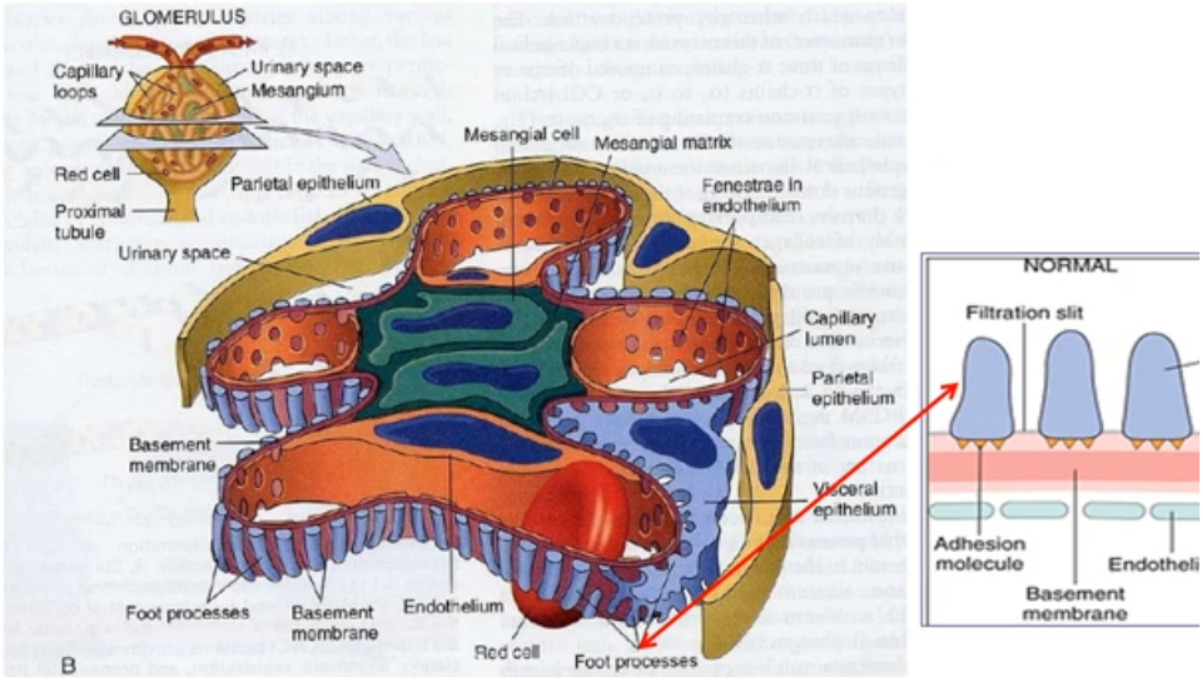
Modified by: Nour Hussein

Nephrotic Syndrome

Dr. Nisreen Abu Shahin



We will be talking about the kidney, which has a function kof filtration of blood which includes toxins and waste products and return of clean blood to the circulation 24/7.

Kidney has a lot of pathological diseases, part of the functional compartments of the kidney is a glomerulus الكبيبة which is responsible for filtration,

A glomerulus is a network of capillaries which are elongated and surrounds itself, it starts with afferent arteriole and ends with efferent arteriole and is responsible for filtration through the membrane of this capillary network which composes of many parts inducing

1. Endothelial cells
2. Basement membrane
3. Podocytes epithelial cells

Problems with filtration are under the umbrella of NEPHROTIC SYNDROME.

The Nephrotic Syndrome

Podocyte = → Damage will cause ↑ permeability

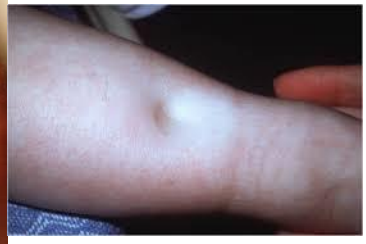
- a clinical complex resulting from glomerular disease & includes the following:
- (1) **massive proteinuria** (3.5 gm /day in adults). → Hallmark. → Heavy. (Most important)
- (2) **hypoalbuminemia** (≤ 3 gm/dL).
- (3) **generalized edema** → ↓ Osmotic Pressure (Albumin) } Due to Proteinuria.
- (4) **hyperlipidemia and lipiduria**. → TAG, LDL 1. ↑ production of lipoproteins in liver due to shift in metabolic pathways
  2. Albumin, responible for the transport of lipids, Hypo Albumenimia???
- (5) little or no azotemia, hematuria, or hypertension.

