

Diuretics

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Diuretics: Classification

CARBONIC ANHYDRASE INHIBITORS

Acetazolamide T 0,25

Brinzolamide Eye drops 1%-5,0

LOOP DIURETICS

Ethacrynic acid

Furosemide Sol. i.v. i.m. 1%-2ml; T 0,04

Toraseamide T 0,001

THIAZIDE DIURETICS

Chlorthalidone

Hydrochlorothiazide T 0,025

Indapamide T 0,0025

POTASSIUM-SPARING DIURETICS

Eplerenone

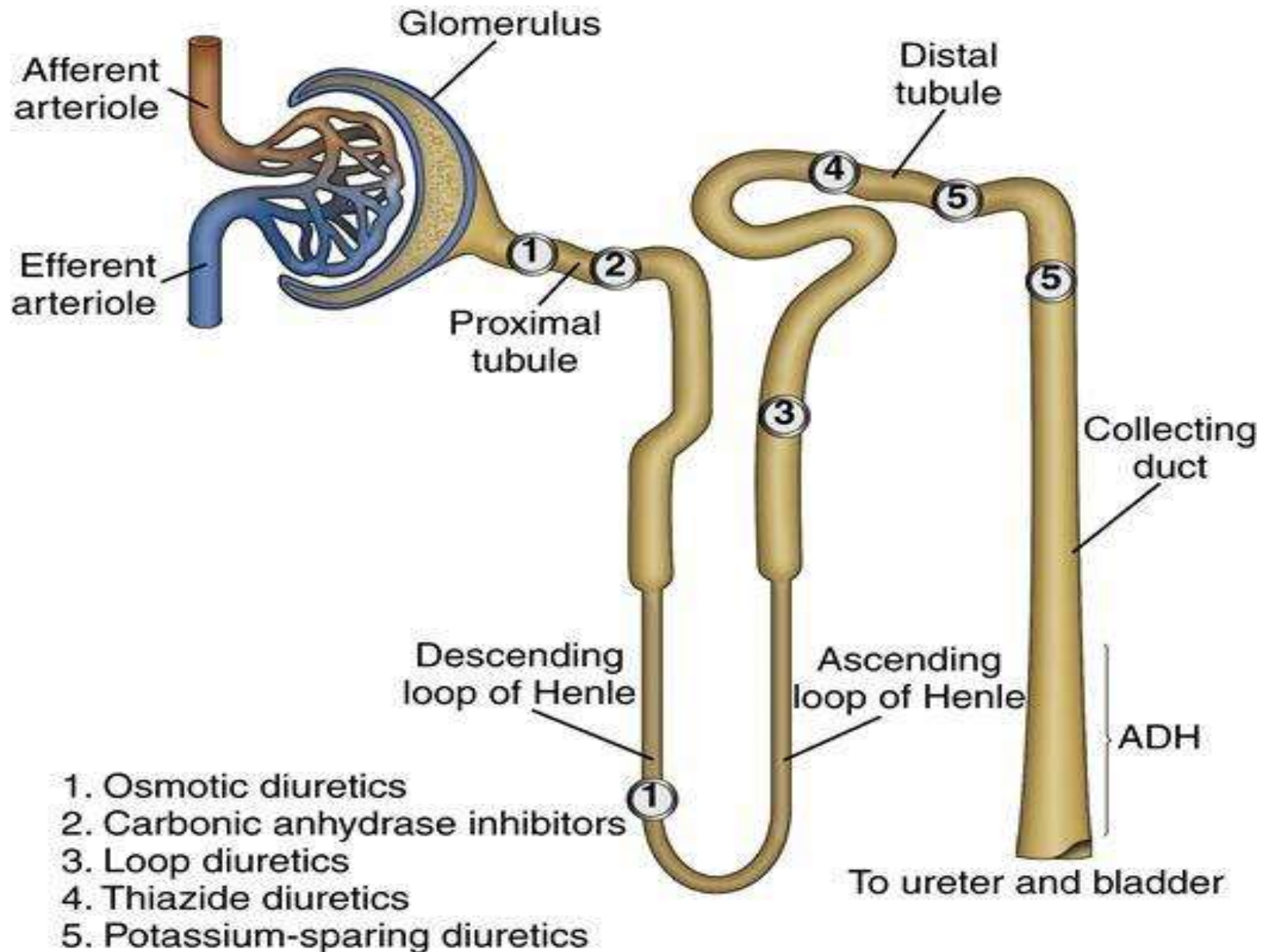
Spironolactone T 0,025

Amiloride

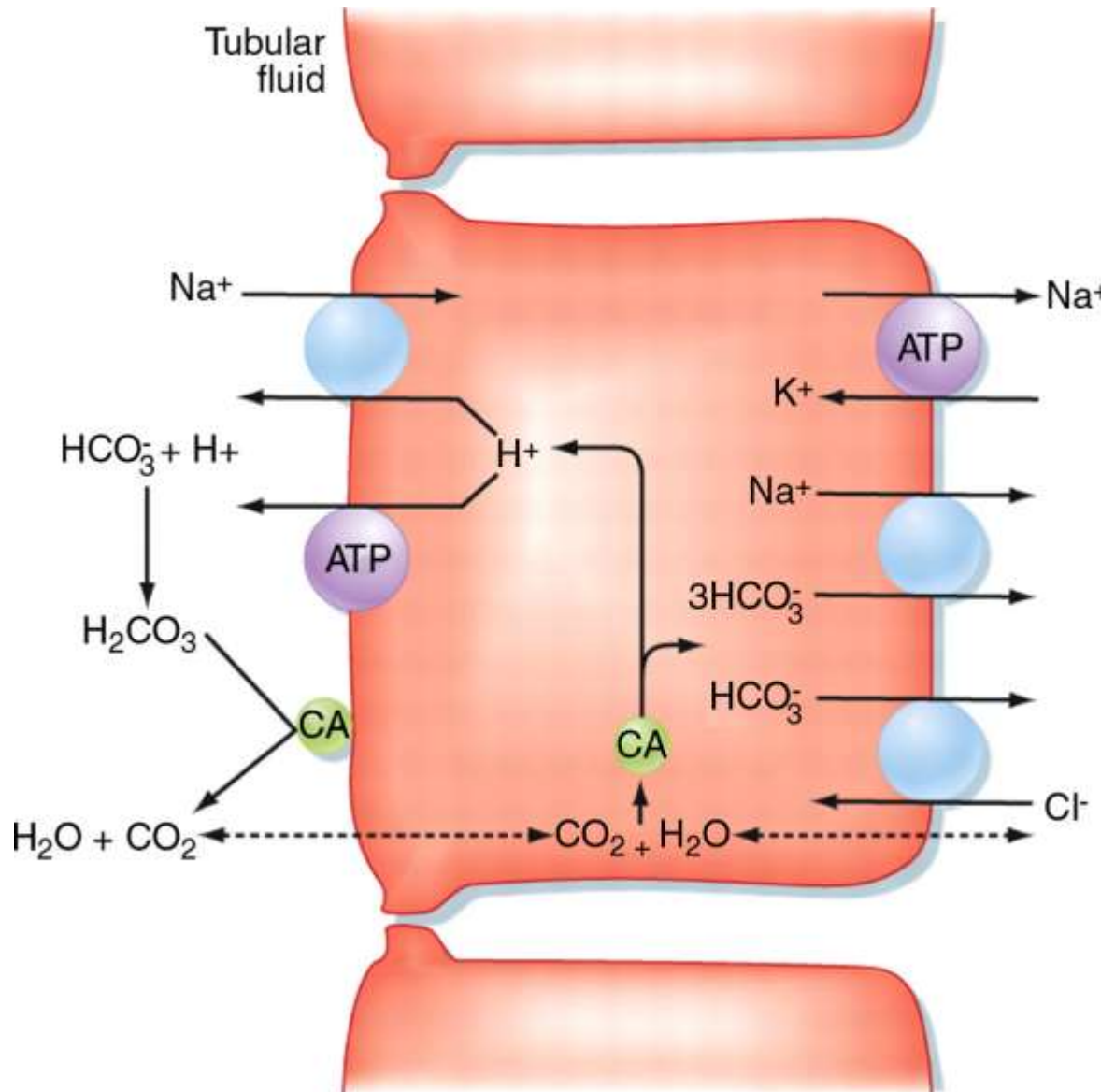
OSMOTIC DIURETICS

Mannitol Sol. i.v. 15% - 200 ml

Diuretics: site of action



CAI: Mechanism of Action



Blood

- ▶ Carbonic anhydrase inhibition, results in:
 - ❑ Decreased H⁺ formation inside cell
 - ❑ Decreased Na⁺/H⁺ antiport
 - ❑ Increased Na⁺ and HCO₃⁻ in lumen
 - ❑ Increased diuresis

