-change disease**
- **2-Focal segmental glomerulosclerosis(FSGS).**
- **3-Membranous nephropathy**
- **4-membranoproliferativeGN type 1 (usually a combination of nephrotic/ nephritic syndrome)**

❑Causes of Nephrotic Syndrome in systemic diseases

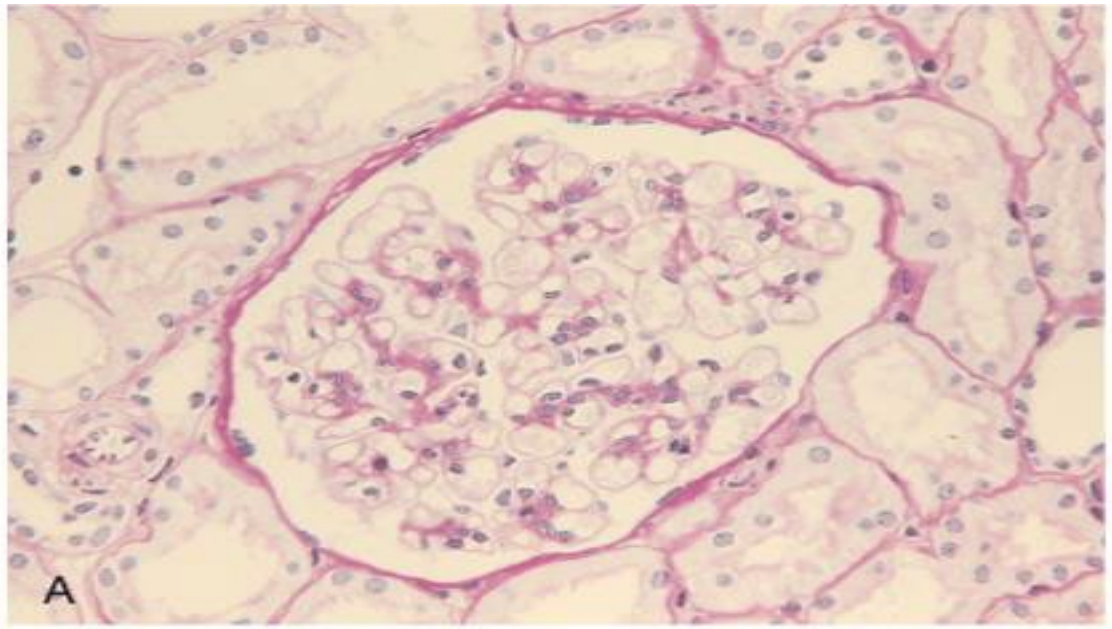
- **B-Systemic Diseases with Renal Manifestations:**

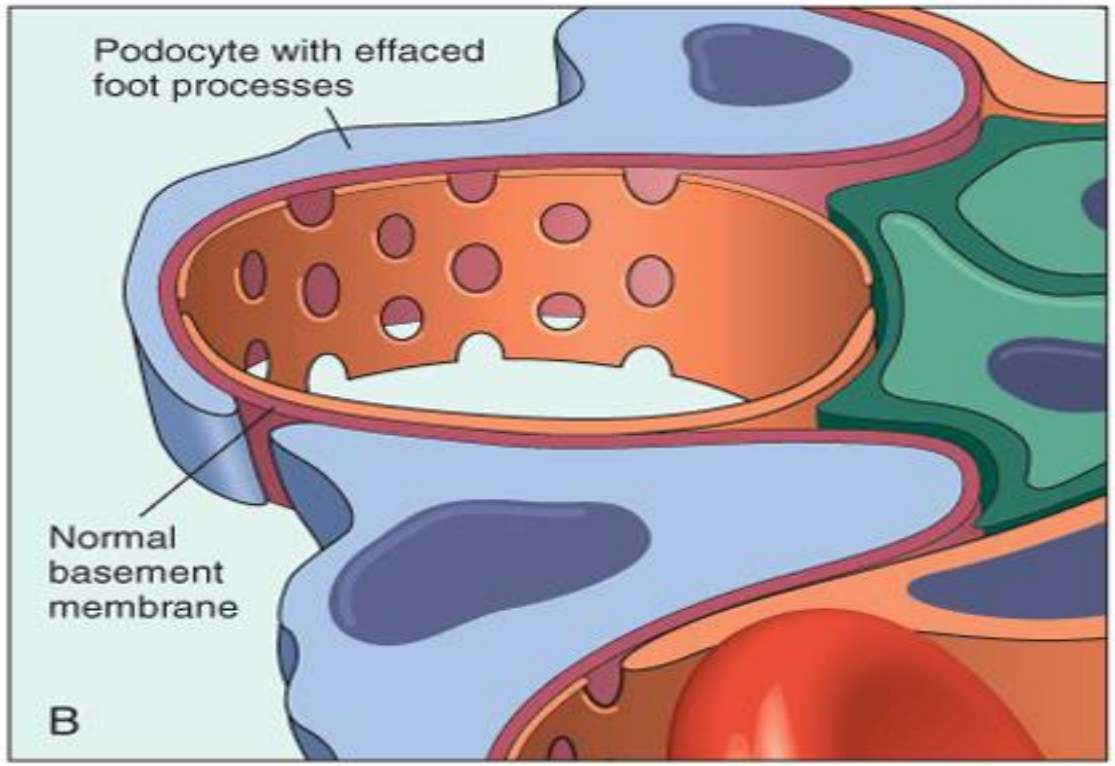
- Diabetes mellitus
- Amyloidosis
- Systemic lupus erythematosus
- drugs (gold, penicillamine, "street heroin")
- Infections (malaria, syphilis, hepatitis B, HIV)
- Malignancy (carcinoma, melanoma)
- Miscellaneous (e.g. bee-sting allergy)

❖ Minimal Change Disease (Lipoid Nephrosis)

MCD is the most frequent (about 65%) cause of the nephrotic syndrome in children. Although it may develop at any age, MCD is most common between ages 1 and 7 years. It is characterized by **G** that have a normal appearance by light microscopy, but when viewed with the **EM it** shows **(1)diffuse effacement of podocyte foot processes(2) without antibody deposits**.

Pathogenesis: The pathogenesis of podocyte injury, which is the underlying mechanism of proteinuria in MCD is **unknown** & it may be the result of nonimmune causes.





Minimal change disease.

A

glomerulusappears normal, with a delicate basement membrane

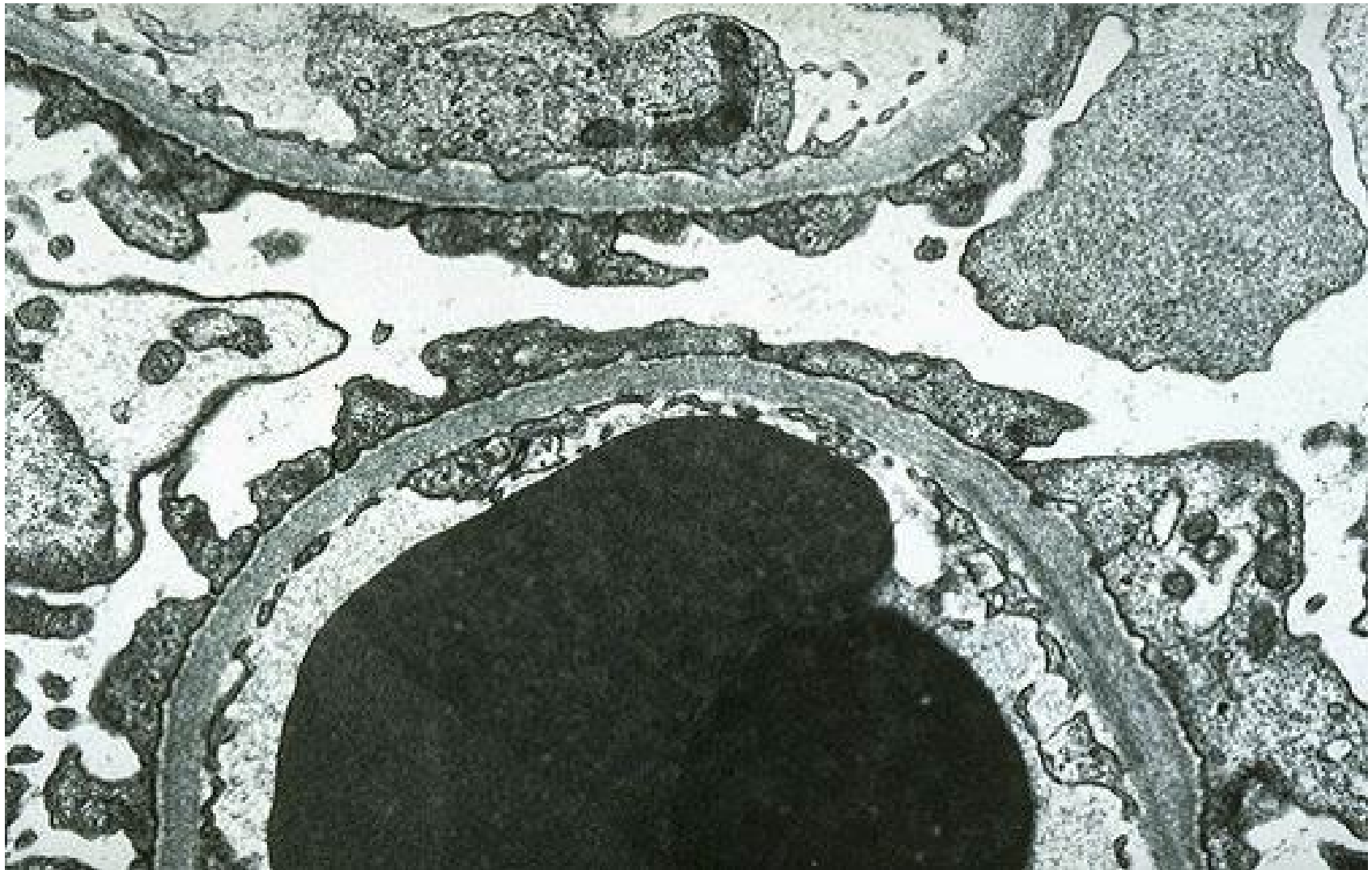
B

diffuse effacement of foot processes of podocyteswith no immune deposits.

