Issues of the differential diagnosis of diseases accompanied with nephrotic syndrome

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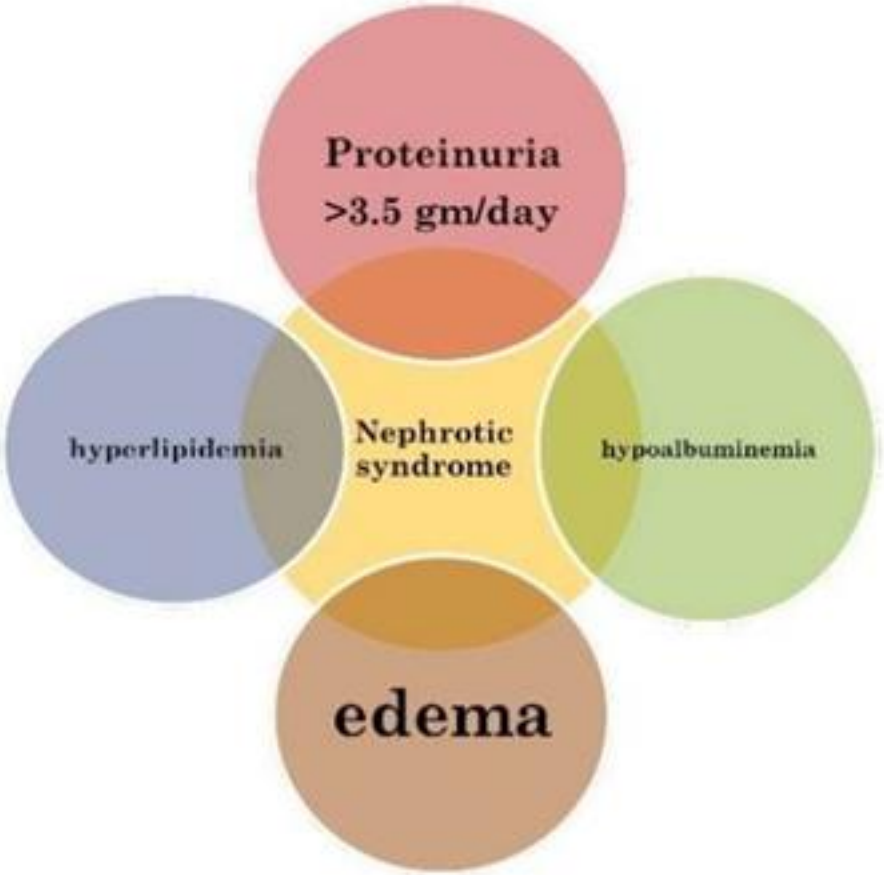
Definition

