Practical Pharmacology

Lab 2

Diuretics

Drug Samples

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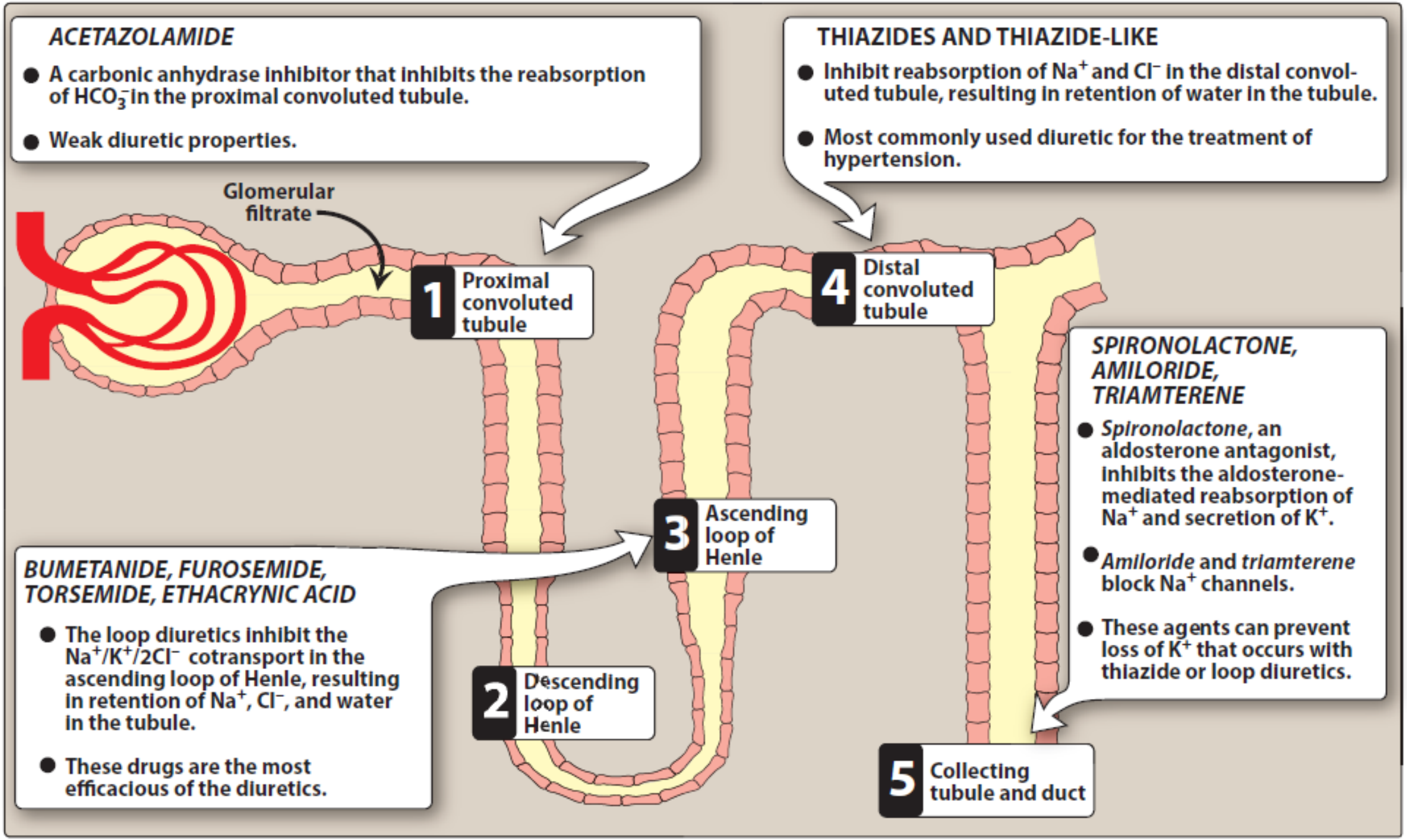
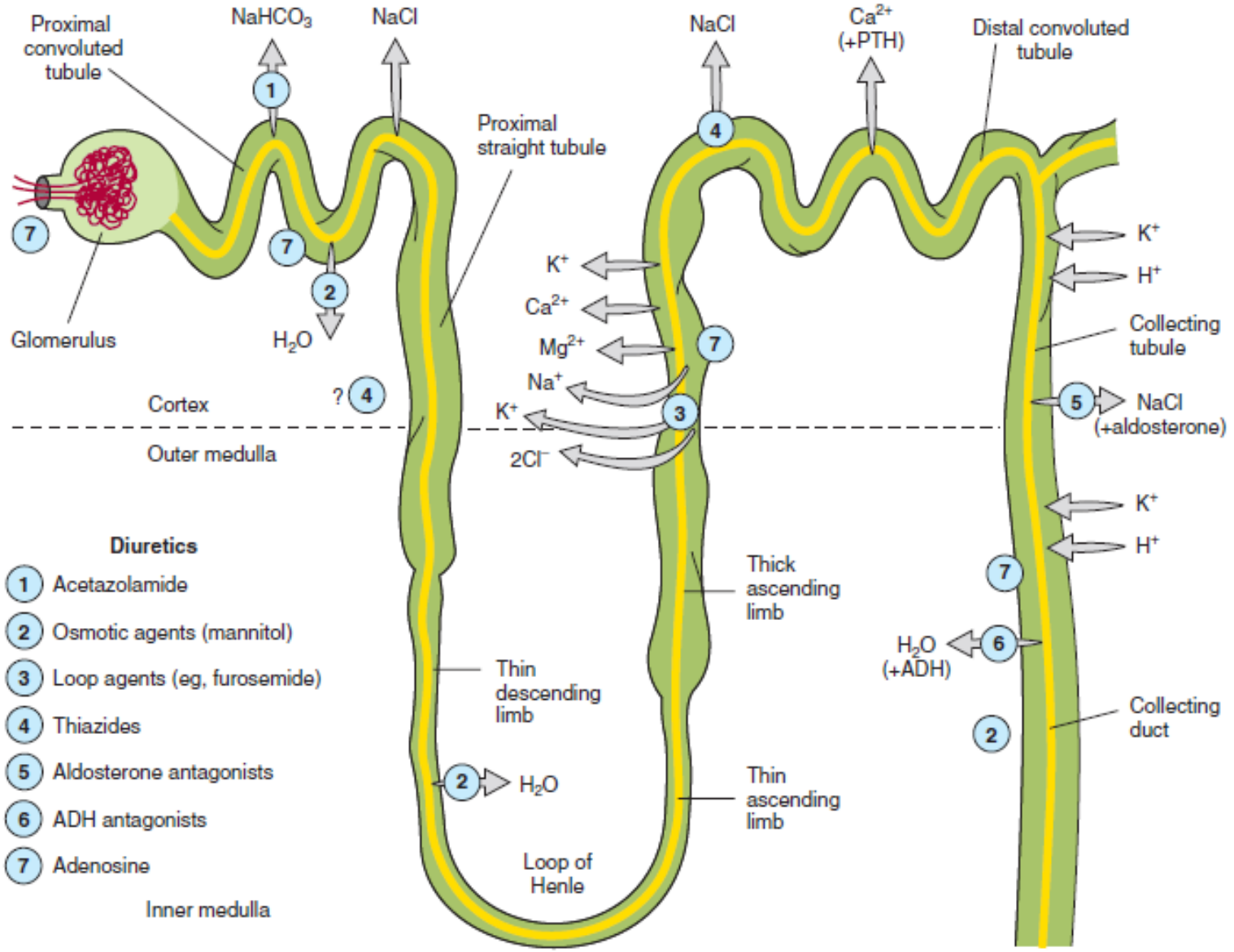
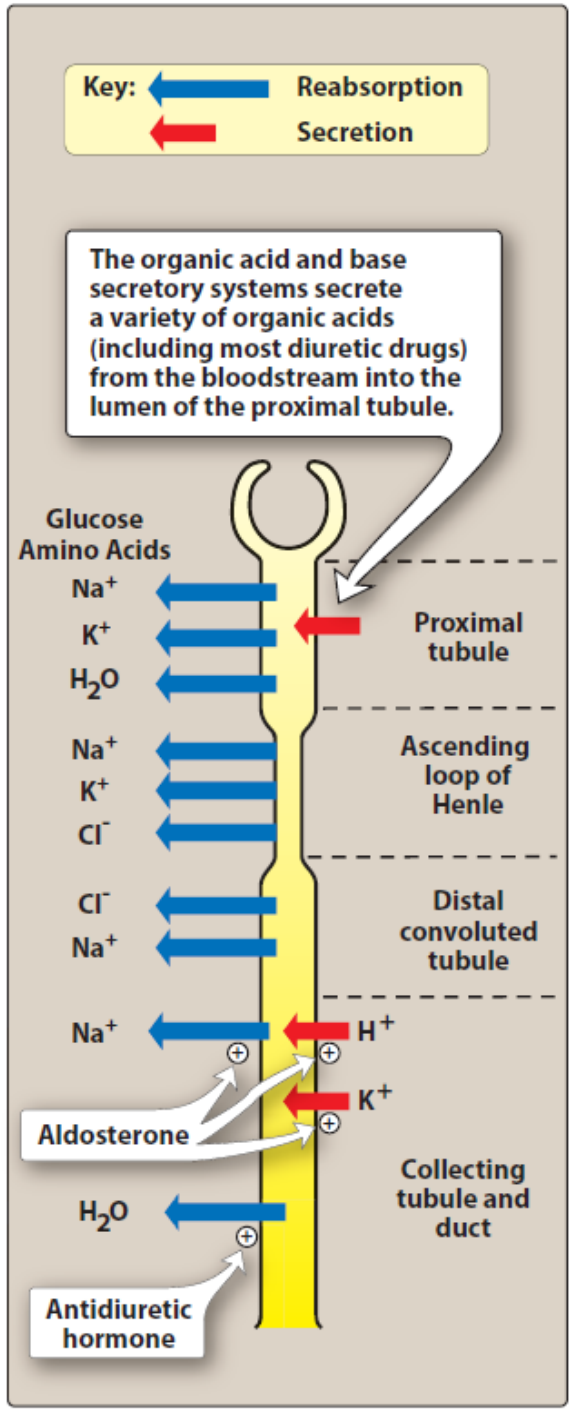
DIURETICS