Morphology

- **LM**
- the glomeruliappear normal.
- **IF**
- negative
- **EM**
- **uniform and diffuse effacement of the foot processes of the podocytes.**
- No immune deposits

MCD-EM the capillary loop in the lower half contains two electron dense RBC's. Fenestrated endothelium is present and the BM is normal. The overlying epithelial cell foot processes are fused (arrows).



❖ MCD Clinical Course

- ❖ • nephrotic syndrome in an otherwise healthy child.
- ❖ •no hypertension
- ❖ •renal function preserved
- ❖ •selective proteinuria (albumin)
- ❖ •prognosis is good .
- ❖ •Treatment : corticosteroids 90 % of cases
- ❖ •< 5 % develop chronic renal failure after 25 years
- ❖ •In Adults with minimal change disease the
- ❖ response is slower and relapses are more common.

❖ Focal and Segmental Glomerulosclerosis (FSGS)

G lesion characterized (1) histologically, by sclerosis affecting some, but, not all **G** (**focal** involvement) & involving only some (**segments**) of each affected **G**
(2) often associated with the **nephrotic syndrome**& can occur:
(1) in **association** with other known conditions, e.g., **HIV nephropathy, heroin nephropathy**;
(2) As a secondary event in other forms of GN(e.g., **[IgA] nephropathy**);
(3) as a **maladaptation after nephron loss.**
(4) in **inherited or congenital**forms resulting from mutations affecting cytoskeletal or related proteins expressed in podocytes (e.g., nephrin), i.e., nonimmune cause;
(Nephrin a transmembrane glycoprotein, is the major component of the slit diaphragms between adjacent foot processes)
(5) as an **primary or idiopathic** FSGS, which accounts for 20% to 30% of all cases of the nephrotic syndrome.
★It is becoming an **increasingly common** cause of nephrotic syndrome in **adults (35%)** & remains a frequent cause in children.

In children it is important to distinguish **FSGS** cause of the nephrotic syndrome from MCD, because the clinical courses are markedly different:

Unlike MCD, **patients with FSGS** have
(1) **Nonselective** proteinuria, & (2) Higher incidence of **hematuria & hypertension**
(3) Generally, a **poor response to corticosteroid therapy, with 50% of cases developing RF within 10 years** of diagnosis. Adults in general feel even less well than children.

❖ Pathogenesis

★The pathogenesis of primary FSGS **is unknown**.
★In any case, nonimmune injury to the podocytes is thought to represent the initiating event of primary FSGS **(as** with MCD)& is the underlying mechanism of proteinuria.
The **permeability-increasing factors produced by lymphocytes** have been proposed in both MCD & FSGS.

★The recurrence of proteinuria in some persons with FSGS, who receive **renal allografts**, sometimes within 24 hours of transplantation, supports the idea that a circulating mediators is the cause of the damage to podocytes.

★The deposition of **hyaline masses** in the **G** in FSGS represents the entrapment of plasma proteins & lipids in foci of injury where sclerosis develops. IgM & complement proteins commonly seen in the lesion are also believed to result from nonspecific entrapment in damaged **G**.

❖ Morphology

Microscopically :, FSGS is characterized by both focal & segmental lesions occurring in (1) some segments within a **G** & sparing of the others (hence the term "**segmental**"), &

(2) the disease first affects only some of the **G**(hence the term "**focal**").
★The affected **G** exhibit **(a)↑mesangial matrix, (b) deposition of hyaline masses**

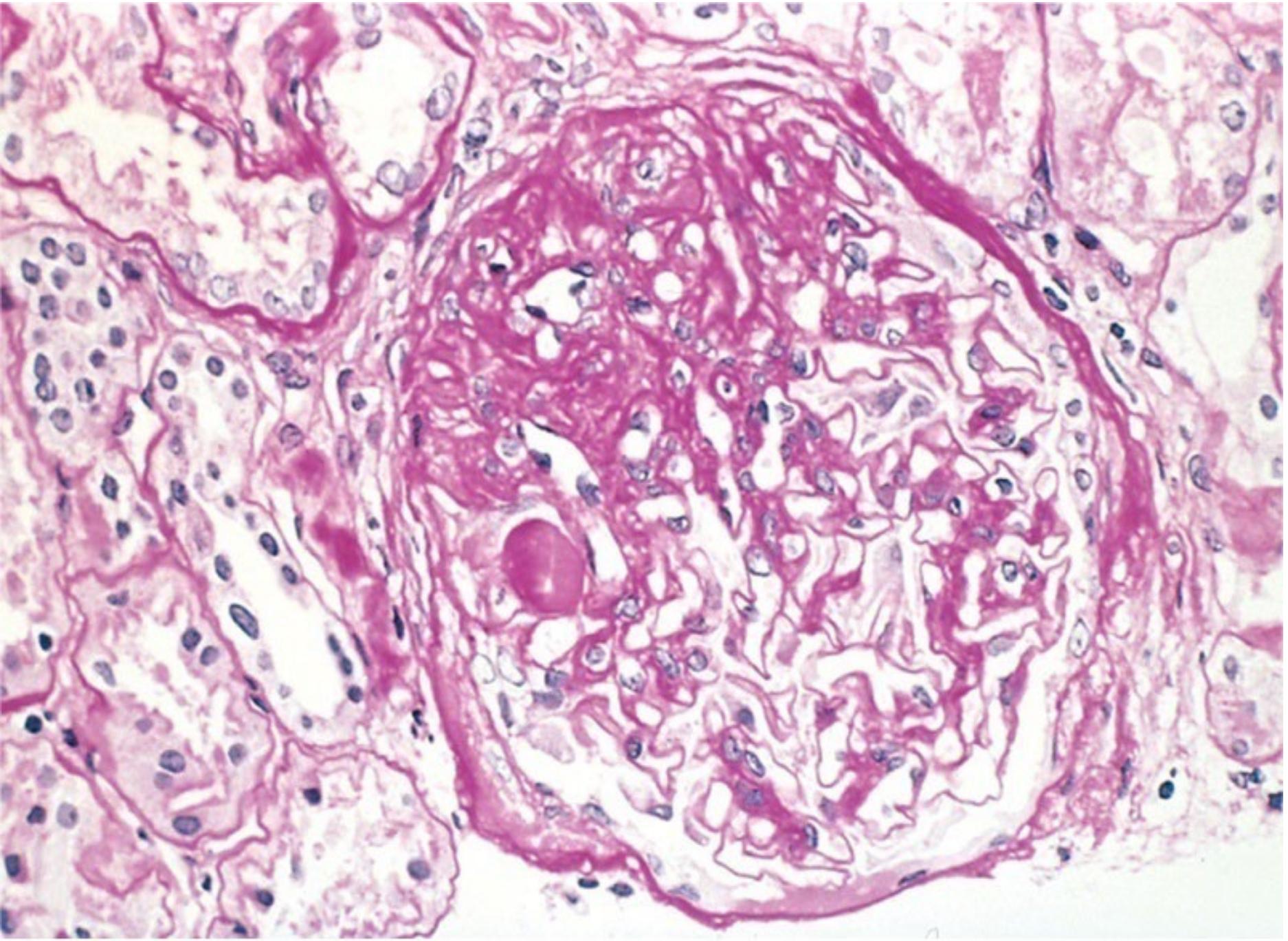
(hyalinosis) & lipid droplets in the affected G, causing….
(C) obliteration of the capillary lumens

immunofluorescence M often reveals nonspecific trapping of immunoglobulins, usually IgM, & complement, in the areas of hyalinosis.

On EM, as in MCD, the podocytes exhibit **effacement of foot processes,**

Clinically,there is **little tendency for spontaneous remission** of idiopathic FSGS, & responses to corticosteroid therapy are poor.

★**Progression** of FSGS, with time, leads to **global sclerosis** of the **G** with pronounced tubular atrophy & interstitial fibrosis, a picture difficult to differentiate from other forms of chronic **G**disease, with progression to RF occuring in 50% of FSGS patients after 10 years.



HP view of **focal & segmental glomerulosclerosis (FSGS),** seen as a mass of **scarred, obliterated capillary lumens with accumulations of matrix material,** that has replaced a portion of the glomerulus.

