

# Issues of the differential diagnosis of diseases accompanied with nephrotic syndrome

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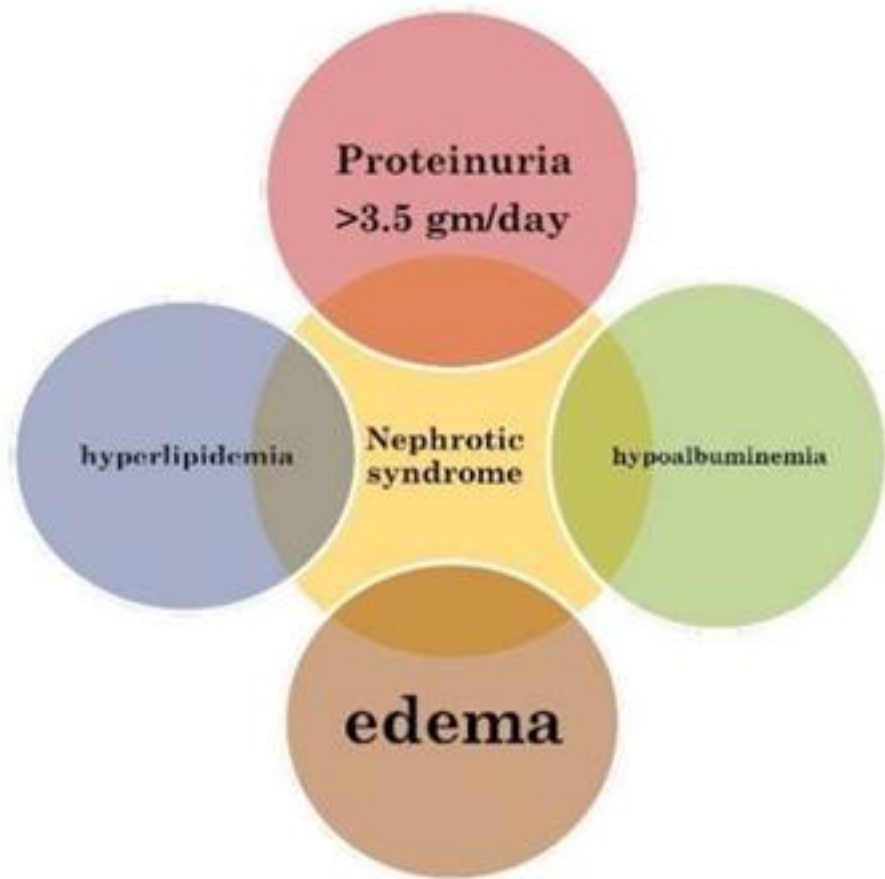
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# Definition

Nephrotic syndrome is a clinical complex characterized by a number of renal and extrarenal features, most relevant of which are:

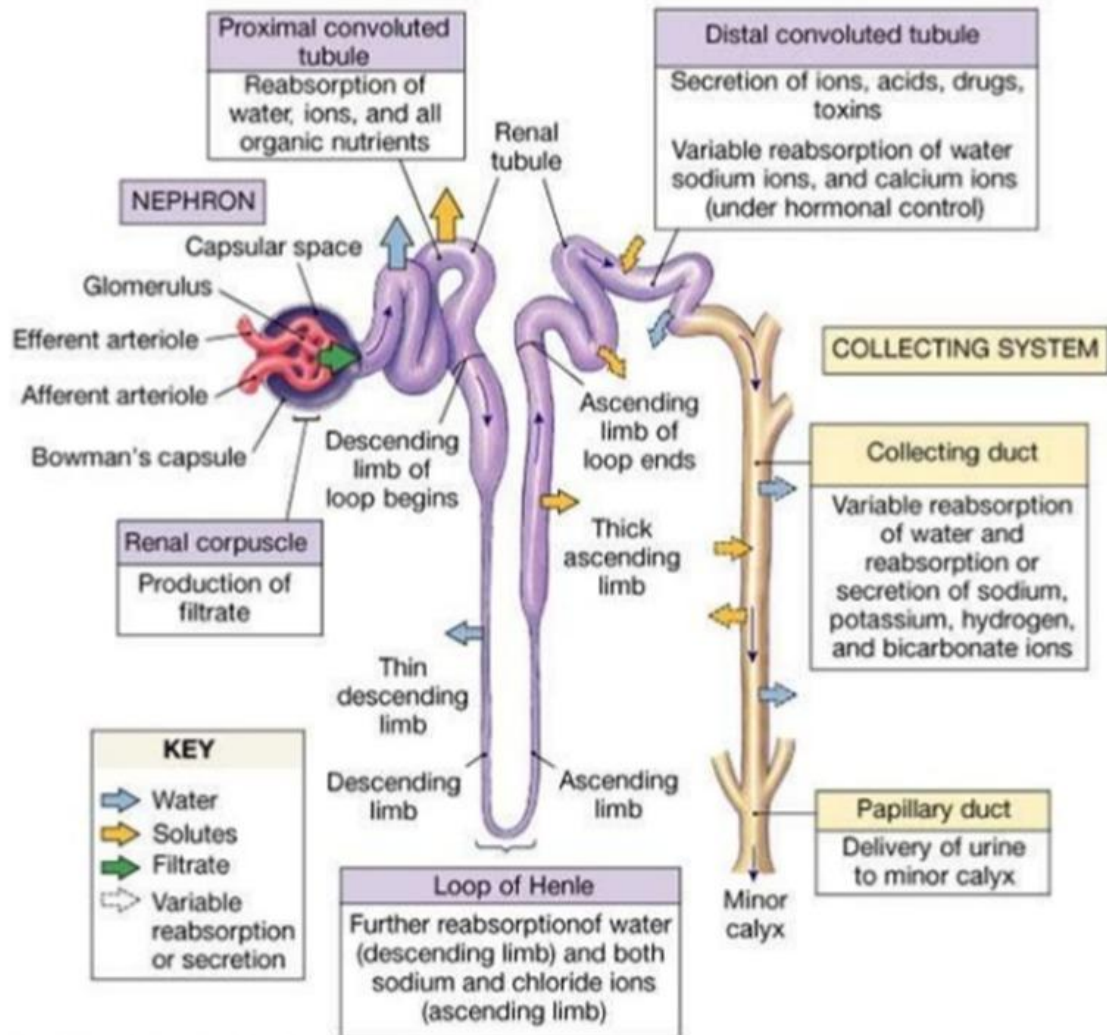
- Proteinuria ( $>3.5$  mg/24h)
- Hypoalbuminemia ( $<2.5$ g/dL)
- Edema
- Hyperlipidemia
- Other