CAI: Pharmacological Effects

- ☐ mild diuresis
- ☐ metabolic acidosis
- ☐ ↓ production of intraocular fluid
- ☐ ↓ production of cerebrospinal fluid

Therapeutic Applications

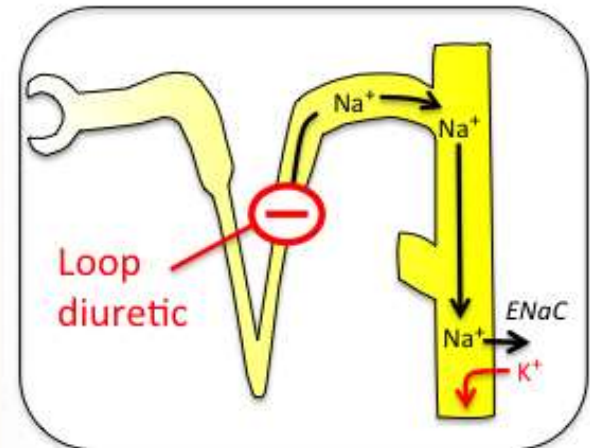
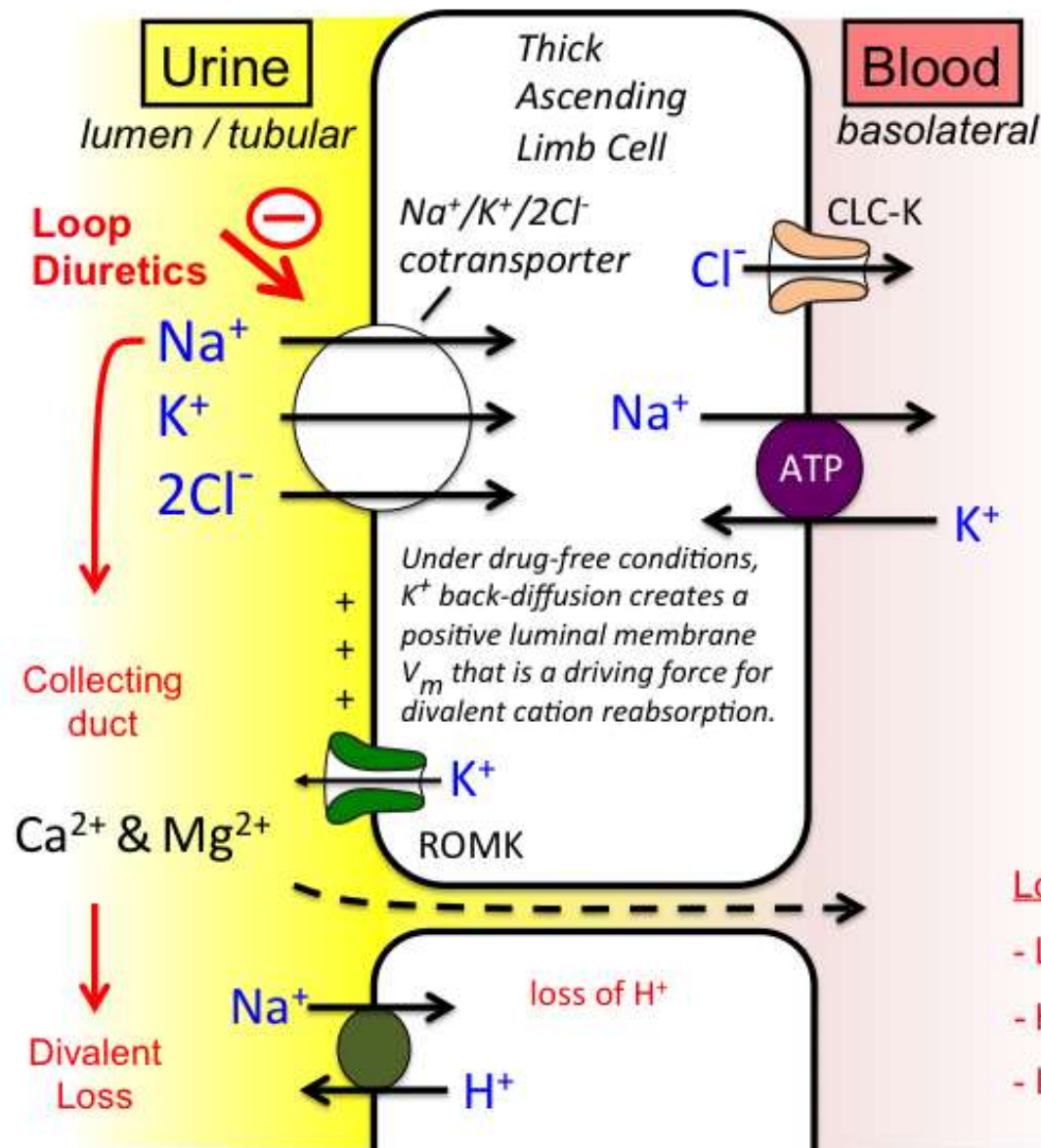
As diuretic is practically not used!

