Pathology Lecture
Nephrotic Syndrome

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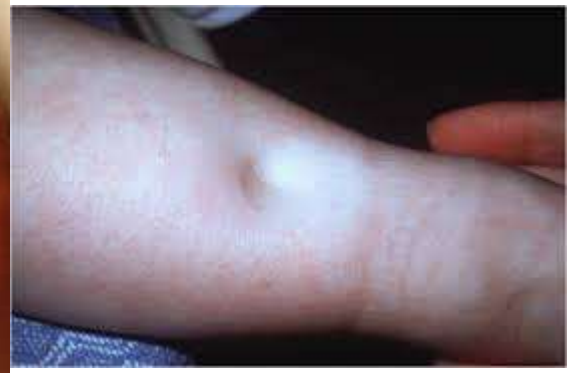
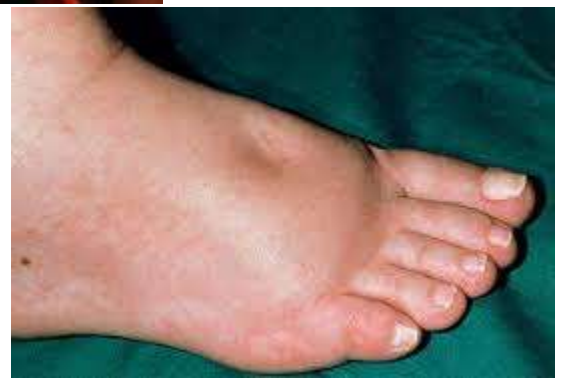
The Nephrotic Syndrome

- a clinical complex resulting from glomerular disease & includes the following signs and symptoms:
- (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- membranoproliferative GN type 1 (usually a combination of nephrotic/ nephritic syndrome)

Causes of Nephrotic Syndrome

1-primary glomerular diseases

Cause	Prevalence (%) Children	Prevalence (%) Adults
Primary Glomerular Disease		
Membranous GN	5	30
Minimal-change disease	65	10
Focal segmental glomerulosclerosis	10	35
Membranoproliferative GN	10	10
IgA nephropathy	10	15

Causes of Nephrotic Syndrome

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)**

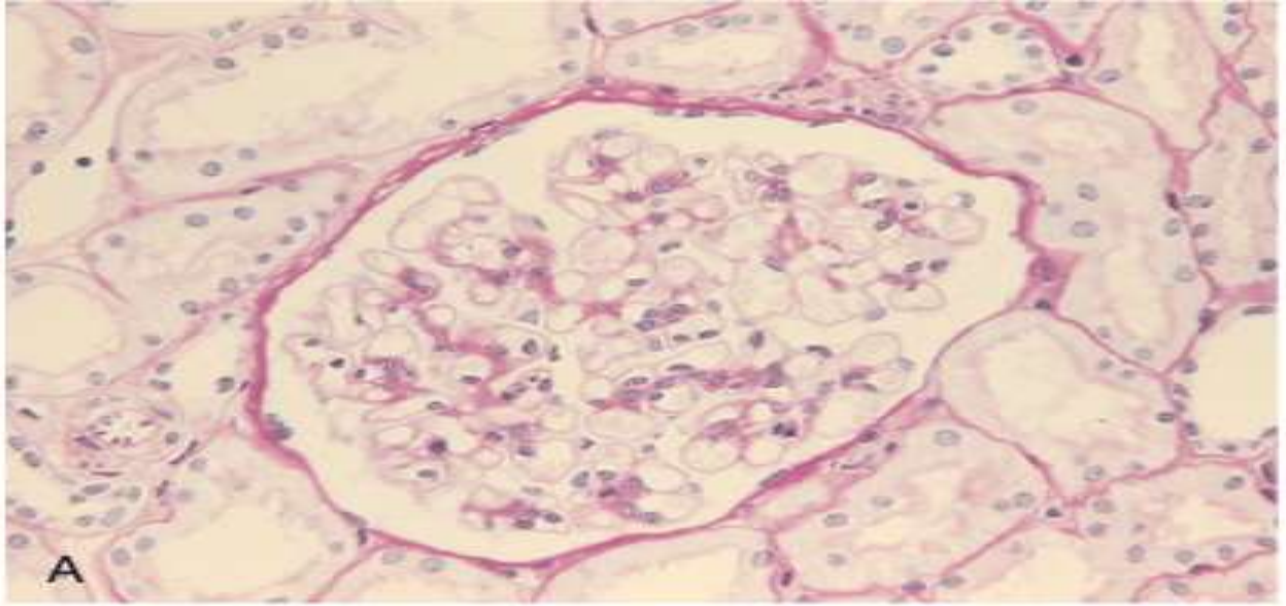
1- Minimal-Change Disease (Lipoid Nephrosis)

