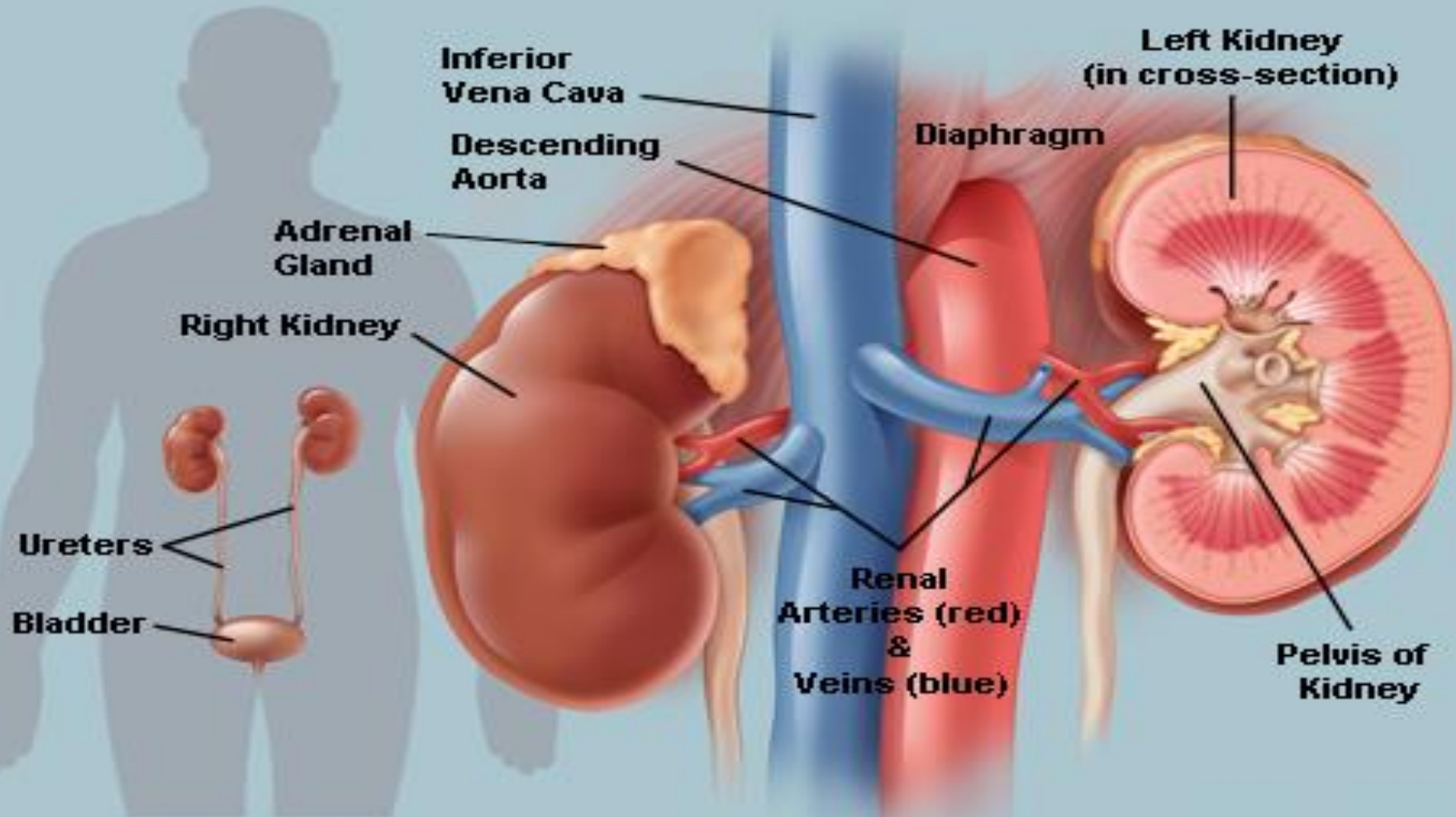
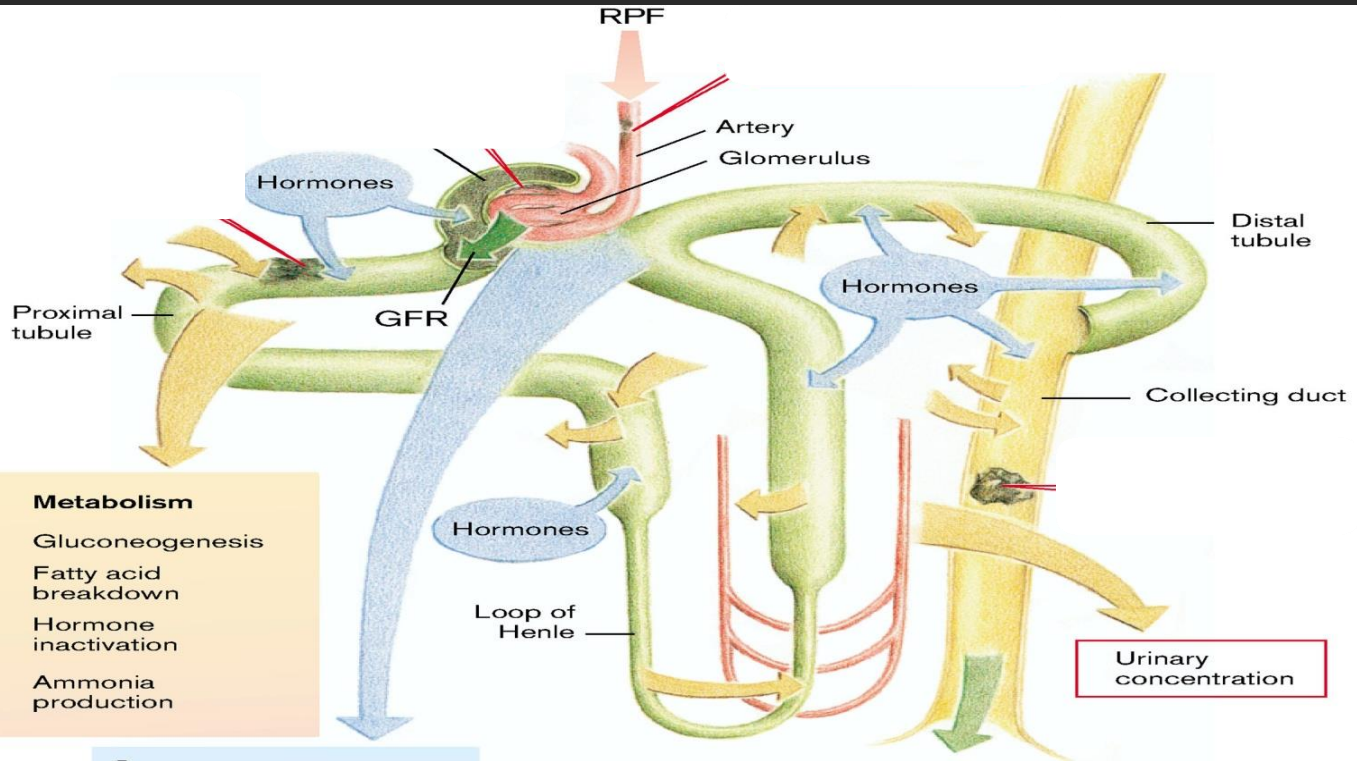


# PATHOPHYSIOLOGY OF THE KIDNEYS



# FUNCTIONS OF THE KIDNEYS



- 1 Metabolism**
- Gluconeogenesis
  - Fatty acid breakdown
  - Hormone inactivation
  - Ammonia production

- 2 Hormone release**
- Erythropoietin
  - Calcitriol
  - Renin, angiotensin
  - Kinins
  - Prostaglandins

**3 Regulation**

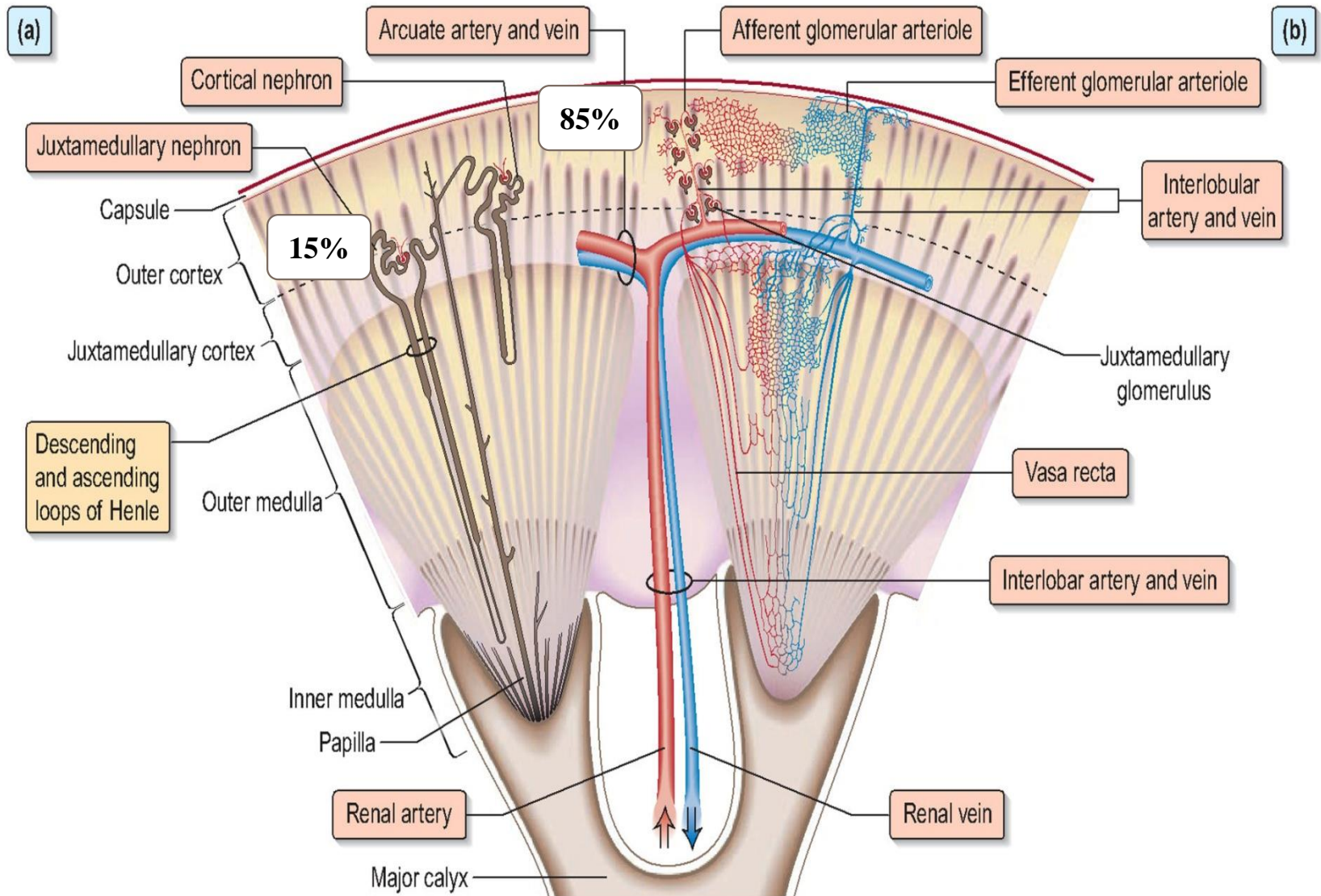
Excretion	Elimination
Loss of useful substances:	Retention of useless or harmful substances:
Glucose	Uric acid
Amino acids	Urea
Proteins	Creatinine
	VnO <sub>4</sub>
	Xenobiotics
	Uremia toxins