	MCG	FSGN
Hematuria	_	+
Hypertension	_	+
Proteinuria	Selective	Non-selective
Respond to corticosteroid therapy	Good	Poor

❖ Collapsing glomerulopathy

- A morphologic type of FSGS.
- poor prognosis.
- collapse of glomerular tuft and podocyte hyperplasia.
- It may be :
- 1-idiopathic .
- 2-associated with **HIV infection**.
- 3-drug-induced toxicities.

❖ Membranous GN(MGN)=Membranous Nephropathy MN)

A slowly progressive disease, most common in the 30-50 years age group, characterized by the presence of:

(I)diffuse thickening of the capillary wall,

(II)subepithelial immunoglobulin-containing deposits.

Pathogenesis

★MGN is a form of **chronic immune complex nephritis**. Although circulating complexes of known exogenous (e.g., hepatitis B virus) or endogenous (DNA in SLE) Ag can cause MGN, it is now thought that most idiopathic MGN are induced by Abs reacting in situ to endogenous, or, planted **G**Ags.

❑ **Types of Membranous glomerulonephritis :**

1-Idiopathic (85% of cases): antibodies against podocyte antigen phospholipase A2 receptor (PLA2R)antigen

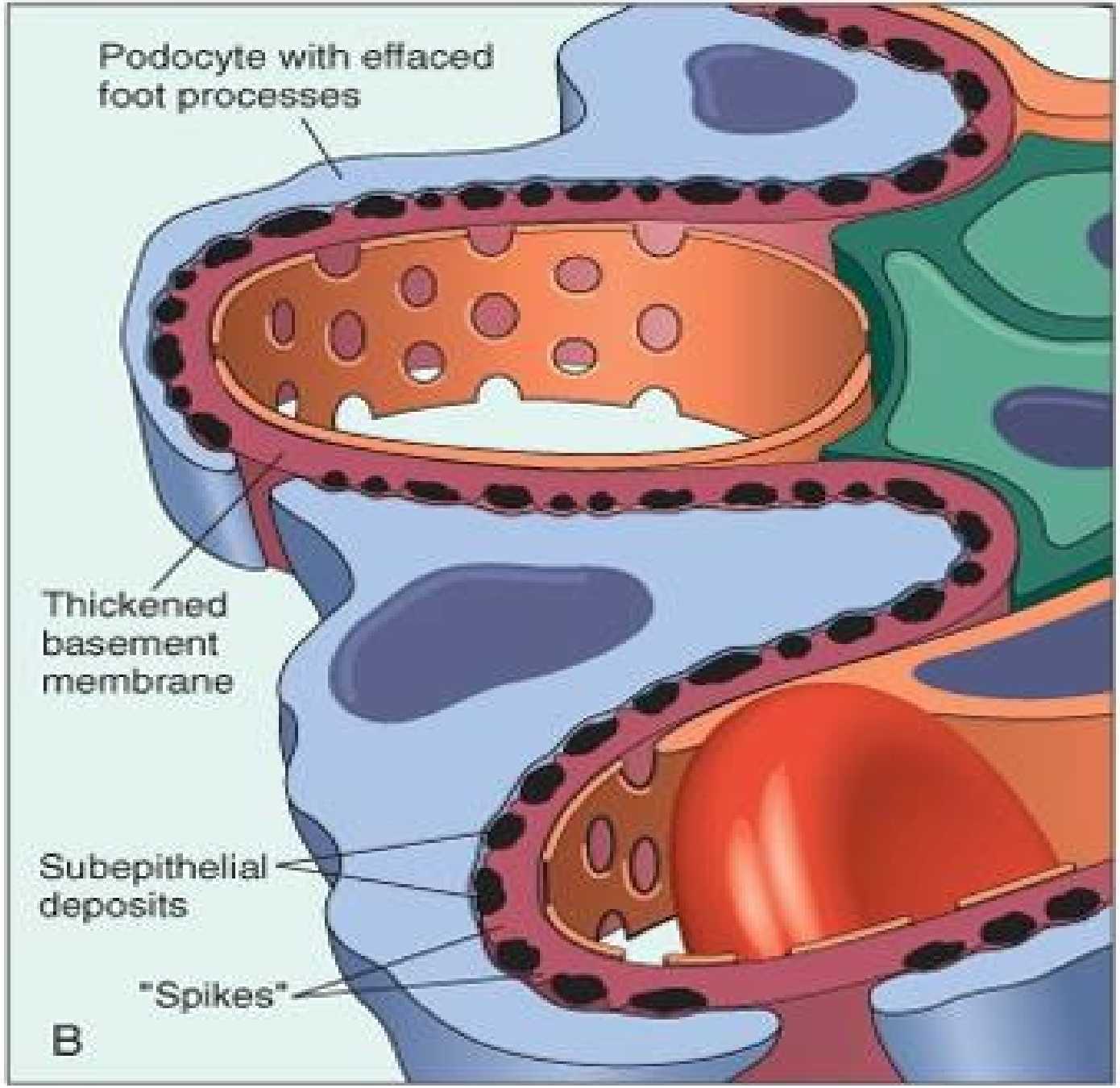
2-Secondary membraneous nephropathy

- **(1) infections (HBV, syphilis, schistosomiasis, malaria).**
- **(2) malignant tumors (lung, colon and melanoma).**
- **(3) autoimmune diseases as SLE .**
- **(4) inorganic salts exposure (gold, mercury).**
- **(5) drugs (penicillamine, captopril,NSAID).**

❑ Morphology

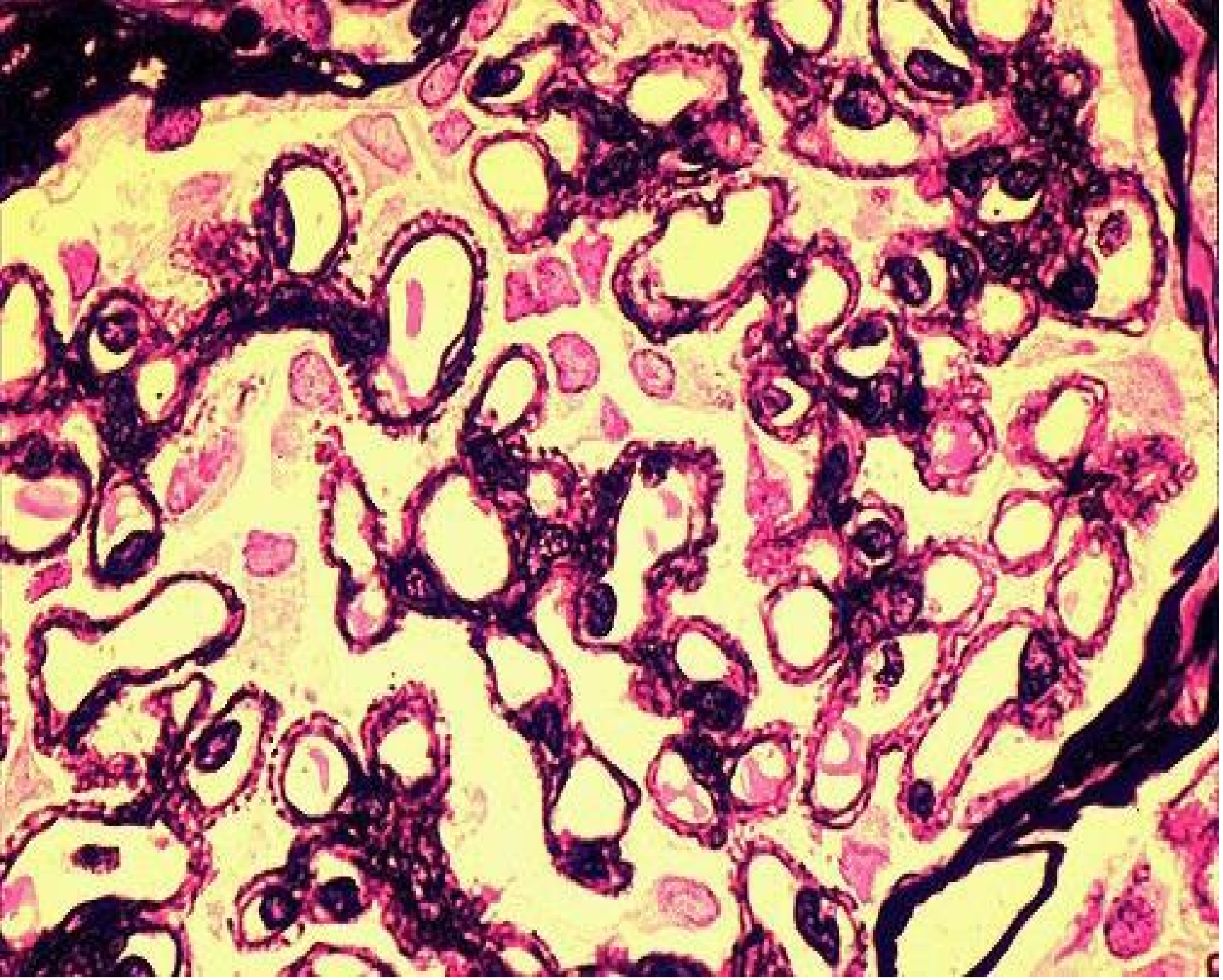
- **LM**
- **diffuse thickening of the GBM**.
- **IF**
- **deposits** of immunoglobulins and complement along the GBM (IgG)
- **EM**

By EM: (1) the podocytes show ,effacement of foot processes, & (2) the diffuse thickening of the GBM is caused in part by subepithelial dome deposits that nestle against the GBM & are separated from each other by small, spike like protrusions of GBM matrix that form in reaction to the dome deposits, resulting in a (spike & dome pattern) As the disease progresses, these spikes close over the deposits, incorporating them into the GBM.

