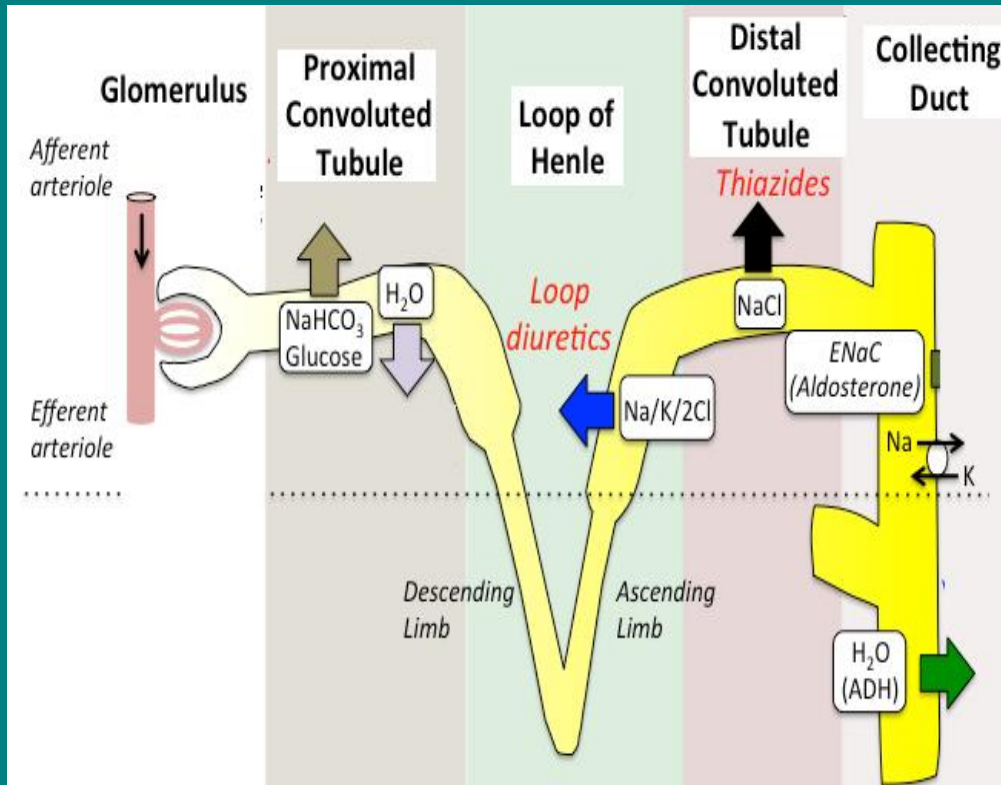


DIURETICS-II

THIAZIDES & LOOP DIURETICS



THIAZIDE DIURETICS

NA-CL SYMPORT INHIBITORS

Thiazide Diuretics

• Thiazide-Like Diuretics

Hydrochlorothiazide

Potency 1, $t_{1/2}$ 3h

Chlorothiazide

Potency 0.1, $t_{1/2}$ 2h

Chlorthalidone

Potency 10, $t_{1/2}$ 26h

Metolazone

Potency 5, $t_{1/2}$ 5h

Indapamide

Potency 20, $t_{1/2}$ 16h



Distal Convoluted Tubules
Thiazide Diuretics

THIAZIDES

PHARMACOKINETICS

Thiazides are **lipid soluble**

Given orally, efficiently absorbed from the GIT

Long duration of action

