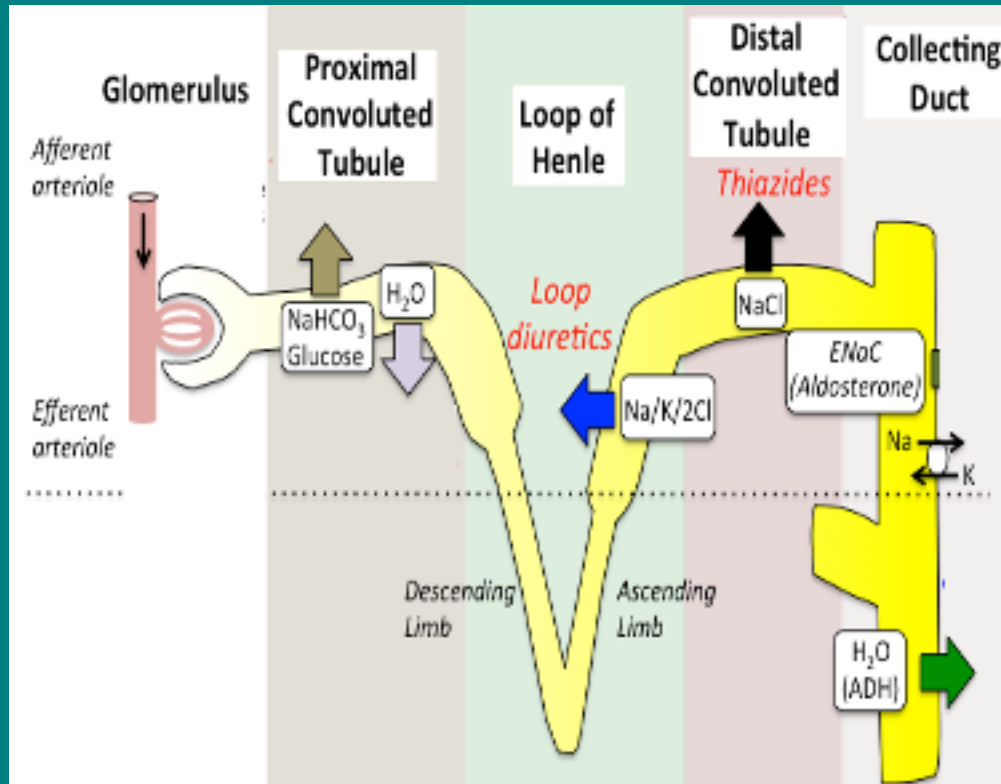


DIURETICS-II

THIAZIDES & LOOP DIURETICS



THIAZIDE DIURETICS

NA-CL SYMPORT INHIBITORS

Thiazide Diuretics
• Thiazide-Like Diuretics

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

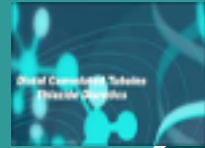
Chlorothiazide
Potency 0.1,
 $t_{1/2}$ 2h