→ Normal Urine contents:- 1. Toxins
2. Salts
3. Water.

* Note how all symptoms are related to each other!!!

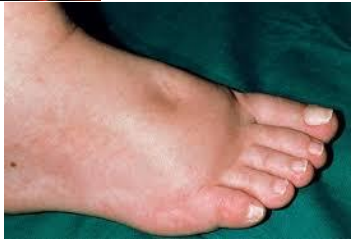
How will doctor know?

1. Generalized Edema
   ↳ Most Alarming

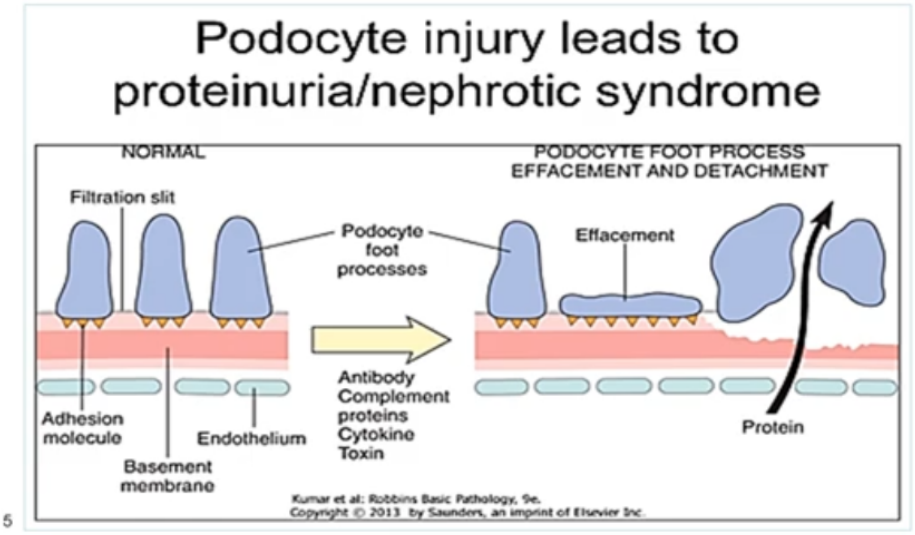


2. Measure BP
   NO HTN !

3. Kidney function test
   ↳ Creatinine, Urea] → Normal
   NO Azotemia !



4. Urine Analysis → Protein !!



Pathogenesis of Nephrotic Syndrome (not mentioned in the slide because the doctor wanted to discuss it verbally in the lecture, because each disease is different meaning different diseases may lead to nephrotic syndrome)

1. Anything that damages filtration membrane which keads to passing of protein leading to proteinuria

a. GBM membrane itself

b. Podocyte epithelial cell: that has fingerlike projections covering the wall from the outside, it is very important in the IMpermeability of proteins.

DAMAGE: Nephrotic Syndrome

Causes of Nephrotic Syndrome

- **1- Primary Glomerular Diseases** → No other Reason.
- **2- Secondary (Systemic Diseases with Renal Manifestations)** → Due to an underlying disease

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

Secondary

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)**

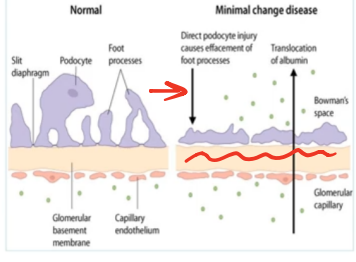
1- Minimal-Change Disease (Lipoid Nephrosis)

