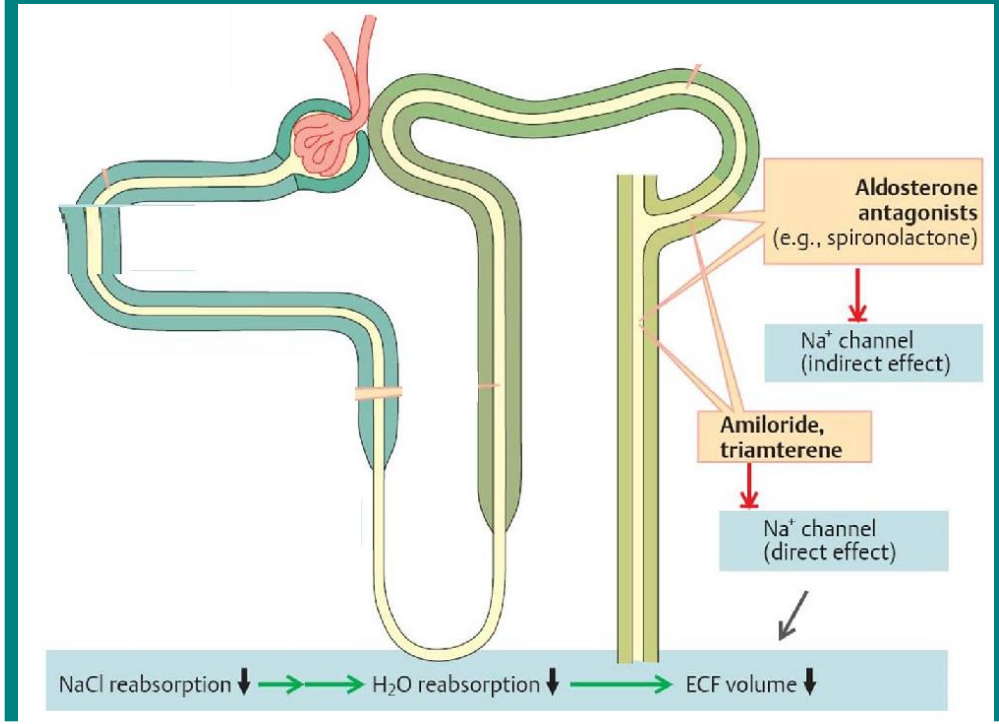
DIURETICS-III

Aldosterone antagonists & Sodium Channel Inhibitors



DIURETICS-III

Potassium-sparing diuretics

Steroidal

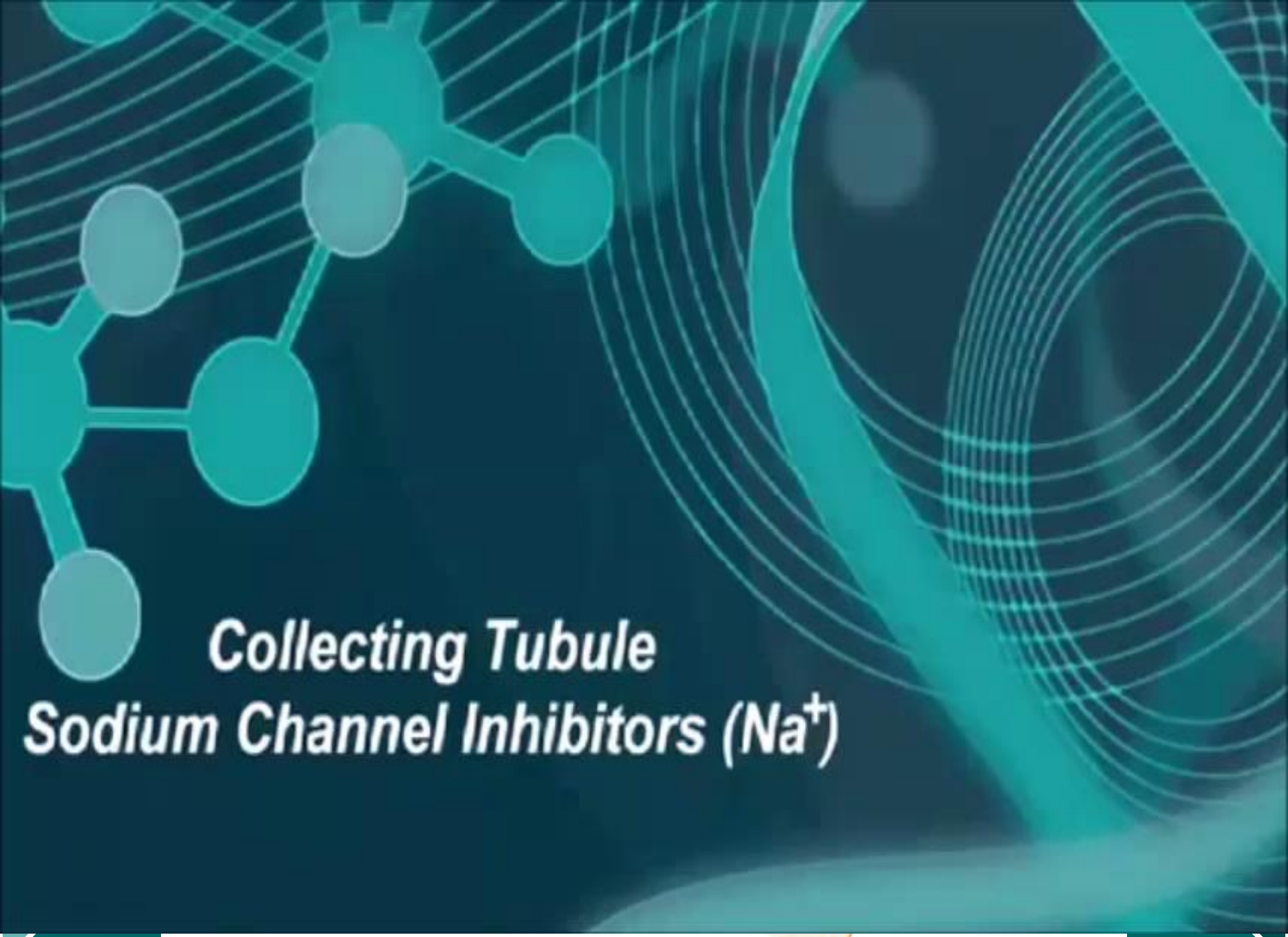
Competitive aldosterone antagonists:

- Spironolactone
- Eplerenone

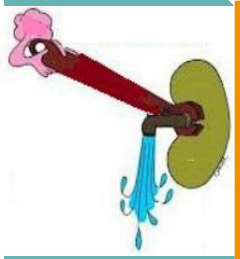
Nonsreroidal

Inhibitors of Na^+ channels:

- Amiloride
- Triamterene


Collecting Tubule
Sodium Channel Inhibitors (Na^+)

DIURETICS-III



MINERALOCORTICOID RECEPTOR ANTAGONISTS

Also Called:

- K-Sparing Diuretics
- Aldosterone Antagonists

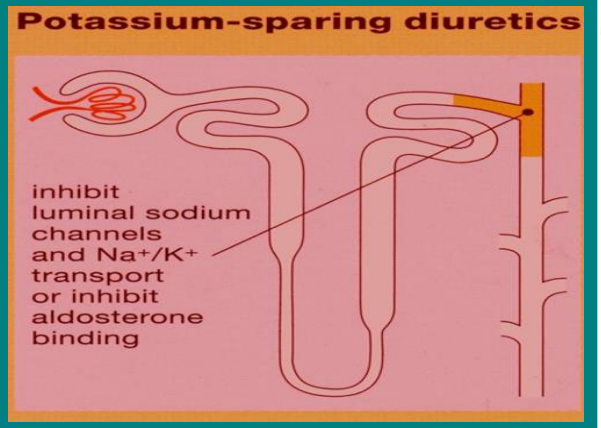
Spironolactone

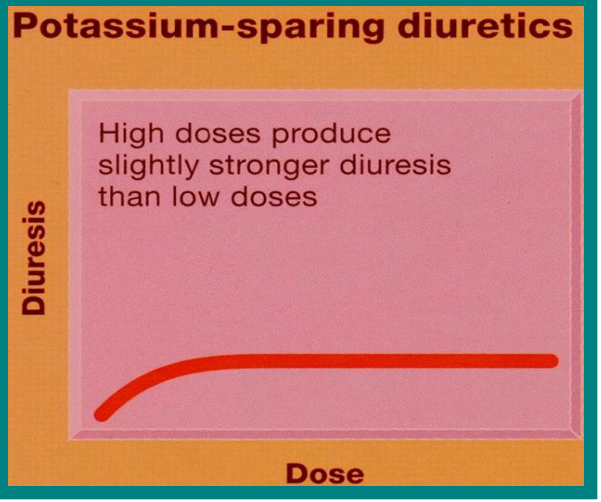
Eplerenone

ALDOSTERONE ANTAGONISTS

- Aldosterone antagonists are competitive antagonist at the collecting duct→↑ Excretion of Na+,Cl-&↓Excretion of K+,H+,NH4

- Actions depend on renal PGs production

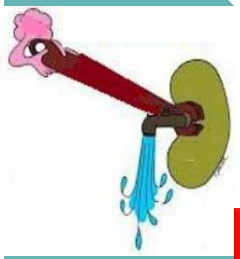




ALDOSTERONE ANTAGONISTS

PHARMACOKINETICS

SPIRONOLACTONE

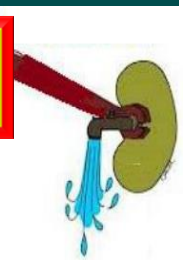


- Well absorbed from the GIT ,t½=1.6h.
- Highly protein- bound
- Undergoes enterohepatic recycling.
- Delayed onset of action (nuclear receptor), maximum diuretic action 4 days.
- Converted in gut & liver to canrenone [active metabolite, t½=16h].

