Study Hub OSCE Sessions- Core Renal Concepts

17-11-20

Presented By

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PRESENTATION OUTLINE

ANATOMY

PHYSIOLOGY

COMMON PATHOLOGIES

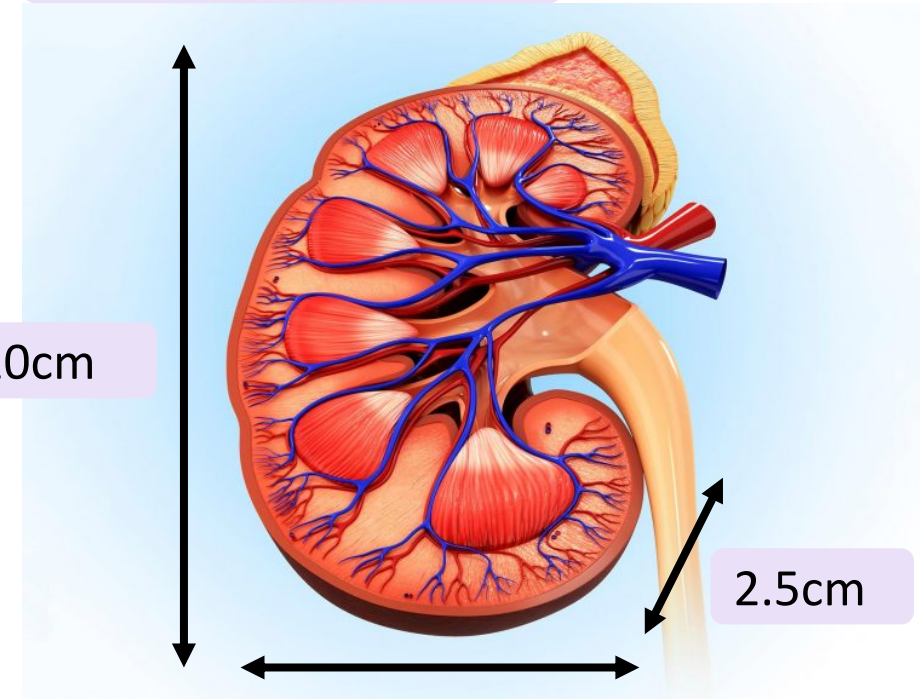
MENTIMETER QUIZ
80 12 10 4

FUNCTIONS

- Removal of metabolic waste products such as
  - Uric acid
  - Urea
  - Creatinine
- Maintain electrolyte, water and pH balance
- Regulation of blood pressure, blood volume and erythropoiesis and vitamin D

ANATOMY

- Dimensions

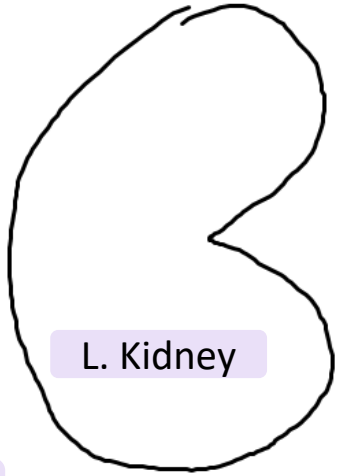


- Ovoid/ bean shaped
- Located
  - Retroperitoneally
  - T12-L3
  - Posteriorly- the superior parts of the kidney lie deep to the 11th and 12th rib
- DEEP
  - Renal capsule -Tough fibrous capsule
  - Perirenal fat- collection of extraperitoneal fat
  - Renal fascia- encloses the kidneys and suprarenal glands
  - Pararenal fat- mainly located on the posterolateral aspect of the kidney
- SUPERFICIAL

ANATOMY- RELATIONS

POSTERIORLY

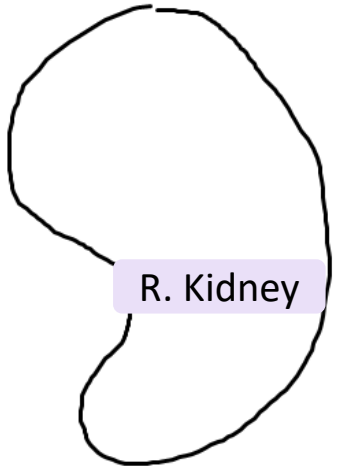
- Diaphragm
- 11th & 12 rib
- Psoas major, quadratus lumborum & transversus abdominis



ANTERIORLY

- Suprarenal gland
- Spleen
- Pancreas
- Left colic flexure
- Jejenum

POSTERIORLY

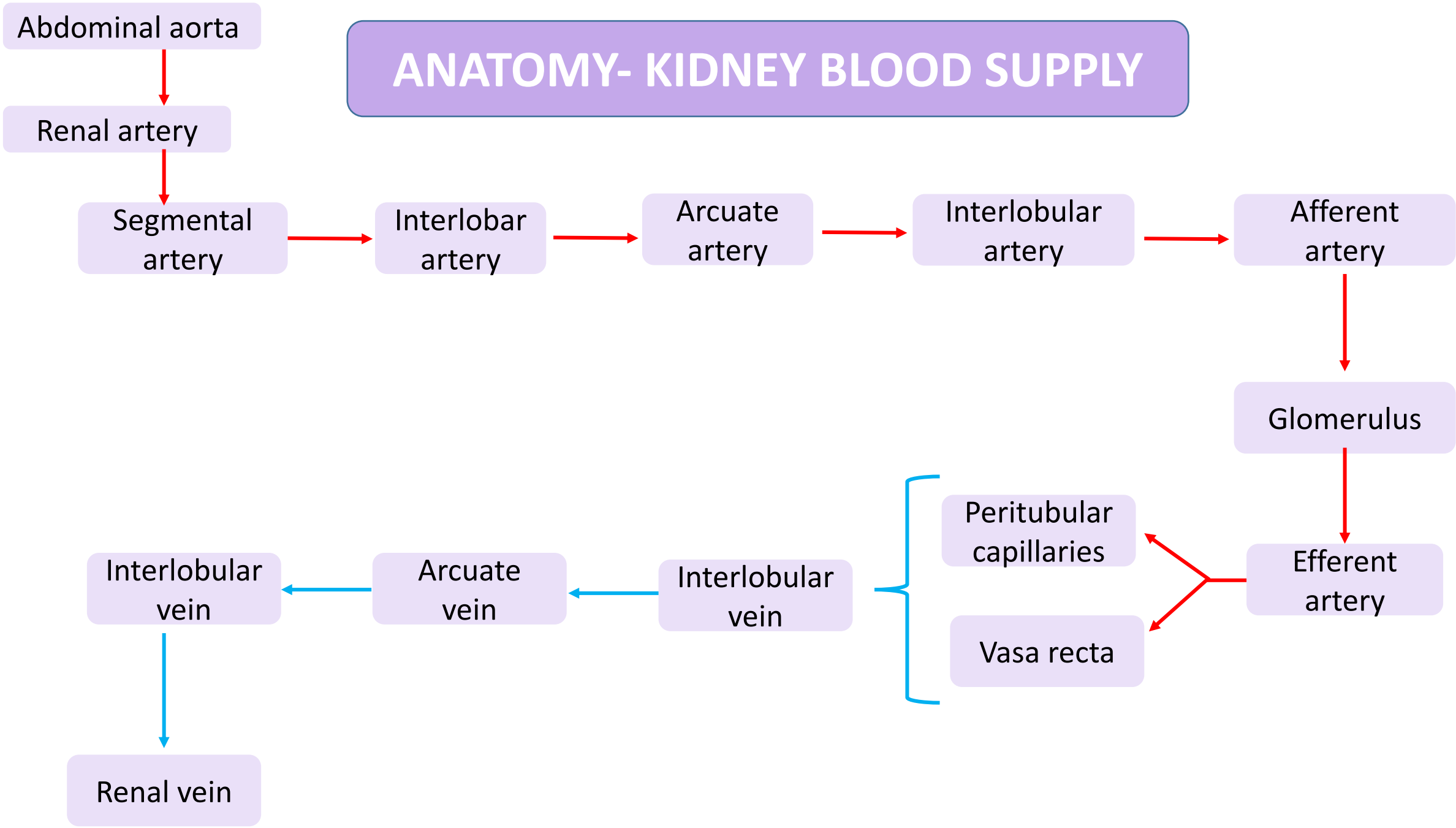


- Diaphragm
- 12th rib
- Psoas major, quadratus lumborum & transversus abdominis
- Subcostal, iliohypogastric & ilioinguinal nerves