Erythropoiesis

Water, electrolyte and mineral balance

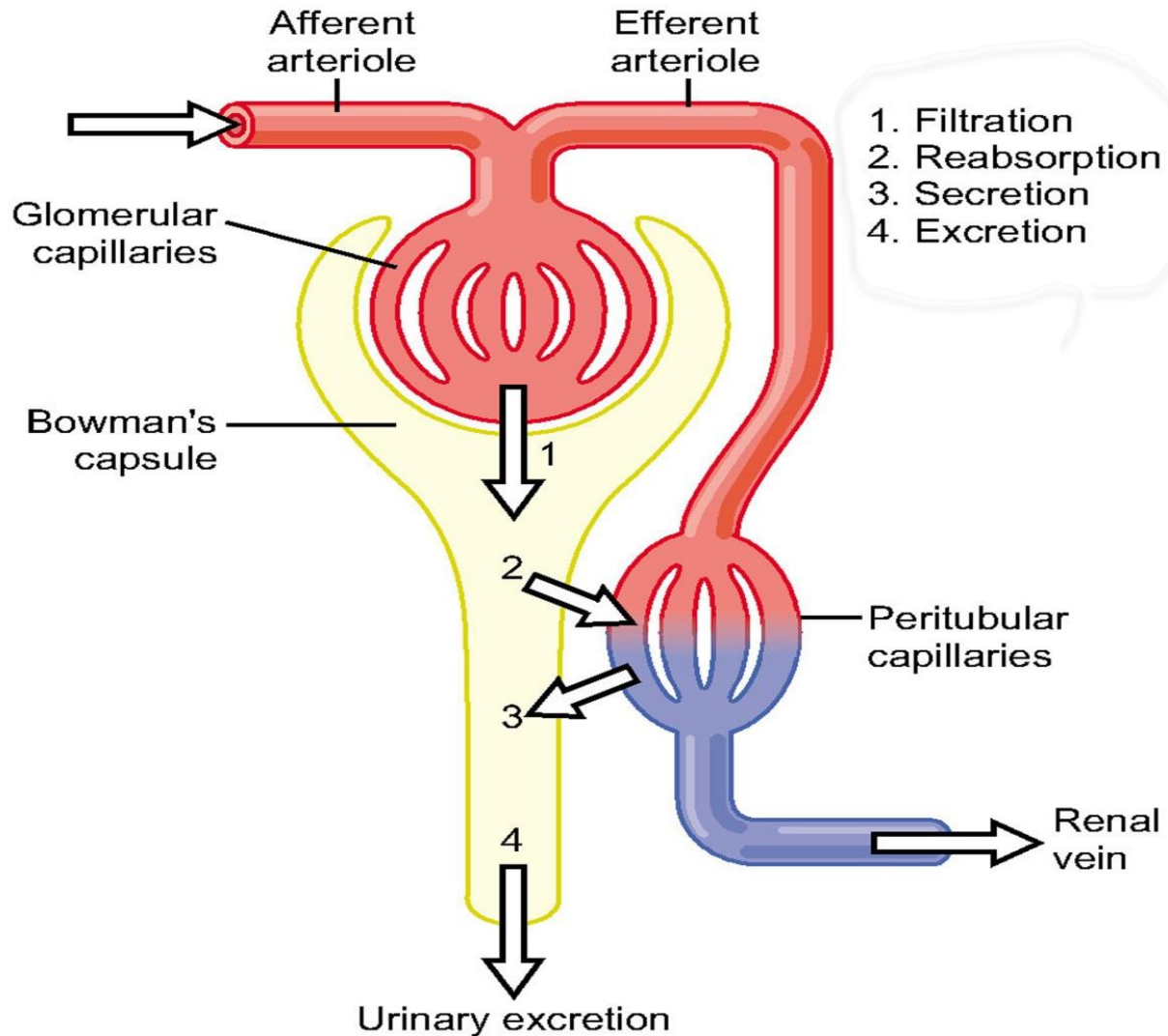
Blood pressure

# FUNCTIONAL ANATOMY OF THE KIDNEY





# PROCESSES AT THE LEVEL OF NEPHRON



$$\text{Excretion} = \text{Filtration} - \text{Reabsorption} + \text{Secretion}$$

## TO DISCUSS TODAY

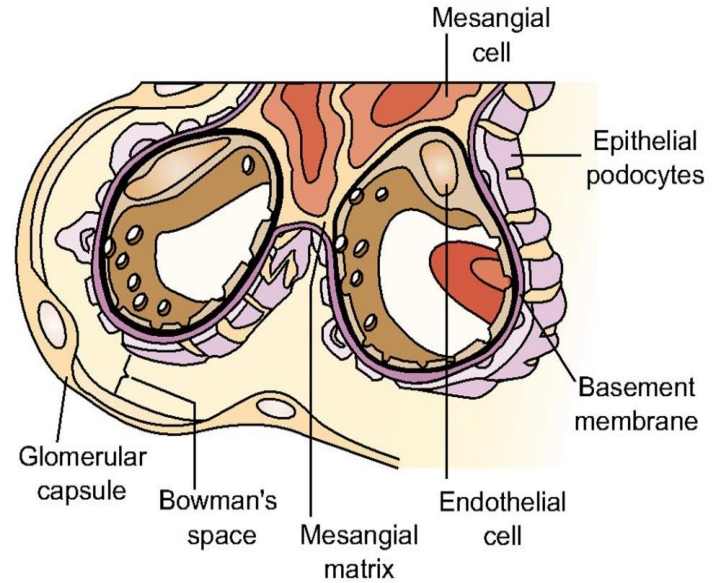
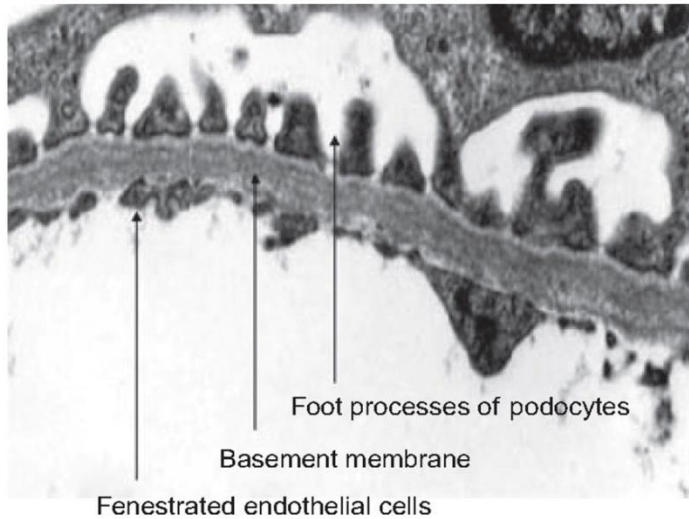
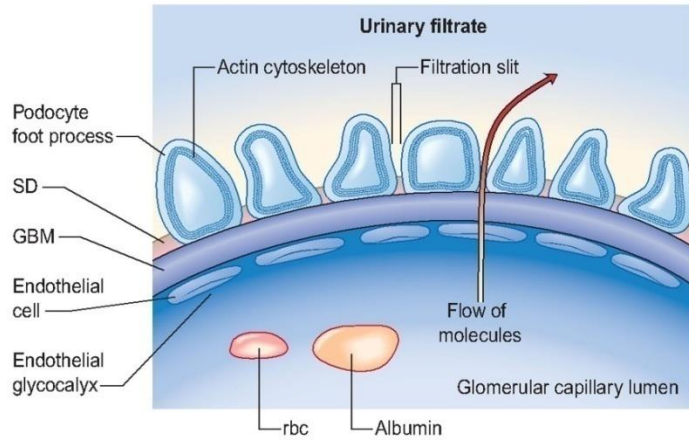
1. Disorders of glomerular filtration

2. Disorders of tubular reabsorption

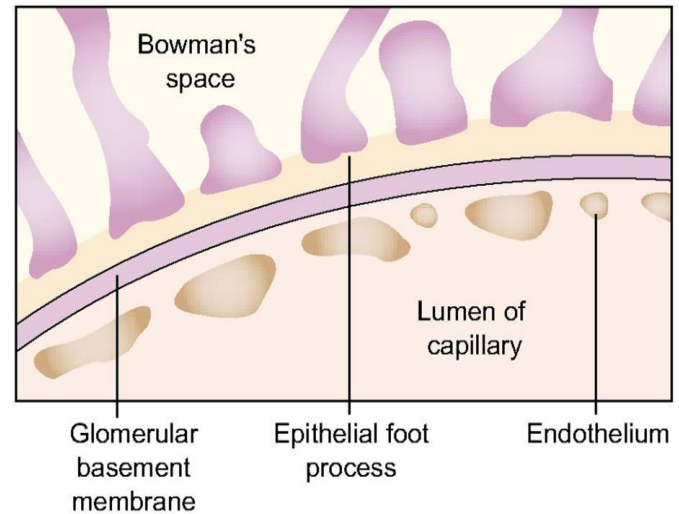
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3. Disorders of tubular secretion

# Disorders of glomerular filtration



B

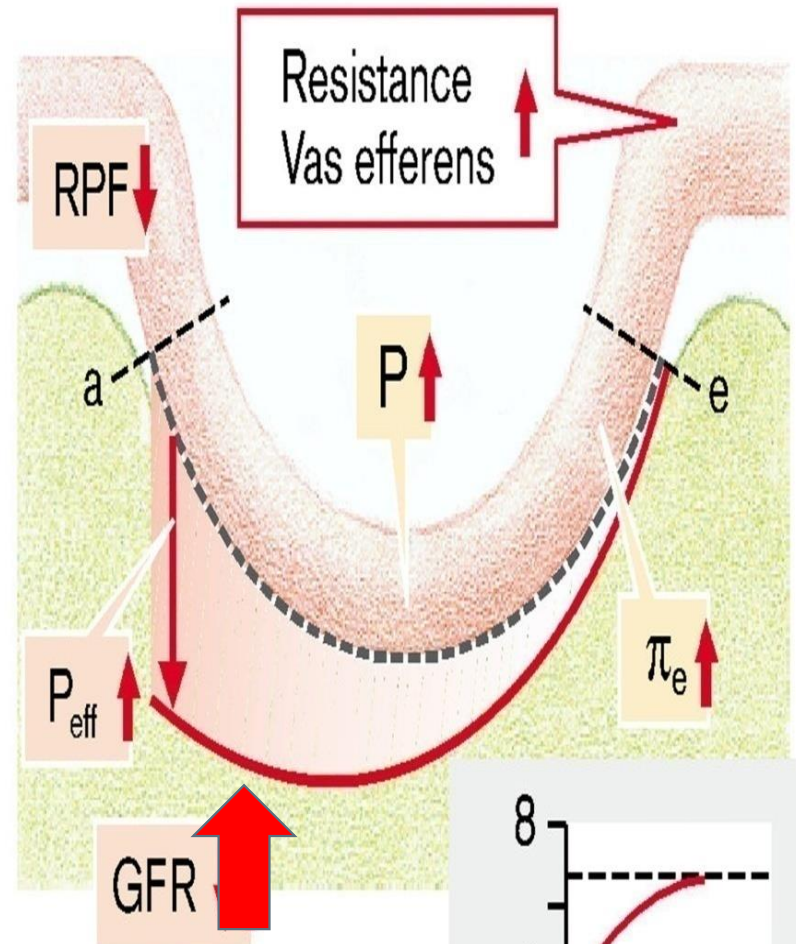


C

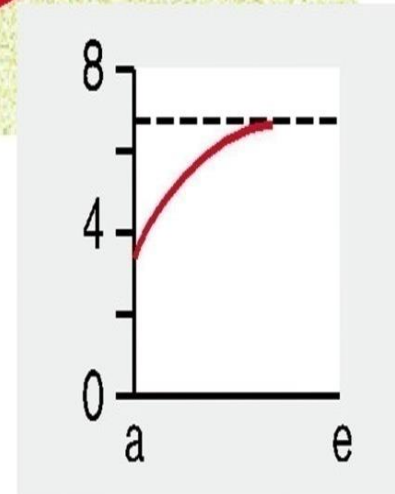


# Increased GFR

- Increased patency of afferent arteriole
- Decreased patency of efferent arteriole
- Systemic hypertension
- Hypoproteinemia:



4





# DECREASED GLOMERULAR FILTRATION

## Pre-renal factors

- Systemic hypotension;
- Construction, compression obliteration of renal arteries;
- Hypertonus of the sympathetic adrenal system, hypersecretion of catecholamine;
- Decreased lumen of afferent arterioles (hypertonic disease, atherosclerosis);
- Increased colloid-osmotic pressure of the blood (dehydration, administration of proteins);

## Intra-renal factors

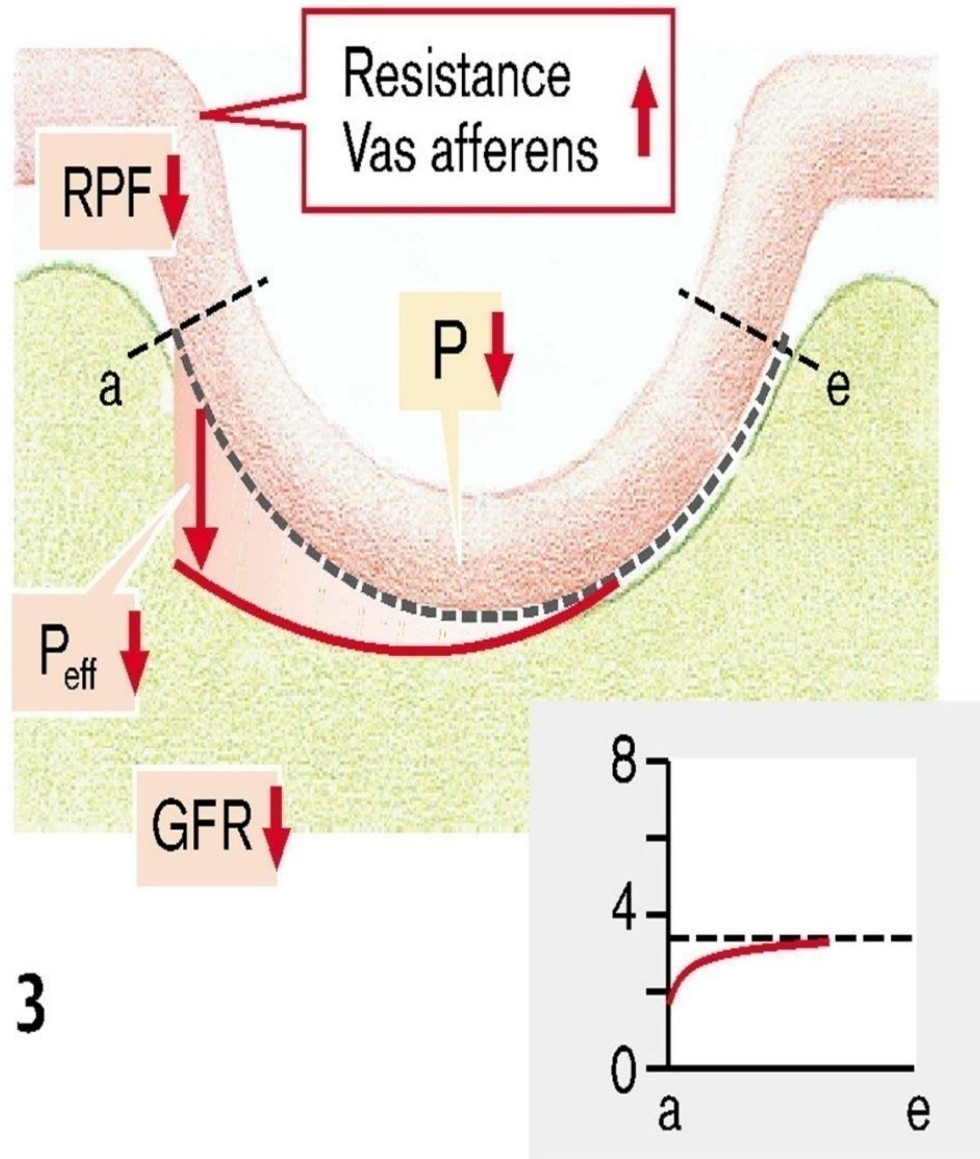
- Decreased mass of nephrons (inflammation, necrosis)
- Glomeruli sclerosis
- Thickening of the basement membrane (immune complex deposition)