ALDOSTERONE ANTAGONISTS

PHARMACOKINETICS

EPLERENONE



Eliminated by metabolism(CYP3A4),t½ 5h

Low affinity for progesterone and androgen receptors

Both ineffective in adrenalectomized patients

ALDOSTERONE ANTAGONISTS

THERAPEUTIC USES

Enhances Natriuresis Caused by Other Diuretics

Prevents Hypokalemia

Used in Combination with Loop & Thiazide Diuretics

Blocks Aldosterone

Secondary hyperaldosteronism

Treatment for Primary Hyper-aldosteronism

Treatment for Edema of Liver Cirrhosis

Treatment for Hypertension

Resistant hypertension

Improve survival

Treatment for Heart Failure

Treatment for Nephrotic syndrome

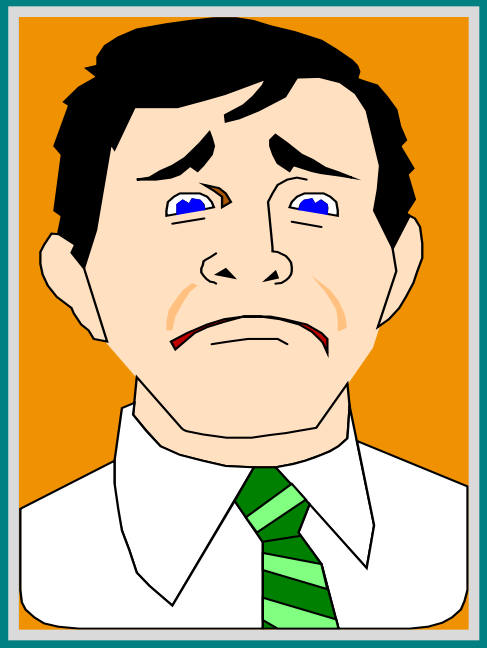
ALDOSTERONE ANTAGONISTS

ADRS

Hyperkalemia

Gastritis

Metabolic Acidosis in cirrhotic patients



Peptic Ulcers

CNS Side Effects

Deepening of Voice

Impotence

Hirsutism

Gynecomastia

Menstrual Irregularities

ALDOSTERONE ANTAGONISTS

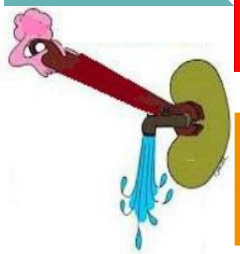
DRUG- DRUG INTERACTIONS

Salicylates → **↓Secretion of canrenone ↓Efficacy of spironolactone**

Digitalis ← **Spironolactone alters clearance**

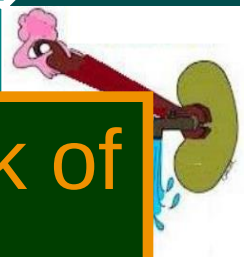
ALDOSTERONE ANTAGONISTS

CONTRAINDICATIONS



Hyperkalemia

Increased Risk of Hyperkalemia



- Renal failure
- Other K+ sparing diuretics
- ACE-I
- K+ suplement

SODIUM CHANNEL INHIBITORS

Also Called:

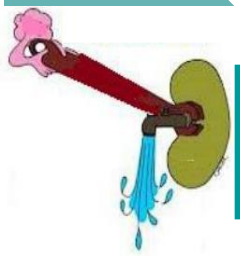
- K-Sparing Diuretics

Triamterene
Potency 0.1,
t½ 4.2 h,
elimination
by metabolism

Amiloride
Potency 1,
t½ 21h,
renal
elimination

SODIUM CHANNEL INHIBITORS

THERAPEUTIC USES



Enhance Natriuresis Caused by Other Diuretics → **Used in Combination with Loop & Thiazide Diuretics**

Prevent Hypokalemia → **Used in Combination with Loop & Thiazide Diuretics**

Block Na+ Channels

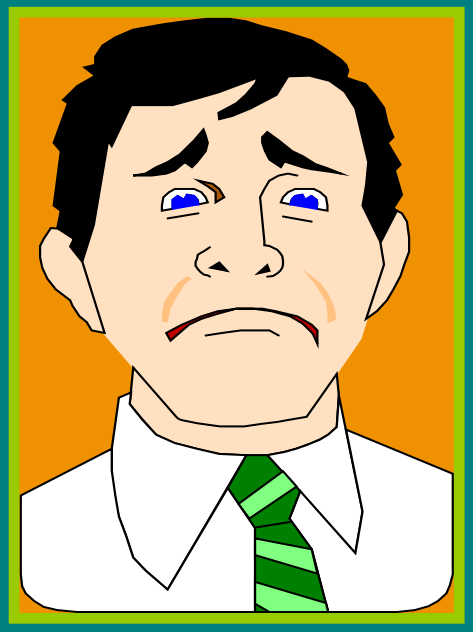
- Treatment for Liddle's Syndrome
- Treatment for Lithium-Induced Diabetes Insipidus

