DIURETICS

PHARMACOLOGY

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Preface :

This handout is just designed by medical students in King Saud University. who take their doctors slides , modify them , and add their notes either from lectures or books.

DIURETICS

Anatomy and Physiology of Renal system

- **Remember the nephron is the most important part of the kidney that regulates fluid and electrolytes.**

- **Urine formation:**
  - Glomerular filtration (is physiologically increased in pregnant ladies and those who eat meat-rich diet)
  - Tubular reabsorption (this is the target of diuretics)
  - Tubular secretion

Everyday:-
✓ **180 L is filtered but only about 2 L are excreted.**

- **How could urine output (volume) be increased ?**
  ↑ Glomerular filtration + ↓ Tubular reabsorption

- **Purpose of Using Diuretics :**

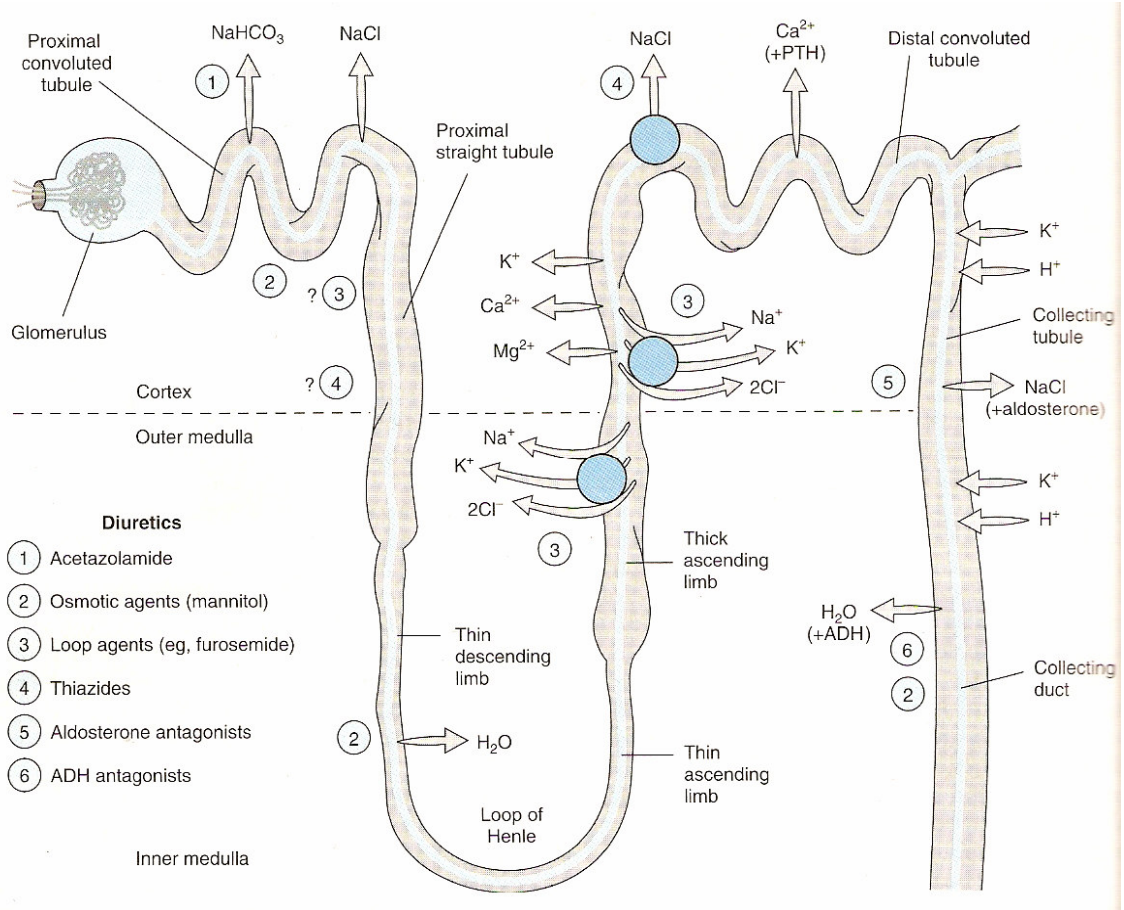
  ✓ To maintain *urine volume* (e.g.: renal failure)

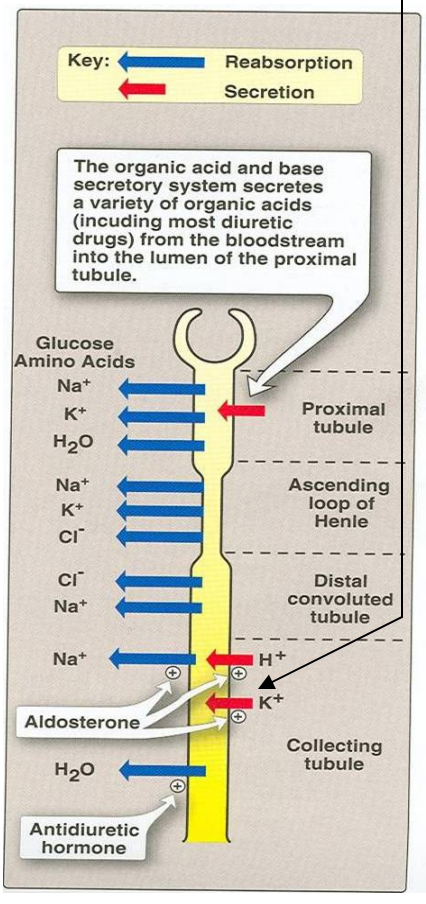
  ✓ To mobilize *edema* fluid (e.g.: heart failure, liver failure, nephrotic syndrome)**.**

  ✓ To control *high blood pressure*.