## Post-renal factors

- Nephrolithiasis
- Hypertrophy of prostate;
- Obstruction/Constriction of ureters or urethra

Oliguria, hyperhydration , hypernatremia, hyperkaliemia, hyperazotemia , acidosis

# ↓ Glomerular filtration



3

## Pre-renal factors

- Systemic hypotension;
- Construction, compression, obliteration of renal arteries;
- Hypertonus of the sympathetic adrenal system, hypersecretion of catecholamine;
- Decreased lumen of afferent arterioles (hypertonic disease, atherosclerosis);
- Increased colloid-osmotic pressure of the blood (dehydration, administration of proteins);

# **INTRARENAL PATHOLOGIC PROCESSES WHICH DIMINISH GLOMERULAR FILTRATION GLOMERULOPATHY**

A general term for a group of disorders in which:

- there is primarily an immunologically mediated injury to glomeruli;
- kidneys are involved symmetrically;
- secondary mechanisms of glomerular injury come into play following an initial immune insult such as fibrin deposition, platelet aggregation, neutrophil infiltration and free-radical induced injury;
- renal damage can be due to a generalized disease such as SLE.

# GLOMERULOPATHY

- Nephritic syndrome;
- Nephrotic syndrome;
- Rapidly progressive glomerulonephritis;
- Isolated urinary abnormalities (glomerular hematuria and/or subnephrotic proteinuria);
- Chronic glomerulonephritis.





## ***Nephritic syndrome***

produces obstruction of the glomerular capillary lumen with decreased permeability of renal filter

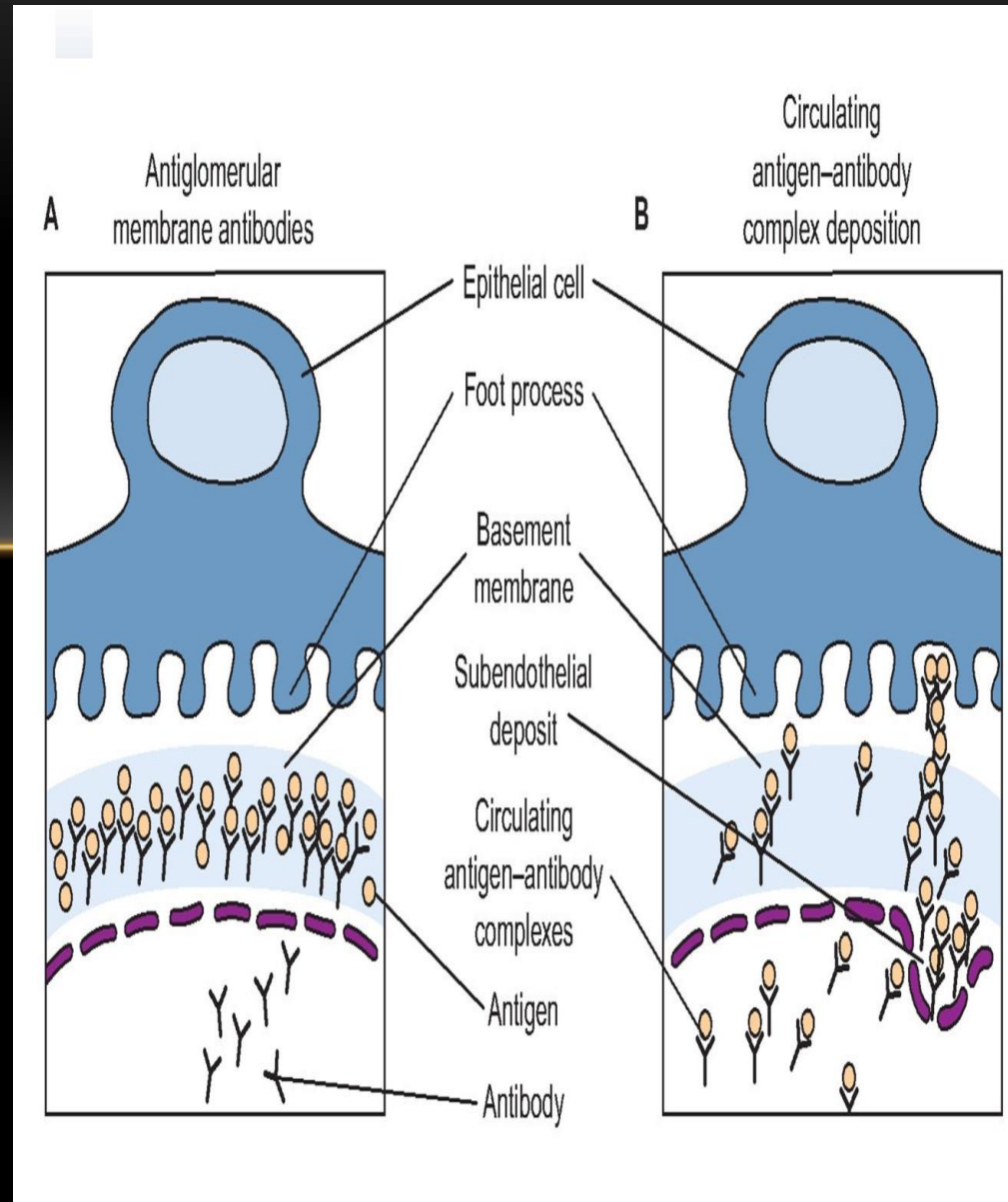
## ***Nephrotic syndrome***

produces an increase in glomerular permeability and

# GLOMERULONEPHRITIS

A. Anti-glomerular membrane antibodies leave the circulation and interact with antigen localized in the basement membrane of the glomerulus.

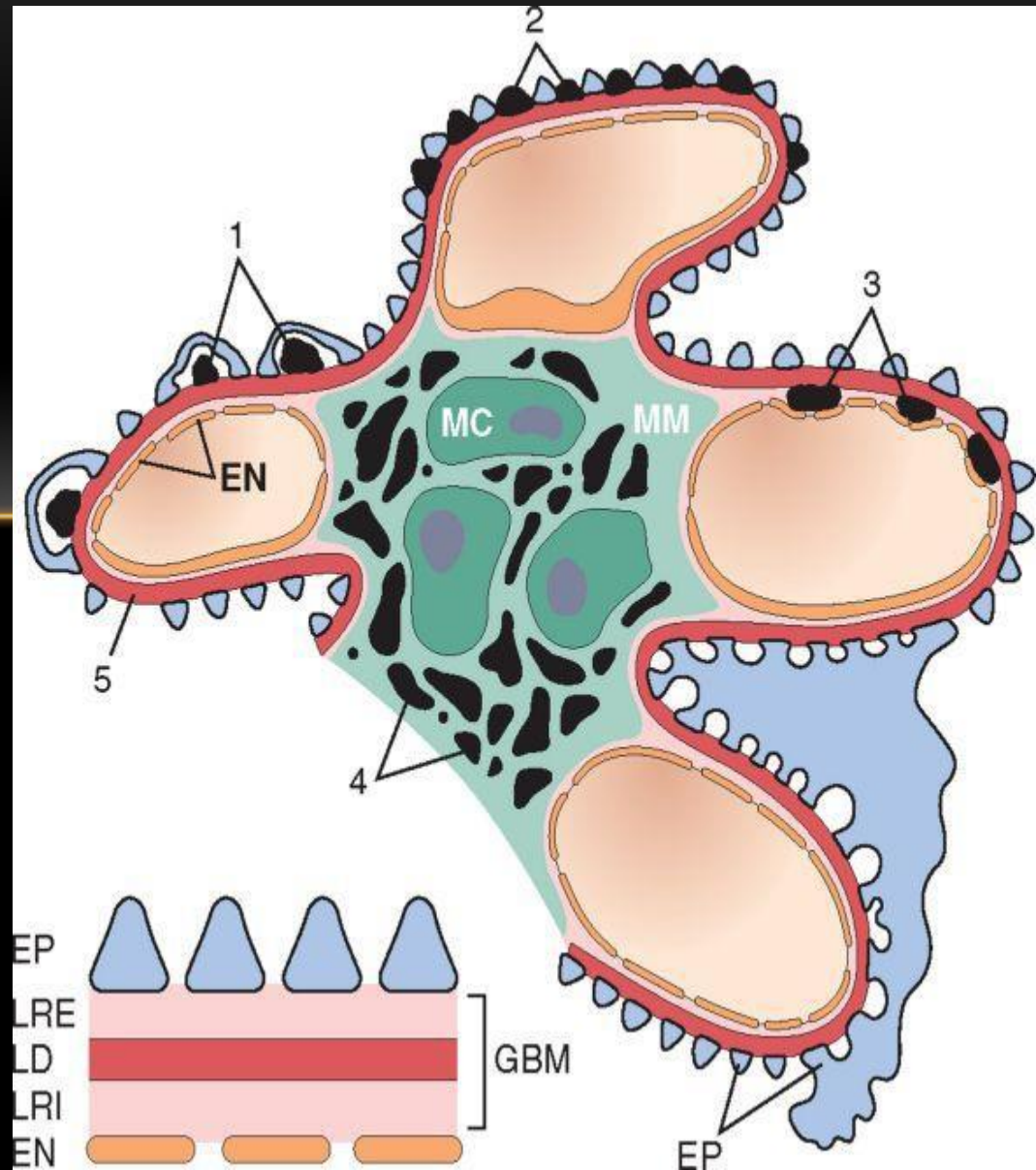
B. Antigen-antibodies complexes circulating in the blood become trapped as they are filtered in the glomerulus



# GLOMERULONEPHRITIS

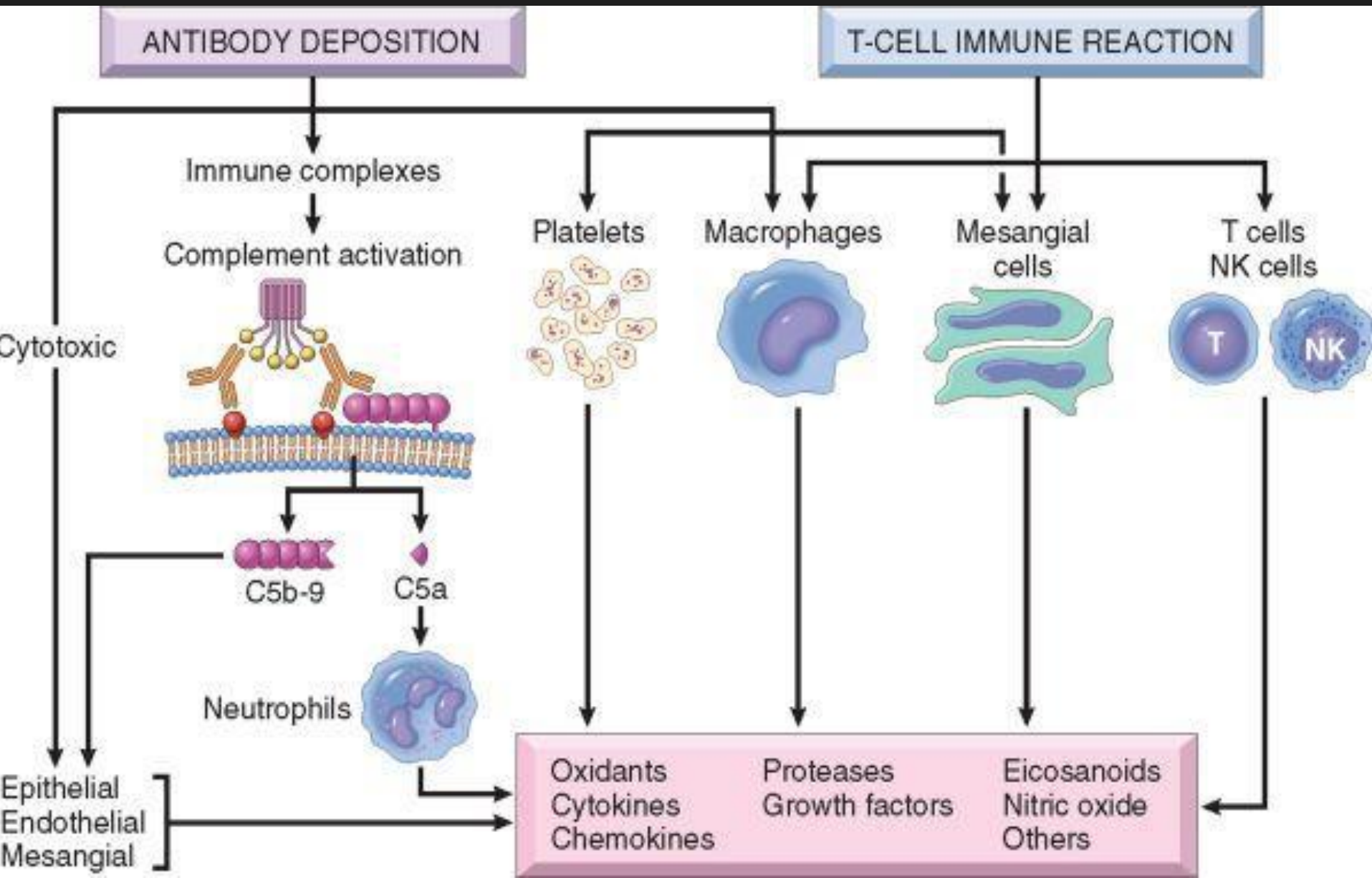
Localization of immune complexes:

1. Subepithelial
2. Epimembranous
3. Subendothelial
4. Mesangial deposits



# GLOMERULONEPHRITIS

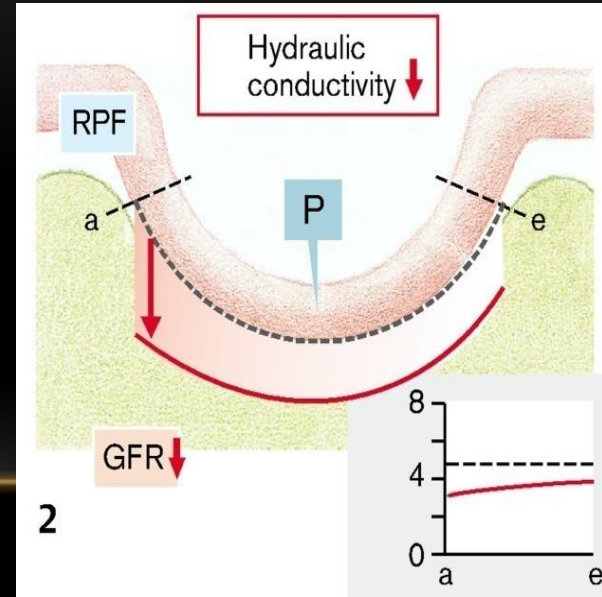
## MEDIATORS AND CELLS OF GLOMERULAR INJURY





# ACUTE NEPHRITIC SYNDROME

It is caused by inflammatory processes that occlude the glomerular capillary lumen and damage the capillary wall



Permitting red blood cells to escape in the urine

Renal ischemia  
Activation RAA

Decreased GFR



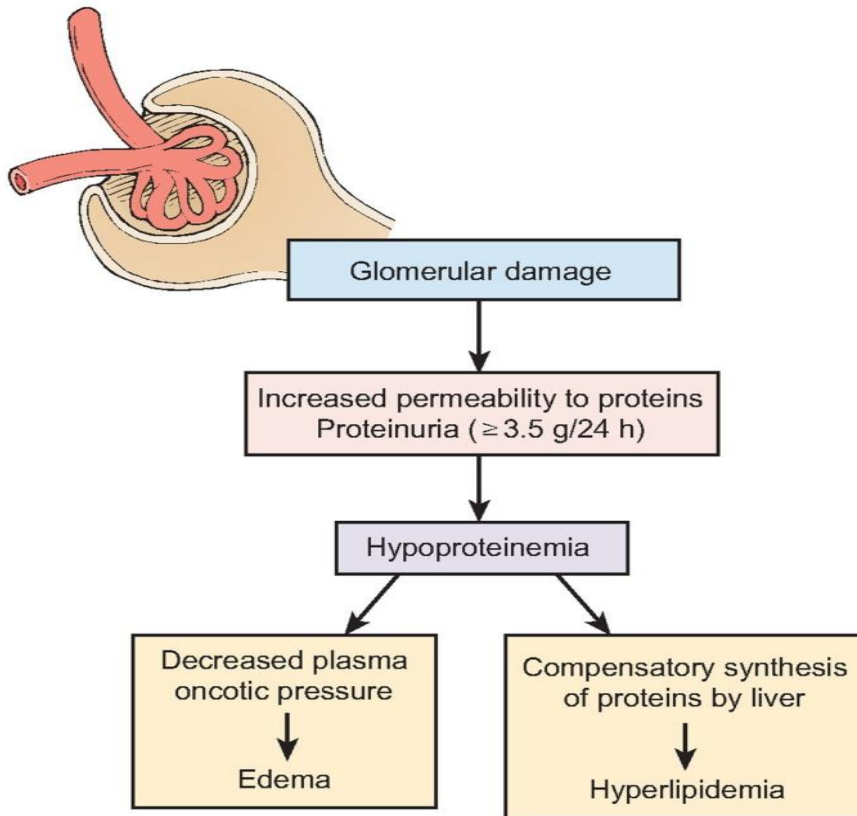
**Hematuria**  
microscopic or visible with presence of red cell casts

**Salt and water retention**

**Oliguria**  
**HTA**  
**Edemas**  
**Azotemia**

# NEPHROTIC SYNDROME

**Non-specific glomerular disease characterized by a constellation of clinical findings that result from an increase in glomerular permeability and loss of plasma proteins in the urine.**



## Criteria of nephrotic syndrome

- Massive proteinuria (>3,5 g/day);
- Lipiduria (free fat, fatty casts);
- Hypoalbuminemia (< 3 g/dL);
- Generalized edemas;
- Hyperlipidemia (triglycerides, LDLs, cholesterol > 300 mg/dL)

# NEPHROTIC SYNDROME



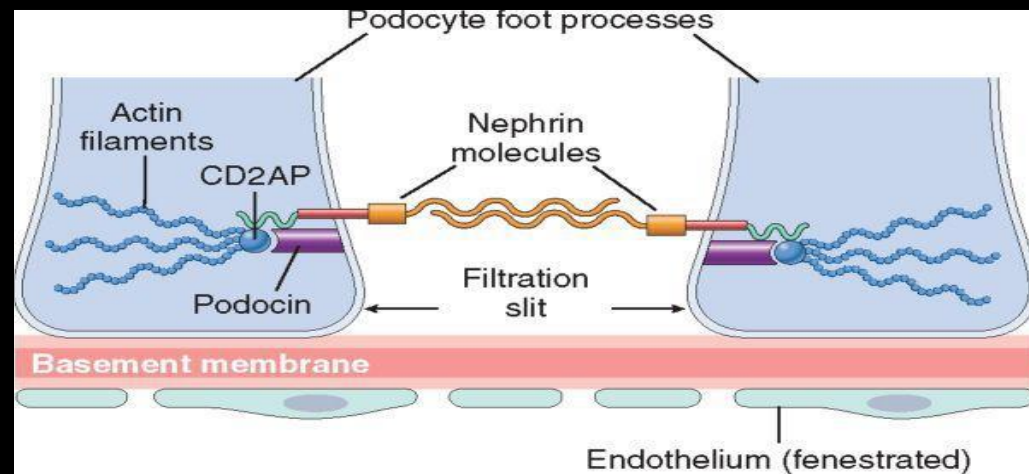
**PRIMARY**

**Congenital nephrotic syndrome,**  
involve mutation in genes that encode  
podocytes protein such as *nephrin,*  
*podocin, alpha-actinin-4 etc..*  
**Lipoid nephrosis,**  
**Focal segmental glomerulosclerosis**  
**Membranous glomerulonephritis**

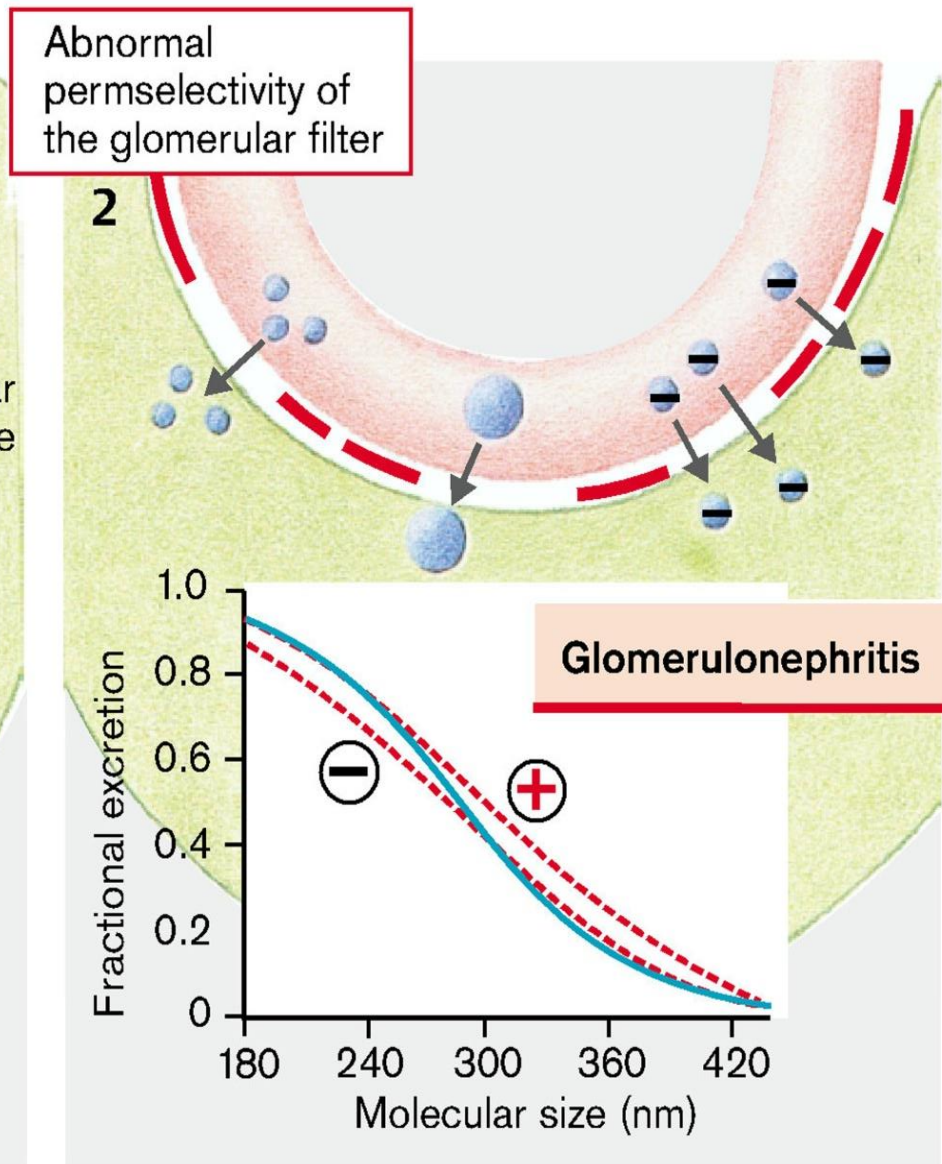
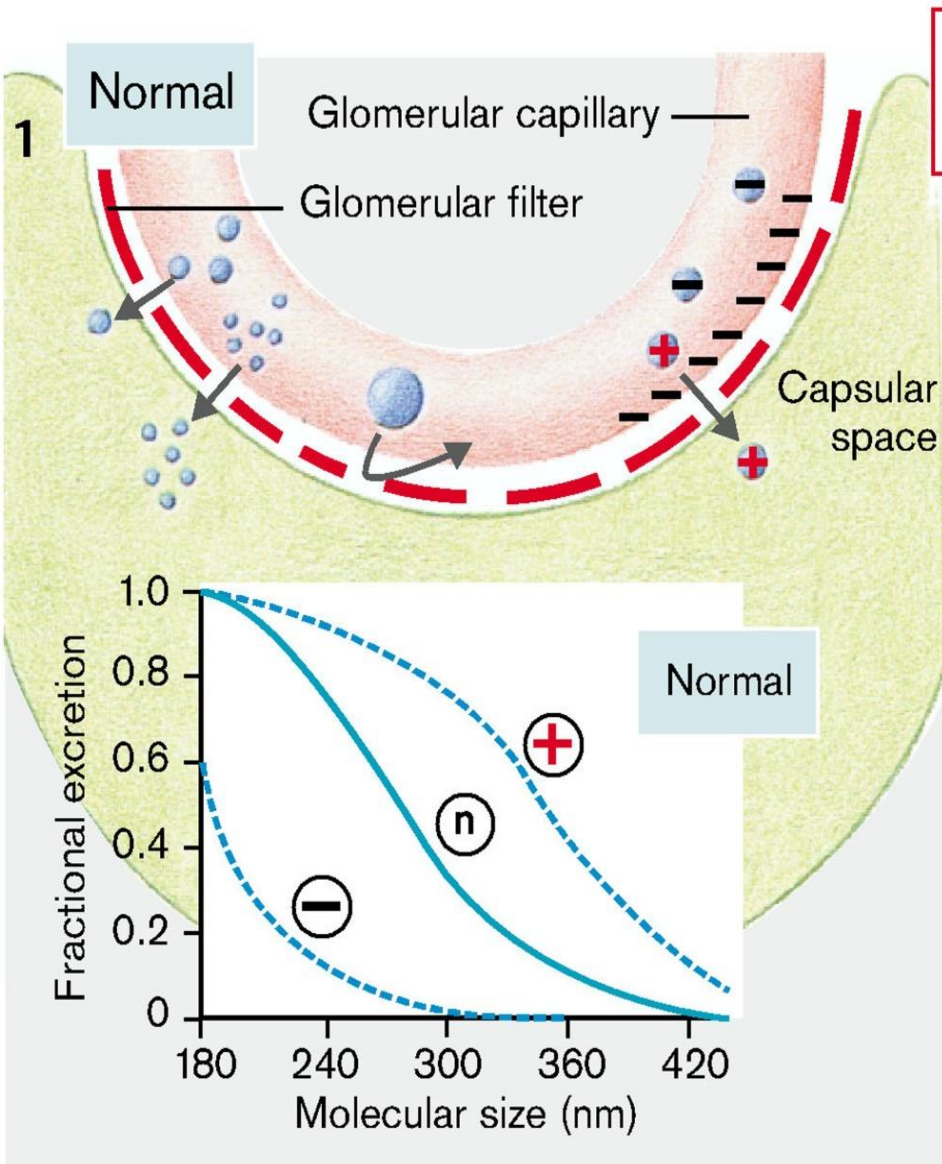