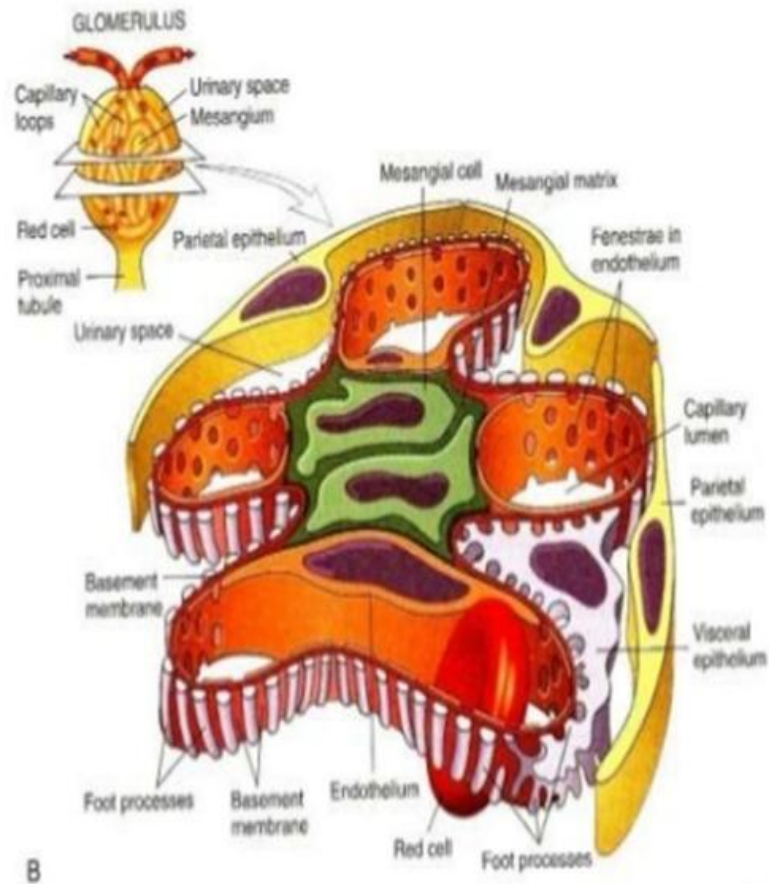
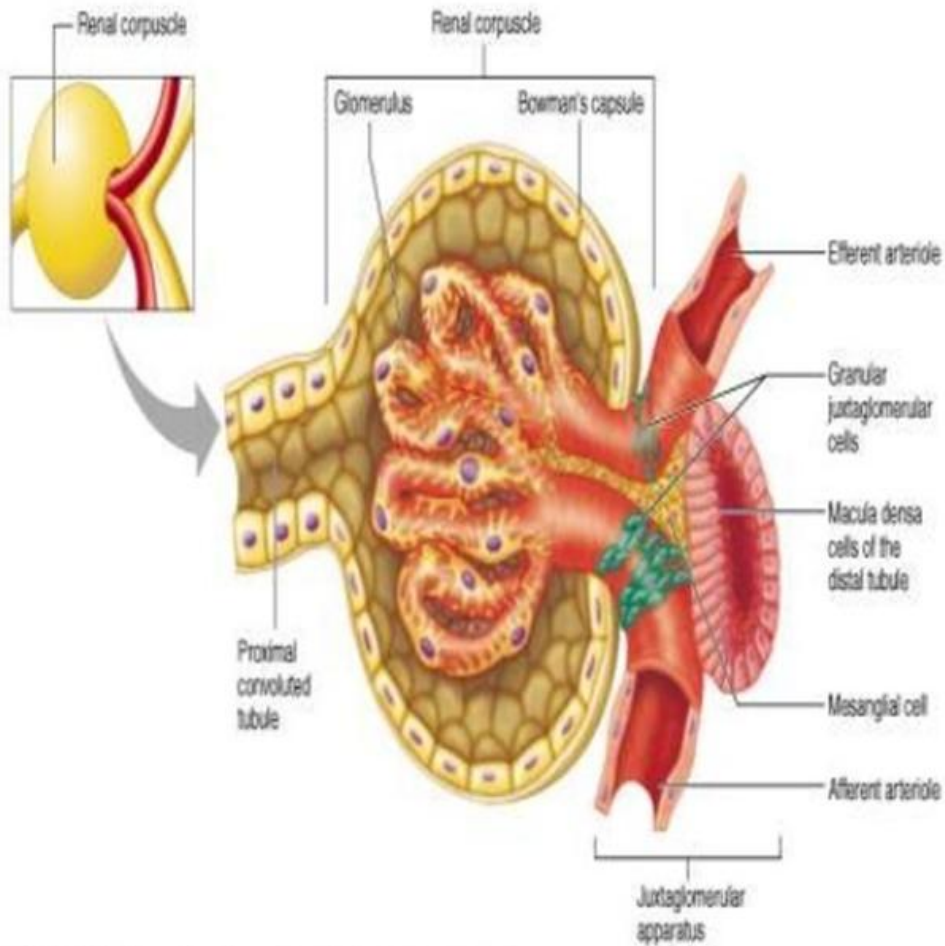
A few other features seen in nephrotic syndrome can be:

- Hypovolemia
- Anaemia (transferrin loss)
- Dyspnea (pleural effusion)
- Lipiduria
- Increased ESR (loss of fibrinogen & other plasma content)
- Hypertension - only in 20%