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

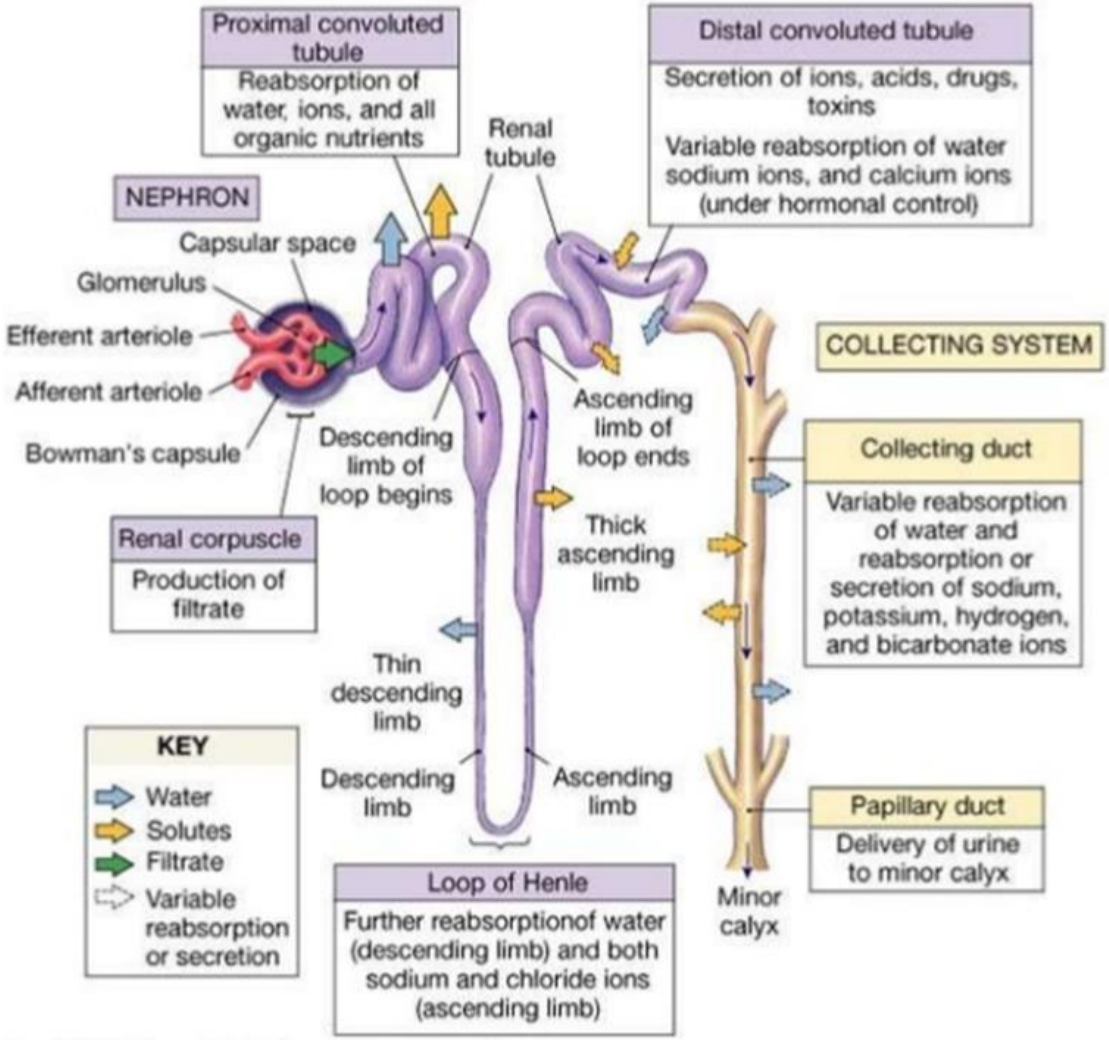
- Proteinuria (>3.5 mg/24h)
- Hypoalbuminemia (<2.5g/dL)
- Edema
- Hyperlipidemia
- Other