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

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

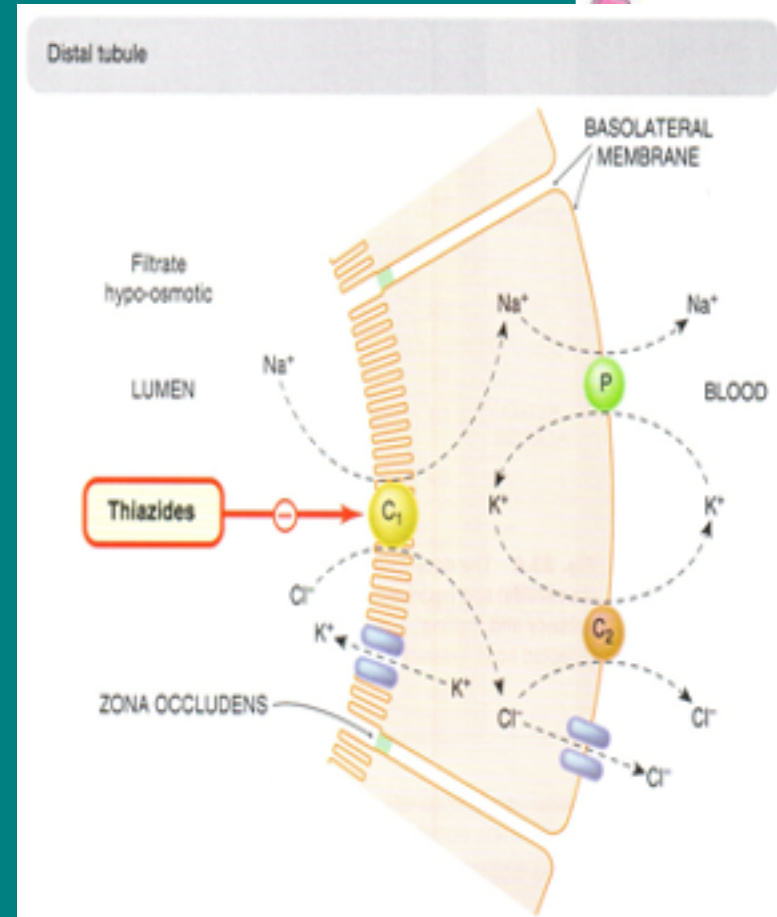
Indapamide
Potency 20,
 $t_{1/2}$ 16h

THIAZIDES



Act on early distal tubule [5-10% of filtered load of sodium is reabsorbed]

- Thiazides inhibit Na/Cl cotransporter
- Weak inhibitors of **carbonic anhydrase**, but this does not contribute to their action



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*

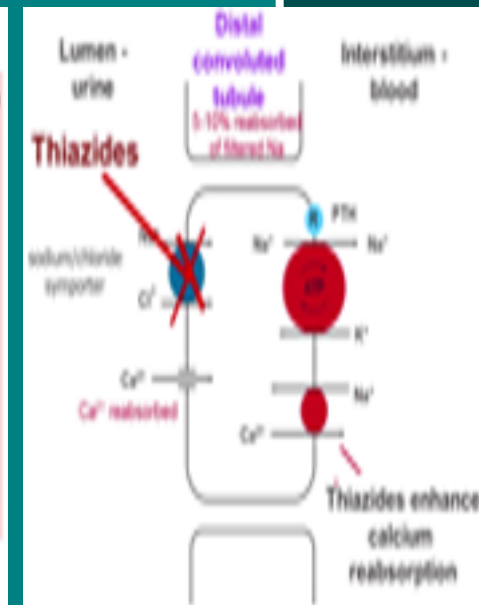
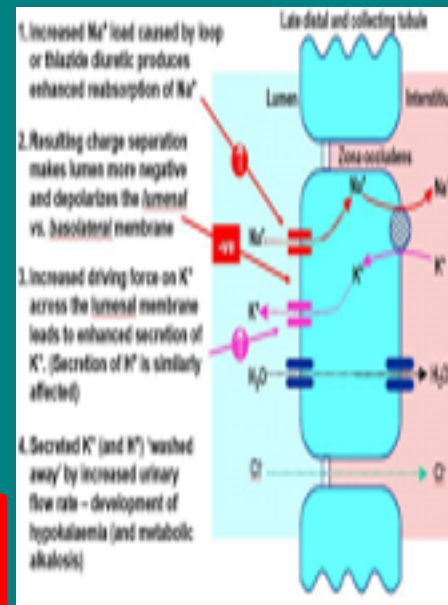
THIAZIDE DIURETICS