15 times more common in children

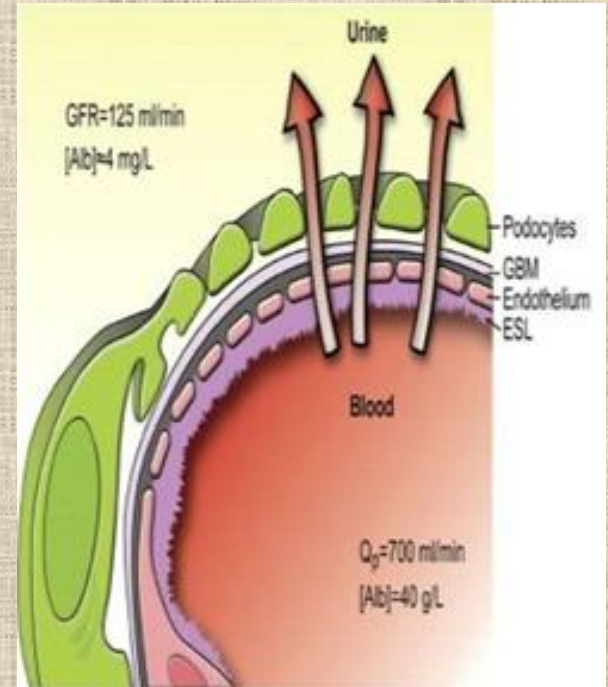






# Pathophysiology of proteinuria

- Normal amount of protein excretion in healthy person -  $<0.1\%$  ( $0.05\text{mg/L}$ )
- Glomerular capillaries are lined by fenestrated endothelium (podocytes) on a glomerular basement membrane
- They have cellular extensions – foot processes; distances between them are filtration slits



## Pathophysiology of proteinuria (2)

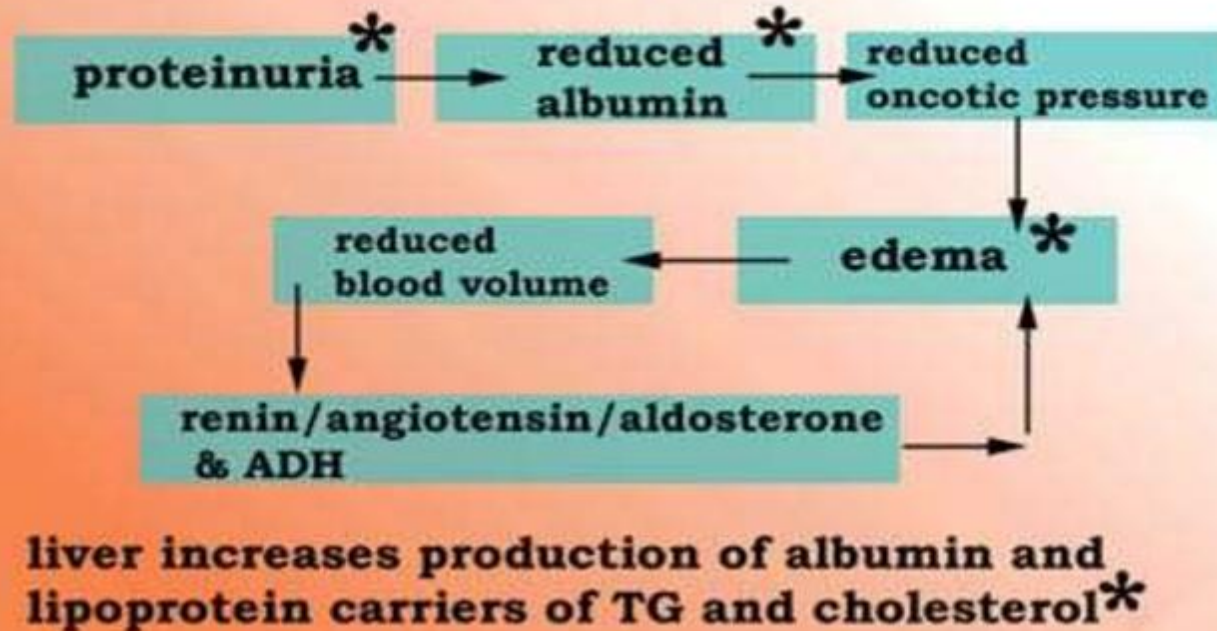
- Therefore, proteinuria can be caused by anything that induces structural damage to endothelial surface, basement membrane or podocytes either
- Selective proteinuria – excretion of relatively low M.W. protein only (albumin, transferrin)
- Non-selective proteinuria – excretion of all types of protein, predominantly high M.W. (IgG, IgM,  $\alpha$ 2-macroglobulin)