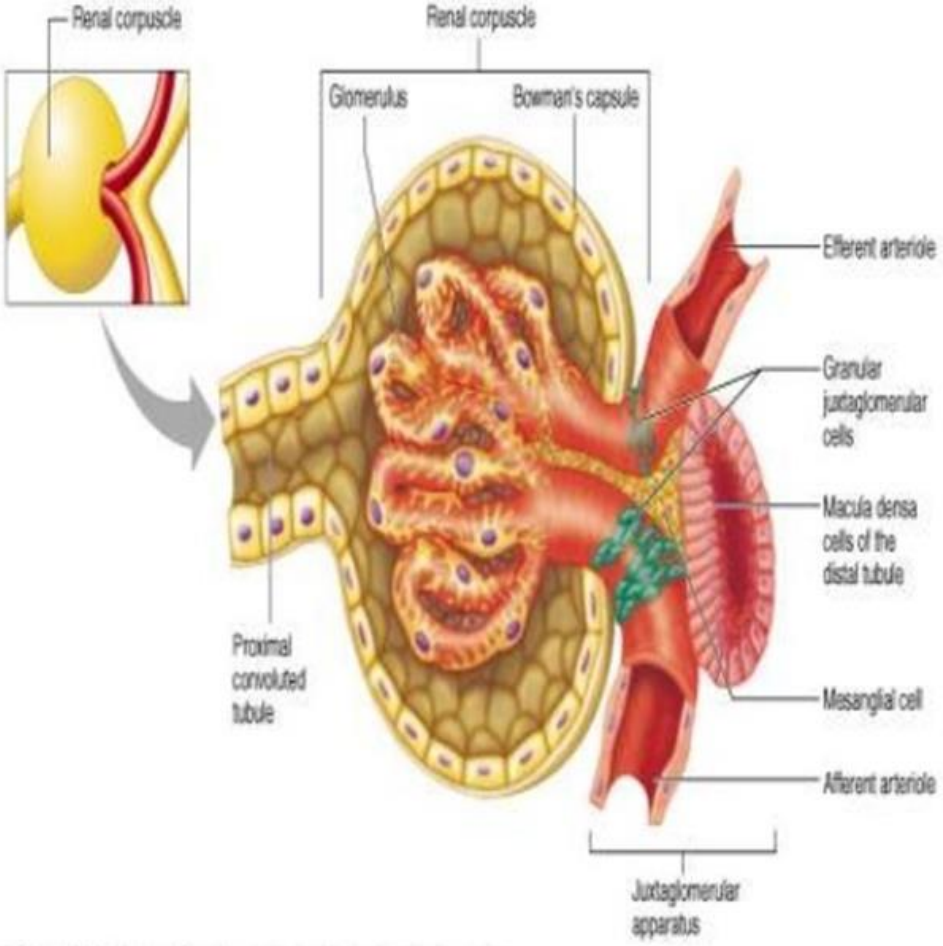

Proteinuria
>3.5 gm/day
hyperlipidemia
Nephrotic syndrome
hypoalbuminemia
edema

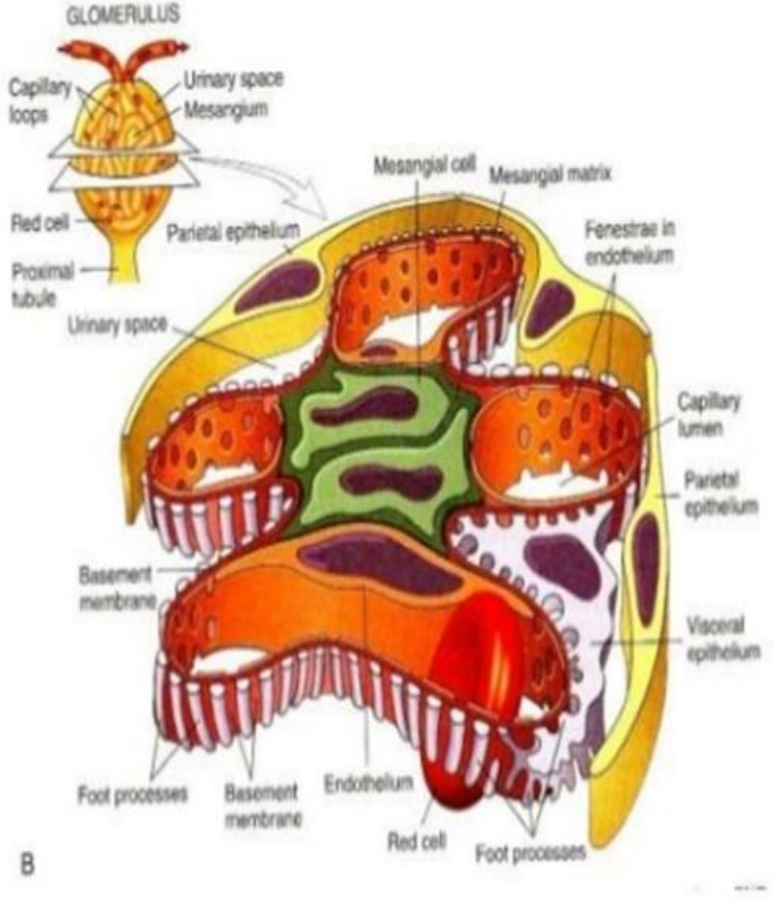
A few other features seen in nephrotic syndrome can be:

- 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

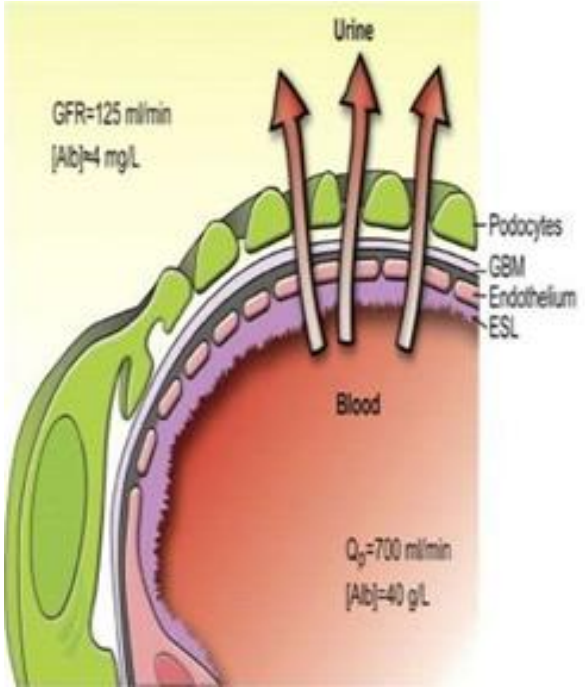

Proximal convoluted tubule
Reabsorption of water, ions, and all organic nutrients
Distal convoluted tubule
Secretion of ions, acids, drugs, toxins
Variable reabsorption of water sodium ions, and calcium ions (under hormonal control)
Renal tubule
NEPHRON
Capsular space
Glomerulus
Efferent arteriole
Afferent arteriole
Bowman's capsule
COLLECTING SYSTEM
Ascending limb of loop ends
Descending limb of loop begins
Collecting duct
Variable reabsorption of water and reabsorption or secretion of sodium, potassium, hydrogen, and bicarbonate ions
Renal corpuscle
Production of filtrate
Thick ascending limb
Thin descending limb
KEY
Water
Solutes
Filtrate
Variable reabsorption or secretion
Descending limb
Ascending limb
Papillary duct
Delivery of urine to minor calyx
Loop of Henle
Further reabsorptionof water (descending limb) and both sodium and chloride ions (ascending limb)
Minor calyx





Pathophysiology of proteinuria

- Normal amount of protein excretion in healthy person - <0.1% (0.05mg/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