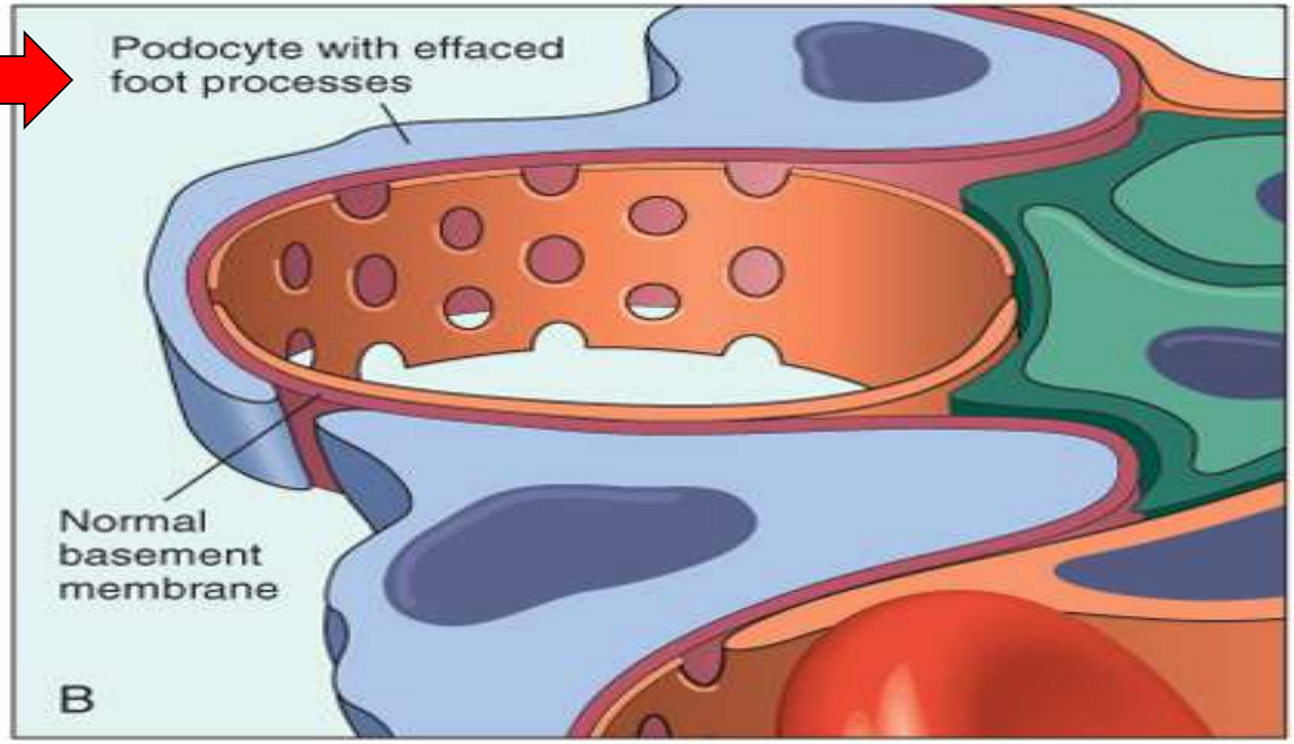
- **benign disorder.**

- **The most frequent cause of the nephrotic syndrome in children (ages 1-7 years).**

- ***Pathogenesis:*** **still not clear.**

? T-cell derived factor that causes podocyte damage and effacement of foot processes.





Minimal change disease.

A

glomerulus appears normal, with a delicate basement membrane

B

diffuse effacement of foot processes of podocytes with no immune deposits.