- **What are the renal transport mechanisms in:**
  - Proximal convoluted tubule 60-70% , *Allows acid secretion*.
  - Thick portion of ascending limb of the loop of Henle. 25%
  - *remember that the thin portion is Only permeable for water.*
  - Distal convoluted tubule 5-10%
  - Cortical collecting tubule 5% (Aldosterone and ADH)

Acid is secreted here to combine with HCO3 forming H2CO3 which dissociates into CO2 and H2O that are both readily reabsorped in contrast to HCO3 which is not reabsorped.





Classification of Diuretics

- Induce a state of increased urine flow , inhibit ion transporters that decrease reabsorption of Na^+

- The best way to classify diuretics is to look for their Site of action in the nephron :

A. Diuretics that inhibit transport in the Proximal Convoluted Tubule:

- Osmotic diuretics :
  - ✓ Mannitol
  - ✓ Sorbitol
  - ✓ Urea

- Carbonic anhydrase inhibitors :
  - ✓ Acetazolamide
  - ✓ Dorsolamide & Brinzolamide (topical)

B. Diuretics that inhibit transport in the Medullary Ascending Limb of the Loop of Henle(Loop diuretics):

- ✓ Furosemide.
- ✓ Torsemide.
- ✓ Bumetanide.
- ✓ Ethacrynic acid.

C. Diuretics that inhibit transport in the Distal Convoluted Tubule:

- ✓ Thiazides : clorothiazide , Hydrochlorthiazide (HCT)
- ✓ Thiazides like : Indapamide , Metolazone

D. Diuretics that inhibit transport in the Cortical Collecting Tubule:

- Potassium spring diuretics :
  - ✓ Spironolactone , Eplerenone
  - ✓ Triametrene
  - ✓ Amiloride.