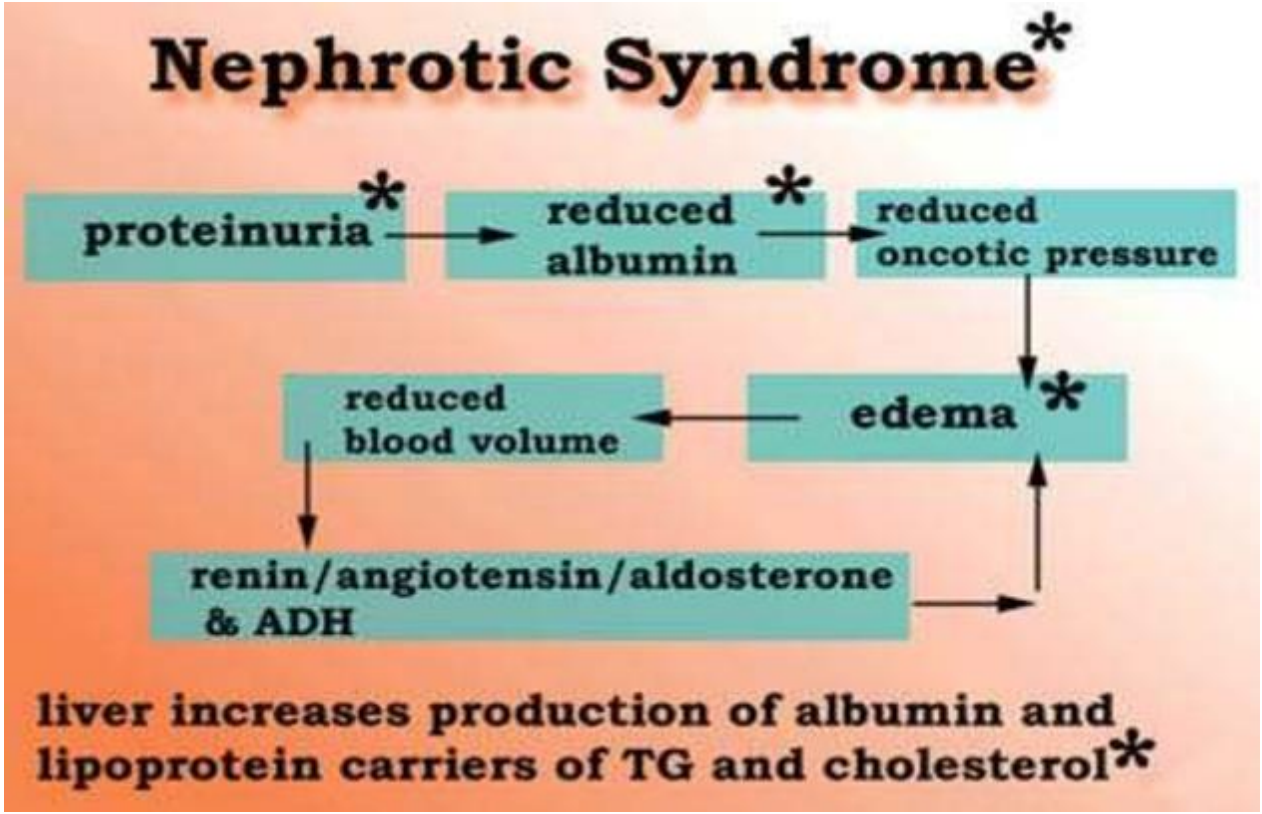


Pathophysiology of proteinuria (2)

- 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, α2-macroglobulin)

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

Pathogenesis of edema



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

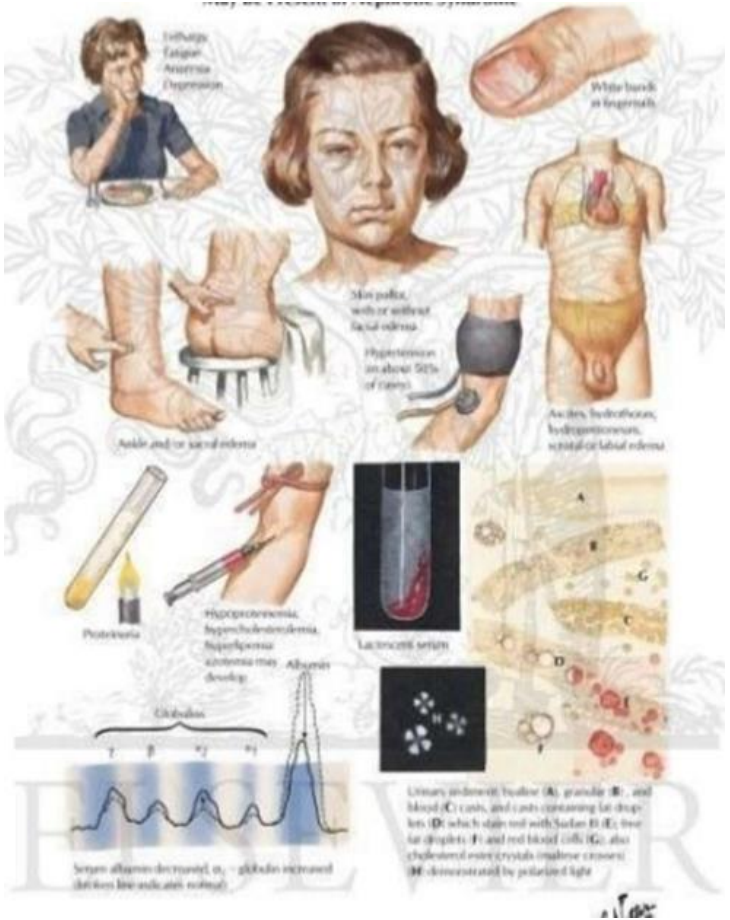
- Reduced oncotic pressure leads to loss of plasma water into interstitium
- That causes a decrease in circulating blood volume
- In perspective it may lead to hypotension – but it’s a late feature