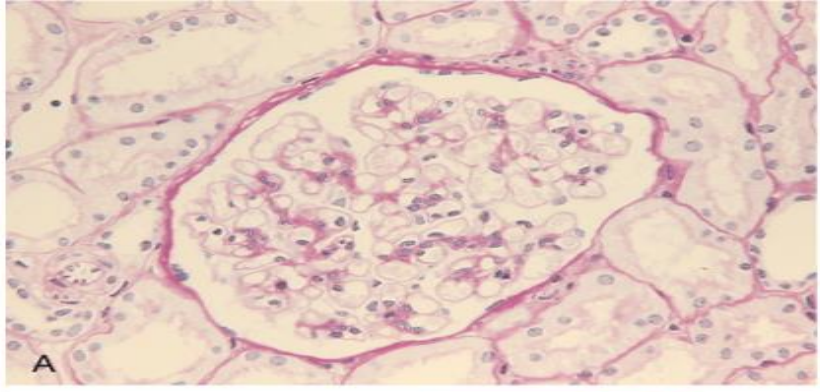
So called because there is no abnormality in the kidney

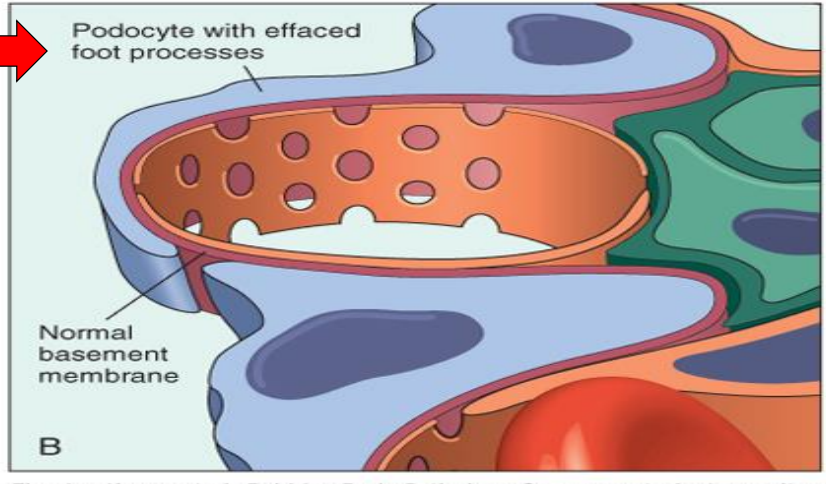
- **benign disorder.**
  - ↳ Good Prognosis
- **The most frequent cause of the nephrotic syndrome in children (ages 1-7 years).**

- ***Pathogenesis:*** **still not clear.**
  - ↱ Alteration in filtration barrier leading to proteinuria

? 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 → LM

B

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

Morphology

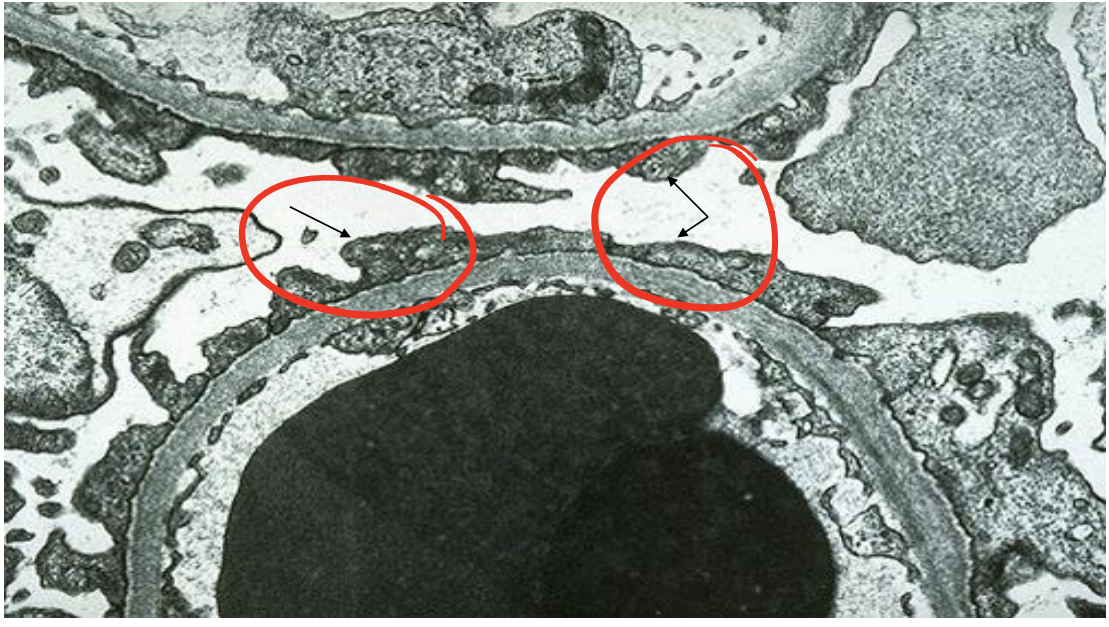
- **LM**
- the glomeruli appear normal.