**SECONDARY**

Systemic disease such  
as diabetes mellitus or  
**SLE**

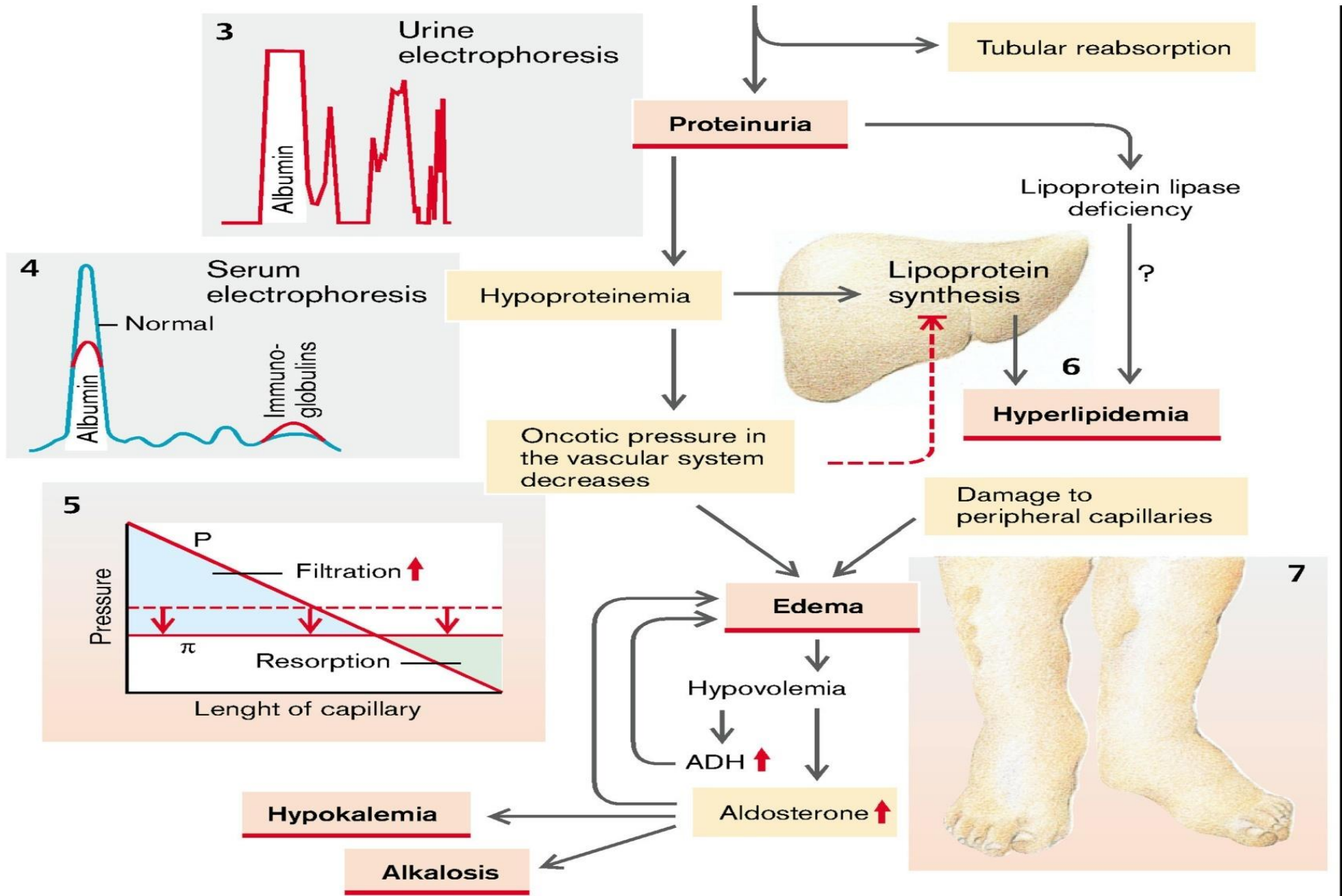


# NEPHROTIC SYNDROME





# NEPHROTIC SYNDROME



**Remember!**



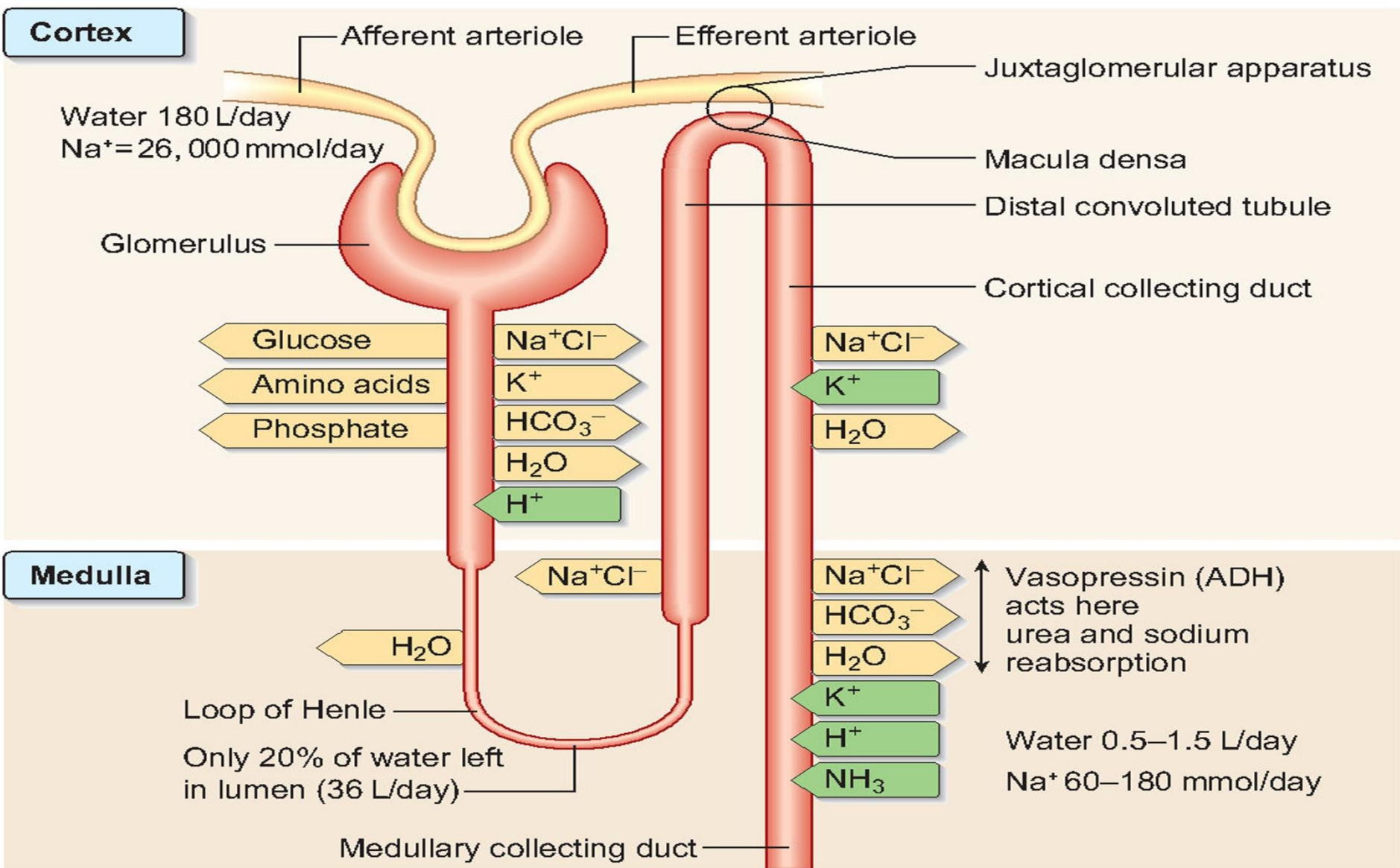
## ***Nephritic syndrome***

Hematuria  
Edema  
Hypertension  
Oliguria  
Azotemia

## ***Nephrotic syndrome***

Overt proteinuria  
Hypoalbuminemia  
Edema  
Hyperlipidemia  
Lipiduria

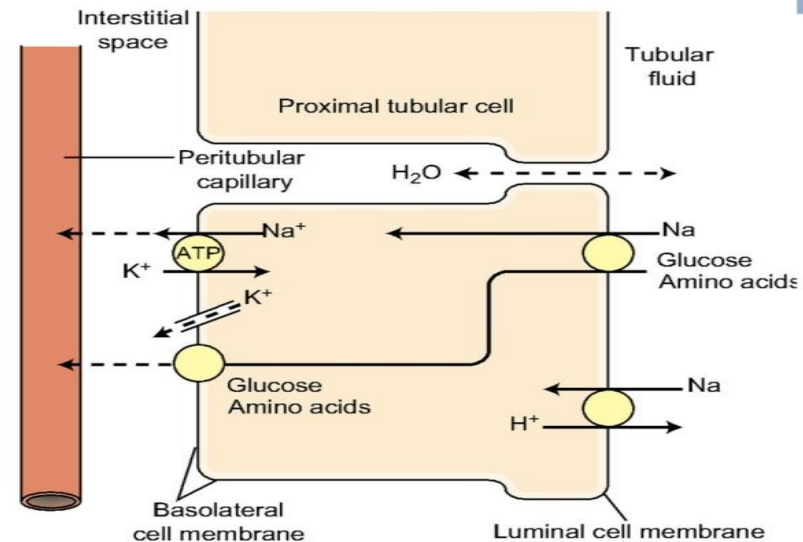
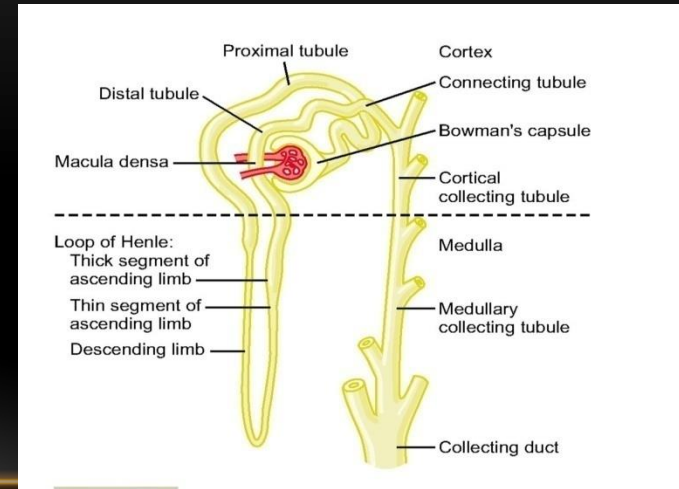
# DISORDERS OF TUBULAR REABSORPTION