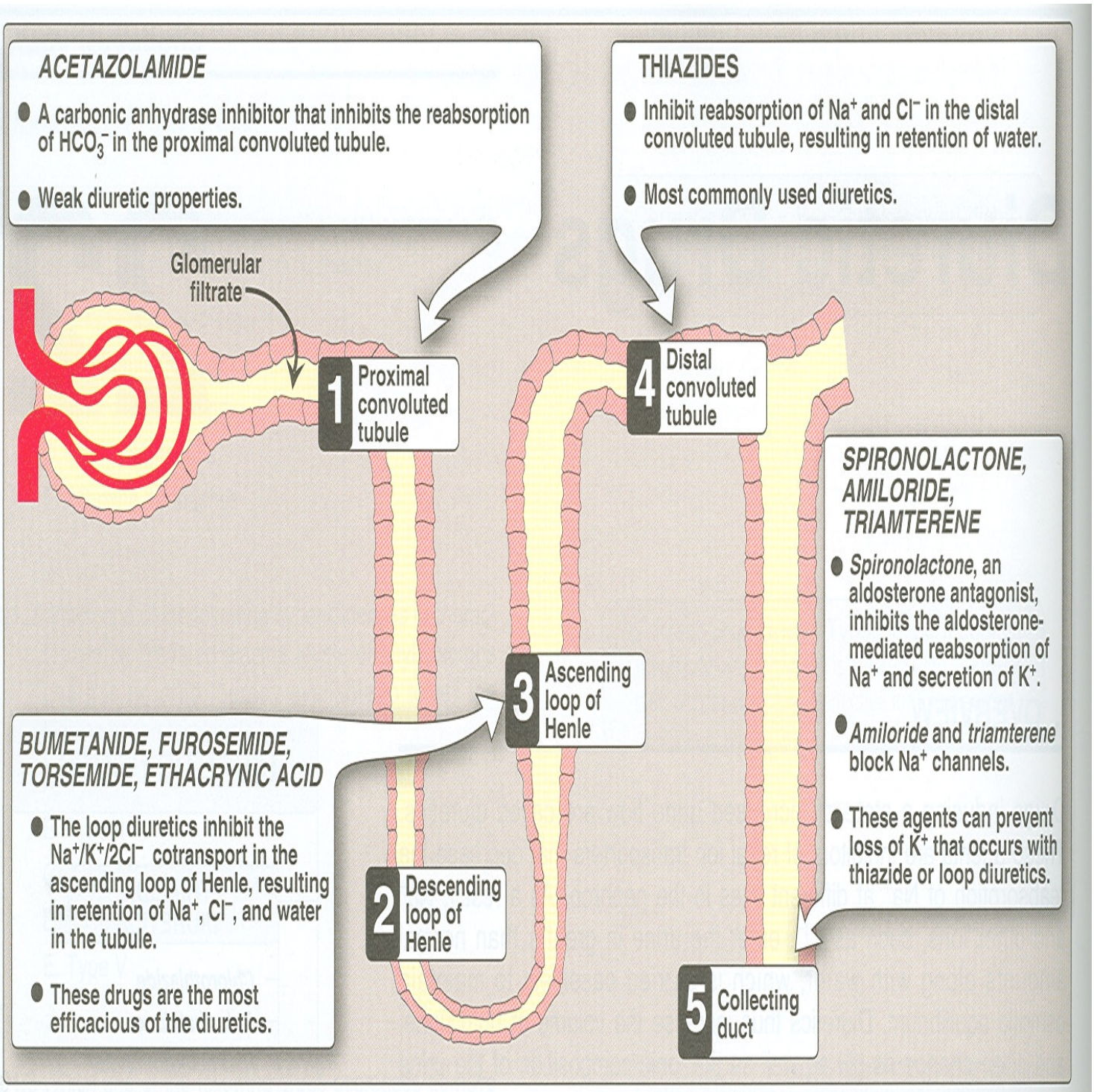


Figure 22.2
Major locations of ion and water exchange in the nephron, showing sites of action of the diuretic drugs.

- **Diuretics that inhibit transport in the Proximal Convoluted Tubule:**

1. Osmotic Diuretics (e.g. : Mannitol , sorbitol & urea)

- **MOA:** They are hydrophilic compounds that are easily filtered through the glomerulus with little reabsorption and thus increase urinary output via osmosis.

  - ✓ drawing water (oedemas also) from all body compartments and organs while circulating in the blood then they get passed in urine with minimal reabsorption.

  - ✓ ***Remember they wrok in the PCT ad thin loop of Henle which are only permeable to water so they draw water with them to be excreted.***

- **PK:** Given I.V (not orally)

mannitol orally → osmotic diarrhea

- **Indications (Clinical uses):**
  - to decrease intracranial pressure in neurological condition.
  - to decrease intraocular pressure in acute glaucoma.
  - to maintain high urine flow in acute renal failure.
  - to excrete large pigments loads to the kidney as in hemolysis and rhabdomyolysis.

- **Adverse Reactions:**
  - Extracellular water expansion (edema) and dehydration.
  - Hypernatremia due to loss more water than sodium.
  - can complicate heart failure and produce pulmonary edema.
  - Headache, nausea & vomiting are also observed.

✓ ***It is contra-indicated in cases of anurea because patients can not excrete ANY volumes of urine which means the fluids drained by these diuretics will remain unexcreted in the kidney***

2. Carbonic Anhydrase Inhibitors :

Acetazolamide: is the prototype of this group.

✓ It is sulfonamide without antibacterial activity.

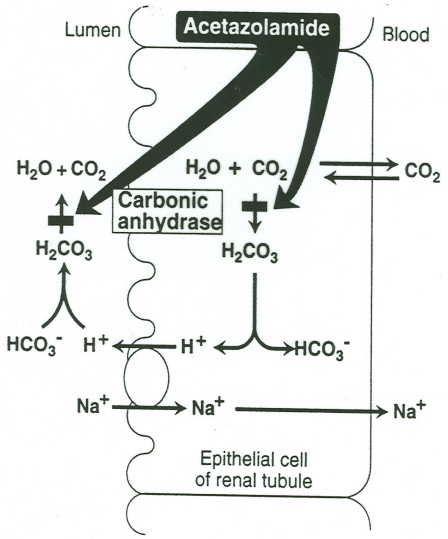


Figure 23.4
Role of carbonic anhydrase in sodium retention by epithelial cells of renal tubule.

- **MOA** :

- inhibit carbonic anhydrase in the proximal tubule

  ✓ the enzyme catalyzes the reaction of CO_2 & H_2O→ H_2CO_3 then ionizes to H^+ & HCO_3^-

- so:

  1. the exchange of Na^+ for H^+ is inhibited by acetazolamide

  2. the retention of HCO_3^- in the lumen → increase urine PH (alkalization)

  3. loss of HCO_3^- → hyperchloremic metabolic acidosis

HCO_3^- = bicarbonate

Acetazolamide increases urinary secretion of Na+ , K+ , Ca+ & HCO3 & water.

Compensatory mechanism :-

✓ Enhancement of Reabsorption of NaCl in tubules (other than the PCT) of the kidney due to depletion of HCO3- in the body which reduces the efficacy of Acetazolamides.

- **Clinical Uses :**

  - Why Acetazolamide is not used as a diuretic ?

  ✓ Because of its extensive compensatory mechanisms.

a) Glaucoma Mechanism?

✓ Inhibit HCO_3^- secretion from blood into aqueous humor in (ciliary body of the eye) -(opposite the direction in PCT) ---> decrease intraocular pressure

✓ topical drug, as **dorzolamide & Brinzolamide** do not cause systemic effects (used as eye drops , local , & to avoid toxicity)

b) Alkalization of urine

to excrete uric acid & cystine.

c) metabolic alkalosis

✓ is due to excessive use of diuretics (loop or thiazides) in patient with sever heart failure or due to respiratory acidosis.

d) **Acute mountain sickness** (dizziness , insomnia , headache & nausea) : by decrease PH and the amount of CSF .. like glaucoma mechanism

✓ Prevention of pulmonary & cerebral edema

✓ It is given 5 days before the ascent.

e) Other Uses As :

- Epilepsy as adjuvant treatment.
- Severe hyperphosphatemia.
- Hypokalemic periodic paralysis.