SODIUM CHANNEL INHIBITORS

ADRS

Amiloride

Hyperkalemia



Triamterene

Hyperkalemia

Renal Stones

Interstitial Nephritis

Megaloblastosis in cirrhotic patients

SODIUM CHANNEL INHIBITORS

CONTRAINDICATIONS

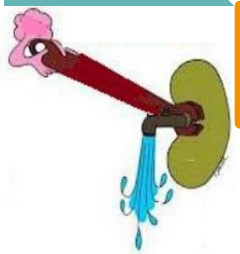
Hyperkalemia

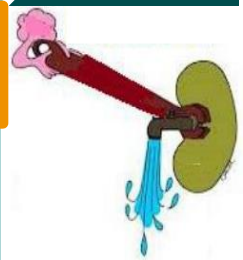
Increased Risk of Hyperkalemia

- Renal failure
- Other K+ sparing diuretics
- ACE-I & ARBs
- Aliskiren
- K+ suplement

SODIUM CHANNEL INHIBITORS

DRUG-Drug INTERACTIONS





ACE Inhibitors
Beta-Blockers
K Supplements
K-Sparing Diuretics
Aliskiren

→ **↑Hyperkalemia-induced by K-Sparing diuretics**

DIURETICS

MNEMONIC FOR TYPES

Leak On The CAN

x Na/Cl/K cotransporter

Leak - Loop Diuretics: Furosemide

On - Osmotics: Mannitol, Urea

x Na/Cl cotransporter

The - Thiazides: Hydrochlorothiazide

C - Carbonic anhydrase inhibitors: Acetazolamide

K sparing

A - Aldosterone inhibitors: Spironolactone

N - Na channel blockers: Amiloride, Triamterene

Diuretics	Mechanism of action	Effects
CA inhibitors **Acetohexamide** **Dorzolamide**	**Inhibition of NaHCO3 reabsorption in PCT**	**– Urinary Na HCO3, K** **Urinary alkalosis** **Metabolic acidosis**
Osmotic diuretic **Mannitol**	**Osmotic effect in PCT & DLH**	**–Urine excretion** **– Little Na**
Loop diuretics **Furosemide**	**Na/K/2Cl transporter in TAL the most effective**	**–Urinary Na, K, Ca, Mg**
Thiazide diuretics **hydrochlorothiazide**	**Na and Cl cotransporter in DCT**	**–Urinary Na, K, Mg** **BUT↓ urinary Ca (hypercalcemia)** **Metabolic alkalosis**
K-sparing diuretic **Spironolactone.**	**competitive antagonist of aldosterone in CCT**	**↑ Urinary Na** **↓ K, H secretion** **Metabolic acidosis**

Diuretics	Uses
CA inhibitors **Acetohexamide** **Dorzolamide (topically) for glaucoma**	**Glaucoma, epilepsy** **Mountain sickness**
Osmotic diuretic **Mannitol**	**• Cerebral edema** **• Acute renal failure**
Loop diuretics **Furosemide**	**Acute pulmonary edema (Drug of choice)** **Heart failure** **Hyperkalemia, Hypercalcemia**
Thiazide diuretics **hydrochlorothiazide**	**Commonly used** **Hypertension, heart failure, hypercalciuria, kidney stones, diabetes inspidus**
K-sparing diuretic **Spironolactone.**	**Hepatic cirrhosis** **(Drug of choice)**

Diuretics	Side effects
CA inhibitors **Acetohexamide** **Dorzolamide**	**Metabolic acidosis , Urinary alkalosis** **Hypokalemia**
Osmotic diuretic **Mannitol**	**Extracellular water expansion** **Dehydration** **Hypernatremia**
Loop diuretics **Furosemide**	**Hypokalemia,** **hypovolemia, hyponatremia,** **hypomagnesemia, hypocalcemia** **Precipitate gout, alkalosis**
Thiazide diuretics **hydrochlorothiazide**	**Hypokalemia, hyponatremia, hypovolemia,** **hypomagnesemia, hypercalcemia** **Alkalosis, precipitate gout** **Hyperlipidemia, hyperglycemia**
K-sparing diuretic **Spironolactone.**	**Gynaecomastia** **Hyperkalaemia, Metabolic acidosis.** **GIT upset and peptic ulcer**