PHARMACODYNAMIC EFFECTS

1-Considerable K^+ loss

2-May give rise to hypokalemic alkalosis

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

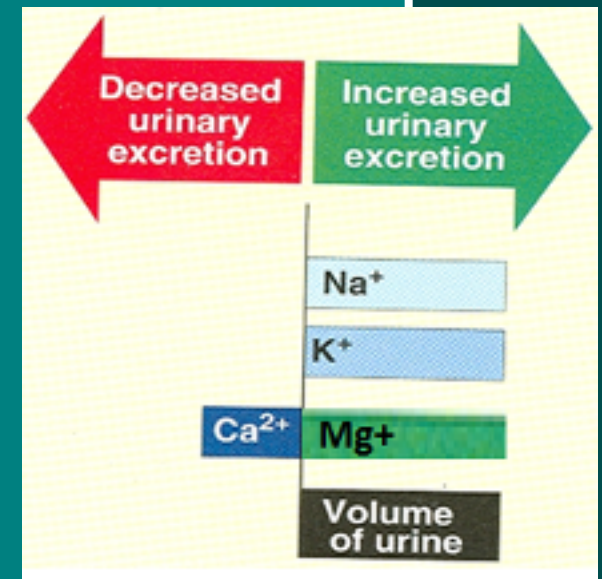


THIAZIDE DIURETICS

PHARMACODYNAMIC EFFECTS

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

• 5- ↓ of urine volume in case of
diabetes insipidus



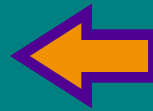
THIAZIDE DIURETICS



DRUG- DRUG INTERACTIONS

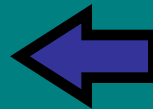


Uricosurics
Sulphonylurea



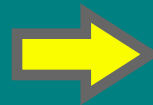
Thiazides
Diminish
effect

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

Increase Na Excretion
to 5% of Filtered Load





Treatment for
Mild Edema

Treatment for
Hypertension

Treatment for
Nephrogenic
Diabetes
Insipidus

Ineffective when the GFR is
less than 30 to 40 ml/min,
except metolazone &
indapamide

Mnemonics
Thiazides Indications
"CHIC"

C	Congestive Heart Failure	
H	Hypertension	
I	Insipidus	
C	Calcium calculi	

Decrease Ca
Excretion

Treatment for
Calcium
Nephrolithiasis

Treatment for
Osteoporosis

LOOP DIURETICS

Na-K-2Cl SYMPORT INHIBITORS

Also Called:

- Loop Diuretics
- High Ceiling Diuretics

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

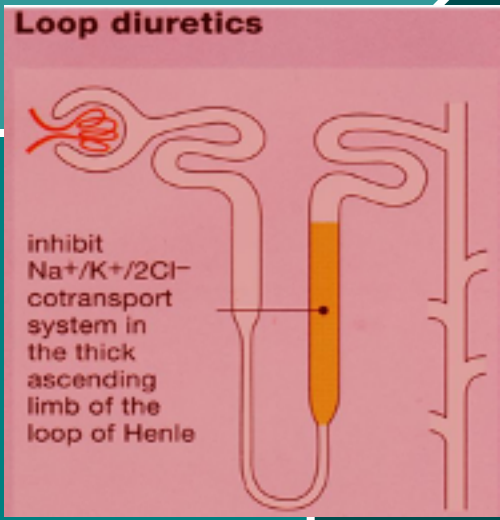
Bumetanide
Potency 40, $t_{1/2}$
0.8 h

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

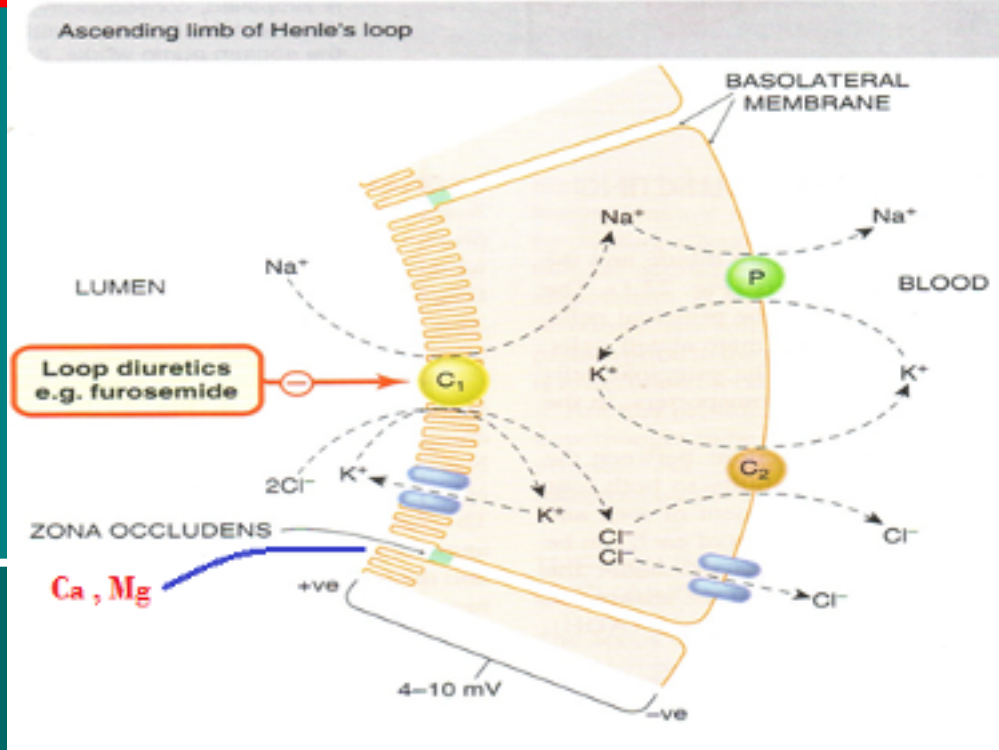
Ethacrynic
Acid
Potency 0.7, $t_{1/2}$
1h