- What are the differences between **acetazolamide** and **dorzolamide** or **brinzolamide? Oral vs Topical**

✓ (**acetazolamide** taken *orally* once daily , ***dorzolamide or brinzolamide*** taken *topically* in the eye).

- **Adverse effects:**

1. hyperchloremic metabolic acidosis.
2. renal K^+ depletion (wasting).
3. renal stone formation (due to phosphaturia & hypercalciuria , Ca^{+2} salts are insoluble in alkaline urine).
4. parethesia & drowsiness..
5. Hypersensitivity.

- The drug is absolutely **contraindicated** in hepatic cirrhosis as it can lead to *decrease excretion of NH_4^+ --> hepatic encephalopathy*

- **Diuretics that inhibit transport in the Medullary Ascending Limb of the Loop of Henle(Loop diuretics):**

Called High-Ceiling Diuretics

e.g. :

- ✓ **Furosemide (LasixR).**
- ✓ **Torsemide.**
- ✓ **Bumetanide.**
- ✓ **Ethacrynic acid.**

- Furosemide ,Torsemide & Bumetanide are sulfonamide derivatives.
- ethacrynic acid is a phenoxy acetic acid derivative containing ketone & methylene group.
- organic mercurial group not used because of high toxicity.

o Pharmacokinetics:

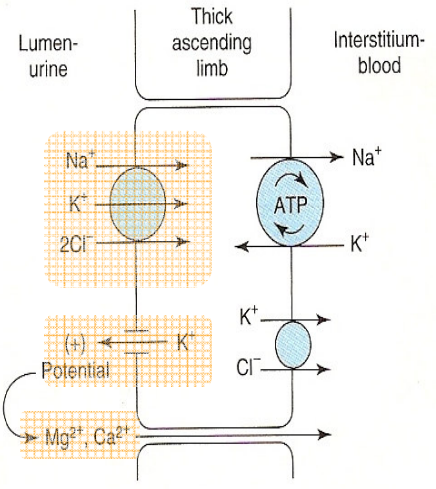
- given orally or parenterally with duration of action from 1 – 4 hours.
- eliminated through kidney (P.C.T) proximal convoluted tubules

so , their secretion is reduced by simultaneous administration of :

- ✓ NSAID's (especially in patients with nephritic syndrome or hepatic cirrhosis).
- ✓ or probenecid

o Mechanism of Action :

A. reduce the reabsorption of NaCl in the ascending limb of the loop of Henle by inhibiting the transport system $Na^+/K^+/2Cl^-$ & also increase Ca^{+2} & Mg^{+2} excretion in urine



how ?

excess K^+ accumulation inside the cell , result in back diffusion of K^+ into tubular lumen and development of lumen-positive potential , this potential provides the driving force for reabsorbtion of **Mg^{+2}** & **Ca^{+2}** paracellularly.

So , when there is blocking of $Na^+/K^+/2Cl^-$ => <u>increase K^+ , Mg^{+2} & Ca^{+2} excretion additional to NaCl excretion</u>

B. increase prostaglandin synthesis that have a role in their diuretic action , also they have potent pulmonary vasodilating effects (PGs).

C. increase renal blood flow by direct action on B.V causing decrease in renal vascular resistance (effective in patients with poor renal function)

- **Furosemide** => ↑ renal blood flow.
- **Furosemide and Ethacrynic acid** => reduce pulmonary congestion & left ventricular filling pressure in heart failure.
- Mainly inhibits Cl^- reabsorption.

What are the compensatory mechanisms?

1. delivary of Cl^- to the distal and collecting tubules which leads to the activation of NaCl pump that will reabsorb Na^+ and Cl^-
2. Aldosterone release due to increased Na^+ in urine.

✓ Generally, the use of loop diuretic causes the followings :-
- **Hypokalemia** + **Hypochloremia** + **alkalosis** + **hypocalcemia** + **hypercalceuria** , all are adverse effects .

Why furosemide is a better diuretic than acetazolamide despite the fact that only 25% of the reabsorption occurs at the ascending loop of Henle?

✓ **Because the compensatory mechanism of Furosmide is way less than those of acetazolamide.**

○ Therapeutic Uses:

1. Edema (Like What?) : acute pulmonary edema (decrease pulmonary congestion).
2. acute heart failure (they have a rapid onset of action).
3. Acute renal failure (increase rate of urine flow & K^+ excretion).
4. Acute hypercalcemia.
5. Hyperkalemia as: they enhance urinary excretion of K^+.
6. Anion overdose: they treat toxic ingestions of bromide-fluoride & iodide.

- **Side effects:**

1. **hypokalemic metabolic alkalosis :** by enhancing renal secretion of K^+ & H^+ .

2. **Ototoxicity : Reversible dose-related hearing loss.**
   - ✓ ethacrynic acid is the most likely to cause deafness
   - ✓ Aminoglycoside should not be use with loop diuretics.

3. **hypersensitivity reactions : Allergic reactions.**
   - ✓ Because it contains sulfate in its chemical structure.
   - ✓ Less with ethacrynic acid.

4. **acute Hypovolemia & dehydration** : *postural hypotension* , shock , cardiac arrhythmias.