Morphology

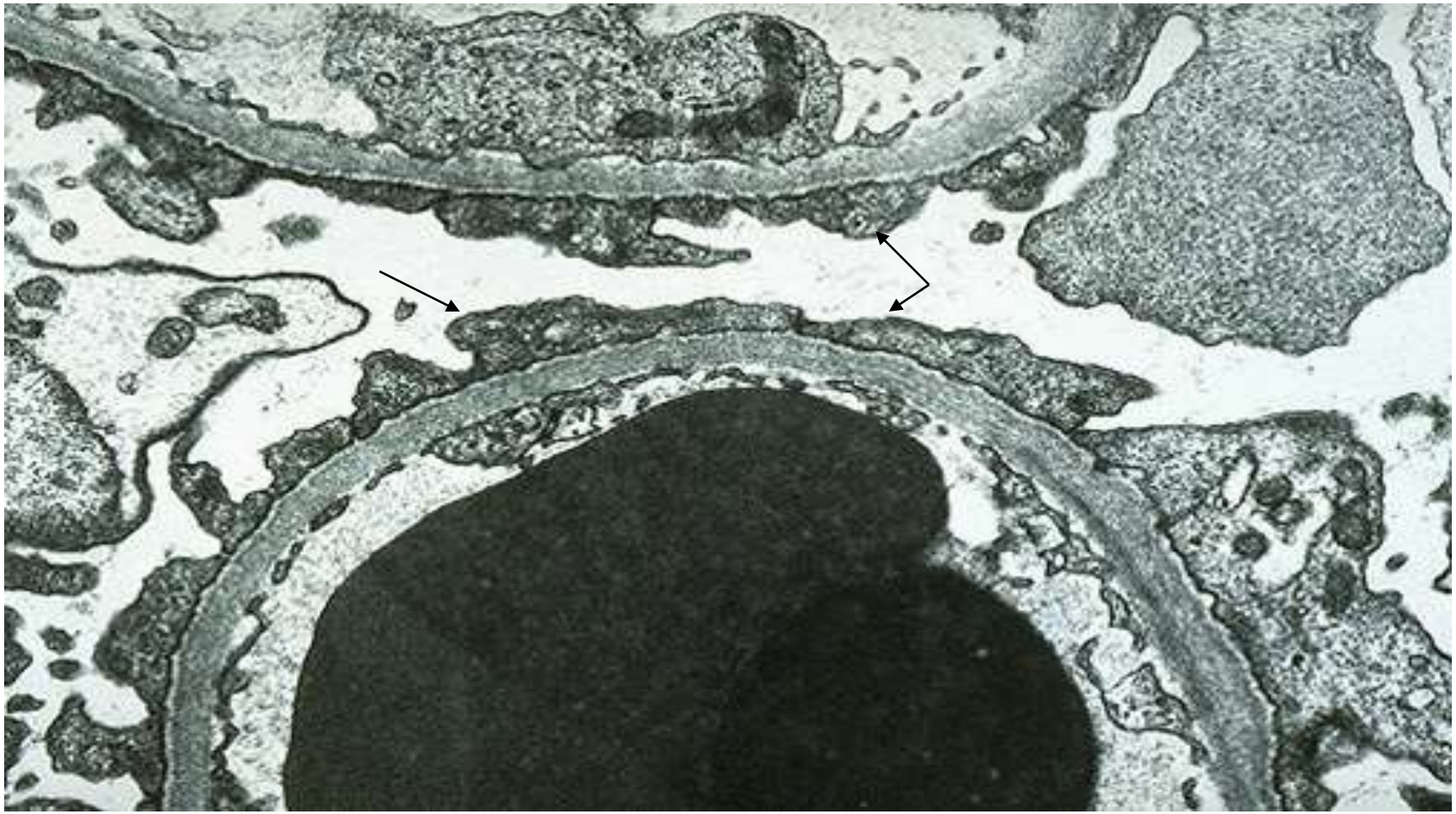
- **LM**
- the glomeruli appear normal.

- **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 respond)**
- **< 5% develop chronic renal failure after 25 years**
- **In Adults with minimal change disease the response is slower and relapses are more common.**

2- Focal and Segmental Glomerulosclerosis (FSGS)

- **sclerosis affecting some but not all glomeruli (focal involvement) and involving only segments of glomerulus.**
- **Usually nephrotic syndrome.**
- **It can occur :**