- **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)

→ Fibrosis

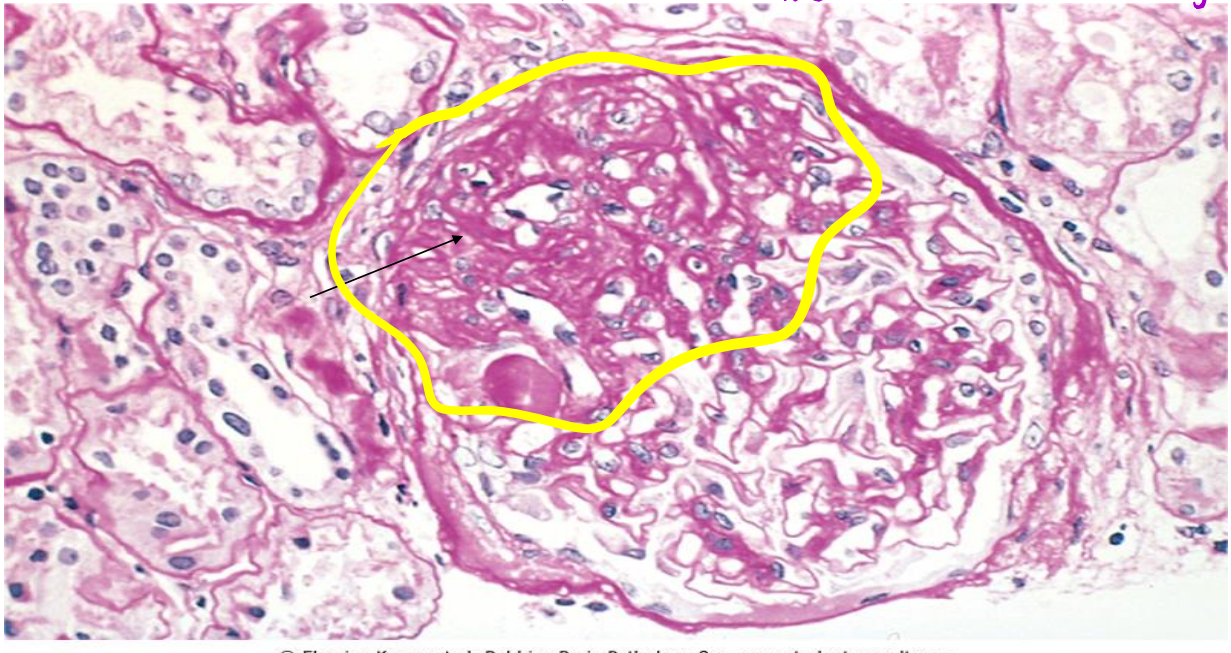
- sclerosis affecting some but not all glomeruli (focal involvement) and involving only segments of glomerulus.
  → Name indications
- Usually nephrotic syndrome.
- It can occur :
- as a primary disease(20% to 30% of NS)
  2- secondary.
- Or: in association with AIDS; heroin abuse; nephron loss; inherited or congenital forms resulting from mutations affecting nephrin; etc….