Hepatic albumin synthesis in nephrotic patients is increased from 150mg/kg/day to 210mg/kg/day



# Pathogenesis of edema

## Nephrotic Syndrome\*



# Pathogenesis of hyperlipidemia

- Reduced oncotic pressure due to protein loss causes, among other, an increase of hepatic lipoprotein synthesis
- Defective lipid catabolism
- Presented mostly by LDL, more seldom – by VLDL
- Increases progression of existing renal disease
- In perspective – increases risk of MI and coronary death

# Pathogenesis of hypovolemia

- Reduced oncotic pressure leads to loss of plasma water into interstitium
- That causes a decrease in circulating blood volume
- In perspective it may lead to hypotension – but it's a late feature

# Symptoms and signs

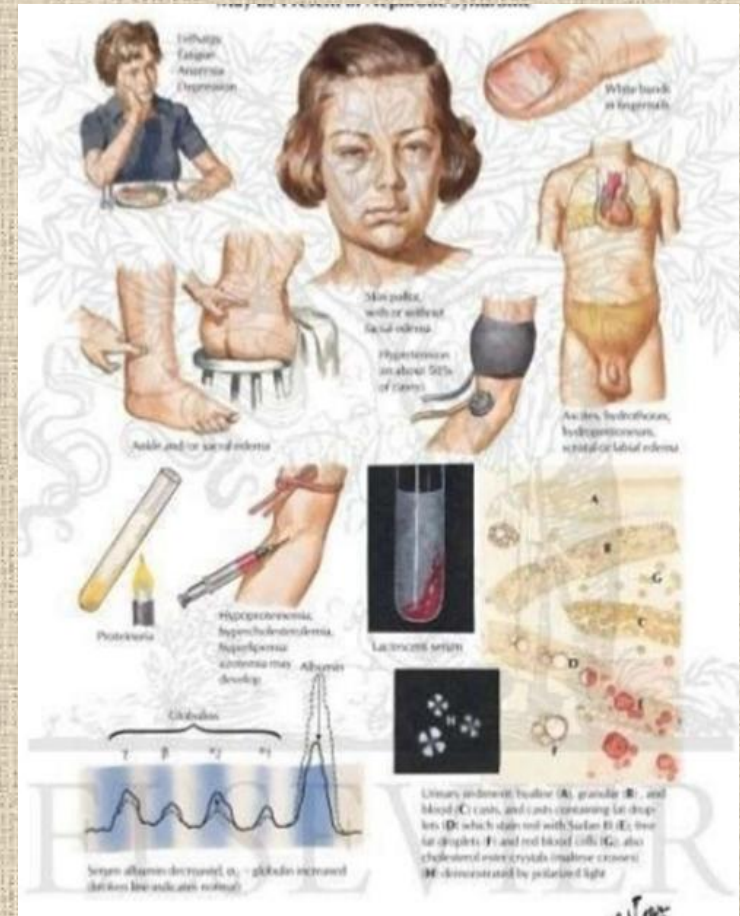
- Frothy urine
- Anorexia, malaise, puffy eyelids, retinal sheen, abdominal pain, wasting of muscles,
- Edema in the eyelids in the morning
- Orthostatic hypotension and shock may develop in children





# Symptoms and signs

- Sometimes oliguria and even acute renal failure due to hypovolemia and therefore hypoperfusion
- Prolonged NS may lead to malnutrition, myopathy, decreased  $\text{Ca}^{++}$ , tetany, coagulation disorders



# Classification

- Primary – being a disease specific to kidneys
- Secondary – being a renal manifestation of a systemic general disease