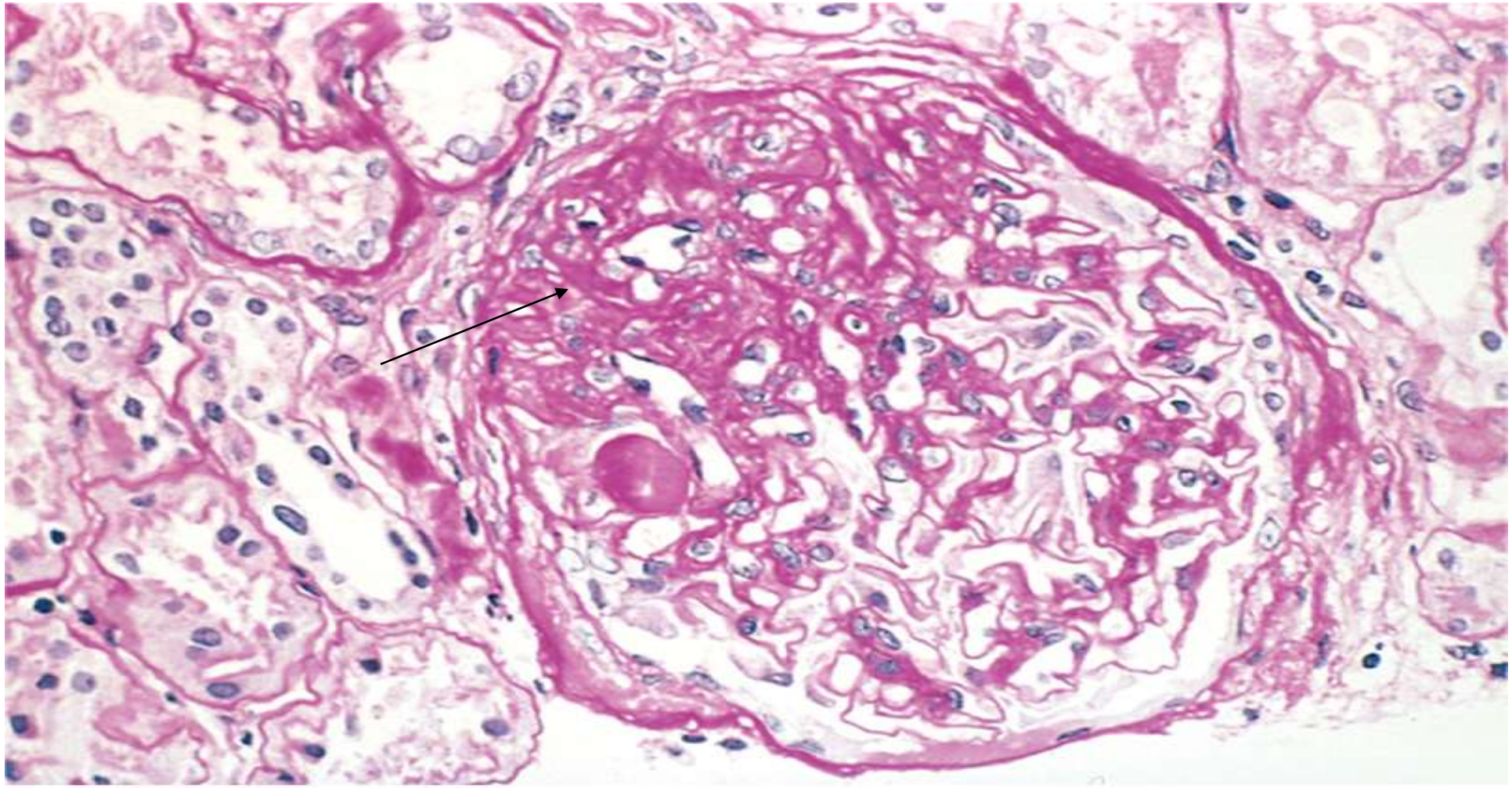
1- as a primary disease(20% to 30% of NS):

- **e.g. inherited or congenital forms resulting from mutations affecting nephrin**

2- Or: in association with underlying condition:

- **e.g.; AIDS; heroin abuse; nephron loss; etc….**

focal and segmental glomerulosclerosis (PAS stain).
a mass of scarred, obliterated capillary lumens with accumulations of matrix material (collagen)



MCD versus FSGS

	MCD	FSGS
hematuria	-	+
hypertension	-	+
proteinuria	selective	nonselective
response to corticosteroid therapy	good	poor

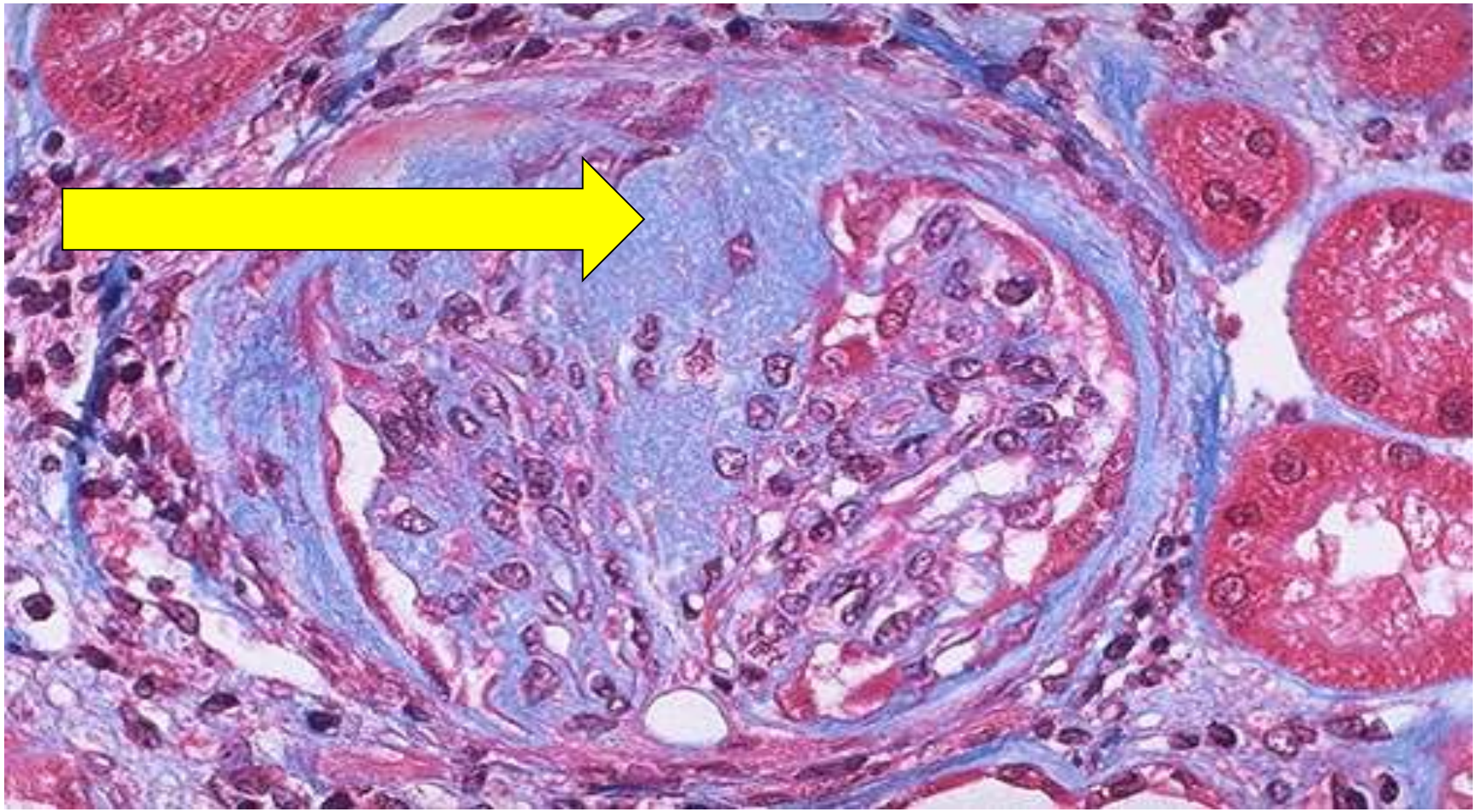
- ***Pathogenesis***
- **unclear**
- ***injury to the podocytes* ? ↑ GFR at first**
- **? Genetics**
- **entrapment of plasma proteins and lipids in foci of injury where sclerosis develops.**