5. **with hyponatremia.**

6. **Hypocalcemia & hypomagnesemia.**

7. **hyperuricemia (precipitation of gout)** : How? By ↑ *reabsorbtion of uric acid in PCT* . is avoided by using lower doses.

- **Drug interactions: NSAIDs (contraindicated).**

What are the *differences* between furosemide and torsemide?

1. **Furosmide is less potent and has slower onset (2.5 hours) than torsemide (1 hour).**

2. **Toresmide has characteristic fast onset of action when taken orally which *reduces the need of Furosmide IV injections* and help avoid its Adverse effects.**

What are the *advantages* of bumetanide over that of furosemide?

1. **It is the most potent diuretic that is used for a refractory oedema.**
2. **Has fast onset and fast offset.**

✓While Furosomide :-Slow onset and slow offset with lower efficacy than bumetanide

- **Dosage of loop diuretics:**

Furosemide	**20-80 mg**
Torsemide(non-popular)	**2.5-20 mg**
Bumetanide	**0.5-2.0 mg**

D. Diuretics that Inhibit Transport in the Distal Convoluted Tubule (e.g.: Thiazides and Thiazide-like)

✓ Thiazides : clorothiazide , Hydrochlorthiazide (HCT)
✓ Thiazides like : Indapamide , Metolazone

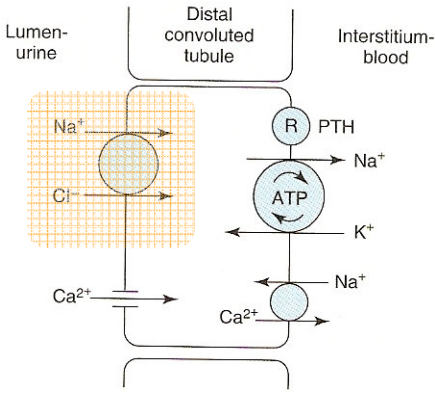
- these diuretics are mainly (NATURETICS)

○ History of Thiazides

✓ Thiazides were thought to be CA inhibitors but when they were tested, people realized that Thiazides were even more potent than CA inhibitors without even inhibting CA.

○ Chemistry & PK:

- They are sulfonamide derivative, are related in structure to the carbonic anhydrase inhibitor.
- They affect the distal tubule.
- <u>All are administered orally.</u>
- <u>Chlorothiazide is given parenterally.</u>
- They are secreted by the organic acid secretory system in PCT competing with uric acid secretion.



○ Pharmacodynamics:

◦ <u>Mechanism of action:</u> <u>-MCQ-</u>

- They inhibit Na^+/Cl^- reabsorption from the distal convoluted tubule by blocking Na^+/Cl^- cotransporter.
- <u>They enhance Ca^{++} reabsorption from DCT.</u>
- Their action depends on renal PG production.
- <u>K^+ depletion</u> because more K^+ is exchanged for Na^+.
- Decrease urinary Ca^{++} excretion by promoting reabsorption of Ca^{++}.
- Reduce peripheral vascular resistance.

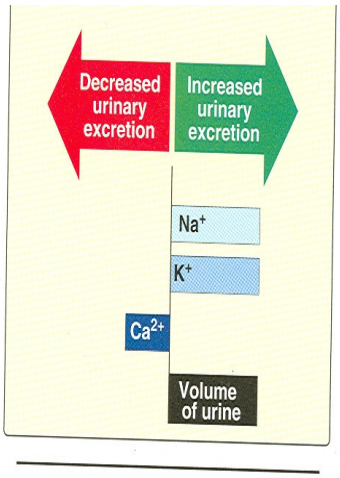


Figure 22.4
Relative changes in the composition of urine induced by thiazide diuretics.

What are the compensatory mechanisms?

1. Aldosterone Release (like furosmide so they will lead to hypokalemia and Alkalosis).
2. ADH release which reabsorps H_2O but not Na^+ causing hyponatremia more pronounced than that with Furosmide.

○ Indications: -MCQ-

1. **Hypertension**: mild to moderate essential hypertension (↓ blood volume)
   - ✓ (Hydrochlorthiazide, Indapamide) used more than loop diuretics.
2. **Congestive heart failure**: (mild to moderate)
3. **Renal impairment**: e.g. nephritic syndrome.
4. **Nephrolitiasis due to idiopathic Hypercalciuria or hypocalcemia** : it is beneficial for patient with Ca^{++} oxalate stones in urinary bladder.
5. **Diabetes insipidus**: because it has the ability to produce hyperosmolar urine, Thiazides can substitute for ADH in the treatment of nephrogenic diabetes insipidus.
6. **Refractory Edema**: together with the Loop diuretics (e.g. Metolazone).

○ Adverse Effects: -MCQ-

1- Hypokalemic metabolic alkalosis:
   - ✓ Hypokalemic can predispose patients on digitalis to ventricular arrythmias we can treatment the case by administration of **Spironolactone, Triametrene.**

2- Hyperuricemia →gout attack
3- Hypercalcemia.
4- Hyperglycemia (impaired glucose tolerance).
5- Hypersensitivity: bone marrow suppression vasculitis, interstatial nephritis.
6- Hyperlipidemia,↑ LDL , ↑serum cholesterol.
7- Hyponatremia .
8- Other toxicities: Weakness, fatigability & parathesias.