- ☐ glaucoma
- ☐ intracranial hypertension
- ☐ as additional drug in the treatment of epilepsy

Contraindications

Liver cirrhosis (decrease excretion of NH_4 → hepatic encephalopathy)

Loop Diuretics: Mechanism of Action



Enhanced Na^+ delivery results in K^+ loss in the collecting duct

25% of filtered Na is normally reabsorbed in the loop of Henle

Loop diuretics:

- Loss of Na & Water
- Hypokalemic metabolic alkalosis
- Increased Ca^{2+} loss

Loop Diuretics: Mechanisms and Effects

Mechanism of action

blockade of $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ transporter of the ascending part of the loop of Henle

synthesis of PGE and PGI and improvement of blood supply to the kidneys

Pharmacological effects

"Powerful" diuresis, accompanied by loss of K^+ , Mg^{2+} , Ca^{2+}

Vasodilation (iv) \Rightarrow \downarrow AD and \downarrow preload

Loop Diuretics: Therapeutic Applications

chronic peripheral edema in:

- ☐ heart failure
- ☐ liver cirrhosis
- ☐ renal failure

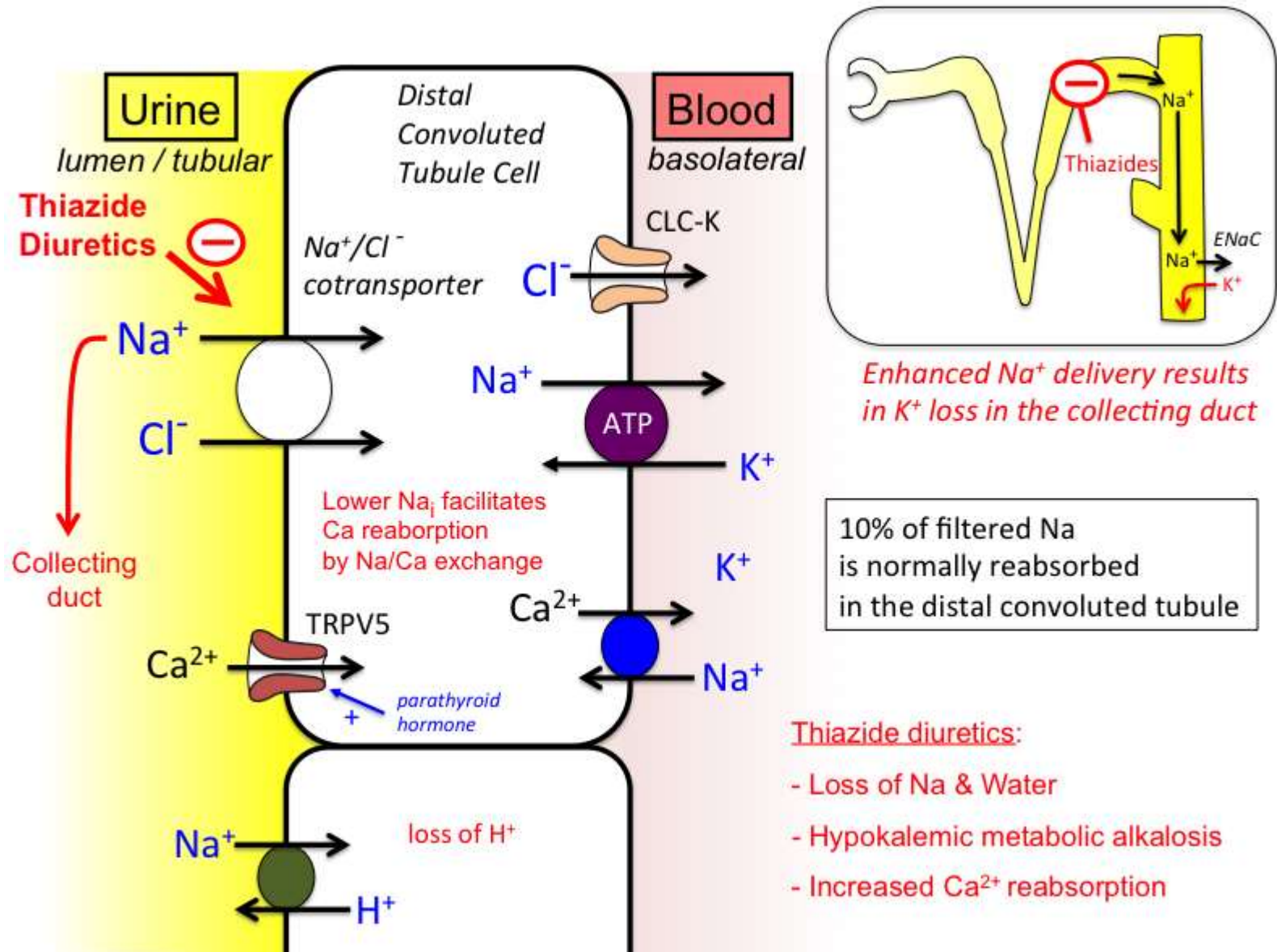
emergency conditions:

- ☐ pulmonary edema, cardiac asthma
- ☐ acute attack of glaucoma
- ☐ poisoning with water-soluble toxins
- ☐ hypercalcemia

Loop Diuretics: Side Effects

- ☐ hypokalemia
- ☐ hypomagnesemia
- ☐ hyperuricemia
- ☐ metabolic alkalosis
- ☐ ototoxicity
- ☐ postural hypotension
- ☐ allergic reactions

Thiazide Diuretics: Mechanism of Action



Thiazide Diuretics: Mechanism of action

- ❑ blocking Na^+/Cl^- -transporter in the distal tubules
- ❑ increase reabsorption of Ca^{2+} in distal tubule
- ❑ inhibit carbonic anhydrase in proximal tubule
- ❑ decrease Na^+ input into smooth muscle of vessels and decrease sensitivity to vasoconstrictors

Pharmacological effects

- ❑ moderate (prolonged) diuresis
- ❑ vasodilation
- ❑ decrease production of intraocular fluid
- ❑ decrease loss of Ca^{2+}

NB! Thiazides do not increase blood supply to the kidneys!

In severe cardiac or renal failure, there is no diuretic effect.

Thiazide Diuretics: Indications

- ❑ Hypertension (drugs of choice)
- ❑ Chronic peripheral edema in:
 - chronic heart failure
 - liver cirrhosis
 - renal failure (except for severe forms)
- ❑ Idiopathic hypercalciuria