ANTERIORLY

- Suprarenal gland
- Liver
- Duodenum
- Right colic flexure

ANATOMY- KIDNEY BLOOD SUPPLY



PHYSIOLOGY

- Urine excretion = glomerular filtration –(tubular reabsorption + tubular secretions)

- Filtration process

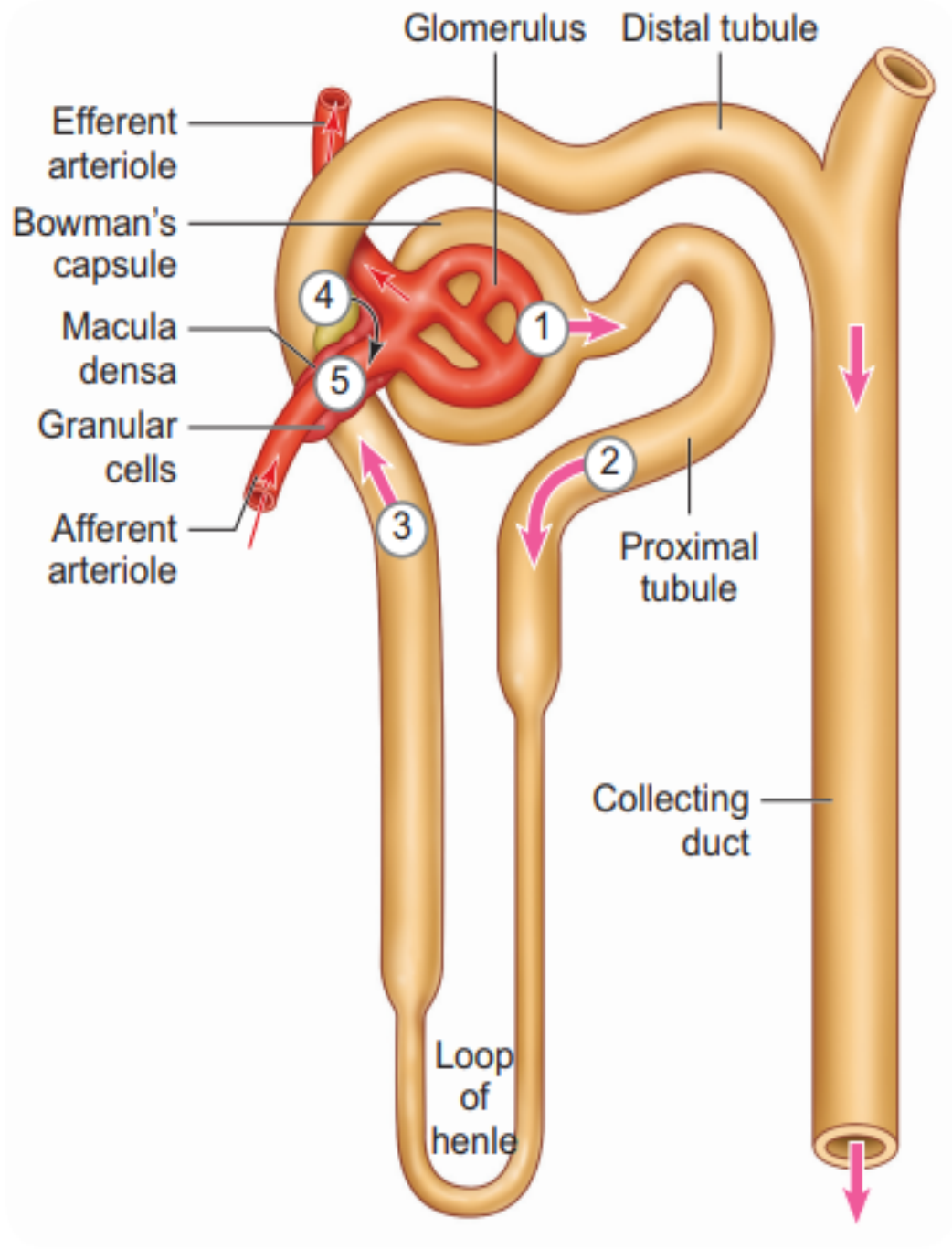
Filtrate passes through fenestrations of the capillary endothelium