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 Ca++, tetany, coagulation disorders



Classification

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

Causes

Primary:

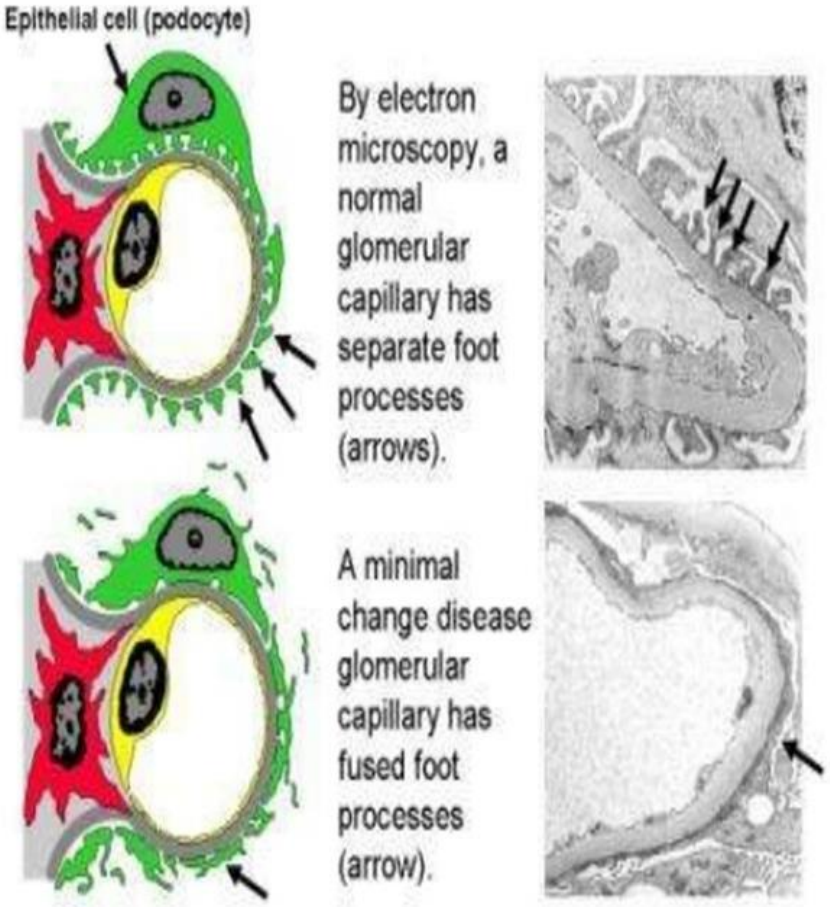
- *Minimal-change nephropathy*
- Focal glomerulonephritis
- Membranous nephropathy
- Mesangial proliferative glomerulonephritis
- Rapidly progressive glomerulonephritis