- **Clinical Course**
- **about 50% of individuals suffer renal failure after 10 years**
- **Poor responses to corticosteroid therapy.**
- **Adults do worse than children**

- **Morphology**
- **LM:**
- Sclerosis in some glomeruli not all of them; and in a segment not all of the affected glomerulus
- **IF microscopy**
- Negative
- **EM**
- **effacement of podocyte foot processes**

FSGS

blue = collagen deposition (MT stain).



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.

3- Membranous nephropathy:

- **Immune complex deposition in glomerulus**

- **<u>Types of Membranous glomerulonephritis :</u>**

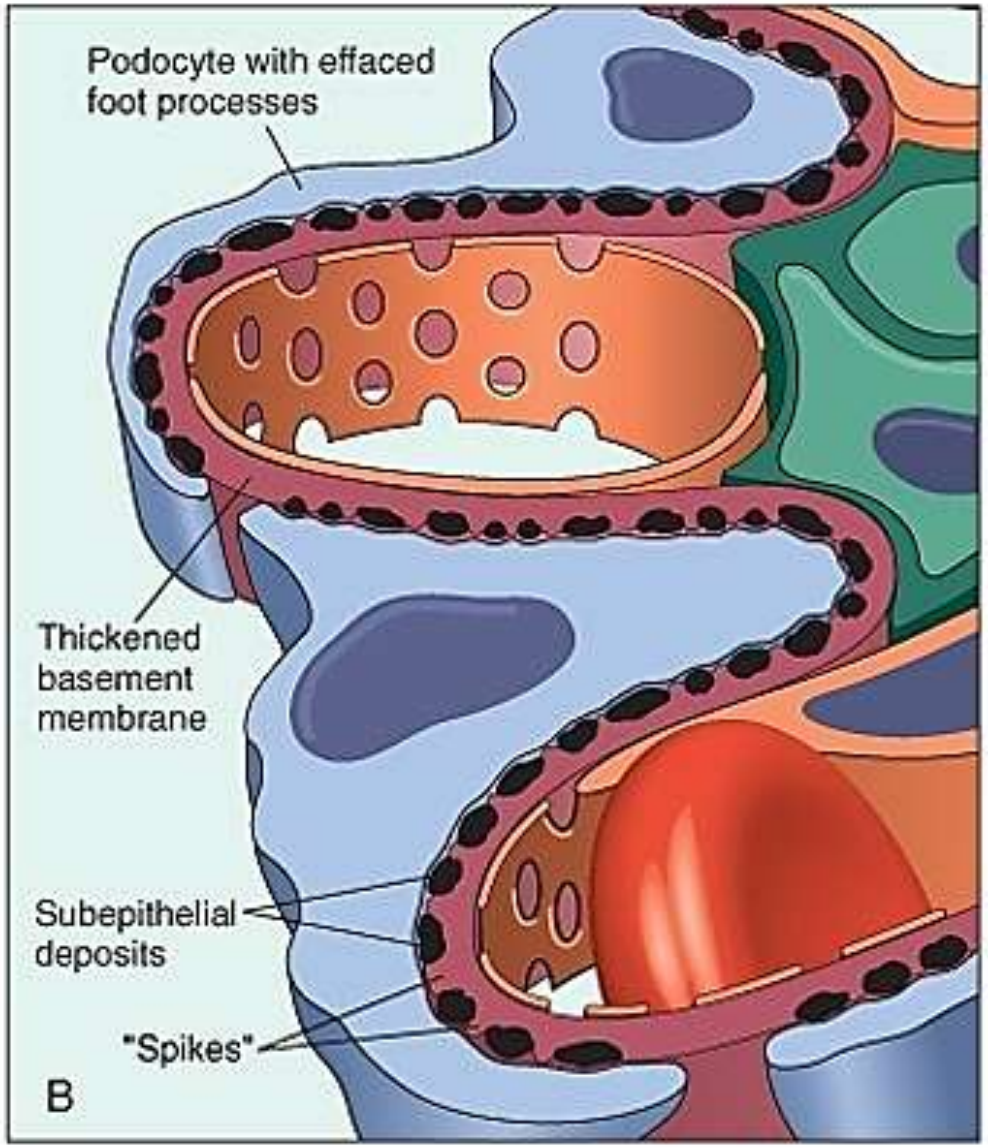
1-Primary (85% of cases): antibodies against podocyte antigen phospholipase A2 receptor (PLA2R) antigen