↓

glomerular basement membrane

↓

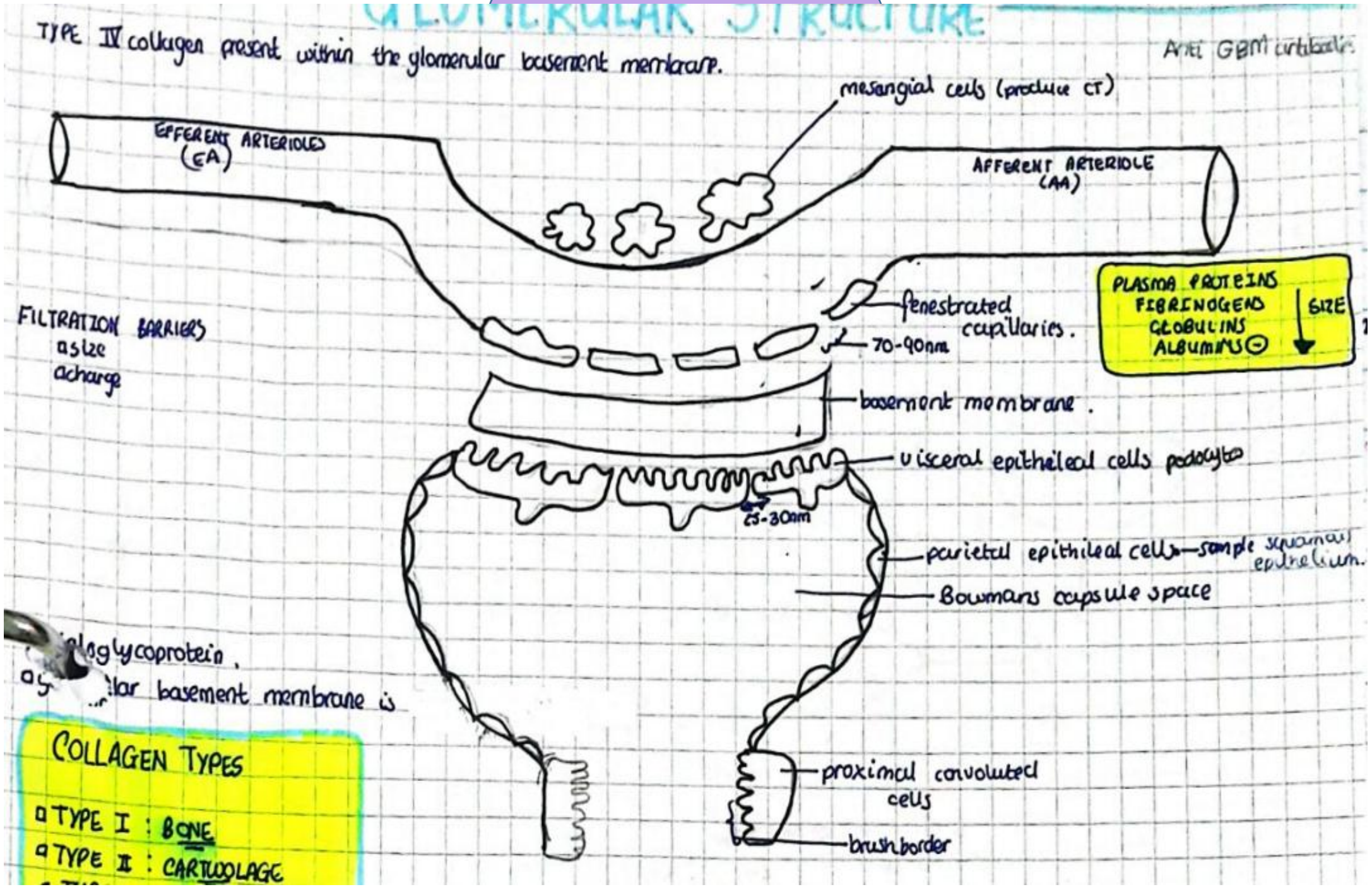
Between pedicels


Glomerulus
Distal tubule
Efferent arteriole
Bowman's capsule
Macula densa
Granular cells
Afferent arteriole
4
1
5
2
3
Proximal tubule
Collecting duct
Loop of henle

GLOMERULAR STRUCTURE

TYPE IV collagen present within the glomerular basement membrane.