Eliminated by glomerular filtration & tubular secretion, some is reabsorbed

May interfere with uric acid secretion and cause **hyperuricemia**

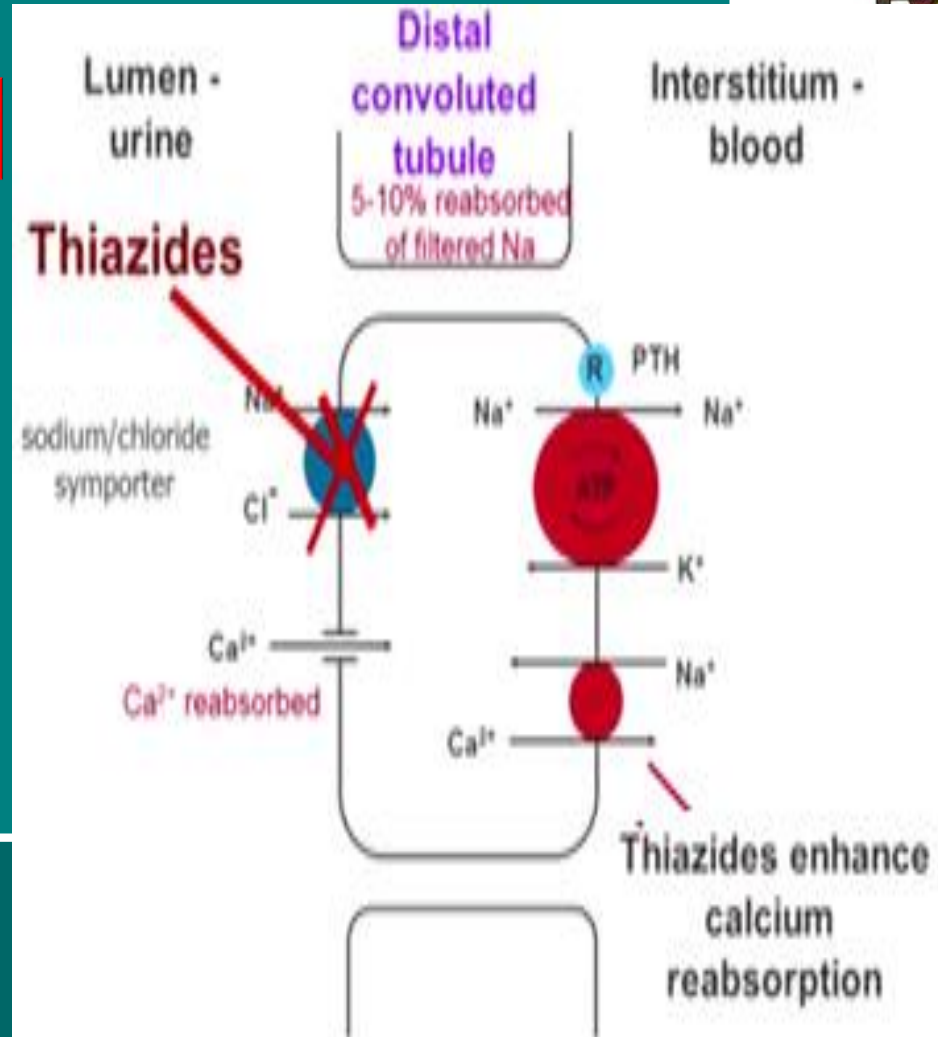
THIAZIDE DIURETICS

PHARMACODYNAMIC EFFECTS

1-Considerable K^+ loss

2-May give rise to hypokalemic alkalosis

3- \downarrow uric acid & \downarrow Ca^{++} excretion & \uparrow Mg^{++} excretion

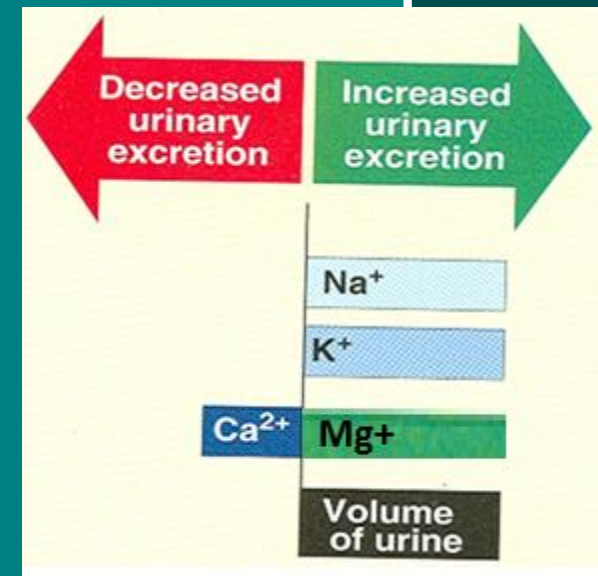


THIAZIDE DIURETICS

PHARMACODYNAMIC EFFECTS

4- Causes vasodilatation , diazoxide , non diuretic thiazide is a potent vasodilator