2-Secondary to another condition or disease

Secondary Membranous glomerulonephritis :

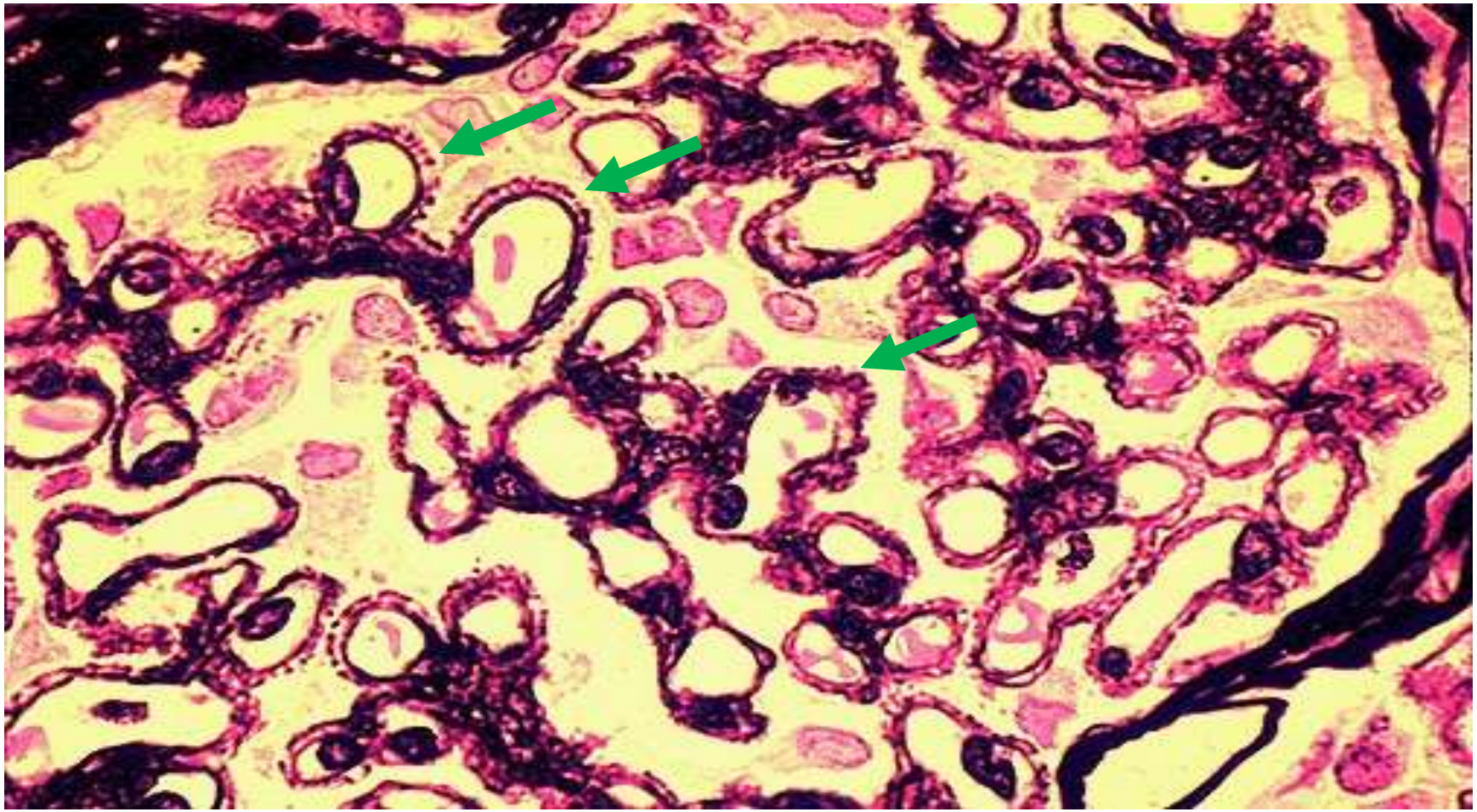
- **(1) infections (HBV, syphilis, schistosomiasis, malaria).**
- **(2) malignant tumors (lung, colon and melanoma).**
- **(3) autoimmune diseases as SLE .**
- **(4) inorganic salts exposure (gold, mercury).**
- **(5) drugs (penicillamine, captopril,NSAID).**