Anti GBM antibodies



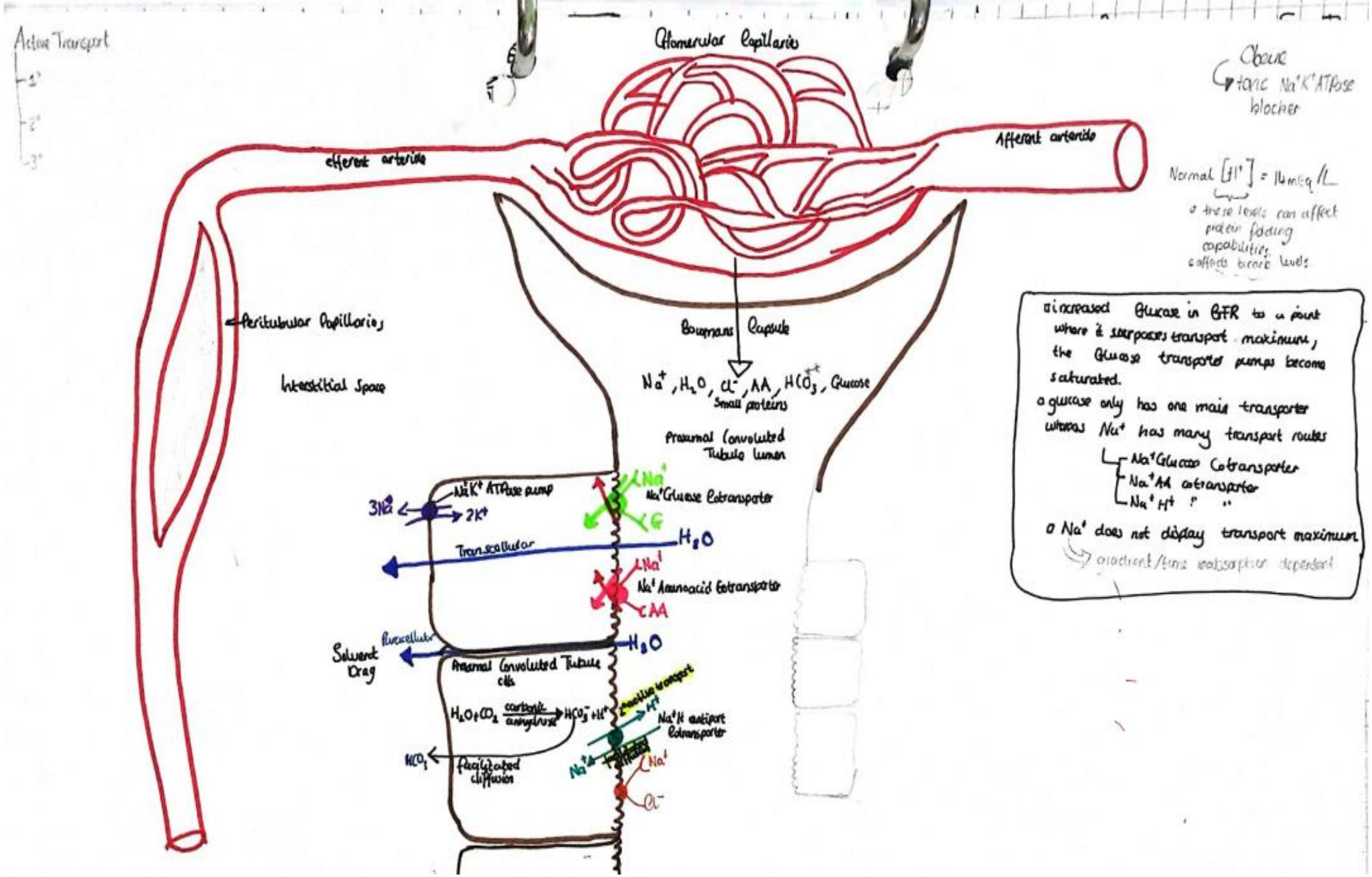
FILTRATION BARRIERS
- a size
- a charge

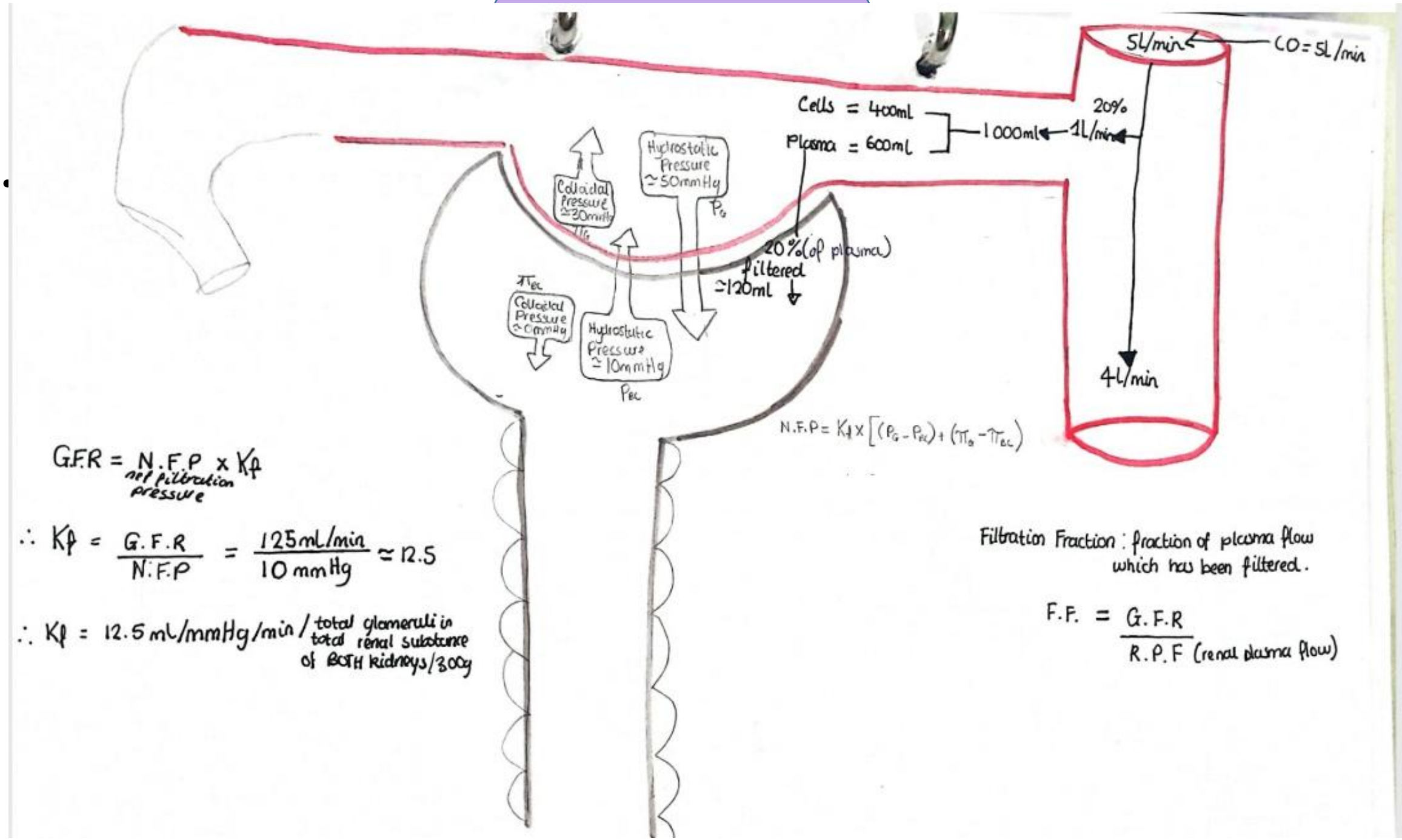
...glycoprotein,

a...lar basement membrane is

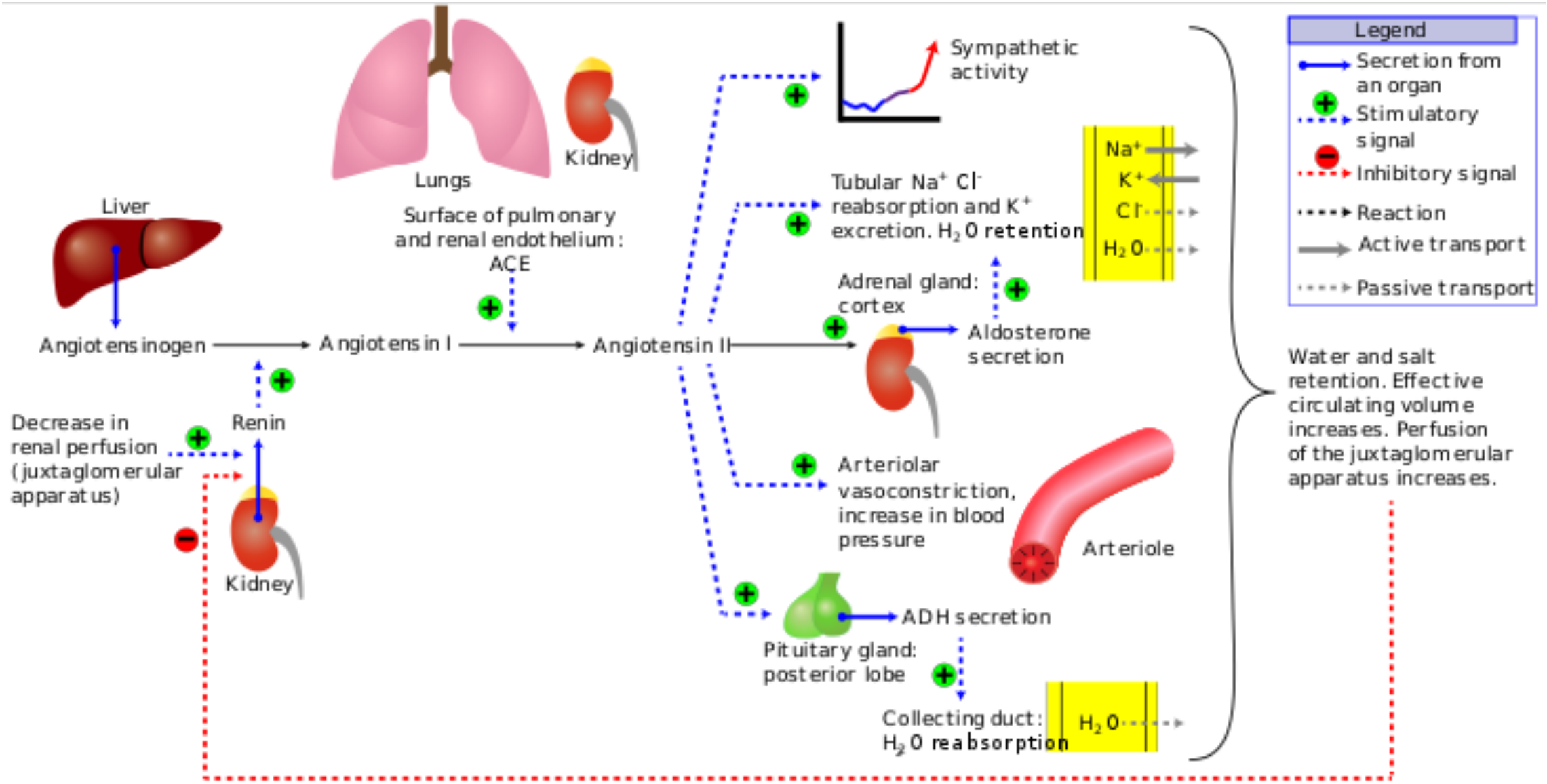
COLLAGEN TYPES

- TYPE I : BONE
- TYPE II : CARTILAGE


Active Transport
1°
2°
3°
Glomerular Capillaries
Choice
Cytoplasmic Na⁺K⁺ATPase blocker
Normal [H⁺] = 1 mmol/L
• these levels can affect protein folding capabilities
• affects blood levels
Efferent arteriole
Afferent arteriole
Peritubular Capillaries
Interstitial Space
Bowmans Capsule
Na⁺, H₂O, Cl⁻, AA, HCO₃⁻, Glucose
Small proteins
Proximal Convoluted Tubule lumen
Na⁺K⁺ ATPase pump
3Na⁺
2K⁺
Na⁺Glucose Cotransporter
Na
G
Transcellular
H₂O
Na⁺ Amino acid Cotransporter
Na
AA
Paracellular
Solvent Drag
H₂O
Proximal Convoluted Tubule cells
H₂O + CO₂ carbonic anhydrase H₂CO₃ → HCO₃⁻ + H⁺
Secondary active transport
H⁺
Na⁺H⁺ antiport Cotransporter
HCO₃⁻
facilitated diffusion
Na⁺
Na⁺
Cl⁻
• increased Glucose in GFR to a point where it surpasses transport maximum, the Glucose transporter pumps become saturated.
• glucose only has one main transporter whereas Na⁺ has many transport routes
Na⁺Glucose Cotransporter
Na⁺AA cotransporter
Na⁺H⁺ ? "
• Na⁺ does not display transport maximum
gradient/ions reabsorption dependent