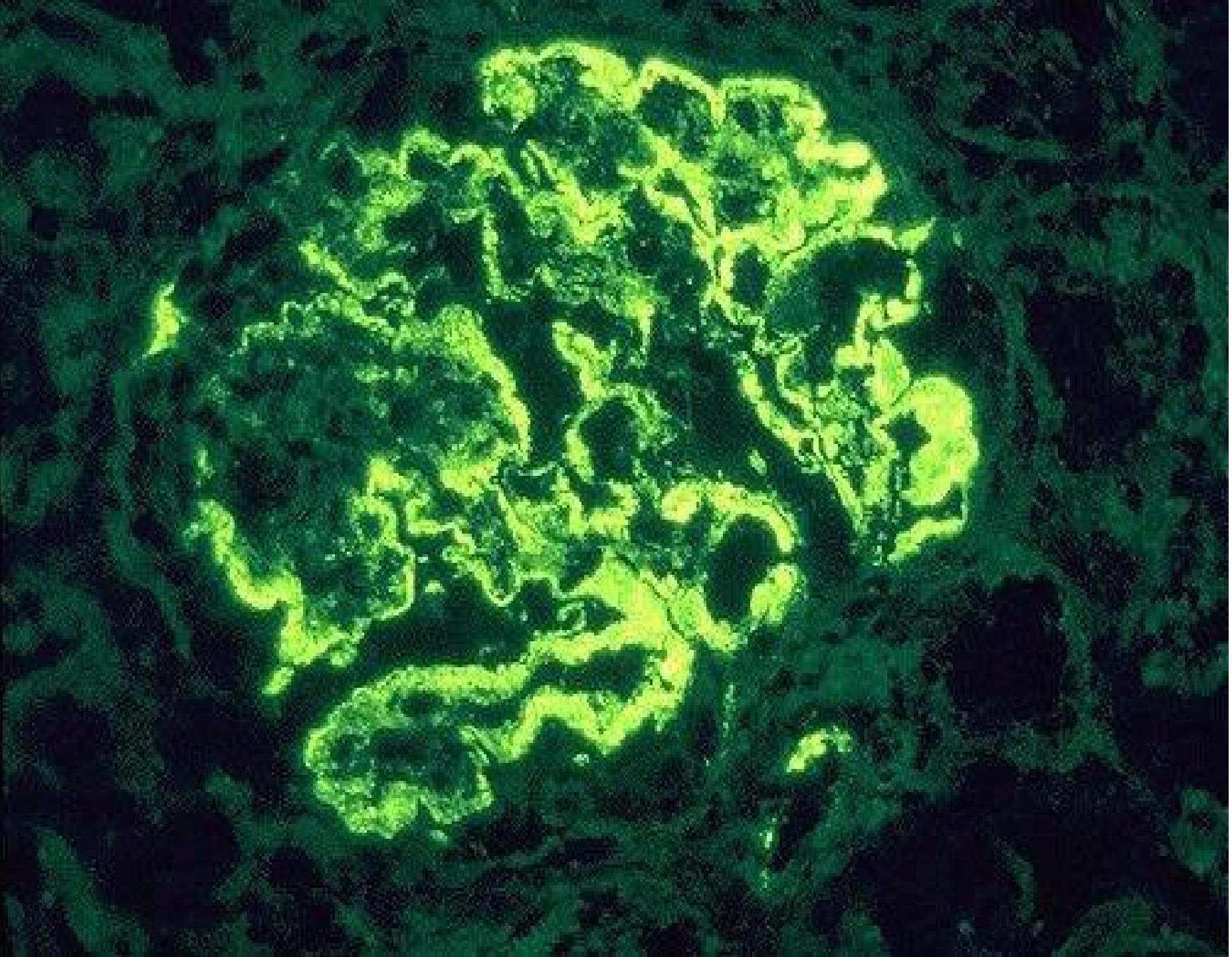


Membranous nephropathy.

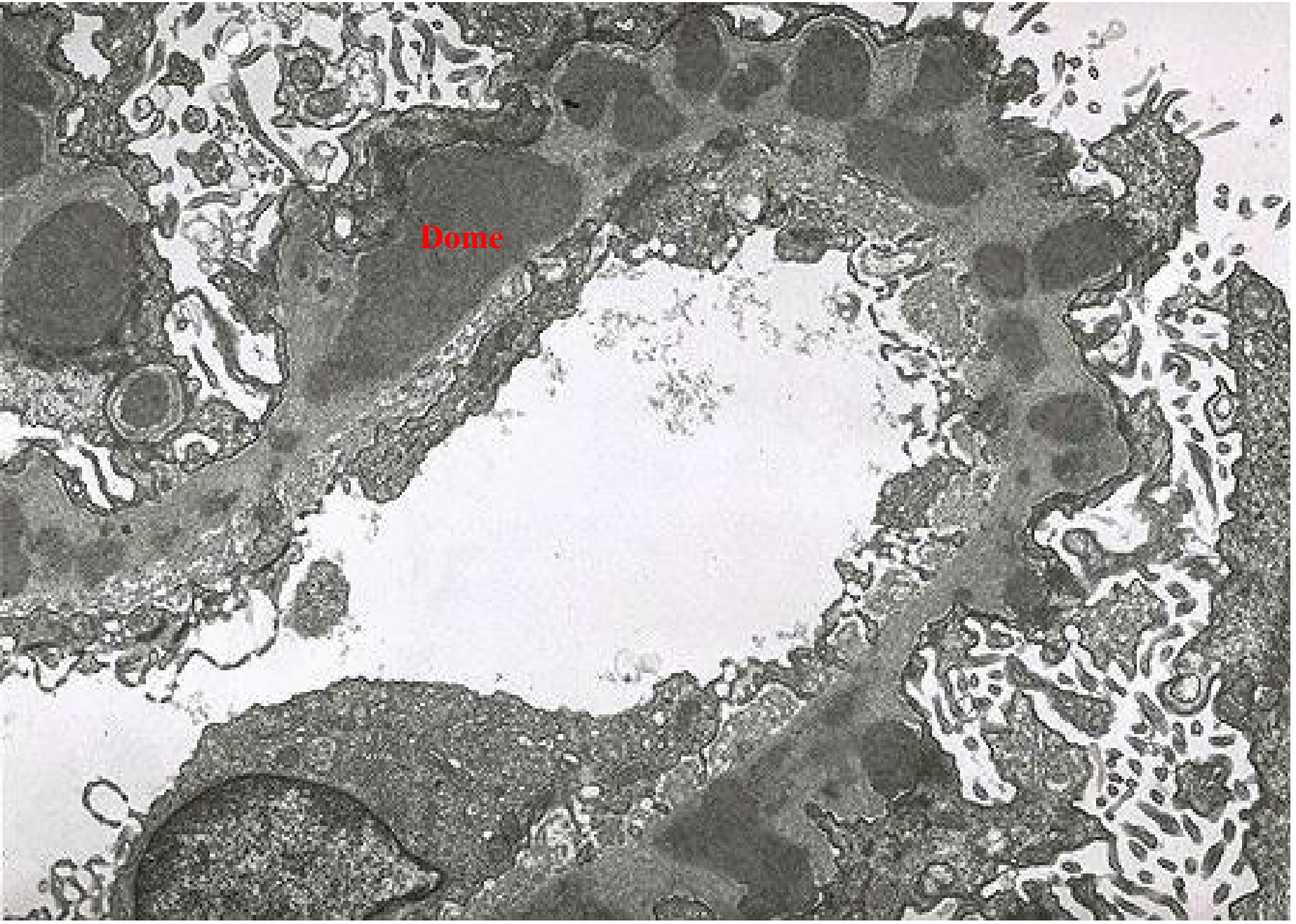
subepithelialdeposits and the presence of "spikes" of basement membrane material between the immune deposits.



A silver stain (black). Characteristic "spikes" seen with membranous glomerulonephritis as projections around the capillary loops.



Membranous GNIF: deposits of mainly IgG and complements



EM-("spike and dome" pattern).

❑ Clinical Course

Clinically, idiopathic MGN characterized by **insidious development of the nephrotic syndrome**, usually without antecedent illness. **In contrast to MCD**, (I) the **proteinuria is nonselective**, & **(II) does not usually respond to corticosteroid** therapy.

- **poor response to corticosteroid therapy.**

Secondary causes of MGN should be ruled out.