- "***Diuretics***" are agents that increase urine volume.
- "***Natriuretic***" causes an increase in renal sodium excretion.
- "***Aquaretic***" increases excretion of solute-free water.
- Because natriuretic almost always also increase water excretion, they are usually called diuretics. So, most **diuretics comprise both *natriuretic* plus *aquaretic***


ACETAZOLAMIDE
A carbonic anhydrase inhibitor that inhibits the reabsorption of HCO_3^- in the proximal convoluted tubule.
Weak diuretic properties.
THIAZIDES AND THIAZIDE-LIKE
Inhibit reabsorption of Na^+ and Cl^- in the distal convoluted tubule, resulting in retention of water in the tubule.
Most commonly used diuretic for the treatment of hypertension.
Glomerular filtrate
1 Proximal convoluted tubule
2 Descending loop of Henle
3 Ascending loop of Henle
4 Distal convoluted tubule
5 Collecting tubule and duct
BUMETANIDE, FUROSEMIDE, TORSEMIDE, ETHACRYNIC ACID
The loop diuretics inhibit the $Na^+/K^+/2Cl^-$ cotransport in the ascending loop of Henle, resulting in retention of Na^+, Cl^-, and water in the tubule.
These drugs are the most efficacious of the diuretics.
SPIRONOLACTONE, AMILORIDE, TRIAMTERENE
Spironolactone, an aldosterone antagonist, inhibits the aldosterone-mediated reabsorption of Na^+ and secretion of K^+.
Amiloride and triamterene block Na^+ channels.
These agents can prevent loss of K^+ that occurs with thiazide or loop diuretics.