5L/min
CO = 5L/min
Cells = 400ml
Plasma = 600ml
1000ml
20%
1L/min
Hydrostatic Pressure ≃ 50mmHg
Colloidal Pressure ≃ 30mmHg
20% (of plasma) filtered
≃ 120ml
Colloidal Pressure ≃ 0mmHg
Hydrostatic Pressure ≃ 10mmHg
4L/min
N.F.P = Kf x [(PG - PBC) + (πG - πBC)]
G.F.R = N.F.P x Kf
net filtration pressure
∴ Kf = G.F.R / N.F.P = 125mL/min / 10mmHg ≃ 12.5
∴ Kf = 12.5 mL/mmHg/min / total glomeruli in total renal substance of BOTH kidneys/300g
Filtration Fraction : fraction of plasma flow which has been filtered.
F.F. = G.F.R / R.P.F (renal plasma flow)

The Renin-Angiotensin-Aldosterone System (RAAS)



HYPERTENSION

- Elevated blood pressure
- Diagnosis requires at least 2 separate readings on 2 separate visits

Stages

Normal	Systolic <120 & diastolic <80mmHg
Elevated	Systolic 120-129 & diastolic <80mmHg
Stage 1	Systolic 130-139 & diastolic 80- 89mmHg
Stage 2	Systolic >140 & diastolic >90mmHg

HYPERTENSION CLASSIFICATION

Primary hypertension

- No known secondary cause
- 90 % of cases
- ↓ renal sodium excretion

↓

↑ plasma volume → ↓ Renin release from juxtaglomerular apparatus

↓

↑stroke volume

↓

↑systolic blood pressure

↓

Low renin hypertension

Secondary hypertension

HYPERTENSION CLASSIFICATION

Secondary hypertension

Causes according to organs involved

Adrenal gland

- Primary hyperaldosternism (conn)
- Sushing syndrome
- Tumours
  - Pheochromocytoma
  - Neuroblastoma

Renal

- Kidney
  - Renal artery stenosis
  - Fibromuscular dysplasia
- Renal parenchymal diseases
  - Diabetic nephropathy
  - Glomerlonephritis
  - Polycystic kidney disease

Thyroid

- Hyperthyroidism
  - ↑ cardiac output
- Hypothyroidism
  - ↑ renal retention of sodium

Parathyroid

- Primary hyperparathyroidism
  - Hypercalcaemia
  - Vasoconstriction of arterioles = ↑ total vasucal peripheral resistance

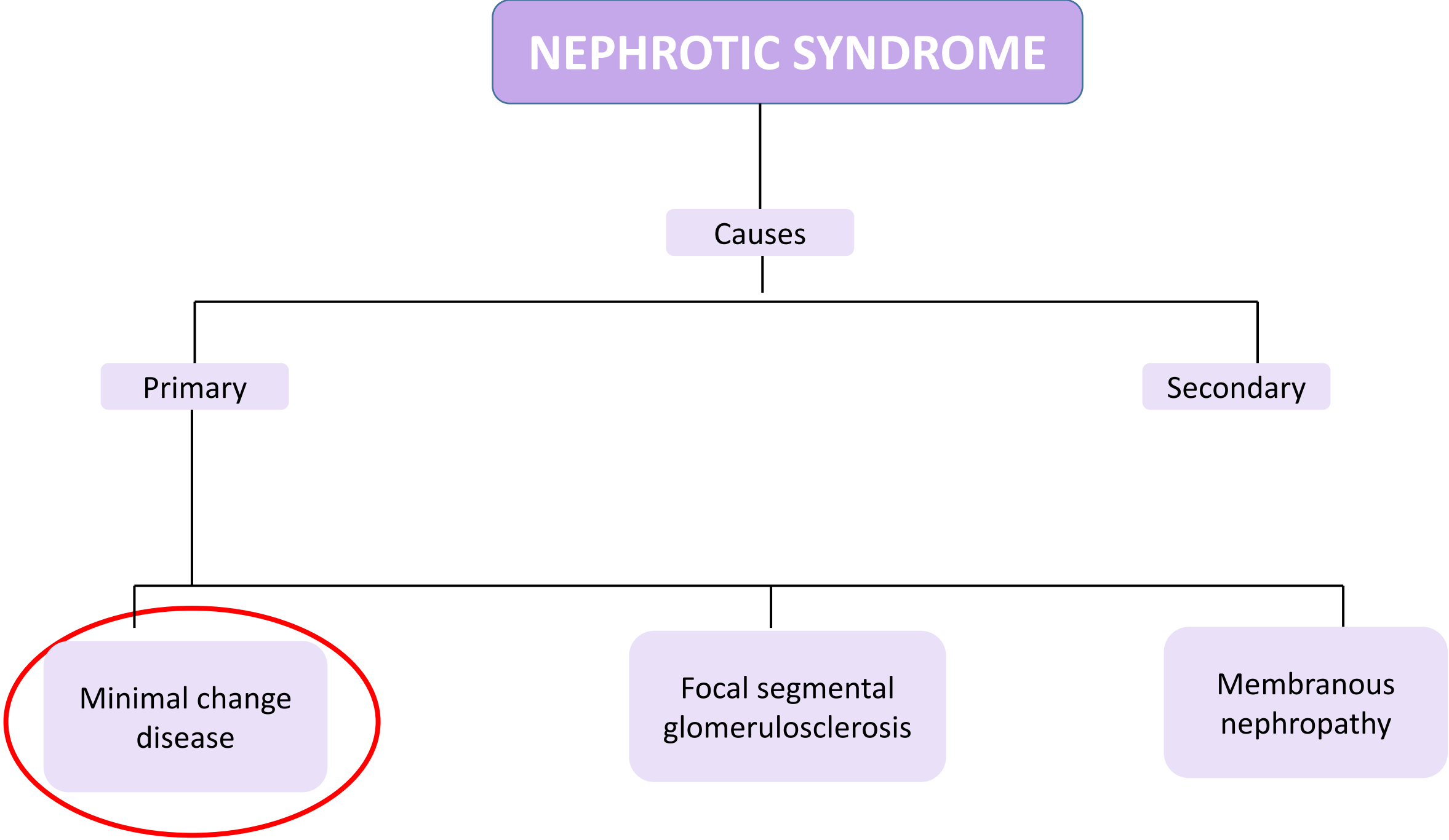
NEPHROTIC SYNDROME

Definition

A combination of symptoms seen in various renal diseases that are associated with dysfunction of the renal filtration system.

Characterized by massive renal loss of protein (> 3.5 g/day) resulting in

- edema
- hypoalbuminemia,
- hyperlipidemia,
- hypercoagulability (antithrombin III deficiency), and
- an increased risk of infection (loss of immunoglobulins).