# Causes

## Primary:

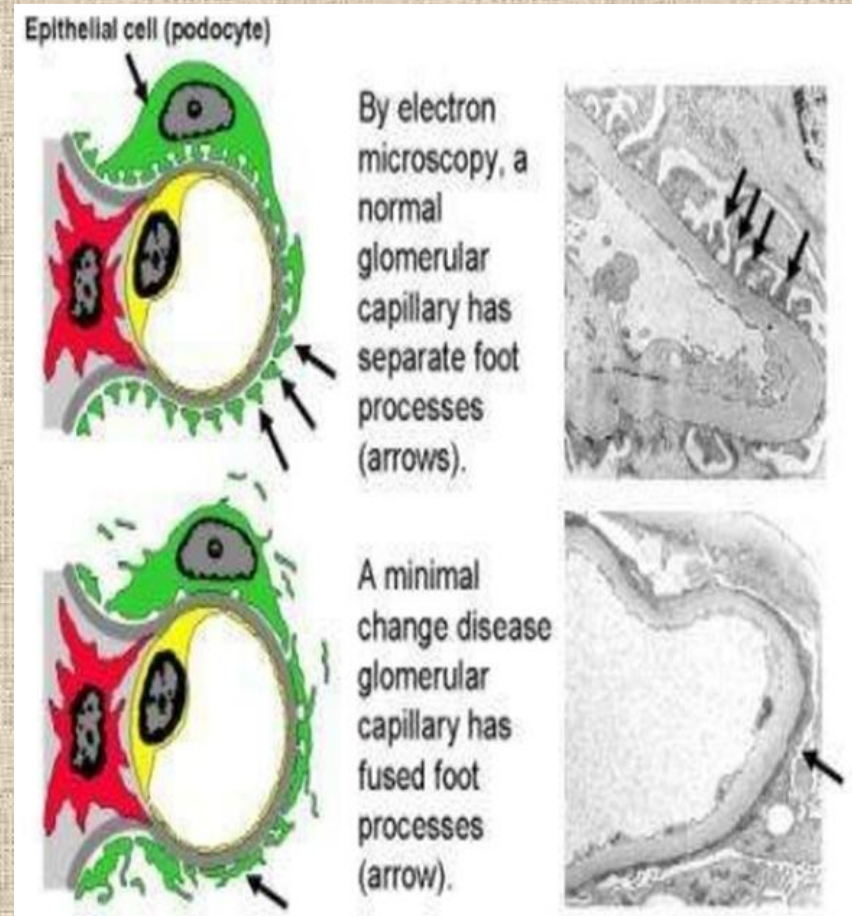
- *Minimal-change nephropathy*
- Focal glomerulonephritis
- Membranous nephropathy
- Mesangial proliferative glomerulonephritis
- Rapidly progressive glomerulonephritis

## Secondary:

- ***Diabetes mellitus***
- SLE
- Amyloidosis/paraproteinemia
- Viral hepatitis B, C
- Preeclampsia

# Minimal change nephropathy

- Synonyms: Neil's disease, Lipoid nephrosis, Foot process disease
- Incidence: 80% - in children (1-8 y.o.), 20% - adults.
- Etiology – mostly idiopathic; in 30% - recent URI; sometimes associated with Hodgkin's lymphoma
- Clinical features: nephrotic syndrome, no other specific signs