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

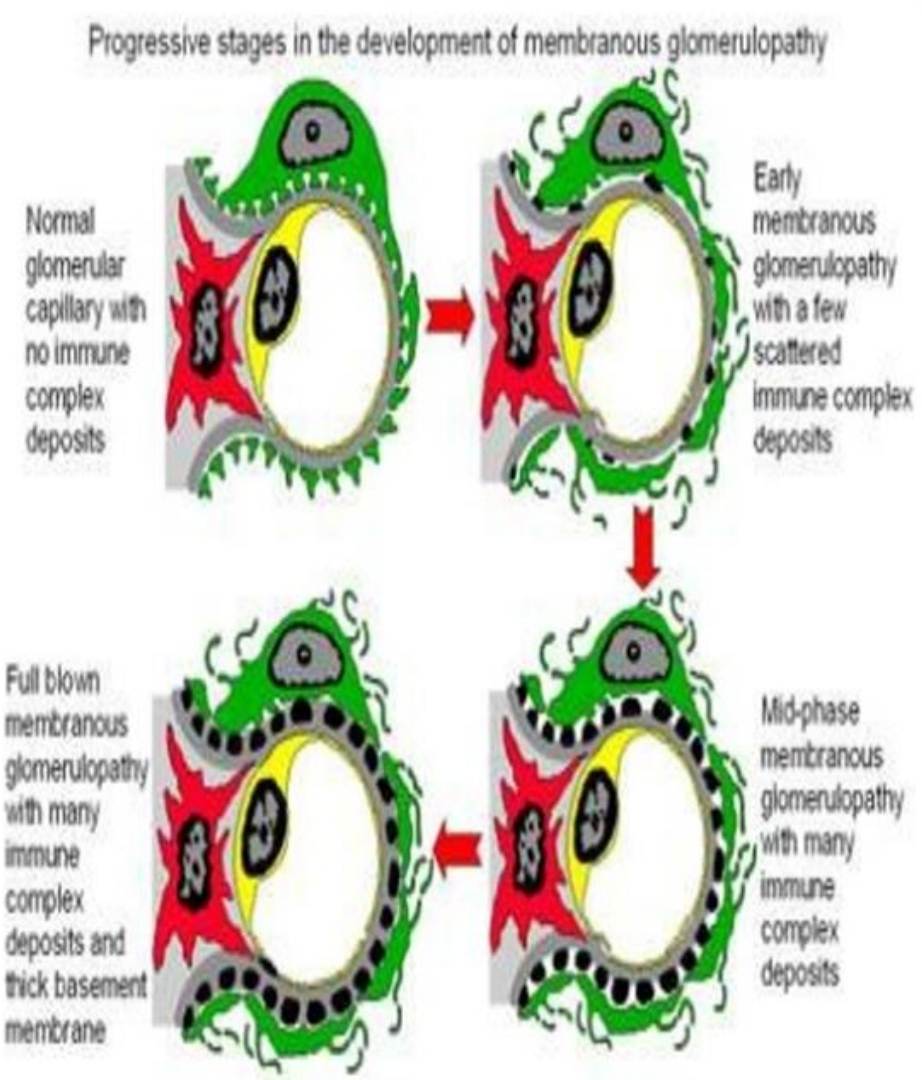


Minimal change nephropathy

- 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, drugs, carcinomas, heavy metals poisoning
- Clinical features: nephrotic syndrome in 80%; asymptomatic proteinuria in 20%.