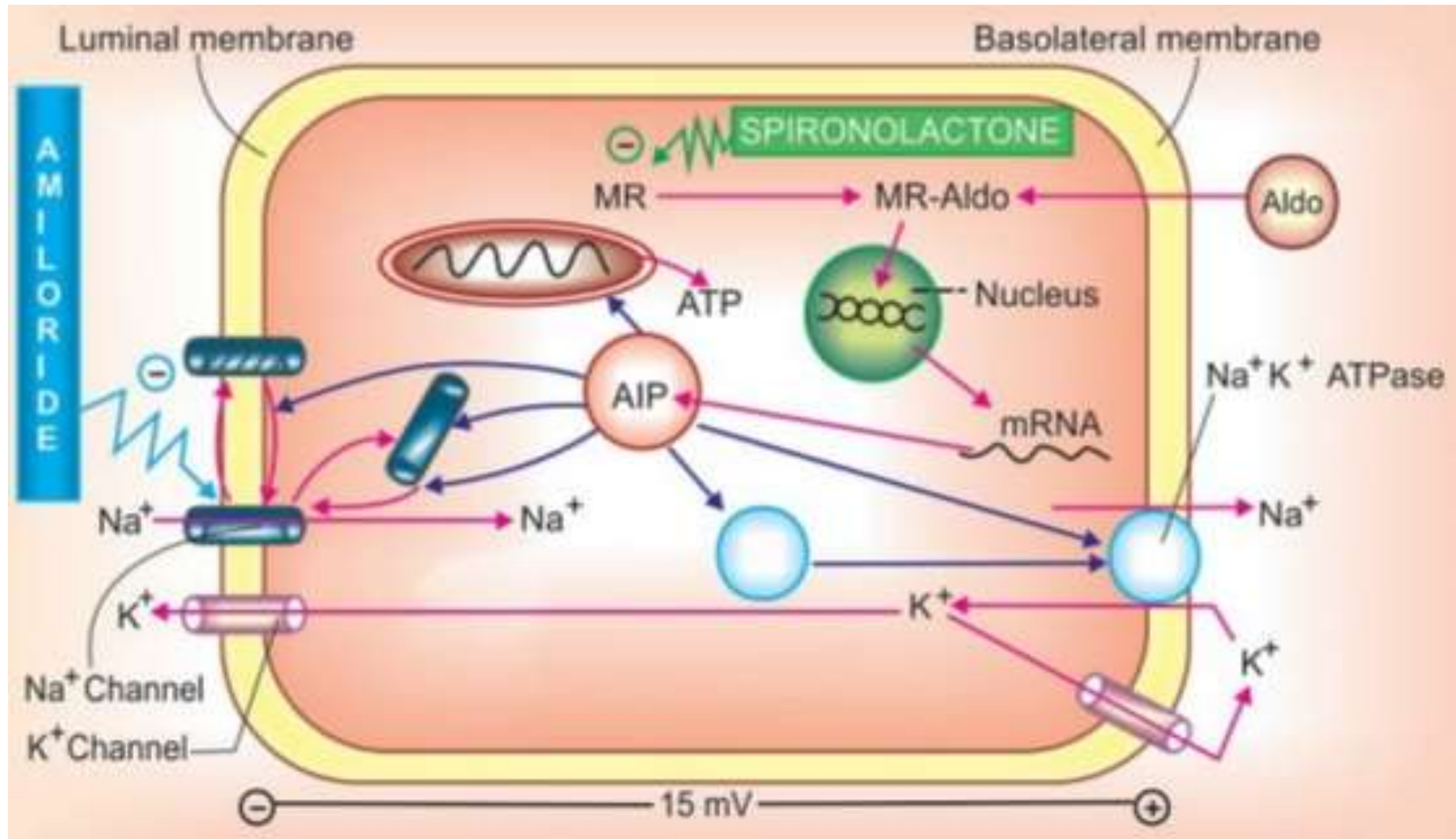
Thiazide Diuretics: Side effects

- ☐ Hypokalemia
- ☐ Hypomagnesemia
- ☐ Hyperuricemia (competition with urates)
- ☐ Hypercalcemia
- ☐ Hyperglycemia
- ☐ Metabolic alkalosis
- ☐ Hypotension (especially in elderly patients)

Currently, the side effects is low, because low doses of drugs are used.

Potassium Sparing Diuretics:

Mechanism of Action



Potassium Sparing Diuretics:

Mechanism and Effects

Spironolactone (competitive aldosterone antagonist)

- ☐ Blocks the mineralocorticoid receptor in distal tubules and collecting ducts
- ☐ Decrease genes expression encoding the synthesis of Na⁺-channel proteins, Na⁺/ K⁺-ATPase
- ☐ Increase excretion of Na⁺ and retention of K⁺
- ☐ Onset of action of after 72 h,
- ☐ Blockade of aldosterone receptors of the heart and blood vessels decrease hypertrophy of the left ventricle and vessels

Amiloride, Triamteren

- ☐ block the entry of Na + to distal tubules and collecting ducts
- ☐ Increase excretion of Na⁺/and retention of K⁺