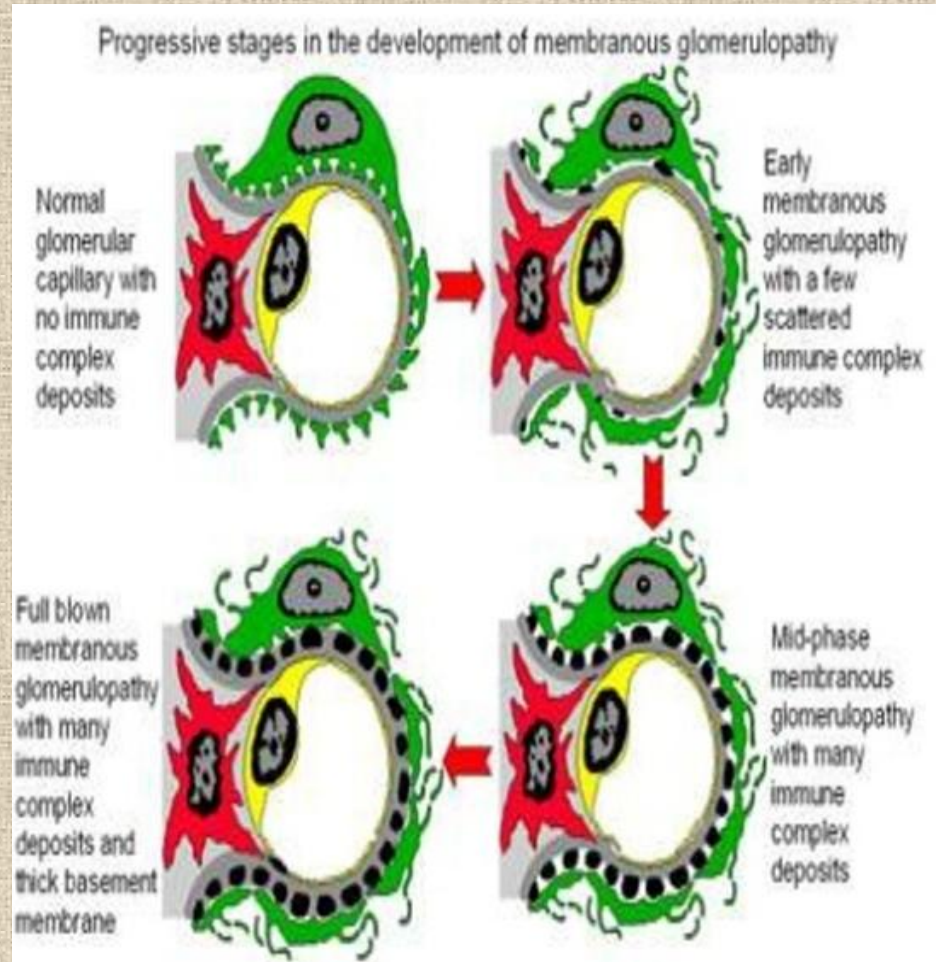


# Minimal change nephropathy

- Lab features: selective proteinuria, no other specific changes
- Course: spontaneous remission in 25-40% patients, complete remission in 65-70%. Steroid resistant patients may progress to FSGS (focal segmental glomerulosclerosis)

# Membranous nephropathy

- Incidence: mostly adults (40-60 y.o.), 50% of all nephrotic syndrome cases
- Etiology: idiopathic in most patients, sometimes associated with infections (immune complexes), drugs, carcinomas, heavy metals poisoning
- Clinical features: nephrotic syndrome in 80%; asymptomatic proteinuria in 20%.