] Endless Reasons. Do not Memorize,

But know that they are many.

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

more pink, connective tissue fibrosis of segment.



MCD versus FSGS

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

- ***Pathogenesis***
- **unclear**
- ***injury to the podocytes*** **? ↑ GFR ? Genetics ?** → mutation in filtration membrane esp. nefrin.
- **entrapment of plasma proteins and lipids in foci of injury where sclerosis develops.**

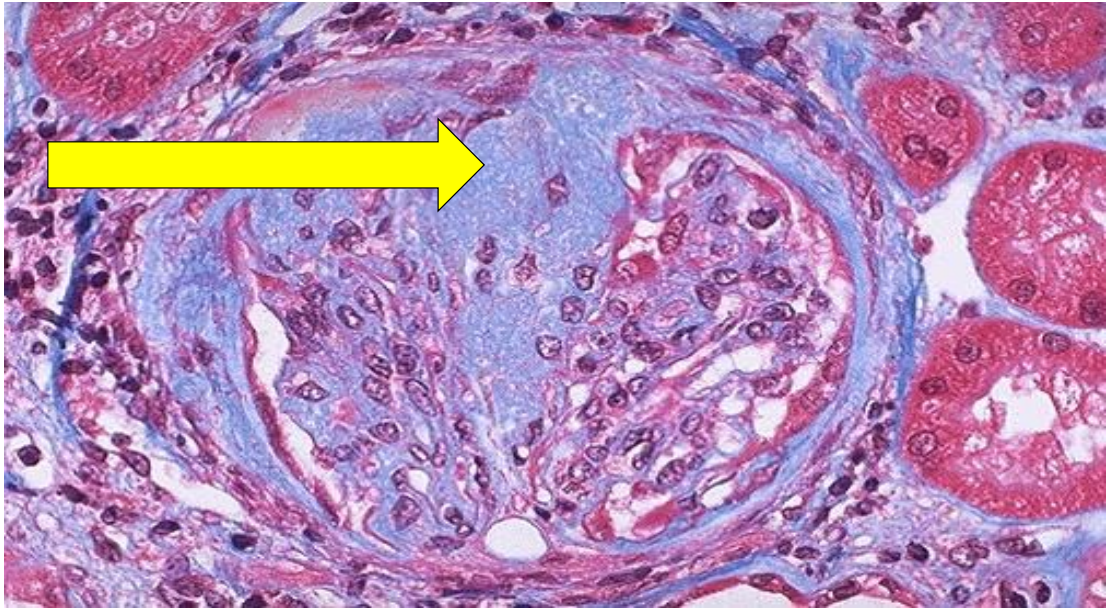
- **Clinical Course** → Poorer prognosis than MCD
- **about 50% of individuals suffer renal failure after 10 years**
- **Poor responses to corticosteroid therapy.**
- **Adults do worse than children**

- **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 foot processes**

FSGS

blue = collagen deposition (MT stain).

Observe connective Tissues



Collapsing glomerulopathy

Doc. Didnt read the slide, only know it has association with HIV!

- 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:

GBM

- **Immune complex deposition in glomerulus** → Lumen
  Ab+Ag ↵
- **Types of Membranous glomerulonephritis :**

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

2-Secondary

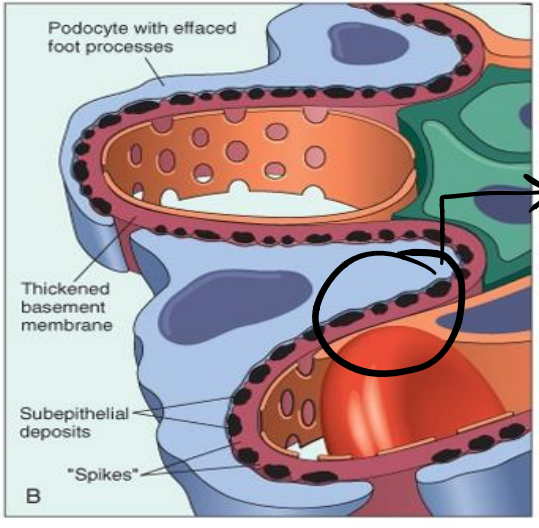
* Disrupts architecture of GBM.