weak (prolonged) diuresis with retention of K⁺

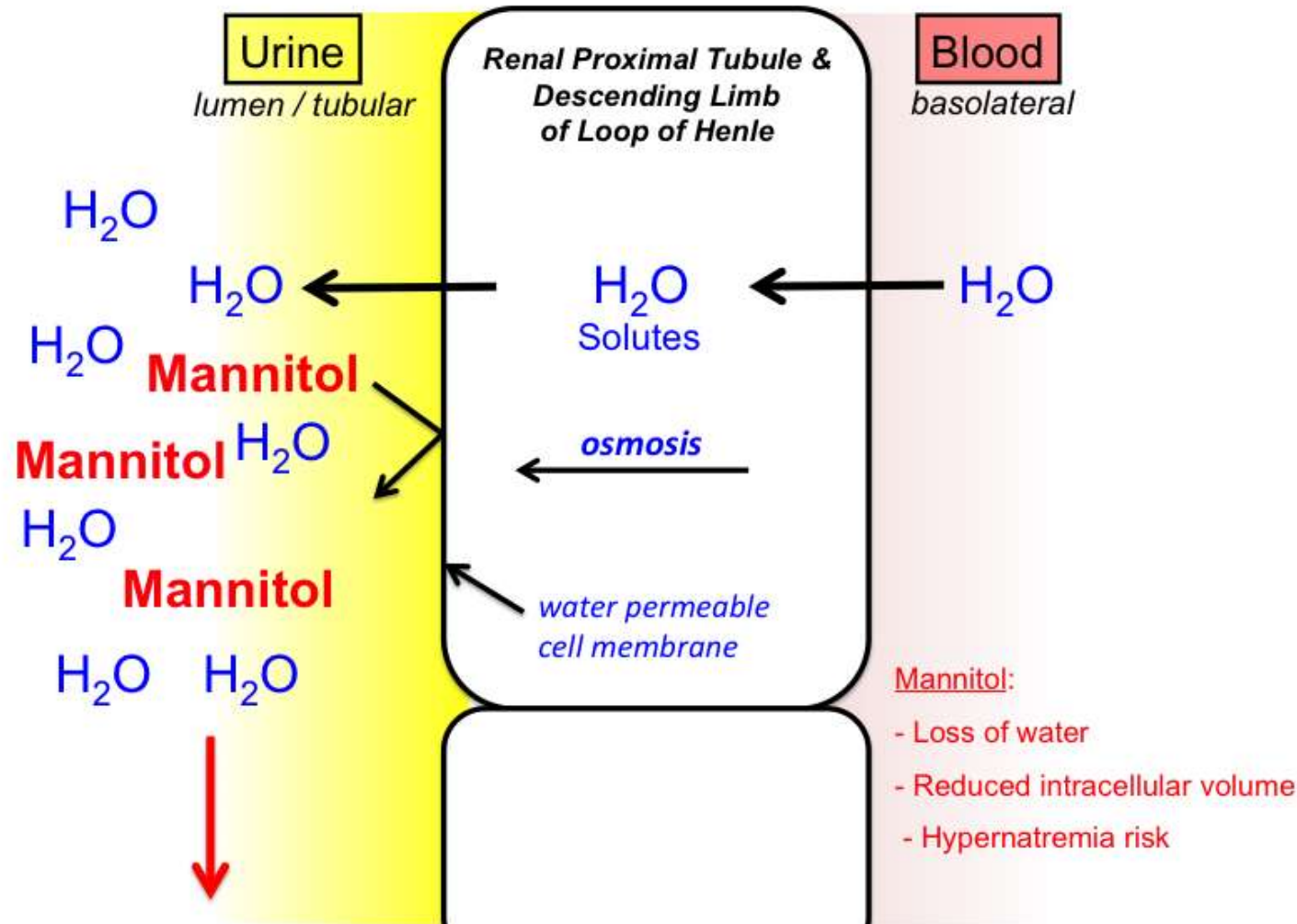
Spironolactone: Indications

- ☐ Primary hyperaldosteronism (Cohn's syndrome)
- ☐ Secondary hyperaldosteronism
 - chronic heart failure
 - liver cirrhosis
- ☐ Hypertension
- ☐ Hypokalemia
- ☐ Hyperandrogenemia in women. It blocks androgen receptors and inhibits steroid synthesis at high doses.

Spironolactone: Side effects

- ☐ Hyperkalemia
- ☐ Gynecomastia (in male) and menstrual irregularities (in female)
- ☐ Erectile dysfunction
- ☐ Irritation of GIT

Osmotic Diuretics: Mechanism of action



↑ osmotic pressure of the urine, preventing the absorption of water practically throughout the nephron (especially in the proximal tubule and Henle loop)

Osmotic Diuretics: Pharmacological effects

It is administered intravenously.

2 phases of action:

1st phase - hypervolemic

↑ blood osmotic pressure → dehydration → ↑ **circulating blood volume**

2nd phase - hypovolemic

as the diuresis develops → ↓ **circulating blood volume**

Osmotic Diuretics: Indications

- ☐ cerebral edema
- ☐ acute attack of glaucoma

Osmotic Diuretics: Contraindications

- ☐ heart failure
- ☐ hypertension

THANKS FOR ATTENTION!