Prognosis:

- **60% of cases → proteinuria persists**
- **about40%→progressive disease and renal failure 2 to 20 yr.**
- **30% →partial / complete remission of proteinuria.**

❖ The Nephritic Syndrome

- Pathogenesis: inflammation
- **proliferation of the cells in glomeruli& leukocyte infiltrate →**
- **Injured capillary walls →escape of RBCs into urine →↓GFR →**
- **oliguria, fluid retention, and azotemia.**
- **Hypertension(a result of both the fluid retention and some augmented renin release from kidneys).**

Nephritic Syndrome: Presentation

- **PHAROH**
- ***P****roteinuria*
  - *<3.5g/1.73m2/day*
- ***H****ematuria*
  - *Abrupt onset*
- ***A****zotemia*
  - *Increased creatinine and urea*
- ***R****BC Casts*
- ***O****liguria*
- ***H****TN*

Peripheral Edema/Puffy Eyes

"Smoky Urine"

GLOMERULAR DISEASES MOSTLY PRESENTING WITH NEPHRITIC SYNDROME

❖ MEMBRANOPROLIFERATIVE GN(MPGN)

Is manifested H, by alterations in the GBM & mesangium & by proliferation of **G** cells.

★**MPGN accounts for 10% of cases of idiopathic nephrotic syndrome** in children & adults.

- Some individuals present only with hematuria or proteinuria in the non-nephrotic range; others have nephritic syndrome or a combined nephrotic-nephritic picture.

•**Types of MPGN:**

1-type I (80% of cases)-immune complex disease (The inciting antigen is not known)

2-type II- excessive complement activation

❑ Pathogenesis of MPGN

Different pathogenic mechanisms are involved in the development of type I & type II MPGN.

Most cases of type I MPGN are caused by **circulating immune complexes, but** the inciting Ag is not known. Like many other GNs, type I MPGN may also occur in association with other known disorders (**secondary MPGN),such as SLE, hepatitis B & C, chronic liver disease or infected A-V shunt**

Type II MPGN (dense-deposit disease)

- Cause: excessive complement activation

- autoantibody against C3 convertase called C3 nephritic factor (it stabilizes the enzyme and lead to uncontrolled cleavage of C3 and activation of the alternative complement pathway).

- Result: Hypocomplementemia

❑ Morphology

- **LM**
- both types of MPGN are similar by LM.
- glomeruli are large with accentuated **lobular appearance** and show **proliferation of mesangial and endothelial cells** as well as infiltrating leukocytes
- **GBM is thickened**(**double contour** or **"tram track"**)
- The **tram track** appearance is caused by "**splitting**" **of the GBM** due to the inclusion within it of processes of mesangial & inflammatory cells extending into the peripheral capillary loops.

Types I & II have different ultrastructural & immunofluorescence microscopic features.

- **Type I MPGN**is characterized by discrete **subendothelial electron-dense deposits**.

✹By immunofluorescence M, C3 is deposited in an irregular granular pattern, & IgG & early complement components (C1q & C4) are often also present, indicative of an immune complex pathogenesis.

Type II MPGN-C3 alone in GBM

In **type II lesions** the lamina densa & the subendothelial space of the GBM are transformed into an irregular, ribbon-like, extremely electron-dense structure, resulting from the deposition of material of unknown composition, giving rise to the term **dense-deposit disease.**

C3 is present in irregular chunky & segmental linear foci in the BMs & in the mesangium but the IgG & the early components of the classical complement pathway (C1q & C4) are usually **absent**.

❑ Clinical Course

• Clinically, 50% of MPGN cases presented with **nephrotic syndrome**, although it may begin as acute nephritis or mild proteinuria.

•prognosis poor.

•No remission.

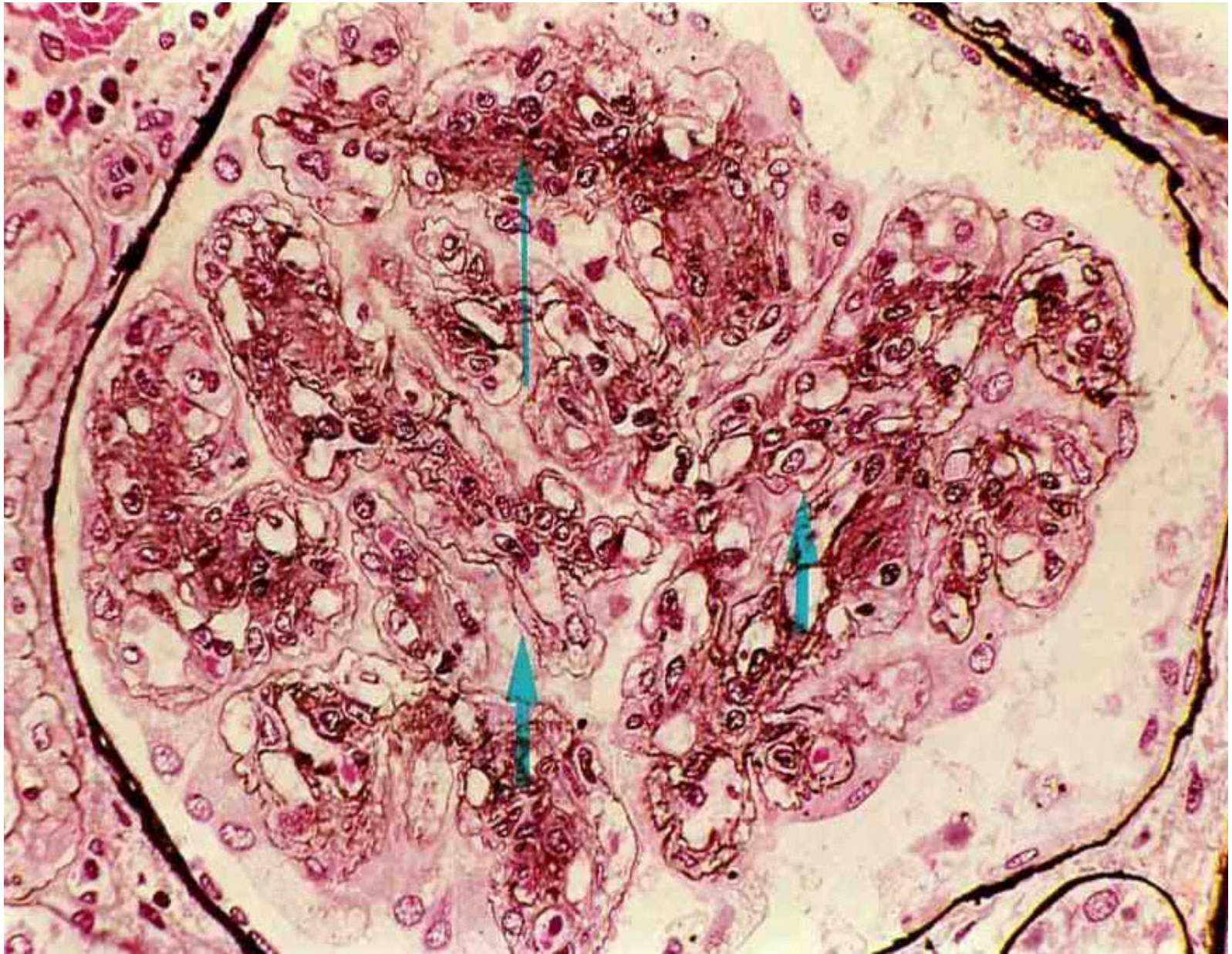
•40% progress to end-stage renal failure.

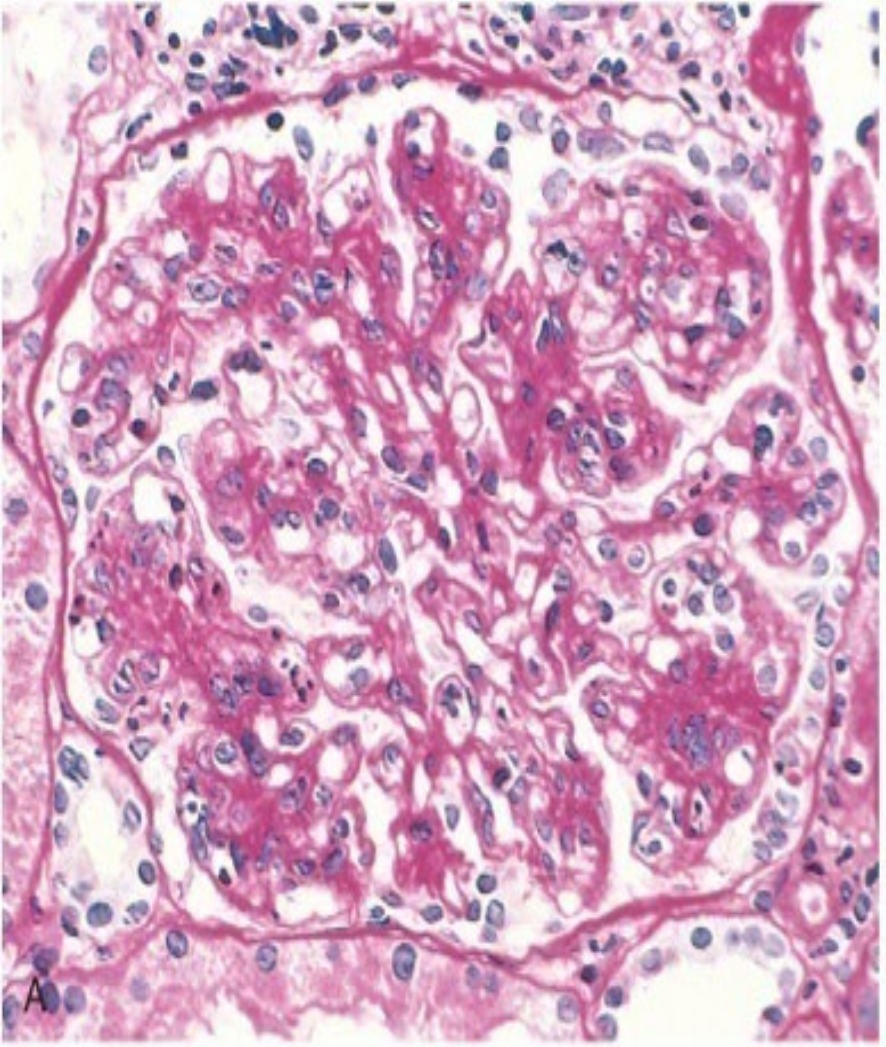
•30% had variable degrees of renal insufficiency. the remaining 30% had persistent nephrotic syndrome without RF.