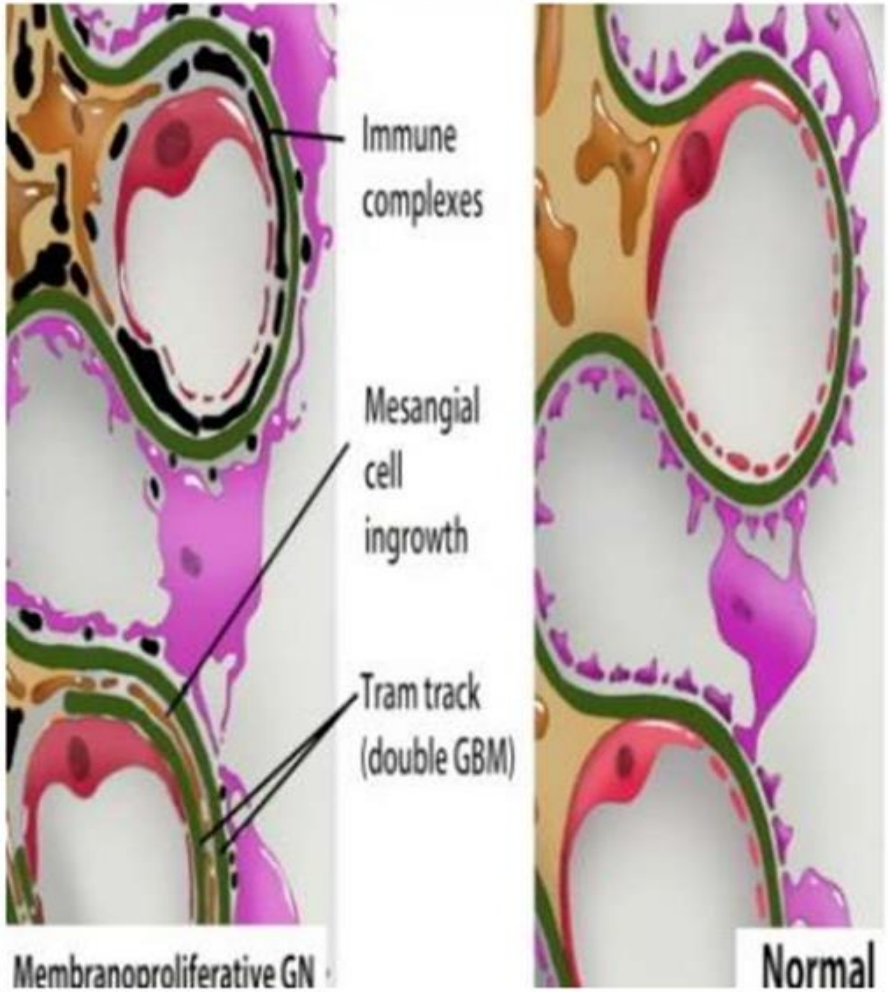


Membranous nephropathy

- 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

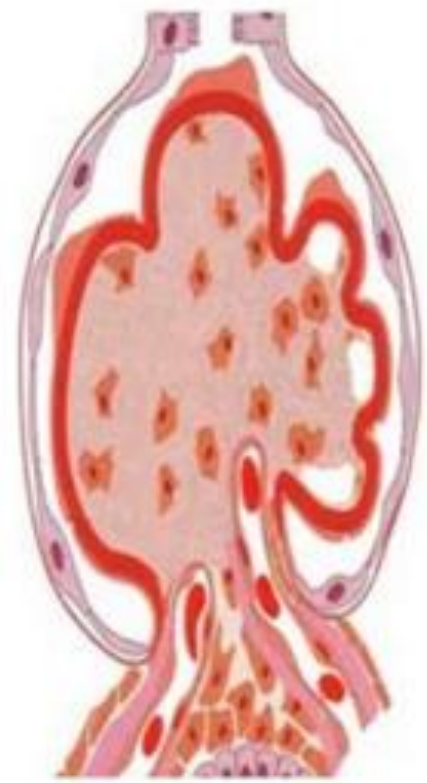


Mesangial proliferative nephropathy

- 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, promonent nodular matrix expansion



- Basement membrane thickening
  - Glomerular
  - Tubular
- Mesangial sclerosis
  - Diffuse
  - Nodular: KW (Kimmelstiel-Wilson)
  - Microaneurysms
- Arteriolar hyaline
- No immune complexes
- Metabolic

THANK YOU!