LOOP DIURETICS

- Act on the **thick segment of the ascending loop of Henle** [25% of glomerular filtrate of Na^+ is reabsorbed]



Inhibit Na-K-2Cl transporter



LOOP DIURETICS

PHARMACODYNAMIC EFFECTS

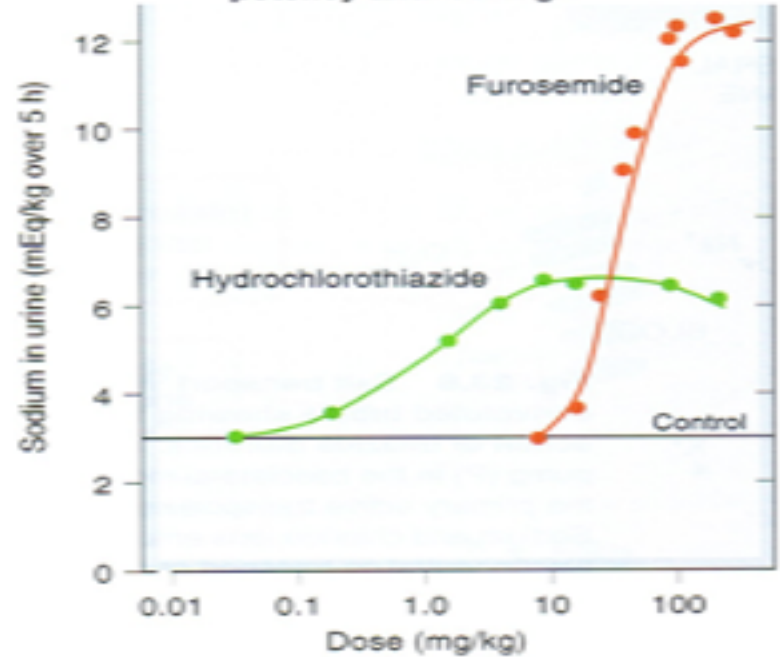


- The most potent diuretics, termed “**high ceiling diuretic**”

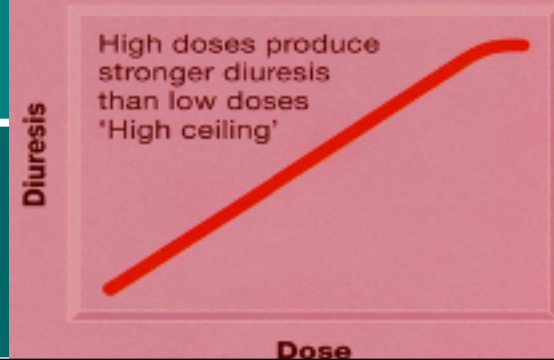
Induce expression of COX, PGE \downarrow salt transport in TAL

- \downarrow Renal vascular resistance & \uparrow renal blood flow \rightarrow PGs