Location → Preferably below podocyte + above GBM
subepithelium

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** . → Immune complex deposition leads to extention of membrane
- **IF**
- **deposits** of immunoglobulins and complement along the GBM (IgG) Positive
- **EM**
- **subepithelial deposits "spike and dome" pattern**.



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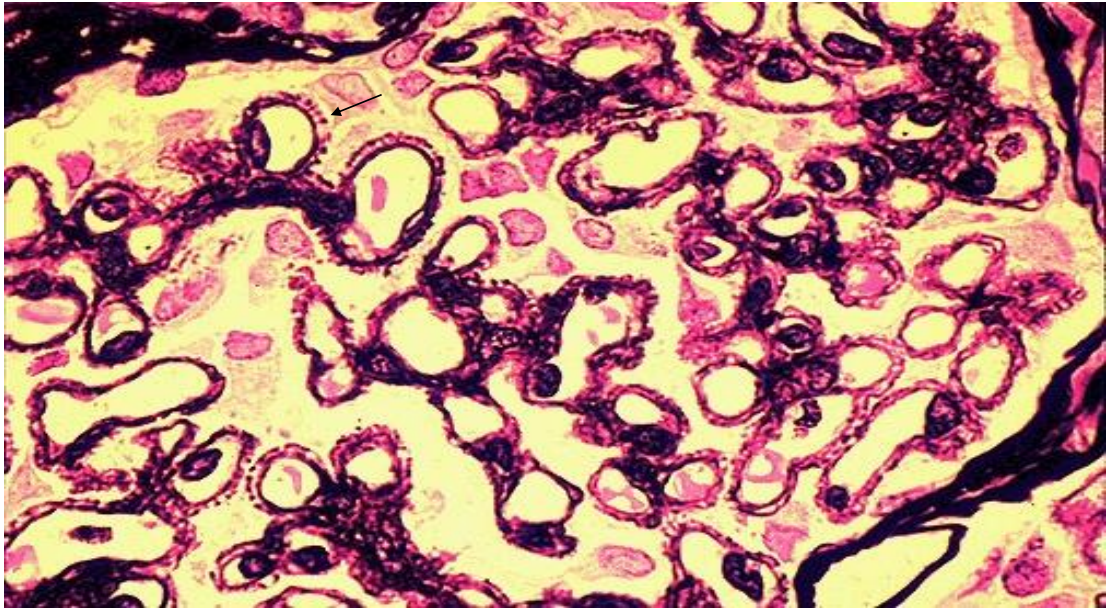
Membranous nephropathy.