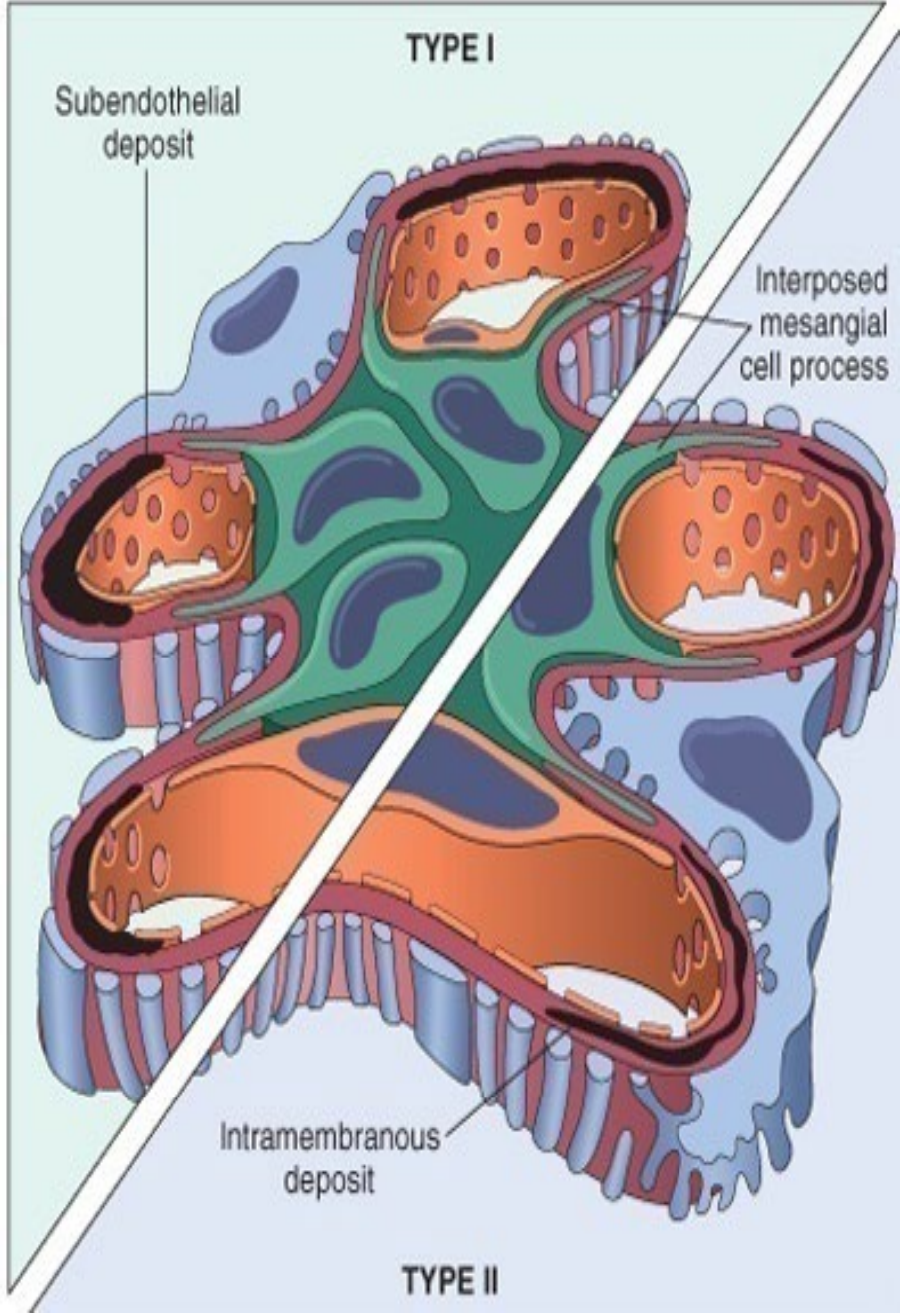
•**Dense-deposit disease (type II) has a worse prognosis.**

•**It tends to recur in renal transplant recipients**

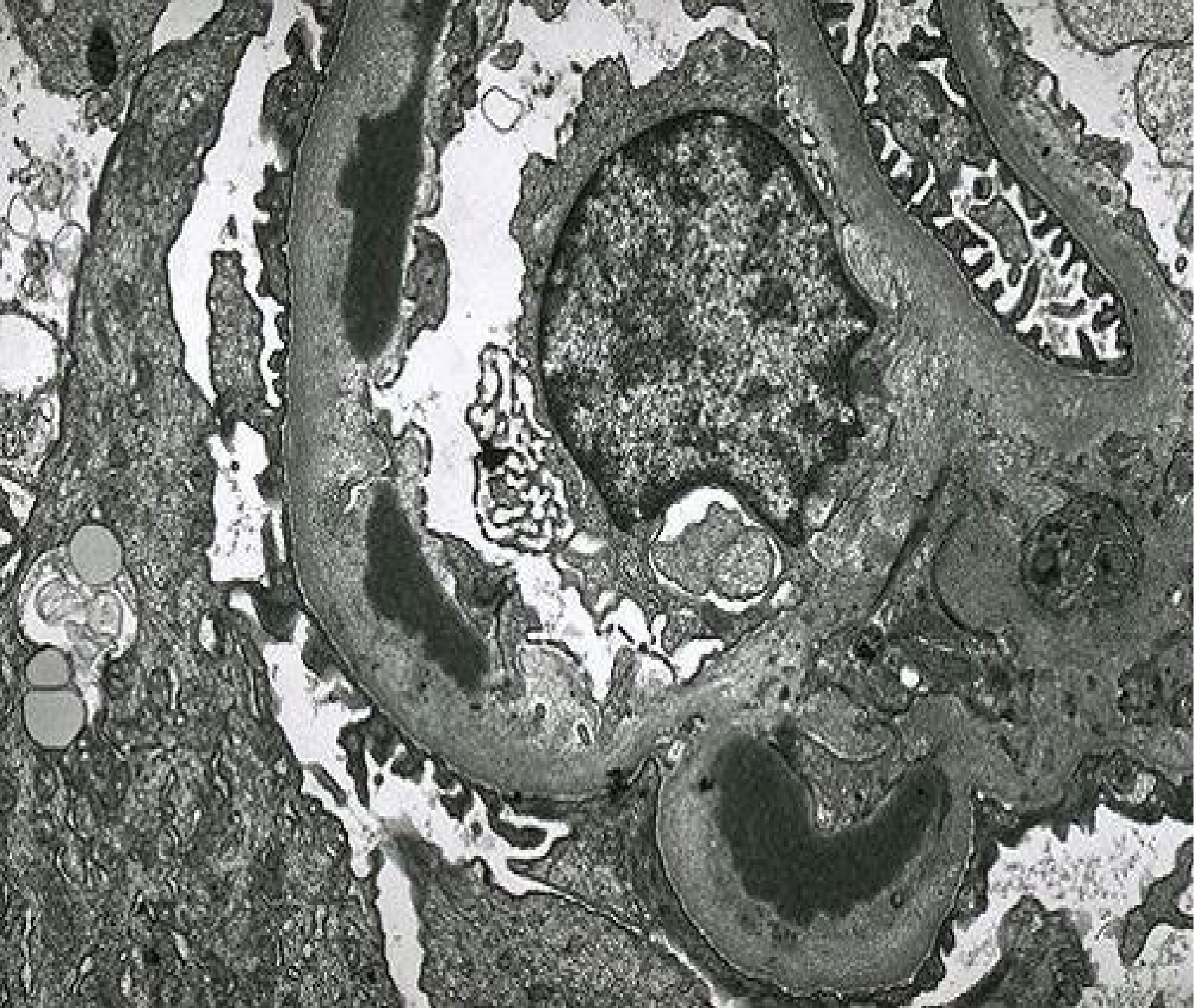
Membranoproliferative GNX450 (silver stain).The **GBM is thickened &**shows typical double contour **"tram track,"** appearance (thick arrow) caused by "**splitting" of the GBM**,due to the inclusion within it of processes of mesangial &inflammatory cells extending into the peripheral capillary loops







A, MPGN, showing BM thickening, WBC infiltration, mesangial cell proliferation, & lobular architecture accentuation. **B,** Schematic representation of patterns in the two MPGN types ★In **type I,**there are **subendothelial** deposits; ★**type II**is characterized by **intramembranous dense deposits**(dense-deposit disease).In both types I&II, mesangial interposition gives the appearance of split BM when viewed by light microscopy.