NEPHROTIC SYNDROME
Causes
Primary
Secondary
Minimal change disease
Focal segmental glomerulosclerosis
Membranous nephropathy

MINIMAL CHANGE DISEASE

- Most common cause of nephrOtic syndrome in children
- On light microscopy, the glomeruli look completely normal.
- The cause is most often idiopathic and it can be triggered by a recent infection, recent vaccination, or by an immune stimulus, like a bee sting.
- Pathophysiology

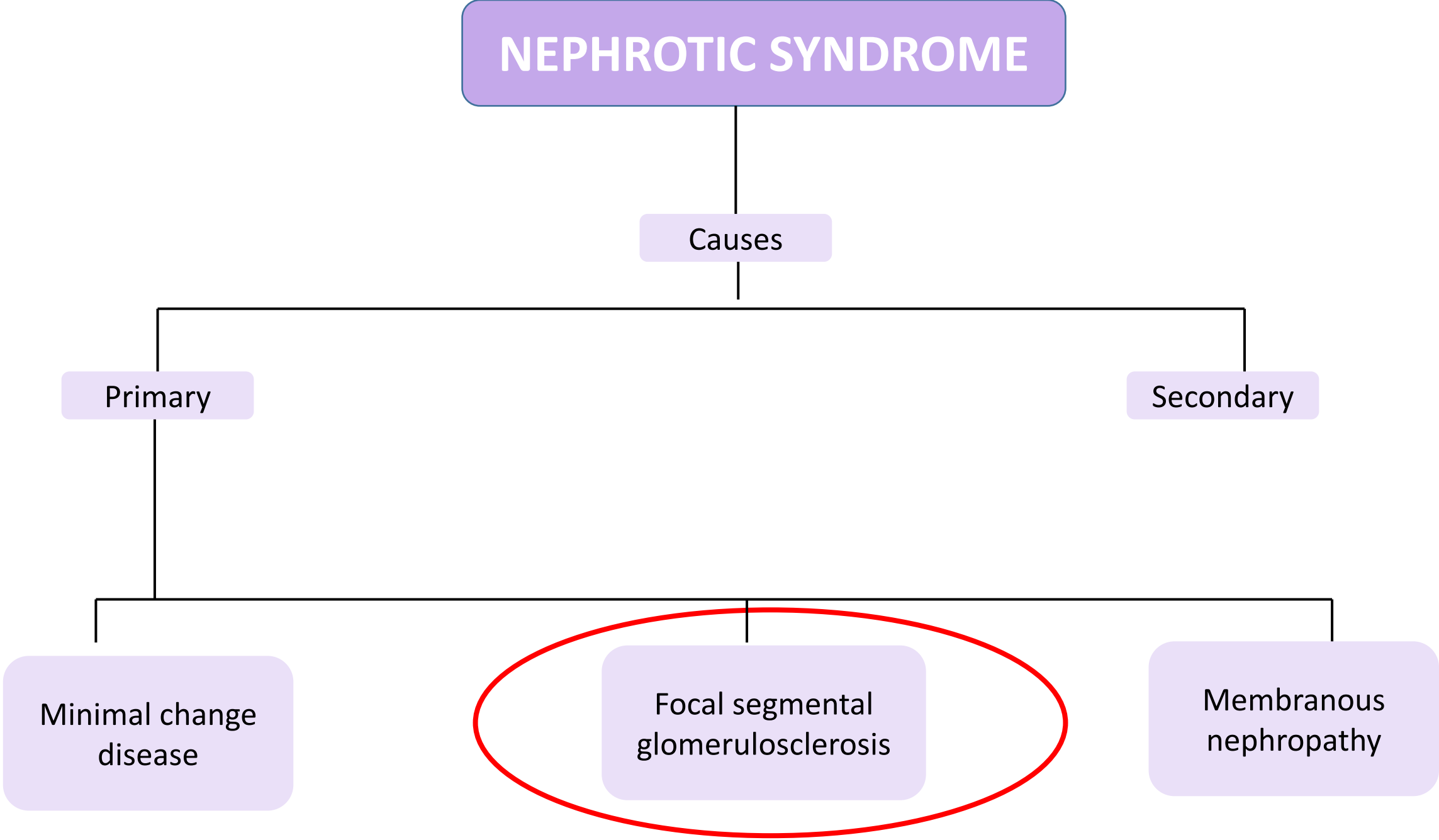
T cells in the blood, releasing cytokines-glomerular-permeability factor, that specifically damages the foot processes of the podocytes, making them flatten out, a process called effacement.

↓

Damaged foot processes lose their negatively charged coat, eventually allowing negatively charged molecules, like albumin, to slip into the nephron.

↓

Even though albumin goes through, other larger proteins like immunoglobulins don't.


NEPHROTIC SYNDROME
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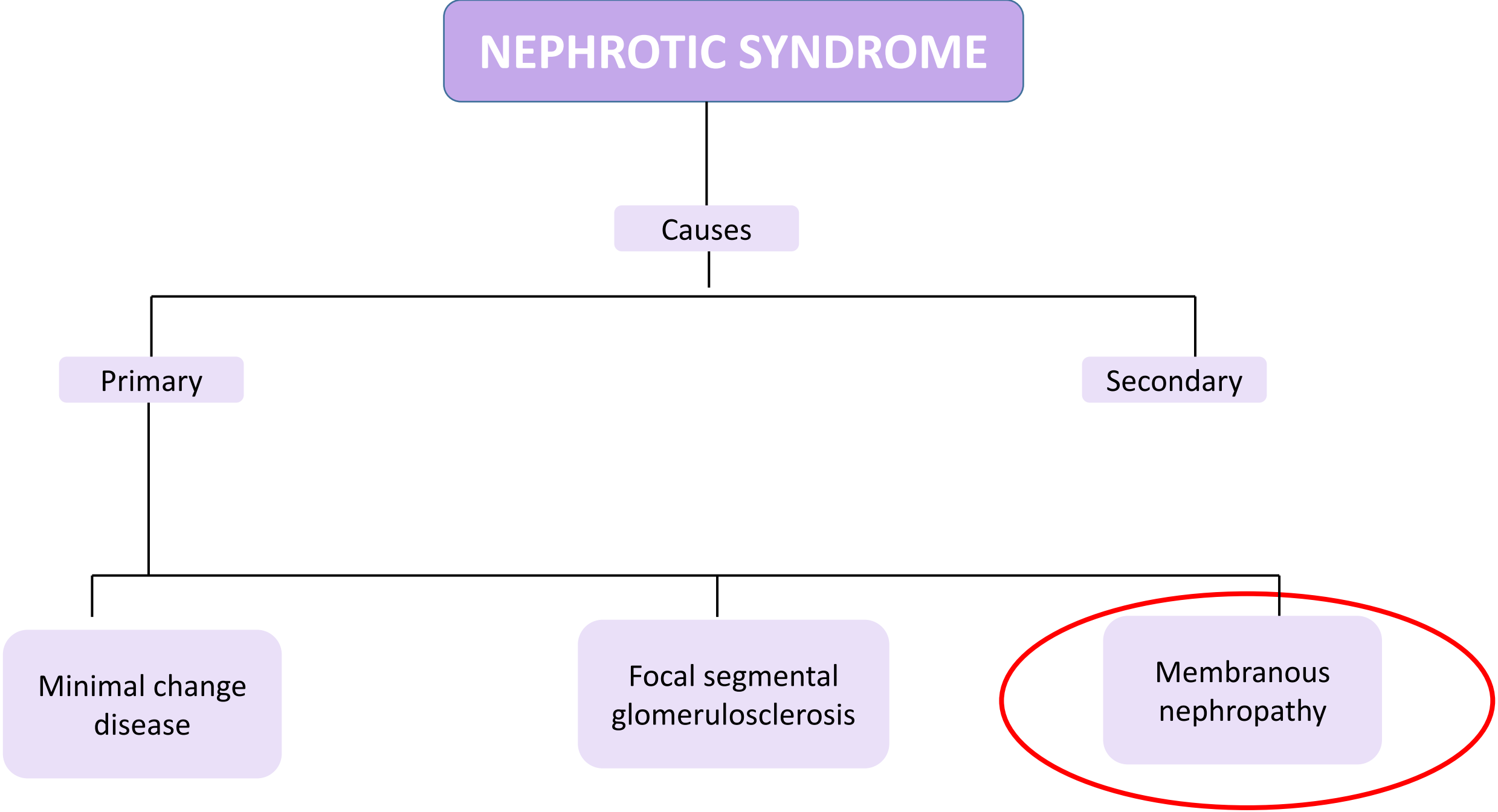
Membranous nephropathy

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

- most common cause of nephrotic syndrome in individuals of African or Hispanic descent.
- More common in adults and can be idiopathic.
- These patients usually have a history of heroin abuse, HIV infection, interferon treatment or congenital malformations.
- The cause of focal segmental glomerulosclerosis is not exactly known yet, but you need to know is that just like minimal change disease, there's effacement of podocyte foot processes.
- With focal segmental glomerulosclerosis, there's also hyalinosis that's caused by deposition of lipids and proteins in the glomerulus.
  Over time, hyalinosis further develops into sclerosis or scar tissue.
- On light microscopy, there's sclerosis and hyalinosis among the glomeruli.