- **Morphology**
- **LM**
- **diffuse thickening of the GBM .**
- **IF**
- **deposits** of immunoglobulins and complement along the GBM (mainly IgG)
- **EM**
- **subepithelial deposits "spike and dome" pattern.**

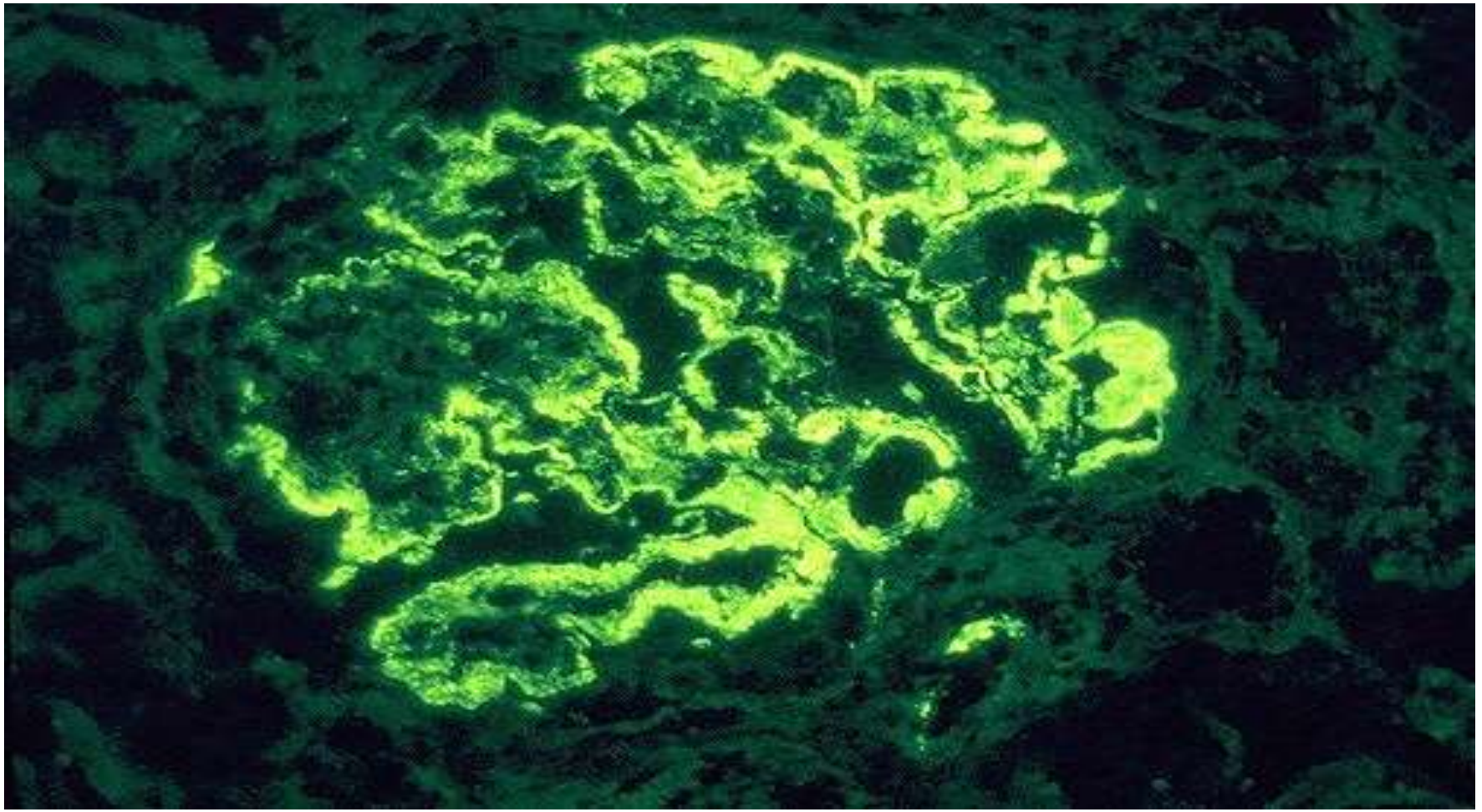


Membranous nephropathy.
subepithelial deposits and the presence of "spikes" of basement membrane material between the immune deposits .