5- ↓ of urine volume in case of diabetes insipidus



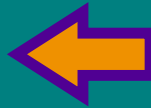
THIAZIDE DIURETICS



DRUG- DRUG INTERACTIONS

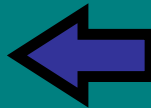


Uricosurics
Sulphonylurea



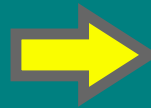
Thiazides
Diminish
effect

Digitalis
Diazoxide



Thiazides
Increase effect

NSAIDs



Reduce thiazide
efficacy

THIAZIDES

ADRS

ECFV
Depletion

Hypokalemia

Hyponatremia

Hypomagnesemia

Impotence

Metabolic
Alkalosis

Hypercalcemia

Hyperuricemia

Hyperglycemia

↑ LDL



THIAZIDES

CLINICAL USES

Mnemonics

Thiazides Indications "CHIC"

C

Congestive Heart Failure



H

Hypertension



I

Insipidus



C

Calcium calculi



[MORE INFORMATION](#)

LOOP DIURETICS

Na-K-2Cl SYMPORT INHIBITORS

Also Called:

- Loop Diuretics
- High Ceiling Diuretics

Furosemide

Potency 1, $t_{1/2}$ 1.5h

**Ethacrynic
Acid**

Potency 0.7, $t_{1/2}$ 1h

Bumetanide

Potency 40, $t_{1/2}$ 0.8 h

Torseamide

Potency 3, $t_{1/2}$ 3.5h



***Loop of Henle
Loop Diuretics***

LOOP DIURETICS

PHARMACODYNAMIC EFFECTS

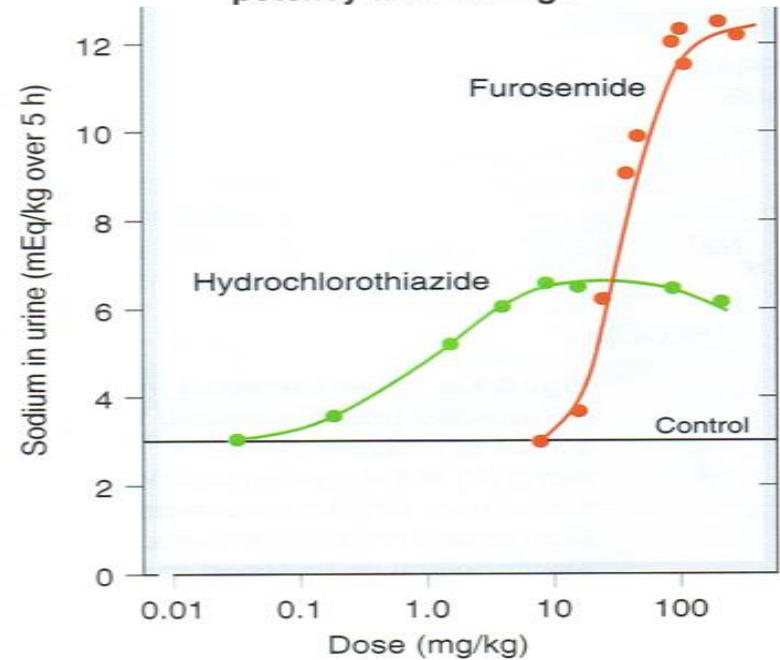


■ The most potent diuretics, termed “**high ceiling diuretic**”

Induce expression of COX, PGE ↓ salt transport in TAL

■ ↓ Renal vascular resistance & ↑ renal blood flow → PGs

The dose-response curves for furosemide and hydrochlorothiazide, showing differences in potency and 'ceiling'.