EM-dense deposits in the basement membrane of MPGN type II in a ribbon-like mass (arrows)

❖ ACUTE POSTINFECTIOUS (POSTSTREPTOCOCCAL) GLOMERULONEPHRITIS(PSGN)

A frequent GN, typically caused by deposition of immune complexes in the **G,** resulting in diffuse proliferation & swelling of resident **G** cells & frequent infiltration by neutrophils.

★The inciting Ag may be **exogenous or endogenous**.

- **Not direct infection of the kidney**

★The **prototypic exogenous pattern** is seen in **poststreptococcal GN**, & a similar proliferative GN may occur in association with infections by other organisms, including certain pneumococcal & staphylococcal infections, several common viral diseases such as mumps, measles, chickenpox, & hepatitis B & C.

★**Endogenous antigens,**as occur in SLE.

★Classically, poststreptococcal GN develops in children 1 to 4 weeks after they recover from a group A, "nephritogenic" strains of β-hemolytic streptococcal infection. In most cases the initial infection is in the pharynx or skin.

PATHOGENESIS OF ACUTE POST STREPTOCOCCAL GN

Is immune complex deposition,because the typical features of immune complex disease are seen, including,

(1) granular deposits of IgG & complement on the GBM

(2) hypocomplementemia

LM

•proliferation of endothelial and mesangial cells and neutrophilic infiltrate.

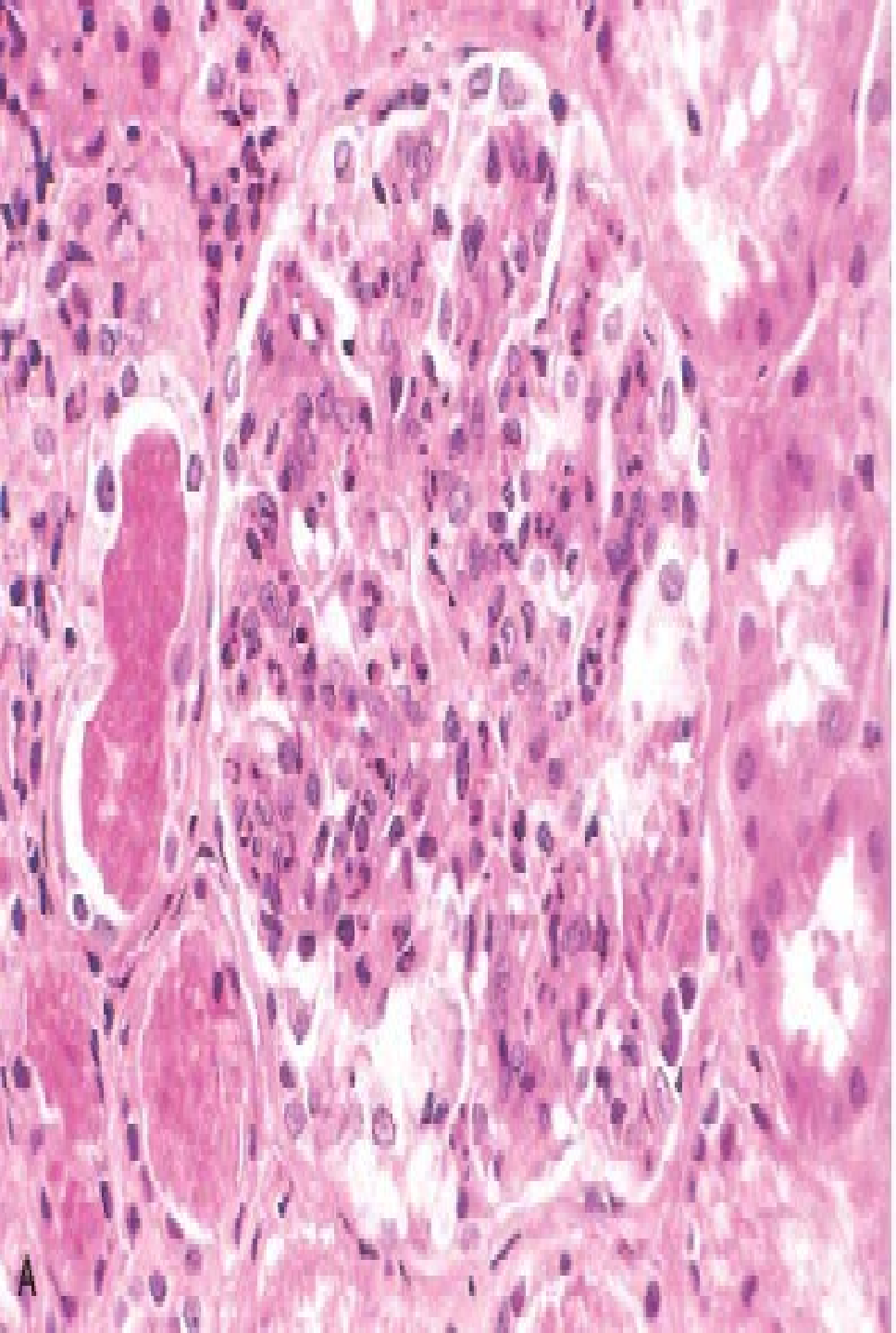
In postinfectious GN, the most characteristic change by light microscopy is a Diffuse (affecting nearly all glomeruli), uniform increased cellularity of the G tufts(caused both by swelling & proliferation of EC & mesangial cells & by a neutrophilic & monocytic infiltrate)

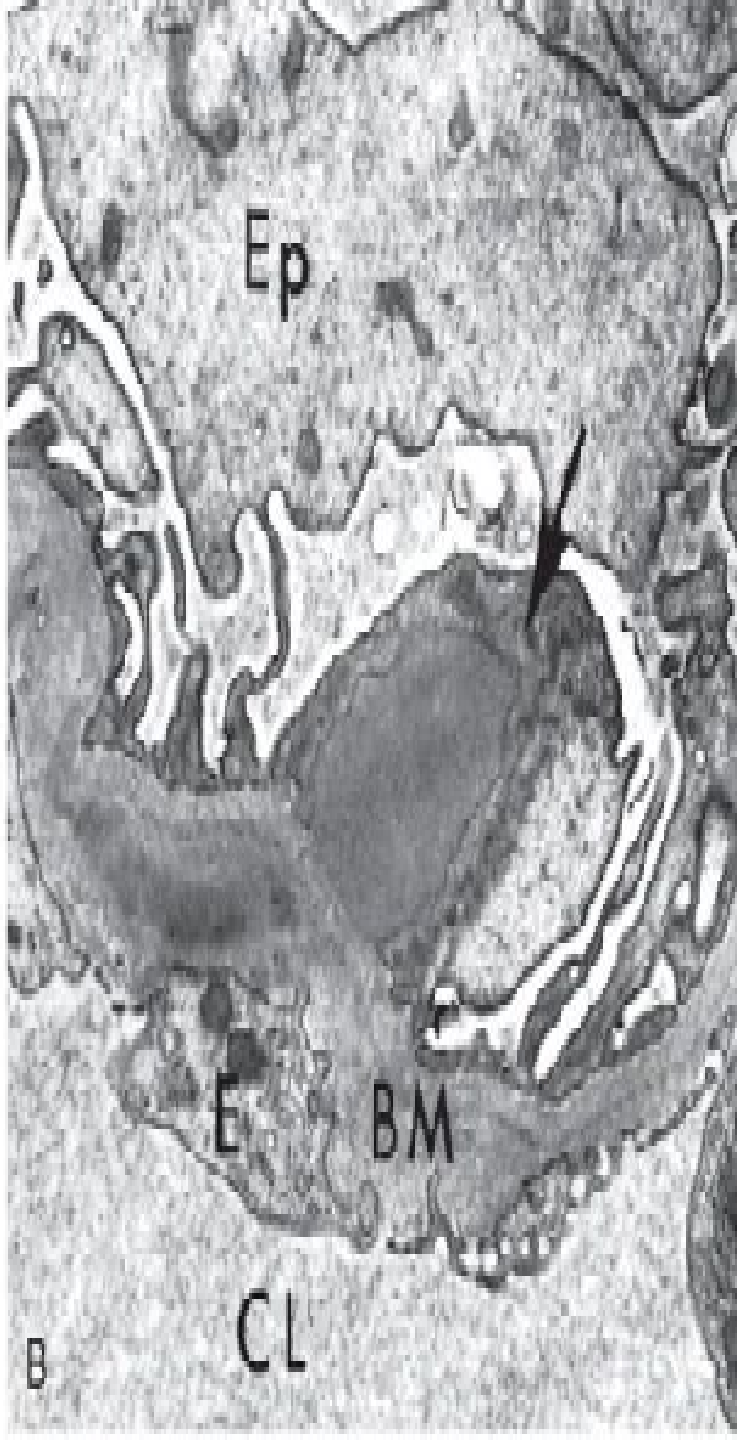
Sometimes there is necrosis of the capillary walls & In a few cases, there may also be "crescents“ within the urinary space in response to the severe inflammatory injury.