# DISORDERS OF WATER AND ELECTROLYTE TUBULAR REABSORPTION

## • Proximal convoluted tubule

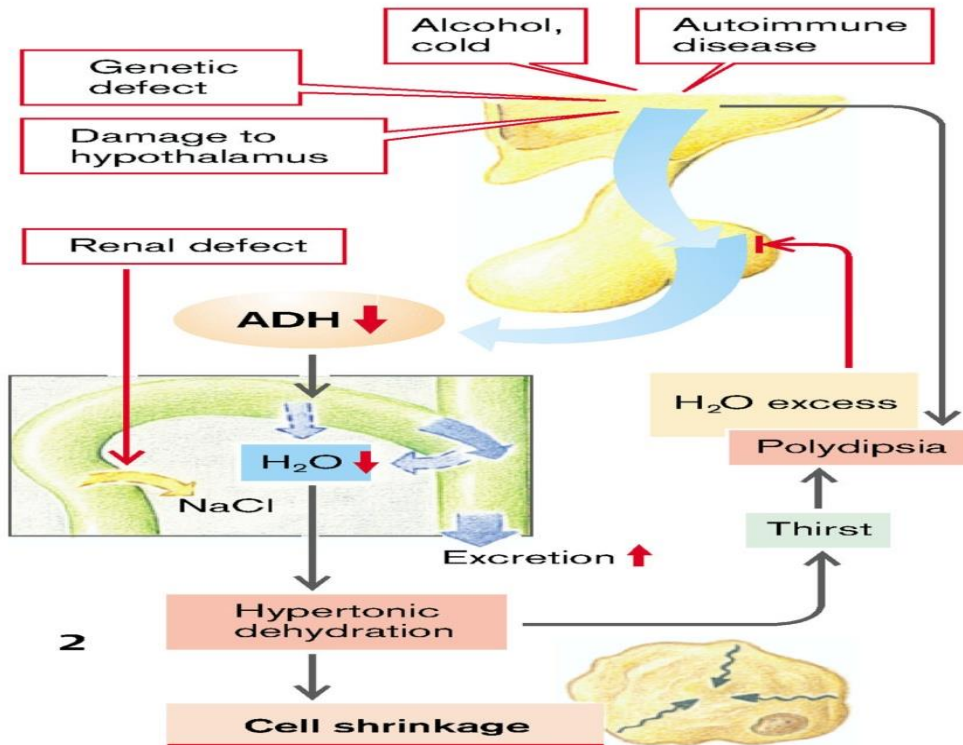
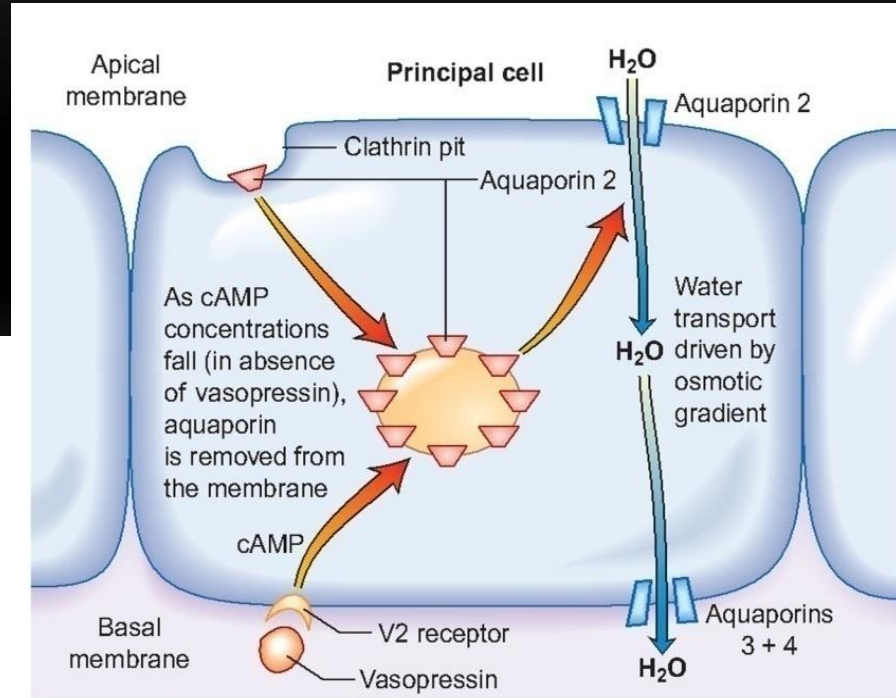
**Osmotic diuresis** (related to presence of osmotic active substances in the glomerular ultrafiltrate – glucose in diabetes mellitus, administration of osmotic diuretics like mannitol)



# DISORDERS OF WATER AND ELECTROLYTE TUBULAR REABSORPTION

## Distal convoluted tubule

- Diabetes insipidus;
- Renal amyloidosis
- Renal sclerosis





# Saline renal diabetes

## Pseudo-hypoaldosteronism

hereditary tubulopathy  
characterised by irresponsiveness  
of distal renal tubules to  
aldosterone



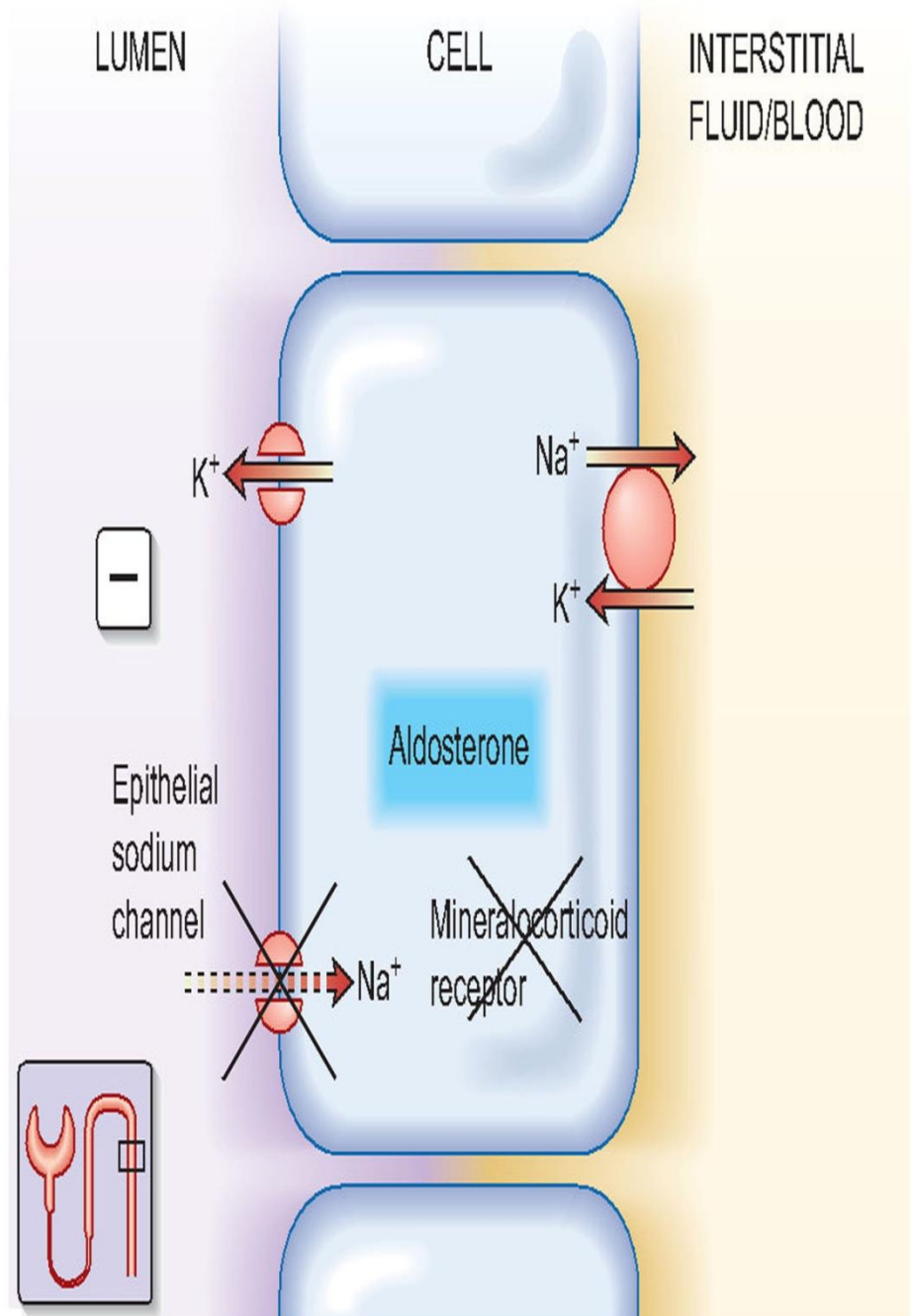
**Hyponatremia**

**Dehydration**

**Hyperkalemia**

**Acidosis**

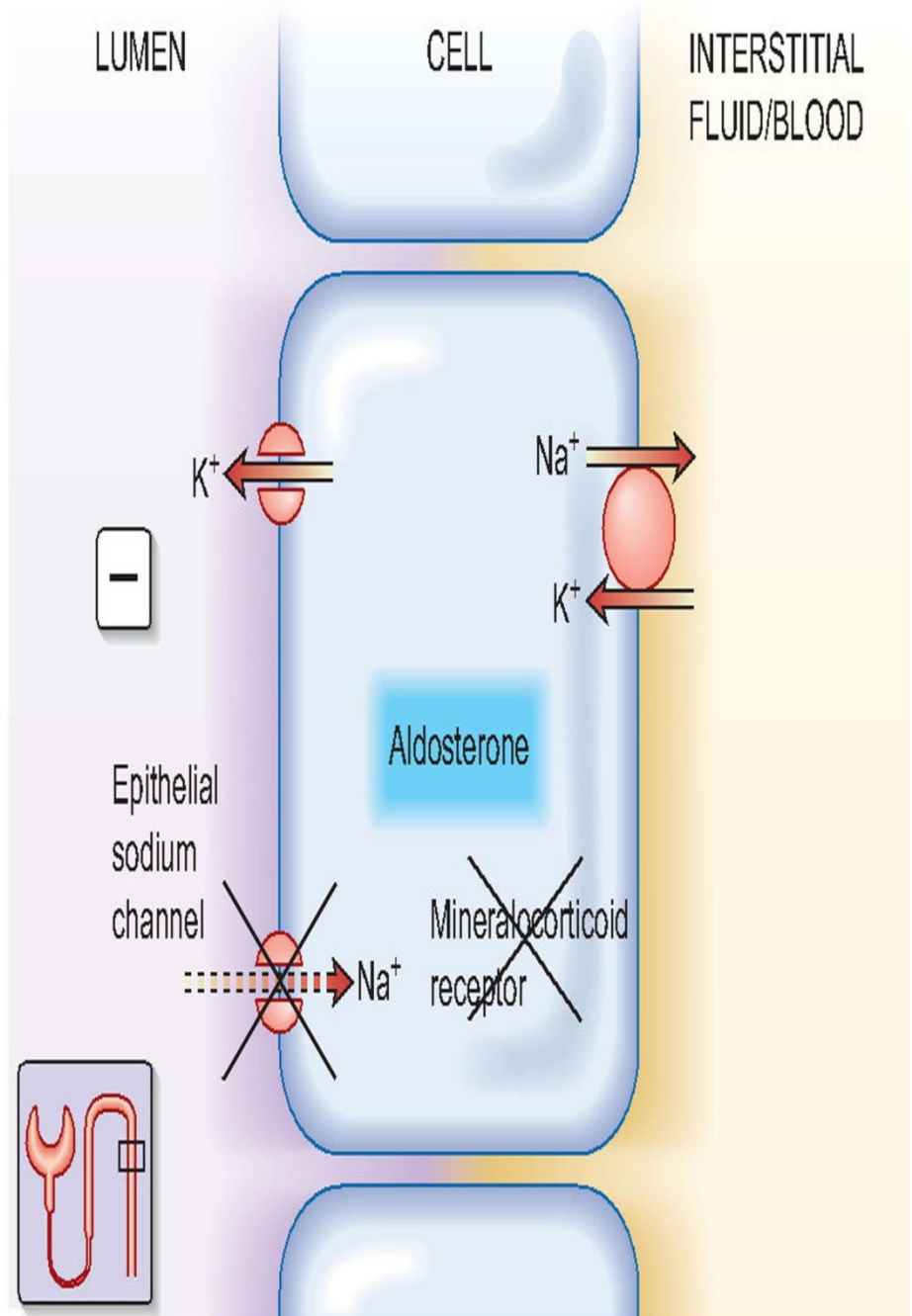
**Polyuria**



# Liddle's syndrome

Hereditary tubulopathy  
characterised by

hyperactivity of epithelial sodium  
channels resulting in excessive  
sodium reabsorption with coupled  
potassium and hydrogen secretion