Loop diuretics

Diuresis

High doses produce stronger diuresis than low doses 'High ceiling'

Dose

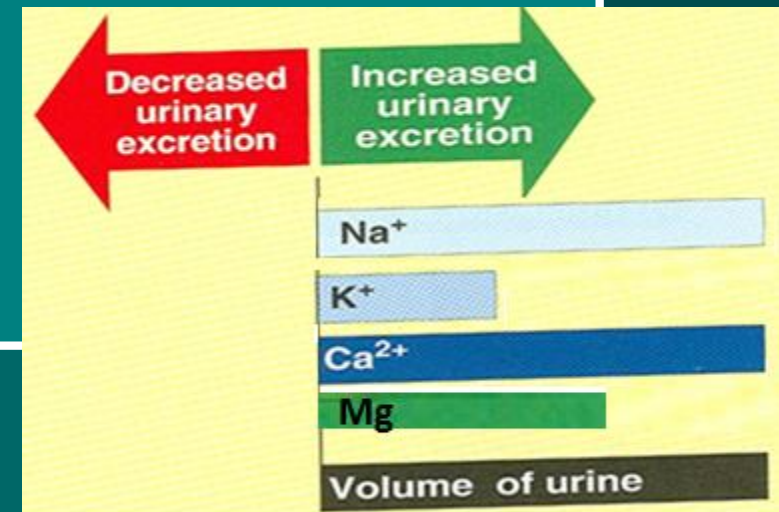
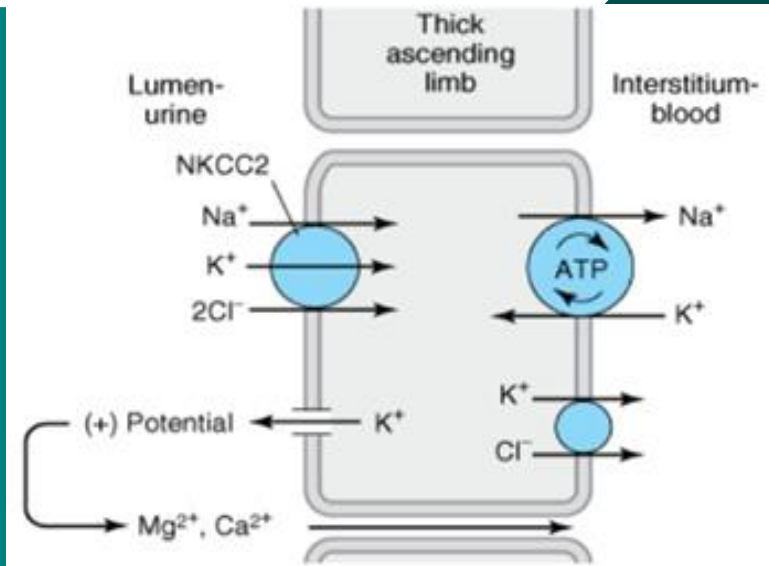
LOOP DIURETICS

PHARMACODYNAMIC EFFECTS



Increase Ca & Mg excretion

Furosemide and ethacrynic acid reduce pulmonary congestion and left ventricular filling pressures in heart failure → ↑ venous capacitance



LOOP DIURETICS

PHARMACOKINETICS

Given orally or IV

Have fast onset of action (suitable for emergency)

Have short duration of action

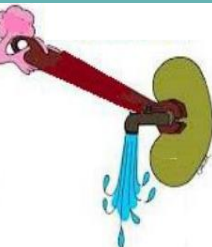
Bumetanide is the most potent

Excreted by active tubular secretion of weak acids into urine (avidly bound to plasma proteins).