- **SIDE EFFECTS:**

- **How do thiazides differ from furosemide?**

1. **Thiazides caused more hyponatremia. WHY?**

✓ Because they cause secretion of ADH leading to Water but not Na+ retention.

2. **Thiazides don't cause ototoxcity while Furosmide causes it at high doses.**

3. **Thiazides cause hypercalcemia and hyperglycemia and hypertriacylglyceremia while Furosmide causees hypocalcemia and Hypertriacylglyceremia with little effect on blood glucose level**

- *They both however cause hypokalemia and alkalosis with Aldosterone release.*

(IMP.)The increased excretion of Na+ is Less than that of water because It leads to little ADH release Stimulation.

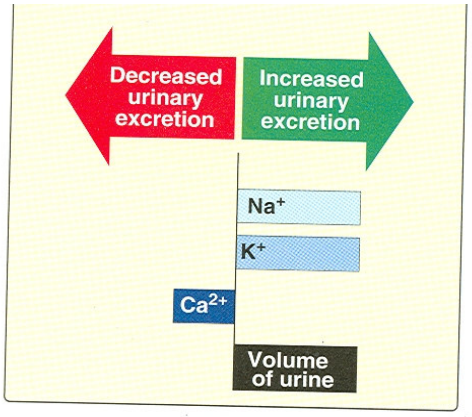


Figure 22.4
Relative changes in the composition of urine induced by thiazide diuretics.

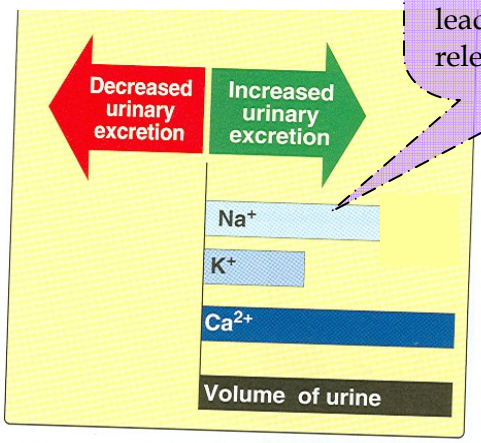


Figure 22.6
Relative changes in the composition of urine induced by loop diuretics.

- **<u>Contraindications:</u>**
  1- Hepatic cirrhosis
  2- Renal failure.

Hydrochlorothiazide:

- It has far less ability to inhibit carbonic anhydrase as compared to Chlorothiazide.
- It is more potent.

Longer Acting Drug:

1- Chlorthalidone:

- as hyperchlorothizide with longer duration of action → treatment of hypertension.

2- Metolazone:

- It is more potent than Thiazides .
- It causes Na^+ excretion in advanced renal failure .

3- Indapamide: -MCQ-

- Lipid soluble.
- Non-thiazide diuretics.
- Long $t_{1/2}$ at low dose.
- It has good antihypertensive action with minimal diuretic.
- It is metabolized & excreted in GIT & kidney
- It is used in renal failure to stimulate additional diuretics on top of that achieved by loop diuretics.

How does indapamide differ from thiazides?

1. **indapamide** is a sulfer-containing compound which is not a thiazide derivative.
2. **Indapamide is both a diuretic and a vasodilator which makes it sutiable for HTN and stroke treatment even if it causes hypokalemia and tachycarida.**

What is metolazone?

- ✓ **Sulfanamides but Not a thiazide though qualitavely similar in action to thiazides.**

Diuretics that inhibit transport in the Cortical Collecting Tubule (e.g. potassium sparing diuretics)

- ✓ Spironolactone , Eplerenone
- ✓ Triametrene
- ✓ Amiloride.

Why does the natriuretic activity of this group has limited range but clinically very important?

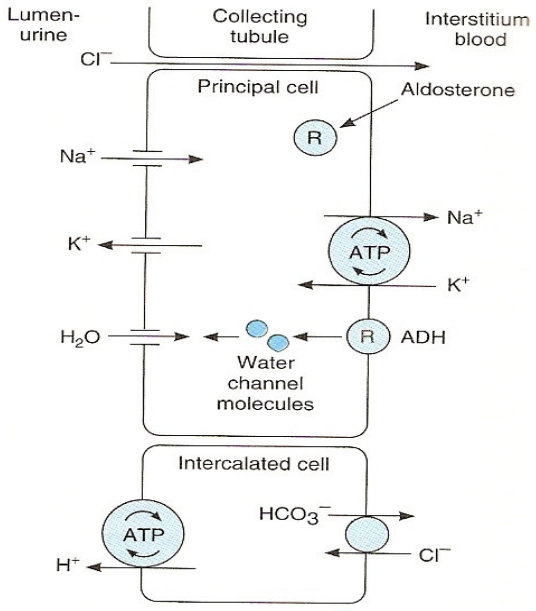
1- it is the only group that actually compensates for K^+ loss. While others cause hypokalemia.

2- it is used to treat diseases that are characterized by elevated Aldosteron level.

- **Classification of Potassium Sparing Diuretics:**

A) *Direct* antagonist of mineralocorticoid receptors (Aldosterone Antagonists (e.g spironolactone(AldactoneR) & Eplerenone)

B) *Indirect* via inhibition of Na^+ flux in luminal membrane therefore inhibiting K^+ secretion (e.g. Triametrene, Amiloride)



A) *DIRECT ANTAGONIST* (SPIRONOLACTONE & EPLERENONE) :

○ Mechanism of action :

- Aldosterone enhance K^+ secretion by increasing Na^+/K^+ ATPase and the same for H^+ . Spironolactone binds to mineralocorticoid receptors this leads to inhibition of secretion of K^+ and acid and stimulation of Na^+ and H_2O excretion.