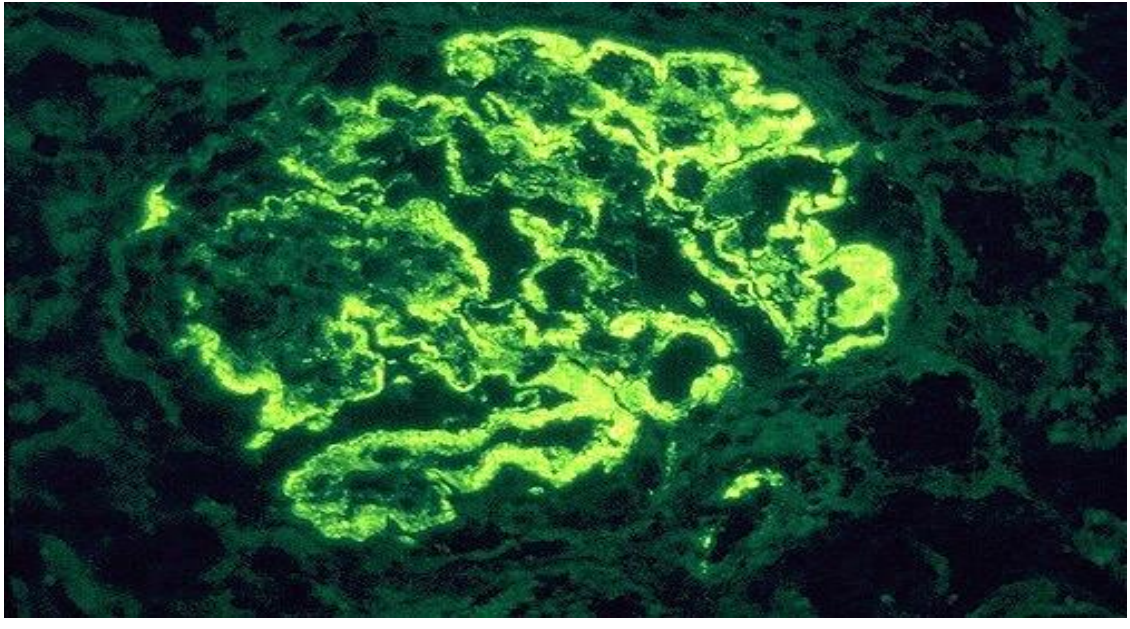
subepithelial deposits and the presence of "spikes" of basement membrane material between the immune deposits .

Damage of filtration.

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

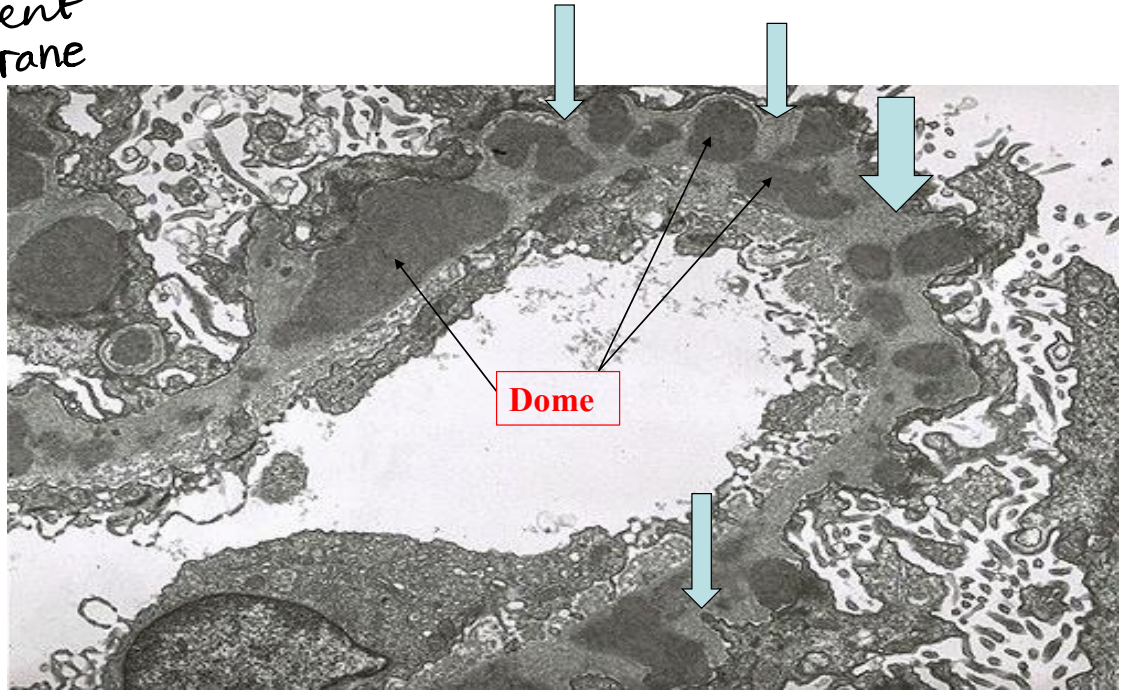


Membranous GN
IF: deposits of mainly IgG and complements



EM- ("spike and dome" pattern).

Basement Membrane



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

Chronic