NEPHROTIC SYNDROME
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Membranous nephropathy

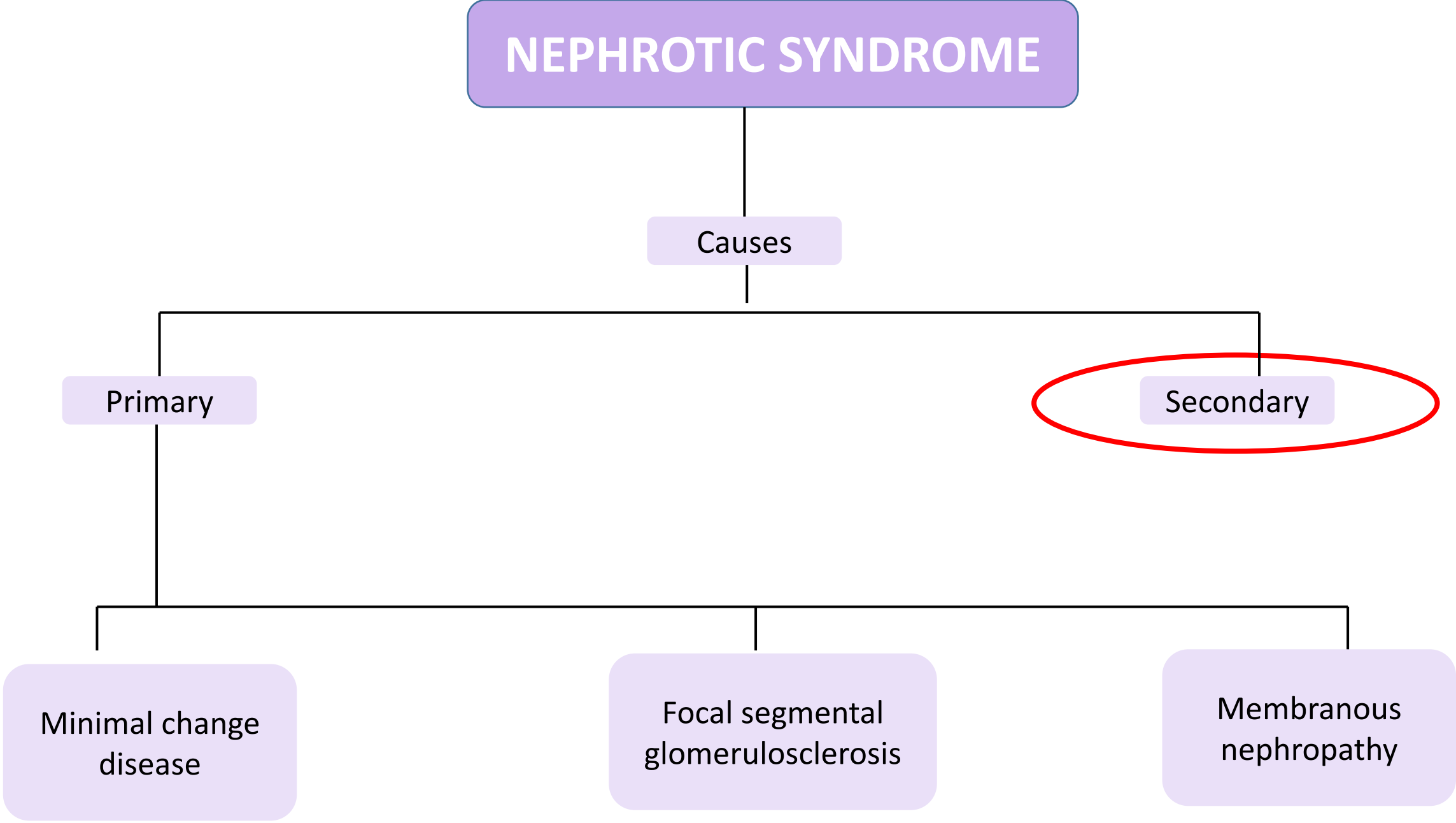
MEMBRANOUS NEPHROPATHY

It can be

- Primary
- Secondary
  - systemic lupus erythematosus,
  - drugs- like NSAIDs,
  - gold or penicillamine,
  - infections- particularly hepB, hep C or syphilis and
  - solid tumors- colorectal carcinoma

With membranous nephropathy, the damage is caused by immune complexes. These immune complexes are called subepithelial deposits because they build up right between the podocytes and the glomerular basement membrane.

These subepithelial deposits are thought to activate the complement system, which directly damages both the podocytes as well as mesangial cells.
One major antigen that's been identified is the phospholipase A2 receptor or PLA2R, so a high yield fact is that in the serum of individuals with membranous nephropathy, you can find IgG antibodies against PLA2R.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NEPHRITIC SYNDROME

Nephritic syndrome is characterized by glomerular capillary damage leading to hematuria, pyuria, water retention, and subsequent hypertension and edema.

Definition

Nephritic syndrome is an inflammatory process that is defined as the presence of one or more of the following.

- Hematuria with acanthocytes
- RBC casts in urine
- Proteinuria (< 3.5 g/24 h)
- Hypertension
- Mild to moderate edema
- Sterile pyuria
- Oliguria
- Azotemia
- NephrItic syndrome indicates glomerular Inflammation.

NEPHRITIC SYNDROME

Causes

Type 3 hypersensitivity reactions

- Poststreptococcal glomerulonephritis
- IgA nephropathy
- Diffuse proliferative glomerulonephritis

Multiple potential causes

- Membranoproliferative glomerulonephritis
- Rapidly progressive glomerulonephritis

Collagen deficiencies

- Alport syndrome

POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

- Most frequently seen in children
- Occurs 2-4 weeks after a group A streptococcal infection of the pharynx or the skin
- Presentation
  - Child develops
    - Fever
    - Malaise
    - Nausea
    - Oliguria
    - Haematuria
- Laboratory findings
  - Blood findings
    - Raised antistreptococcal antibody titres
    - HypOcomplimentaemia

Urinary findings
- Oliguria
- Mild proteinuria < 1g/day
- Haematuria
- Red cell casts

- Pathophysiology
- Some group A strep strains carry the M protein virulence factor in the walls
- Antibodies within the body form immune complexes with the bacterial antigen
- These immune complexes deposit in the basement membrane of the glomerulus
- Stimulates inflammation resulting in C3 complement, cytokines, oxidants, proteases being depsoited

IgA NEPHROPATHY AKA BERGERS DISEASE

The most common primary glomerulonephritis worldwide

Usually triggered by upper respiratory tract or gastrointestinal infections

Epidemiology

- Peak incidence- 2nd – 3rd decades of life
- More common in males 2:1
- Ethnicity – more common in Asian population worldwide

Pathophysiology

- The cause is still not entirely understood.
- Most likely mechanism: an increased number of defective, circulating IgA antibodies are synthesized (often triggered by mucosal infections, i.e., upper respiratory tract and gastrointestinal infections) → IgA antibodies form immune complexes that deposit in the kidney.