○ Pharmacokinetics:

- Spironolactone is completely absorbed orally, metabolized to active metabolite which has the mineralo-corticoid blocking activity.
- Spironolactone induce cytochrome P450.
- Synthetic steroids.

○ Therapeutic uses:

○

1- Diuretics: they are used with thiazide & loop diuretics to prevent K^+ excretion.

2- Hyperaldosteronism:

I. **Primary :** (conn's syndrome , ectopic ACTH production)
II. **Secondary :**
   - ✓ Congestive heart failure "CHF" (because heart failure causes the activation of Sympathetic Nervous system leading to Renin-Angiotensin-Aldosteron activation).
   - ✓ hepatic cirrhosis
   - ✓ nephritic syndrome

3- To overcome the hypokalemic action of diuretics

4- Hirsutism

► **Keep in mind that Aldosterone not only retains Na^+ and H2O but also excretes acids and K^+. Therefore, cushing syndrom(↑ed Ald) is characterized by hypokalemia and hypernatremia.**

- **Toxicity:**

1. Hyperkalemia , which increases in :
   - ✓ Increased diet intake (e.g. dates).
   - ✓ usage of Aldosteron inhibitors such as ACEI, Angiotensin antagonists, β-blockers.
   - ✓ Renal Diseases .

2. Hyperchloremic metabolic acidosis (also caused by Acetazolamide toxicity).

3. Anti-Androgenic effects causing Endocrine abnormalities as Gynecomastia in male & menstrual disturbance in female (hormonal activity).

Keep in mind that in cases of alkalosis (caused by overdose of Loop or thiazides diuretics, NH3 will be excessively formed and then translocated to the brain crossing the BBB which leads to neurologic symptoms while Acidosis causes formation of the polar molecule NH_4^+ which does not cross BBB. So above all, Alkalosis is by far more dangerous than acidosis.

B) *INDIRECT ACTING* (TRIAMETRENE & AMILORIDE) :

- **Mechanism of action:**

- They interfere directly with Na^+ entry through sodium selective ion channels in the collecting tubules. Since K^+ secretion is couple with Na entry. Therefore their usage → K^+ sparing.

- **Therapeutic uses:**
  - ✓ With thiazides & loop diuretics.

- **Toxicity:**
  - Leg cramps.
  - ↑ Blood urea nitrogen, uric acid & K^+ .
  - **Triametrene** is poorly soluble → precipitation in urine → ***kidney stone.***
  - Acute renal failure if **Triametrene** is used with **indomethacin.**

- **Contraindications:**
  - Chronic renal insufficiency.

Table 15–2. Electrolyte changes produced by diuretic drugs.

Drug Group	Urine			Body pH
	NaCl	$NaHCO_3$	K^+	
Carbonic anhydrase inhibitors	↑	↑↑↑	↑	Acidosis
Loop diuretics	↑↑↑↑	—	↑	Alkalosis
Thiazides	↑↑	—	↑	Alkalosis
Potassium-sparing diuretics	↑	—	↓	Acidosis

Diuretics Combination preparations :

Examples:

- **DyazideR =** Triametrene 50 mg + Hydrochlorohtiazide (HCT) 25 mg
- **AldactazideR=** Spironolactone 25 mg + HCT 25 mg
- **ModureticR =** Amiloride 5 mg + HCT 50 mg

✓ ***Why? To overcome effects of hypokalemia and enhance the diuretic activity.***

Note : thiazides should always be there.

Contraindications: Oral K^+ administration

Choose the ONE best answer.

22.1 An elderly patient with a history of heart disease and who is having difficulty breathing is brought into the emergency room. Examination reveals that she has pulmonary edema. Which of the following treatments is indicated?

A. Spironolactone
B. Furosemide
C. Acetazolamide
D. Chlorthalidone
E. Hydrochlorothiazide

22.2 A group of college students is planning a mountain climbing trip to the Andes. Which of the following drugs would be appropriate for them to take to prevent mountain sickness?

A. A thiazide diuretic
B. An anti-cholinergic
C. A carbonic anhydrase inhibitor
D. A loop diuretic
E. A β-blocker

22.3 An alcoholic male has developed hepatic cirrhosis. In order to control the ascites and edema, he is prescribed which one of the following?

A. Hydrochlorothiazide
B. Acetazolamide
C. Spironolactone
D. Furosemide
E. Chlorthalidone

2.4 A 55-year-old male with kidney stones has been placed on a diuretic to decrease calcium excretion. However, after a few weeks, he develops an attack of gout. Which diuretic was he taking?

A. Furosemide
B. Hydrochlorothiazide
C. Spironolactone
D. Triamterene

2.5 An 75-year-old woman with hypertension is being treated with a thiazide. Her blood pressure responds and reads at 120/76 mm Hg. After several months on the medication, she complains of being tired and weak. An analysis of the blood indicates low values for which of the following ?