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



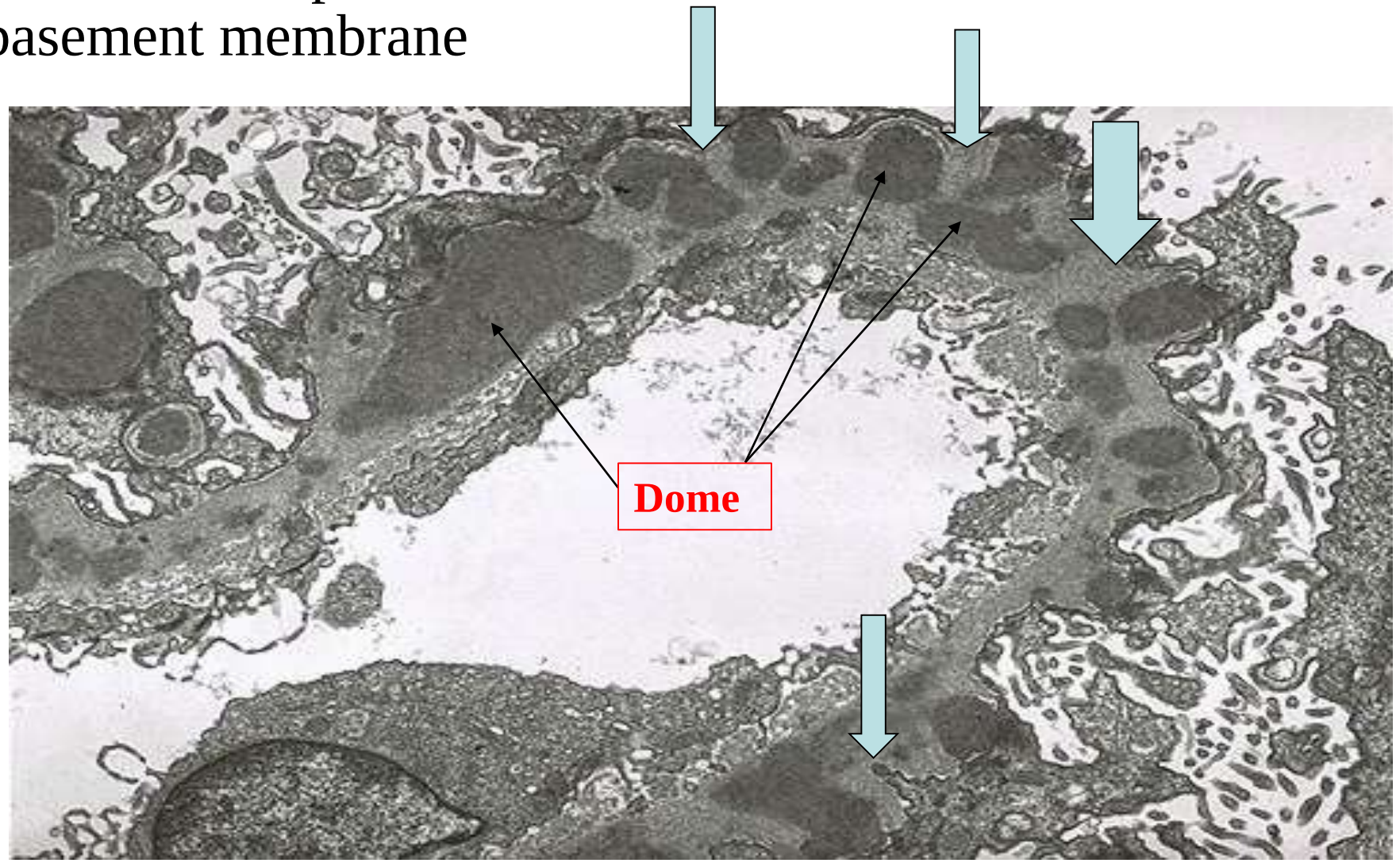
Membranous GN
IF: granular deposits of IgG and complements along the capillary walls



EM: "spike and dome" pattern is characteristic

Dome= immune complex

spike= basement membrane



- **Clinical Course**
- **nephrotic syndrome**
- **poor response to corticosteroid therapy.**
- **60% of cases→ proteinuria persists**
- **~ 40%→ progressive disease and renal failure within 2 to 20 yr.**
- **30% →partial / complete remission of proteinuria.**