# DISORDERS OF GLUCOSE REABSORPTION

Glucose renal threshold = Transport maximum  
170 -180 mg/dL = 10 mmol/L

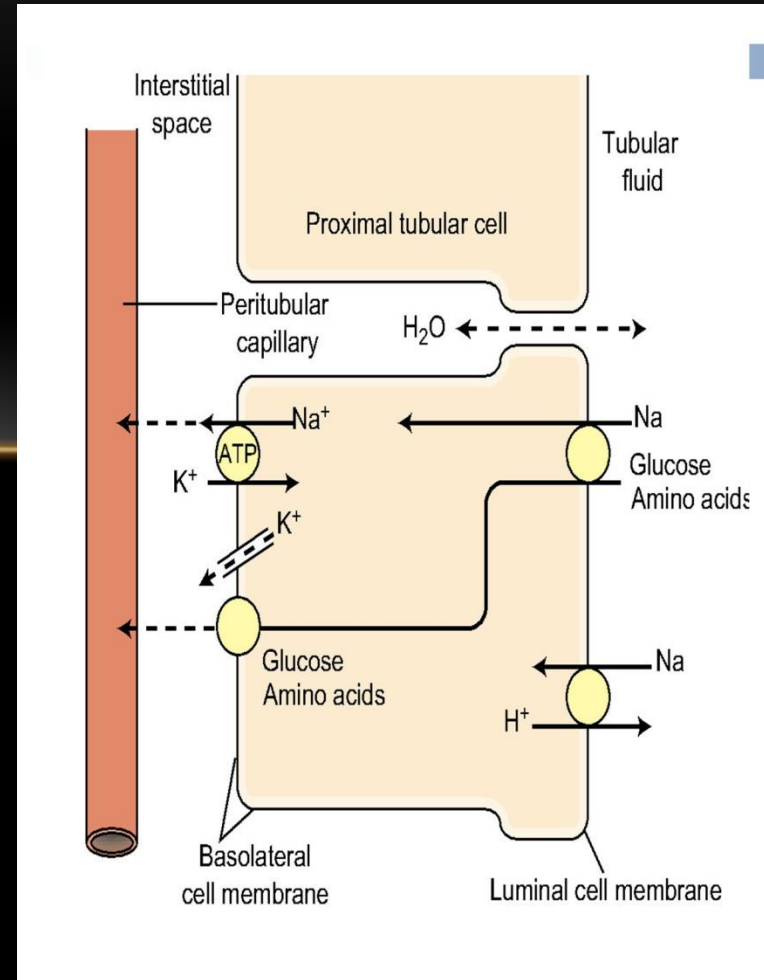
Diabetes mellitus, alimentary hyperglycemia

**Glucosuria**

**Osmotic diuresis**

**Polyuria**

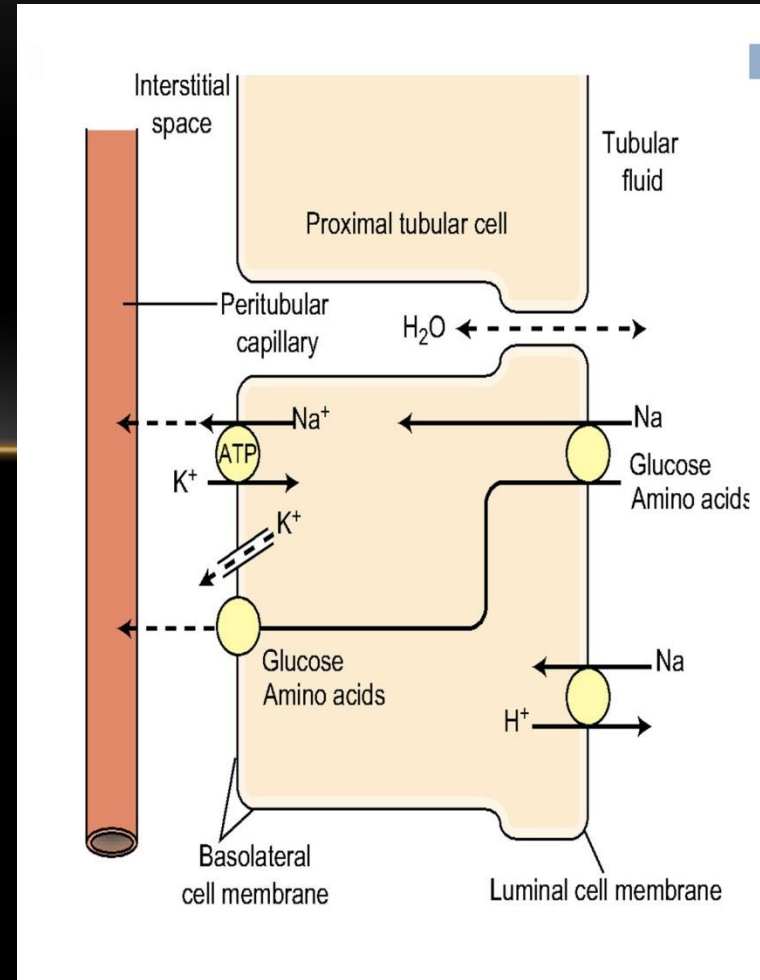
**Dehydration**



# DISORDERS OF GLUCOSE REABSORPTION

## Renal glucosuric diabetes

Hereditary tubulopathy when glucosuria develops at normal glycemia value as result of disorders of proximal active glucose reabsorption (disorders of mechanisms of glucose transportation).