Interfere with uric acid secretion

LOOP DIURETICS

THERAPEUTIC USES



Increase Na Excretion
to 25% of Filtered
Load

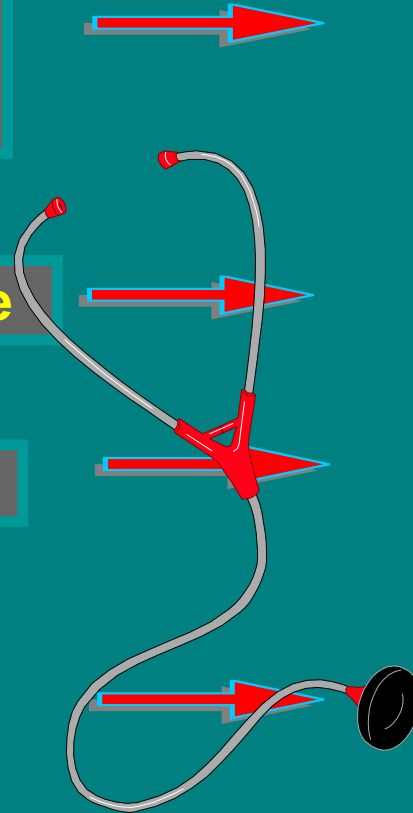
Increase Urine Volume

Increase Ca Excretion

Increase Venous
Capacitance

Increase K⁺ Excretion

Anion overdose



Treatment for
Severe Edema

Treatment for
Oliguric ARF

Treatment for
Hypercalcemia

Treatment for
Pulmonary
Edema

Acute
Treatment for
Hyperkalemia

Toxicity of Br, F & I



LOOP DIURETICS

ADRS

**Profound ECFV
Depletion**

Hypokalemia

Hypocalcemia

Hypomagnesemia

**Metabolic
Alkalosis**

Ototoxicity

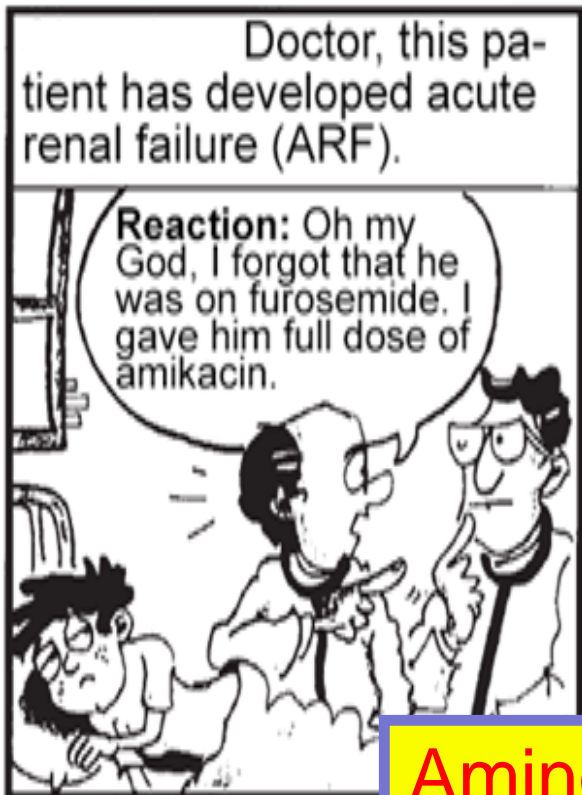
Hyperuricemia

Hyperglycemia

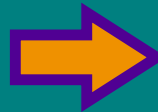


LOOP DIURETICS

DRUG- DRUG INTERACTIONS



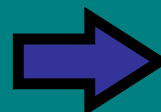
NSAIDs
Probenecid



↓ Diuretic Response

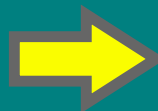


Digitalis



Arrhythmias

Aminoglycosides



↑ Ototoxicity of Loop Diuretic

↑ Nephrotoxicity of Aminoglycosides



Loop Diuretic

LOOP DIURETICS

CONTRAINDICATIONS



Severe Na⁺
& volume
depletion

Hypersensitivity
To sulphonamides

Anurea
unresponsive
to a trial dose of
loop diuretic