Sites of transport of solutes and water along the nephron



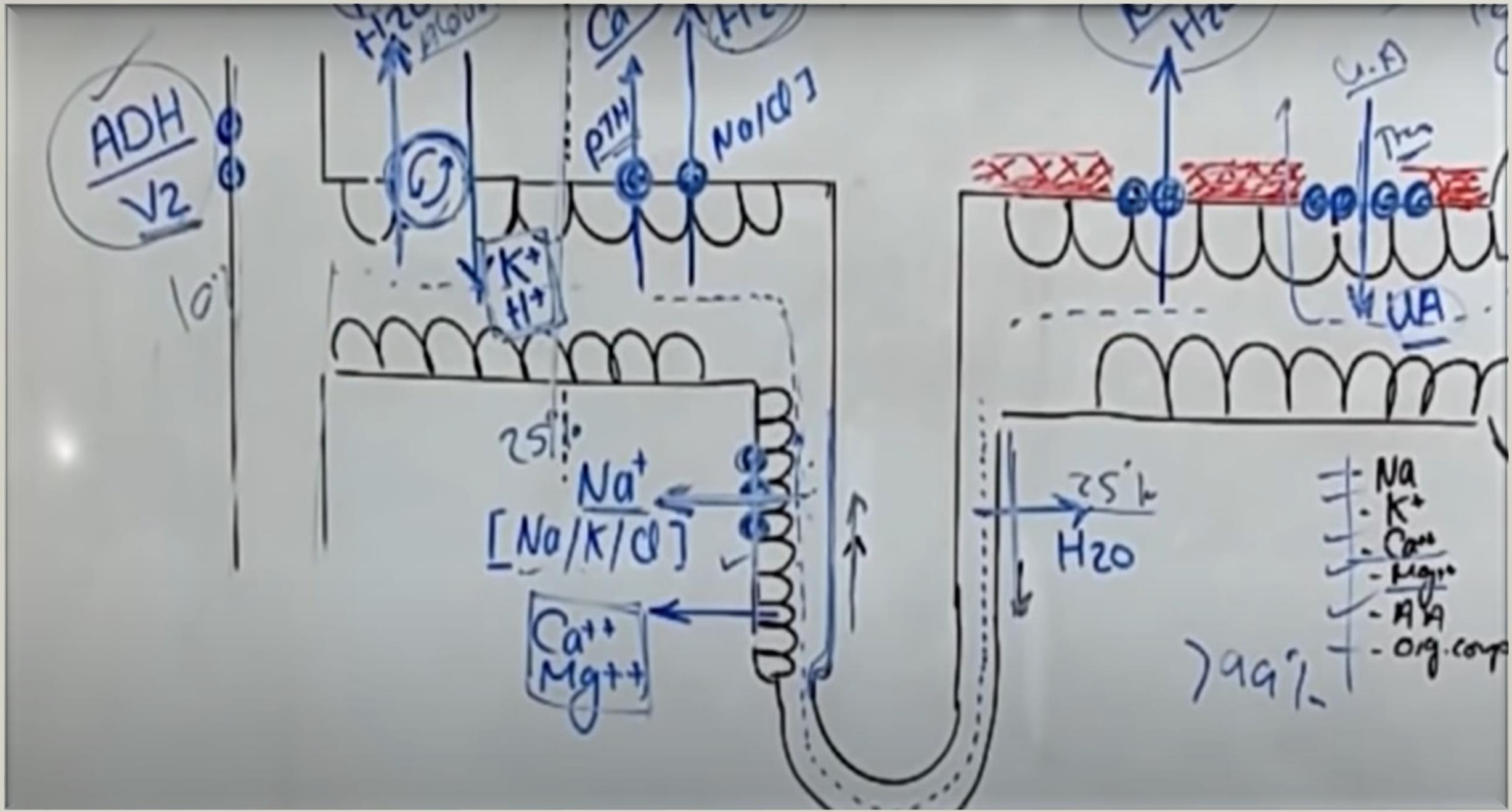


CLASSIFICATION OF DIURETICS

High efficacy: excretes 15-25 % of the filtrated sodium as ***loop diuretics***.

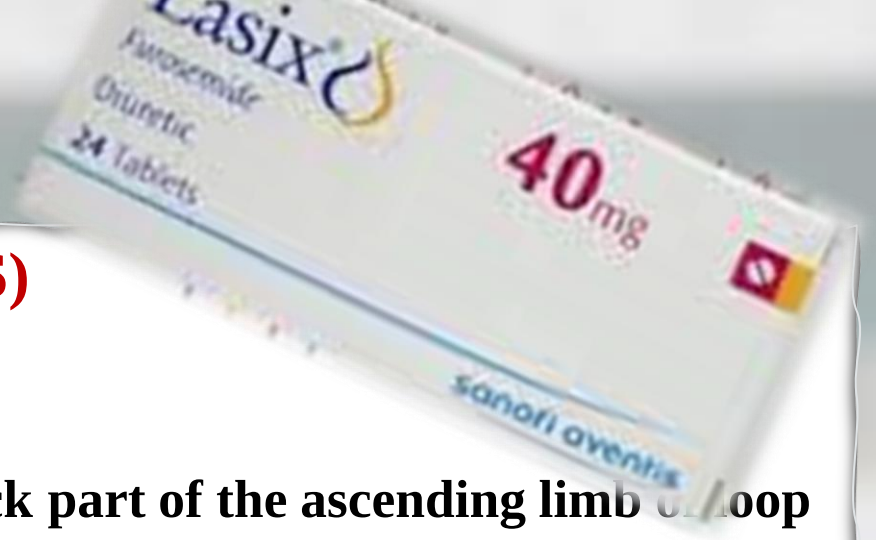
Moderate efficacy: excretes 5-10 % of the filtrated sodium as ***thiazides***.

Low efficacy: excretes less than 5 % of the filtrated sodium as ***K-sparing diuretics and osmotic*** diuretics.


ADH
V2
10%
H2O
Ca
PTH
NaOH
K+
H+
25%
Na+
[Na/K/Cl]
Ca++
Mg++
H2
U.A
UA
25%
H2O
- Na
- K+
- Ca++
- Mg++
- AA
- Org. comp
>99%

Diuretics
Drug Samples

Lasix "Loop diuretics"



- **Generic name:** furosemide **(HIGH CEILING DIURETICS)**

- **Mechanism of action:**

They act by inhibition of Na+ / K+ /2Cl- co-transport mechanism in thick part of the ascending limb of Loop of Henle. They also increase the excretion of Ca++ and Mg++.