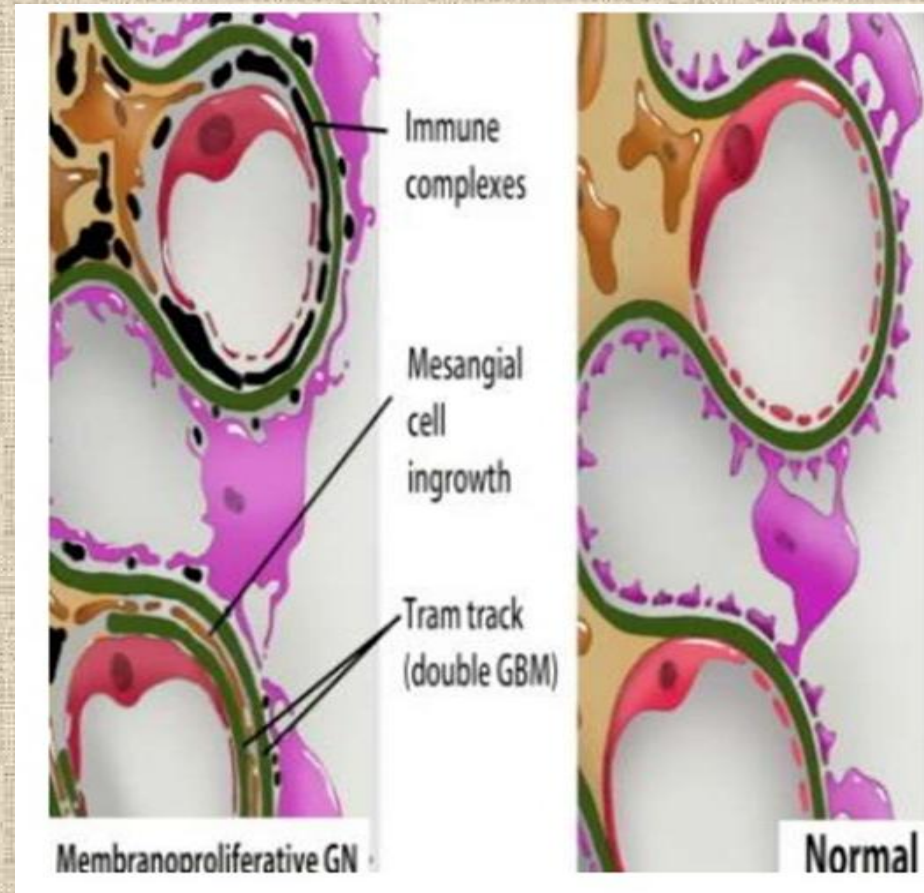


# Membranous nephropathy

- Lab features: non-selective proteinuria, microhematuria
- Course: complete remission in children, in adults – probability of graduate progression to renal failure
- Requires exclusion of other related diseases

# Mesangial proliferative nephropathy

- Incidence: children and young adults (5-25 y.o.)
- Etiology: chronic immune complex nephropathy; associated with chronic URI, SLE, cancer growth, liver cirrhosis, drug abuse etc.
- Clinical features: nephrotic syndrome in 50%, acute nephritic syndrome in 20%, seldom – renal failure



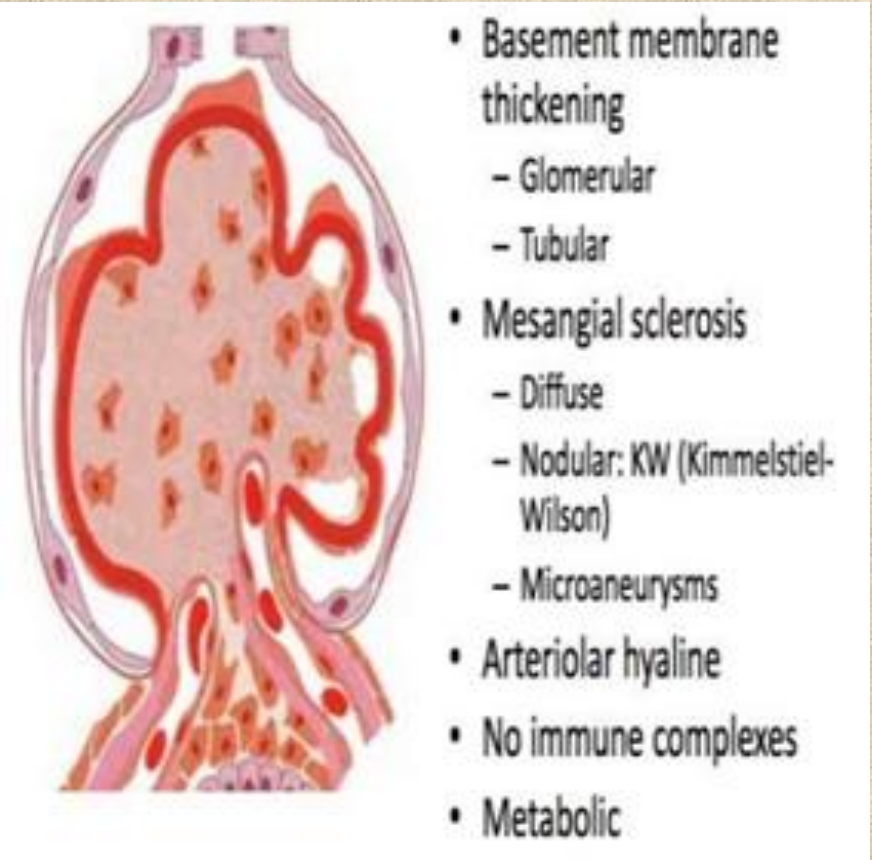


# Mesangial proliferative nephropathy

- Lab features: reduced factors of complement system; increased C3 hepatic factor; circulating immune complexes are found
- Course: progressive deterioration of renal function with short remissions. Chronic renal failure develops within 10 years in 50% of children and 80% of adults.

# Diabetic nephropathy

- Complicates 30% of cases of type I DM and 20% of cases of DM II
- Clues: anamnesis research; presence of proliferative or non-proliferative diabetic retinopathy (in 60-90% of all DM cases)
- The earliest morphologic abnormalities are thickening of a basement membrane and mesangium expansion, prominent nodular matrix expansion



THANK YOU!