A. Calcium
B. Uric acid
C. Potassium
D. Sodium
E. Glucose

1. A 70-year-old man is admitted with a history of heart failure and an acute left ventricular myocardial infarction. He has severe pulmonary edema. Which of the following drugs is LEAST likely to prove useful in the treatment of acute pulmonary edema?
   (A) Bumetanide
   (B) Ethacrynic acid
   (C) Furosemide
   (D) Hydrochlorothiazide
   (E) Torsemide
2. A 50-year-old man has a history of frequent episodes of renal colic with high-calcium renal stones. The most useful agent in the treatment of recurrent calcium stones is
   (A) Mannitol
   (B) Furosemide
   (C) Spironolactone
   (D) Hydrochlorothiazide
   (E) Acetazolamide
3. When used chronically to treat hypertension, thiazide diuretics have all of the following properties or effects EXCEPT
   (A) Reduce blood volume or vascular resistance, or both
   (B) Have maximal effects on blood pressure at doses below the maximal diuretic dose
   (C) May cause an elevation of plasma uric acid and triglyceride levels
   (D) Decrease the urinary excretion of calcium
   (E) Cause ototoxicity
4. Which of the following drugs is correctly associated with its site of action and maximal diuretic efficacy?
   (A) Thiazides—distal convoluted tubule—10% of filtered Na^+
   (B) Spironolactone—proximal convoluted tubule—40%
   (C) Bumetanide—thick ascending limb—15%
   (D) Metolazone—collecting tubule—2%
   (E) All of the above
5. A patient with long-standing diabetic renal disease and hyperkalemia and recent-onset congestive heart failure requires a diuretic. Which of the following agents would be LEAST harmful in a patient with severe hyperkalemia?
   (A) Amiloride
   (B) Hydrochlorothiazide
   (C) Losartan
   (D) Spironolactone
   (E) Triamterene
6. Which of the following diuretics would be most useful in a patient with cerebral edema?
   (A) Acetazolamide
   (B) Amiloride
   (C) Ethacrynic acid
   (D) Furosemide
   (E) Mannitol
7. Which of the following is not a complication of therapy with thiazide diuretics?
   (A) Hypercalciuria
   (B) Hyponatremia
   (C) Hypokalemia
   (D) Hyperuricemia
   (E) Metabolic alkalosis
8. Which of the following therapies would be most useful in the management of severe hypercalcemia?
   (A) Amiloride plus saline infusion
   (B) Furosemide plus saline infusion
   (C) Hydrochlorothiazide plus saline infusion
   (D) Mannitol plus saline infusion
   (E) Spironolactone plus saline infusion
9. A 60-year-old patient complains of paresthesias and occasional nausea associated with one of her drugs. She is found to have hyperchloremic metabolic acidosis. She is probably taking

(A) Acetazolamide for glaucoma
(B) Amiloride for edema associated with aldosteronism
(C) Furosemide for severe hypertension and congestive failure
(D) Hydrochlorothiazide for hypertension
(E) Mannitol for cerebral edema

10. A 70-year-old woman is admitted to the emergency room because of a "fainting spell" at home. She appears to have suffered no trauma from her fall, but her blood pressure is 110/60 when lying down and 60/40 when she sits up. Neurologic examination and an ECG are within normal limits when she is lying down. Questioning reveals that she has recently started taking "water pills" (diuretics) for a heart condition. Which of the following drugs is the most likely cause of her fainting spell?
(A) Acetazolamide
(B) Amiloride
(C) Furosemide
(D) Hydrochlorothiazide
(E) Spironolactone

11. A 55-year-old patient with severe post-hepatitis cirrhosis is started on a diuretic for another condition. Two days later he is found in a coma. The drug most likely to cause coma in a patient with cirrhosis is
(A) Acetazolamide
(B) Amiloride
(C) Furosemide
(D) Hydrochlorothiazide
(E) Spironolactone

12. A drug that has its major effect in the distal convoluted tubule is
(A) Acetazolamide
(B) Amiloride
(C) Demeclocycline
(D) Desmopressin
(E) Ethacrynic acid
(F) Furosemide
(G) Metolazone
(H) Mannitol
(I) Spironolactone
(J) Triamterene

13. A drug that increases the formation of dilute urine in water-loaded subjects and is used to treat SIADH is
(A) Acetazolamide
(B) Amiloride
(C) Demeclocycline
(D) Desmopressin
(E) Ethacrynic acid
(F) Furosemide
(G) Metolazone
(H) Mannitol
(I) Spironolactone
(J) Triamterene

14. A drug that is useful in glaucoma and high-altitude sickness is
(A) Acetazolamide
(B) Amiloride
(C) Demeclocycline
(D) Desmopressin
(E) Ethacrynic acid
(F) Furosemide
(G) Metolazone
(H) Mannitol
(I) Spironolactone
(J) Triamterene

✓ **B**
✓ **C**
✓ **C**
✓ **B**
✓ **C** – remember that a low levels of K^+ cause weakness . Also that the answer is not Na^+ because it is an acute effect that will not wait until several months to show up and because it is the required (desired) effect.

✓ **D**
✓ **D**
✓ **E**
✓ **A**
✓ **B**
✓ **E**
✓ **A**
✓ **B**

✓ **B**
✓ **C**
✓ **C**
✓ **C**
✓ **H**
✓ **A**