Clinical features

- Asymptomatic
- Recurring episodes of:
- Gross or microscopic hematuria
- Flank pain
- Low-grade fever
- Usually during or immediately following a respiratory or gastrointestinal infection
- Can progress to RPGN and/or nephrotic syndrome (< 10% of patients)
- Up to 50% of patients progress to end-stage renal disease within 20–25 years.

DIFFUSE PROLIFERATIVE GLOMERULONEPHITIS

Most commonly associated disease is systemic lupus erythematosus

Diffuse- indicating that 50% of the glomeruli in BOTH kidneys are affected

Clinical presentation

- Microscopic or gross hematuria
- Nonnephrotic or nephrotic range proteinuria or an increase in proteinuria from baseline
- Serum creatinine of more than 0.4 mg/dL above the reference range or the baseline
- Oligoanuria and symptoms of uremia in severe cases of rapidly progressive glomerulonephritis (RPGN) with crescent formation

Pathophysiology

Immune complexes formed & deposition in subendothelial space. (between endothelial wall & basement mebrane -most common site of deposition)

Inflammatory reaction

NEPHRITIC SYNDROME

Causes

Type 3 hypersensitivity reactions

- Poststreptococcal glomerulonephritis
- IgA nephropathy
- Diffuse proliferative glomerulonephritis

Multiple potential causes

- Membranoproliferative glomerulonephritis
- Rapidly progressive glomerulonephritis

Collagen deficiencies

- Alport syndrome

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

Clinical presentation

- Hematuria with acanthocytes
- RBC casts in urine
- Proteinuria (< 3.5 g/24 h)
- Hypertension
- Mild to moderate edema

There are 3 types, which all cause mesangial & endothelial damage to cells in glomerulus

Pathophysiology

- Type 1- most common
- Type 3 hypersensitivity reaction which results in circulating immune complexes from antibodies attaching to HEP B and HEP C antigens

↓

Immune complexes deposited at glomerulus in the subendothelium (between the subendothelial wall abs glomerular basement membrane) and activate the complement pathway

↓

Recruits inflammatory cells-→causing inflammation

↓

Thickening of the basement membrane

- Inappropriate activation of the alternative pathway of the complement pathway
- No immune complexes
- Also known as dense deposit disease

C3 convertase

C3 → C3a & C3b

↓

Complement deposits in the basement membrane

↓

Inflammation & thickening of the basement membrane

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Rapidly progressive glomerulonephritis (RPGN) is an inflammatory disease of the kidneys characterized by rapid destruction of the renal glomeruli that often leads to end-stage renal disease.

3 types

- Type I: anti-glomerular basement membrane antibody disease (Goodpasture syndrome)
- Type II: immune complex-mediated glomerulonephritis IgA nephropathy, membranoproliferative nephropathy, Henoch-Schönlein purpura (HSP)
- Type III: glomerulonephritis associated with vasculitis (pauci-immune GN, ANCA-associated)

a type II hypersensitivity reaction caused by anti-glomerular basement membrane, or GBM, antibodies that target the α3 chain of collagen type IV, in the GBM and the alveolar basement membrane.

Once these autoantibodies, usually IgG, bind to the α3 chain, they activate the complement system, which damages the basement membrane as well as the nearby endothelium and the underlying organ itself.

A similar process is also happening in the basement membrane of the lungs, and causes widespread damage to the alveoli, leading to hemoptysis.

NEPHRITIC SYNDROME

Causes

Type 3 hypersensitivity reactions

- Poststreptococcal glomerulonephritis
- IgA nephropathy
- Diffuse proliferative glomerulonephritis

Multiple potential causes

- Membranoproliferative glomerulonephritis
- Rapidly progressive glomerulonephritis

Collagen deficiencies

- Alport syndrome

ALPORT SYNDROME

Mutation in type 4 collagen gene

Pathophysiology

- Lack of collagen causes GBM to become thin --→ therefore splits

Clinical presentation

- Peripheral oedema
- Periorbital oedema
- Oliguria
- Retinopathy & lense dislocation
- Hearing loss

	Nephritic syndrome	Nephrotic syndrome
Presentation	• Proteinuria (< 3.5 g/day) (can be in nephrotic range in severe cases) • **Hematuria** with acanthocytes • **RBC casts** in urine • Mild to moderate edema • Oliguria • Azotemia • **Hypertension** • Sterile pyuria	• **Heavy proteinuria (> 3.5 g/day)** • Hypoalbuminemia • **Generalized edema** • **Hyperlipidemia** and **fatty casts** in urine → frothy urine • Hypertension • ↑ Risk of thromboembolism: (via loss of antithrombin III) • ↑ Risk of infection (via loss of IgG and tissue edema which compromises the local blood supply and immune response)
Pathophysiology	• Inflammatory response within glomeruli → GBM disruption → loss of renally excreted RBCs (acanthocytes) and ↓ GFR → hematuria, oliguria, azotemia, and ↑ renin → edema and hypertension	• Damage to podocytes → structural damage of glomerular filtration barrier → massive renal loss of protein

Causes	• **Poststreptococcal glomerulonephritis**
	• **IgA nephropathy** (Berger disease)
	• Granulomatosis with polyangiitis (Wegener's)
	• Microscopic polyangiitis
	• Churg–Strauss syndrome
	• **Goodpasture syndrome** (anti-GBM disease)
	• **Alport syndrome** (hereditary nephritis)
	• Thin basement membrane disease
	• **Rapidly progressive glomerulonephritis** (RPGN)
	• Lupus nephritis
	• Most common causes of nephritic–nephrotic syndrome:
	  • Membranoproliferative glomerulonephritis
	  • Diffuse proliferative glomerulonephritis
		• Due to primary or secondary podocyte damage
		  • **Minimal change disease**
		  • **Focal segmental glomerulosclerosis**
		  • **Membranous nephropathy**
		• Due to secondary podocyte damage
		  • **Diabetic nephropathy**
		  • Amyloid light-chain (AL) **amyloidosis**, light chain deposition disease
		  • Lupus nephritis

Quiz time

On the nephrology ward, two people came in with the same symptoms: peripheral and periorbital edema, along with cola-colored urine, arterial hypertension and decreased urine output.

The first person is 10 year old Timmy who had a throat infection two weeks ago.

The second one is 45 year old Dorothy, who also presents with hemoptysis.

Lab tests show that both of them have increased creatinine and BUN.

On urinalysis, there's hematuria and red blood cell casts in the urine.

A 24-hour protein collection was done and showed that both Timmy and Dorothy had proteinuria, but in both cases it was less than 3.5 grams per day.

Now, both Timmy and Dorothy have nephritic syndrome.

Quiz time

Timmy is a young boy who has had a throat infection 2 weeks prior to the renal manifestations, which is consistent with poststreptococcal glomerulonephritis.

This usually resolves on its own and his prognosis is excellent.

Then there's 45 year-old Dorothy that presents with hemoptysis and oliguria which suggests Goodpasture disease.

Further investigations showed that anti-GBM antibodies were positive and the kidney biopsy showed the characteristic crescent shape seen with RPGN.