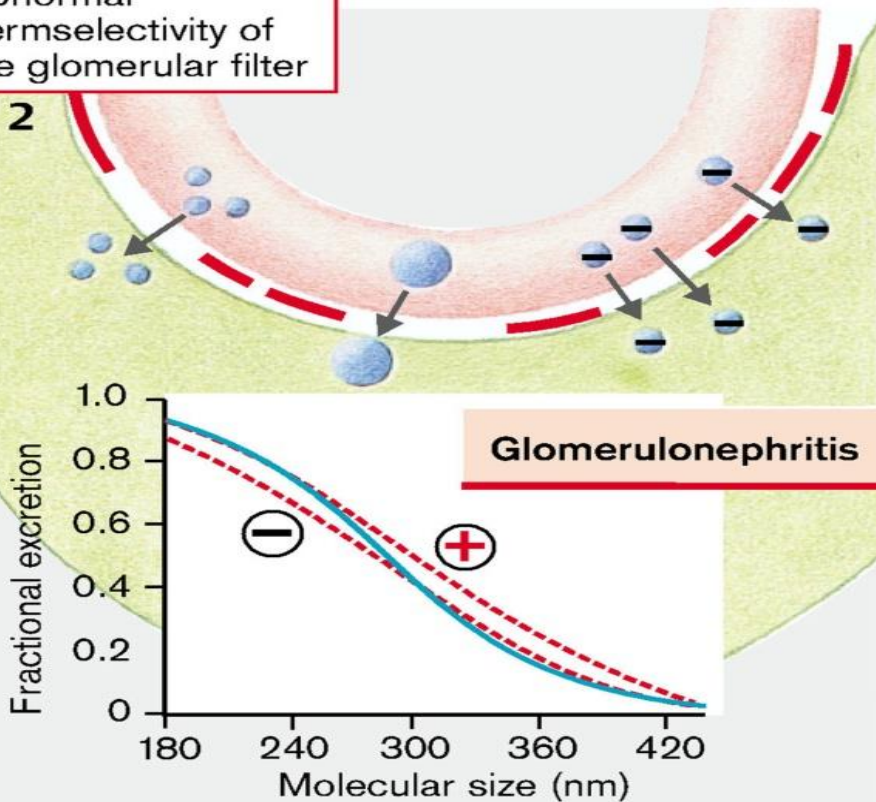
# PROTEINURIA



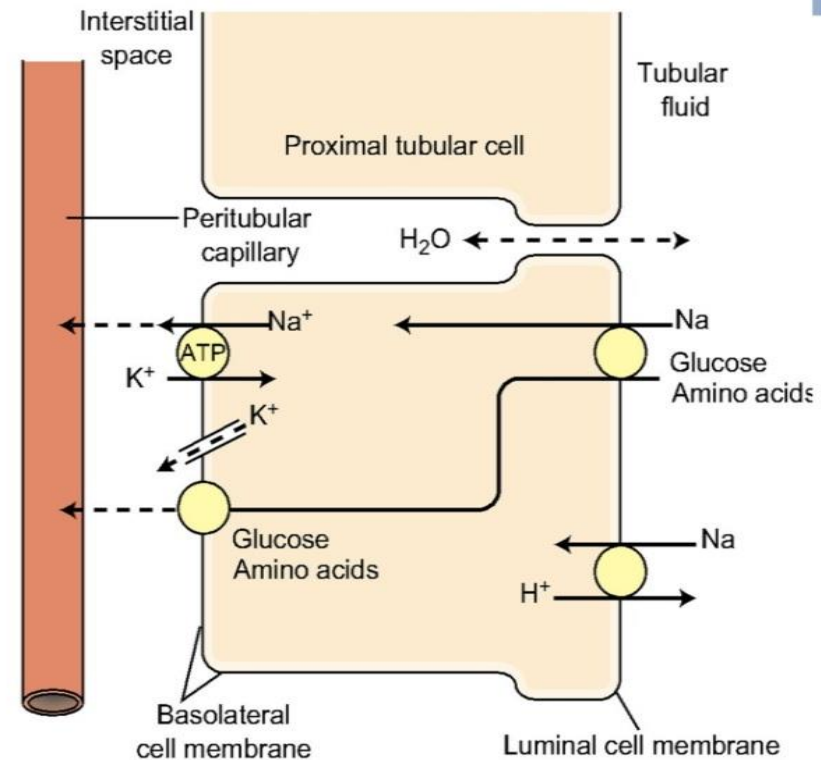
## GLOMERULAR

Abnormal permselectivity of the glomerular filter

2



## TUBULAR

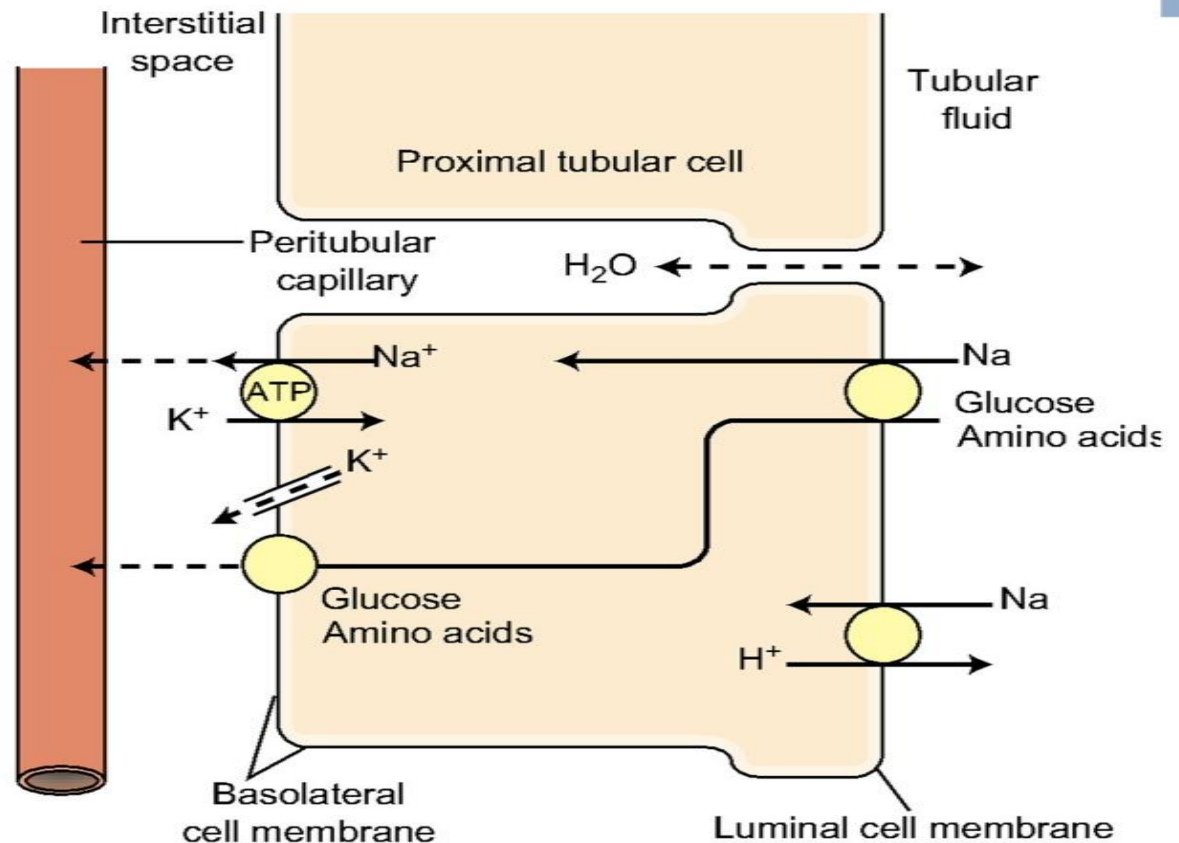




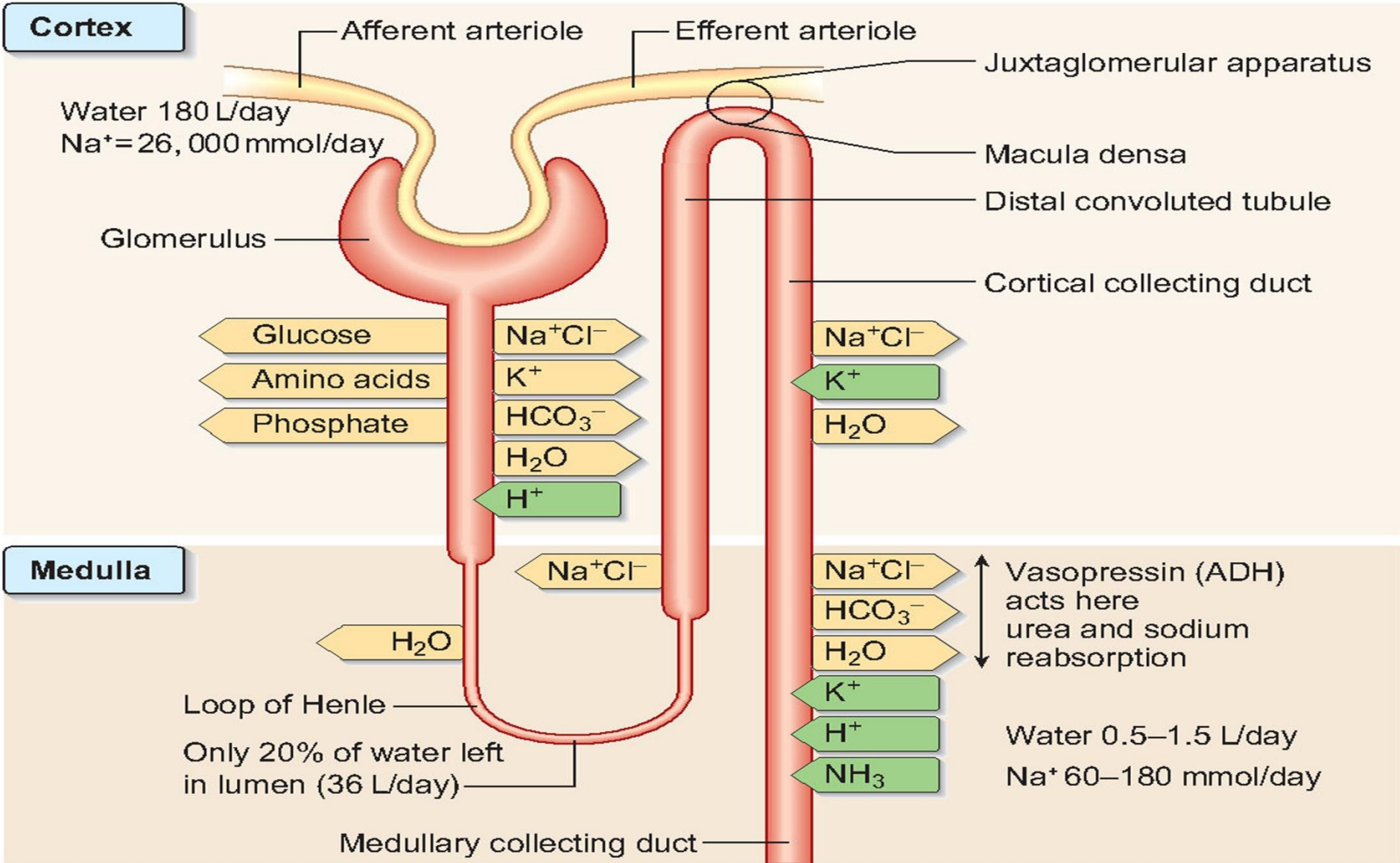
# DISORDERS OF AMINOACID TUBULAR REABSORPTION

Cistinuria

Hurtnup syndrome

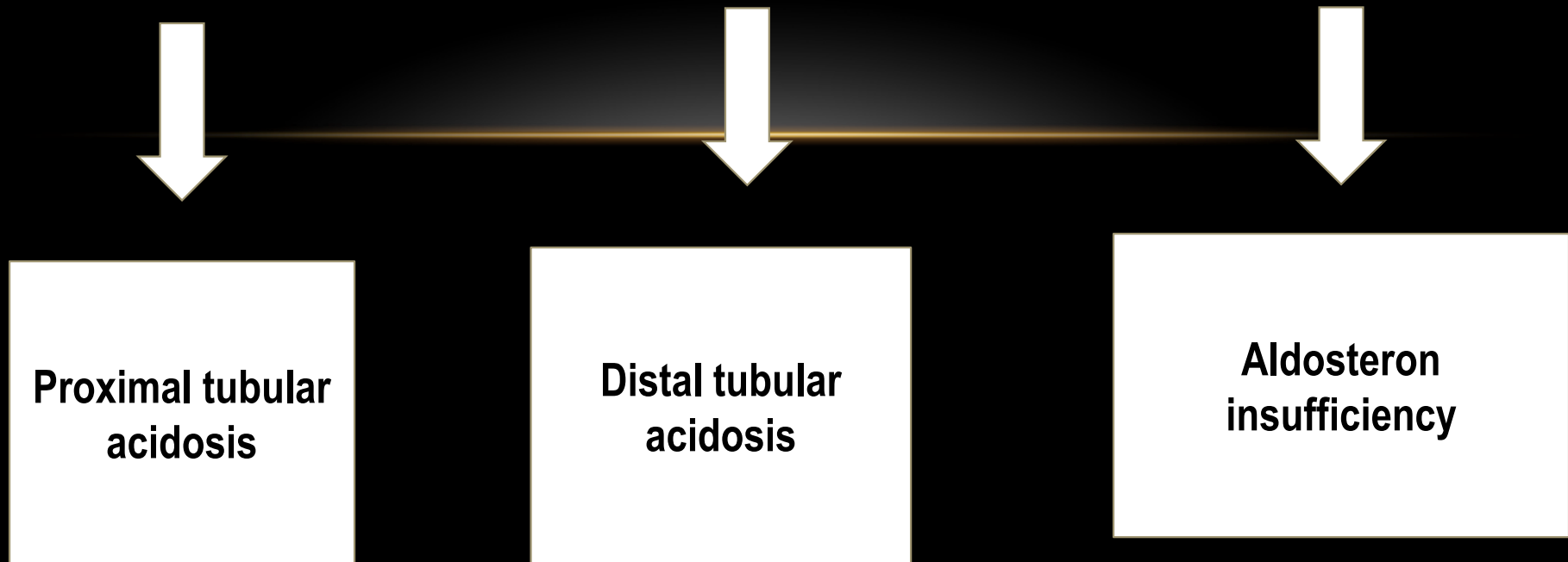


# DISORDERS OF TUBULAR SECRETION



# RENAL TUBULAR ACIDOSIS

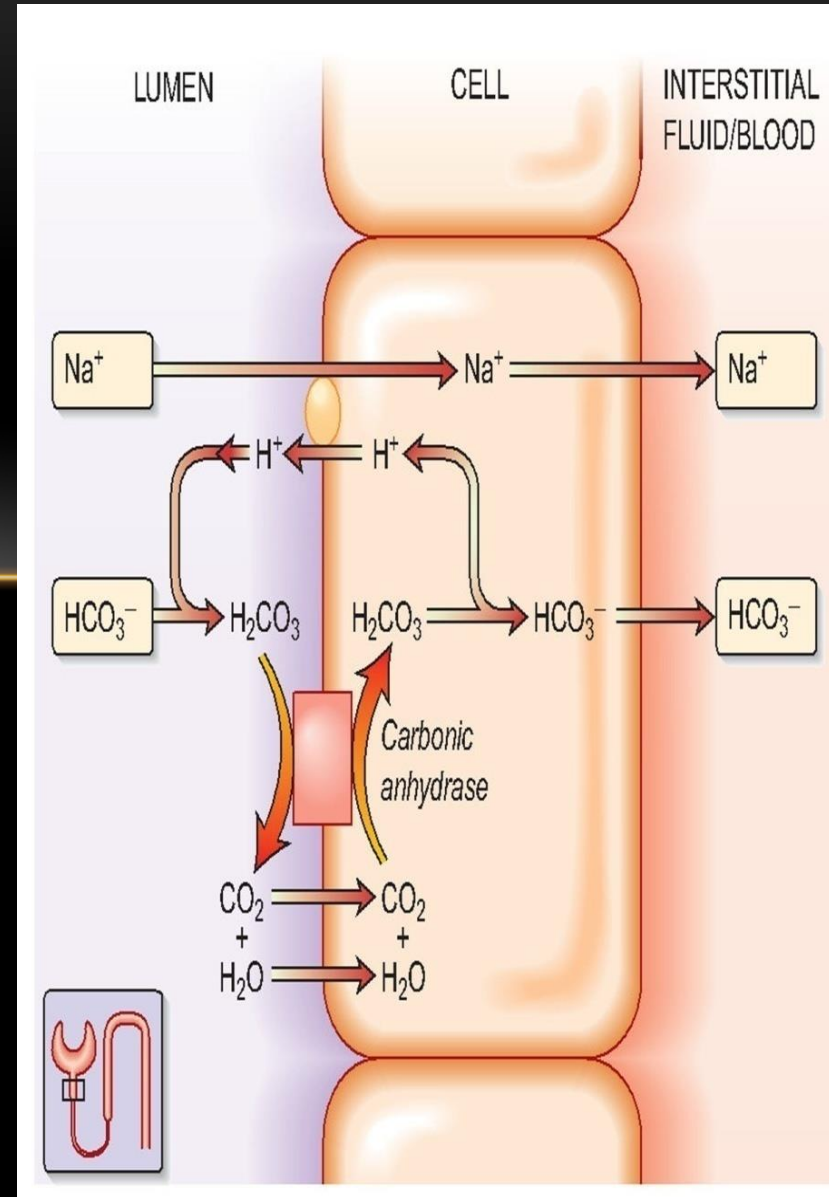
A group of tubular defects in reabsorption of bicarbonate ions ( $\text{HCO}_3^-$ ) or excretion of hydrogen ions ( $\text{H}^+$ ) that result in metabolic acidosis and its subsequent complication, including metabolic bone disease, kidney stones and growth failure in children.



# Proximal renal tubular acidosis

Most often there is decreased activity of the  $\text{Na}^+/\text{K}^+$   $\text{NHE}_3$  pump or that of co-transporter  $\text{Na}^+-3\text{HCO}_3^-$   $\text{NBC}_1$ .

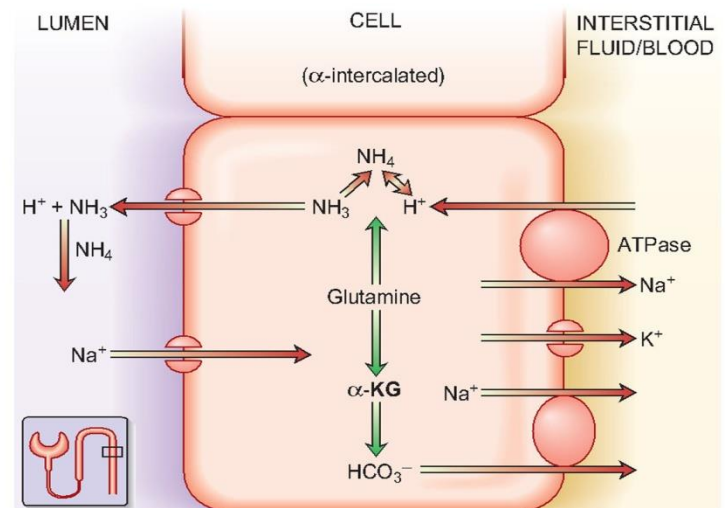
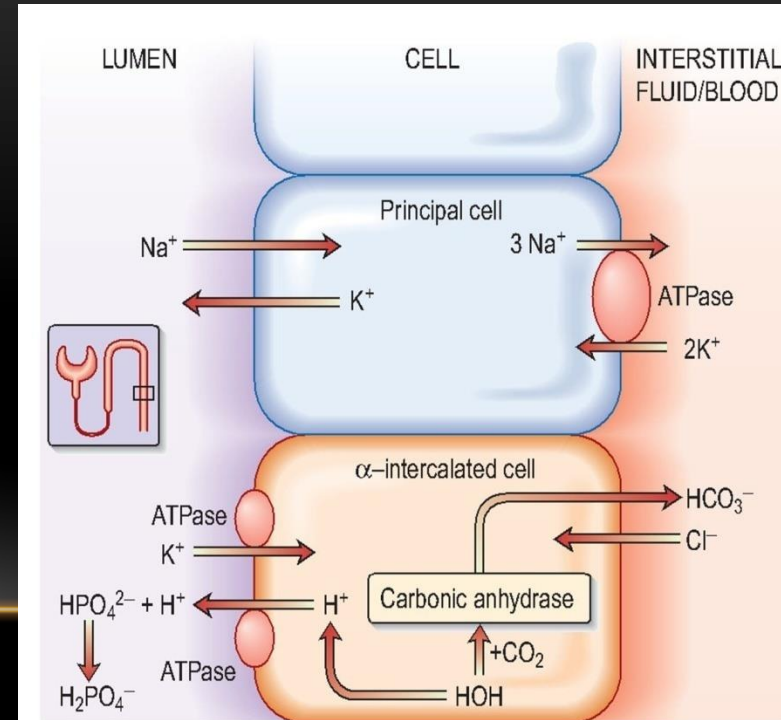
With the onset of impaired tubular  $\text{HCO}_3^-$  reabsorption, there is a loss of this with urine and reduced plasma levels of  $\text{HCO}_3^-$ .



# Distal renal tubular acidosis

Distal RTA results from a distal tubular defect to secrete  $H^+$  ions with failure to acidify the urine and most often is due to defects at the level of  **$H^+$ -ATP-ase,  $H^+$ / $K^+$ -ATP-ase.**

Failure to secrete  $H^+$  results in a net loss of sodium bicarbonate in the urine. This results in **hypovolemia** with compensatory increase in aldosterone level and development of **hypokalemia**.





# Renal tubular acidosis

## Proximal tubular acidosis

-Acidosis

-Hypokalemia

-Inability to lower the urine pH below 5,5 despite systemic acidosis

-



## Distal tubular acidosis

-Acidosis

-Hypokalemia

-Inability to lower urine pH below 5,5 despite systemic acidosis

THANK YOU  
NEVER STOP YOUR CURIOSITY