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



Loop diuretics

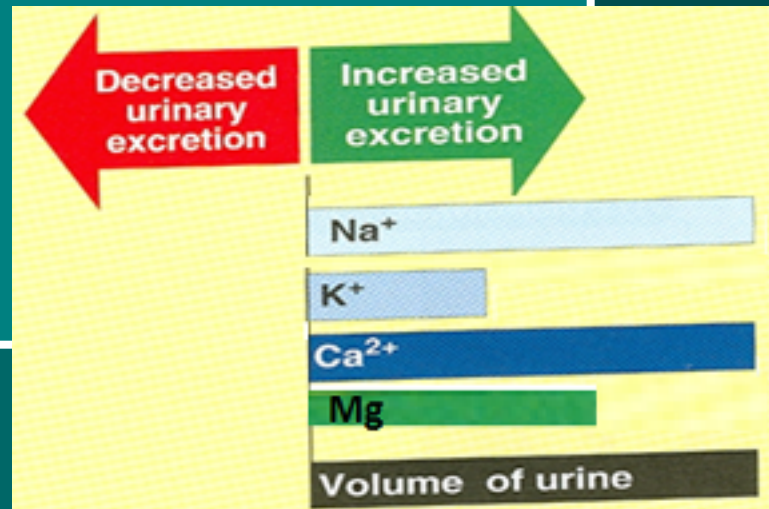
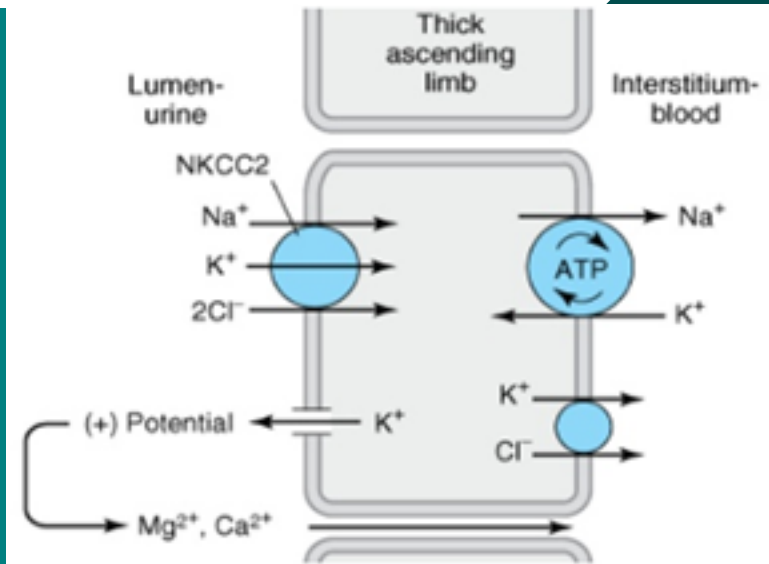


LOOP DIURETICS

PHARMACODYNAMIC EFFECTS

Increase Ca & Mg excretion

Furosemide and ethacrynic acid reduce pulmonary congestion and left ventricular filling pressures in heart failure \rightarrow \uparrow 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



Treatment for
Severe Edema

Increase Urine Volume



Treatment for
Oliguric ARF

Increase Ca Excretion



Treatment for
Hypercalcemia

Increase Venous
Capacitance



Treatment for
Pulmonary
Edema

Increase K⁺ Excretion



Acute
Treatment for
Hyperkalemia

Anion overdose



Toxicity of Br, F & I

LOOP DIURETICS

ADRS



Profound ECFV
Depletion

Hypokalemia

Hypocalcemia

Hypomagnesemia



Metabolic
Alkalosis

Ototoxicity

Hyperuricemia

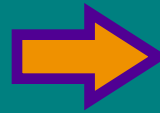
Hyperglycemia

LOOP DIURETICS

DRUG- DRUG INTERACTIONS



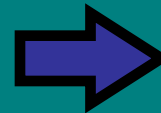
NSAIDs
Probenecid



↓ Diuretic Response

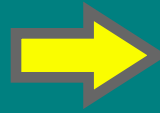


Digitalis



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