❑ In general, both of these findings are ominous.

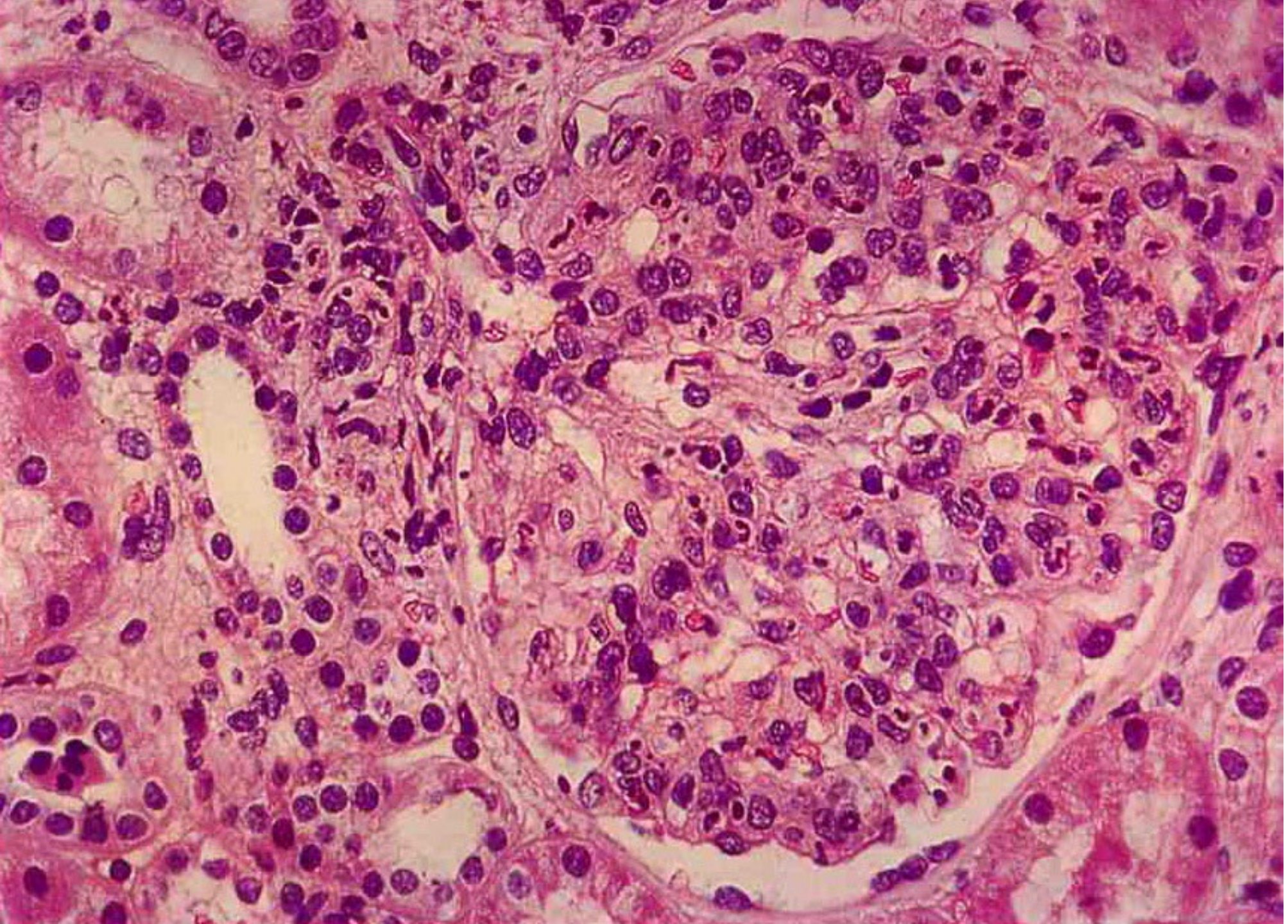
- **IF**
- **deposits of IgG and complement** within the **capillary walls**

- **EM**
- immune complexes “**subepithelial"humps“** in GBM.



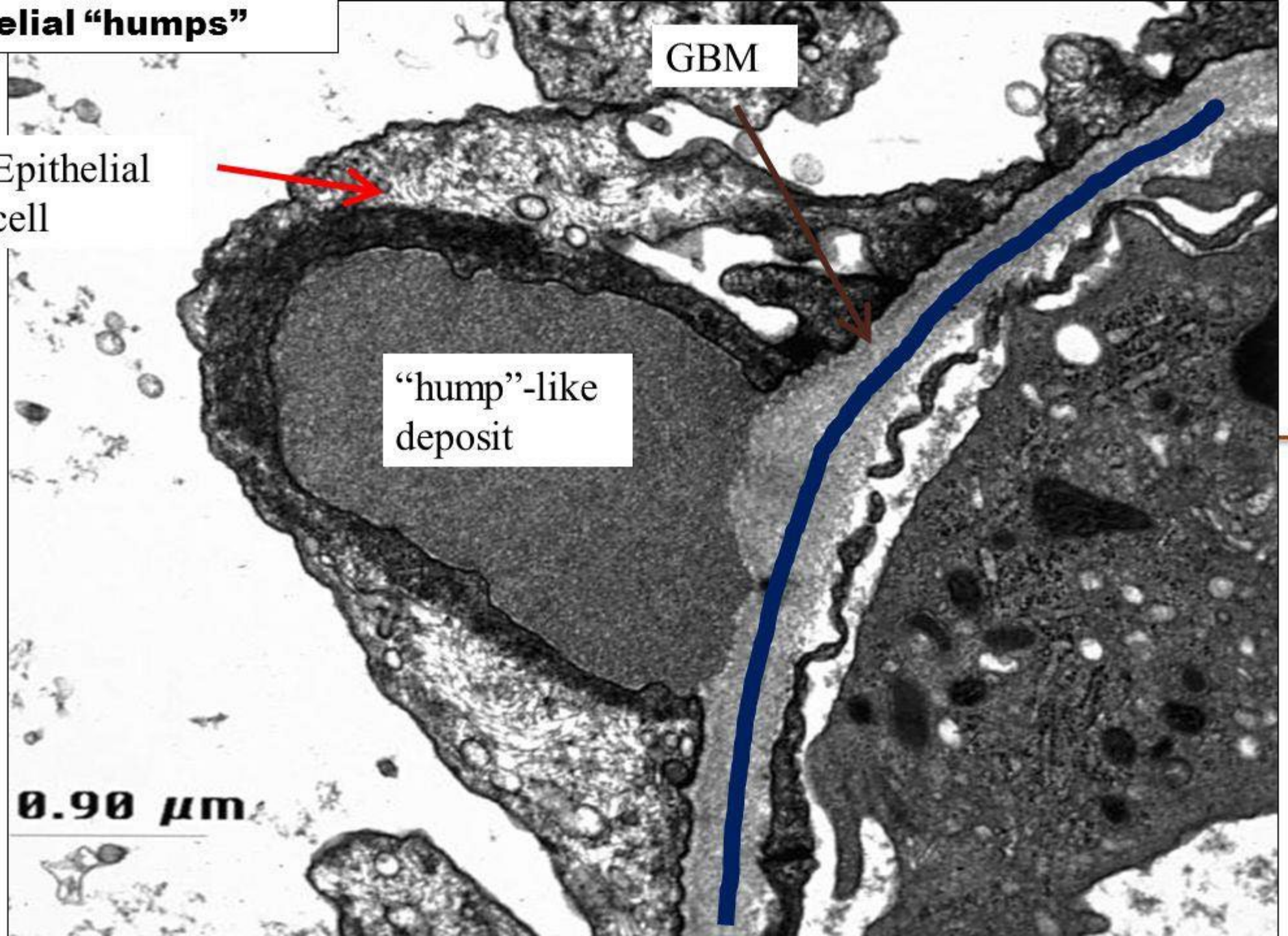


Poststreptococcal GN.A, G hypercellularity is caused by WBC infiltration& proliferation of intrinsic G cells. Note the red casts in the tubules. **B,**Typical EM electron-dense subepithelial “hump” (arrow) + intramembranous deposits. **E**= endothelial cell; **BM**= basement membrane.



Acute Postinfectious (Poststreptococcal) GN X335.showing diffuse(affecting nearly all glomeruli) uniform increased cellularity of the G tufts (caused by both neutrophilic cell infiltration and proliferation & swelling of EC & mesangial cells)

Subepithelial "humps"



❑ PSGN-Clinical Course

- **acute onset .**
- **fever, nausea, and nephritic syndrome.**
- **gross hematuria with smoky brown** rather than bright red urine **.**
- **Mild proteinuria.**
- **Serum complement levels are low during the active phase of the disease.**
- **↑serum anti-streptolysinO antibody titers.**
- **Recovery occurs in most children.**

Thank you