Why furosemide is suitable in emergency Situations?

Rapid onset of action within 1 hour of oral use, peak effect within 30 min.after I.V. use with Short duration (3-6h.)

- **Side effects:**

Hypocalcemia
Hypomagnesemia

Torseretic "Loop diuretics"

- **Generic name:** torsemide

- **Mechanism of action:**

They act by inhibition of Na+ / K+ /2Cl- co-transport mechanism in thick part of the ascending limb of loop of Henle. They also increase the excretion of Ca++ and Mg++.

- **Side effects:**

- Hypokalemia: , Teratogenicity: if used during pregnancy.
Allergic Reactions

- **Uses : Acute Renal Failure , Hypertension**

- **Precaution when use with chronic case of hypertension** due to their short duration

Averothiazide "Thiazide diuretics"

- **Generic name:** hydrochlorothiazide

- **Mechanism of action:**

- They act by inhibition of Na+ / Cl- co transport mechanism in early segment of distal tubules, so they increase the
excretion of Na+ Cl-and water. They also increase the excretion of K+.
- They increase the excretion of Mg++.

- **Uses : The first choice for treatment of mild to moderate hypertension.**

✓ **Can be combined with other antihypertensive drugs in moderate to severe hypertension.**

- **Side effects:**

✓ Hypomagnesemia.
✓ Hypercalcemia.

Co-Vasotec "Thiazide diuretics"

- **Generic name:** valsartan-hydrochlorothiazide

- **Mechanism of action:**

➢ **Hydrochlorothiazide**

They act by inhibition of Na+ / Cl co transport mechanism in early segment of distal tubules, so they increase the excretion of Na+ Cl-and water. They also increase the excretion of K+ and They increase the excretion of Mg++.

➢ **valsartan**

Angiotensin II antagonists (renin-angiotensin-aldosterone system)

- **uses : treatment hypertension**
- **Advantages**

- Safe, inexpensive, effective, well tolerated, once daily dosage and have additive or synergistic effects when combined with other antihypertensive agents.

Spiromide (Generic name : Spironolactone)

- **Mechanism of action:** Diuretic effect through increases the excretion of sodium chloride and water while conserving potassium and hydrogen ions

- **Therapeutic uses:**

- Edema
- Some cases of Hypertension

- **Side effects:**

- Dehydration.
- Decreased sodium , magnesium and calcium level in blood.
- Breast enlargement in male.
- Increased blood uric acid.

- **Why use Spironolactone and hydrochlorothiazide combination preferred ?**

Due to it may also be used to treat water retention (edema) in patients with congestive heart failure, liver cirrhosis, or a kidney disorder called nephrotic syndrome , **with avoidance of hypokalemia causes by thiazide monotherapy.**

lasilactone (Generic name : Spironolactone)

- **Mechanism of action:** Diuretic effect through increases the excretion of sodium chloride and water while conserving potassium and hydrogen ions

- **Contraindication**

✓ **CRF**

✓ **Beta blocker , ACEI**

Why Spironolactone is consider a weak diuretics ?

These drugs are weak diuretics since the amount of Na+-reabsorbed at this site of nephron is only 2-5 % of the filtered Na load.

Cidamex

Generic name : Acetazolamide

(CARBONIC ANHYDRASE INHIBITORS)

Mechanism of action:

- ✓ **They act by inhibition of carbonic anhydrase enzyme in the proximal tubules of kidney, so they inhibit bicarbonate reabsorption and increase its secretion**
- ✓ **CAIs can inhibit carbonic anhydrase–dependent bicarbonate transport at the ciliary body of the eye and hence reduce the formation of aqueous humor (used in glaucoma).**

- **Therapeutic uses:**
- ✓ **Glaucoma**
- ✓ **Acute Mountain Sickness**
- **side effect**

- Metabolic acidosis (mild)
- potassium depletion
- renal stone formation,
- drowsiness

Dorsolamide

Generic name : CARBONIC ANHYDRASE INHIBITORS

Mechanism of action:

CAIs can inhibit carbonic anhydrase–dependent bicarbonate transport at the ciliary body of the eye and hence reduce the formation of aqueous humor (used in glaucoma).

- **Therapeutic uses:**

✓ **Glaucoma**

- **side effect**

- Metabolic acidosis (mild)
- potassium depletion
- renal stone formation,
- drowsiness

Mannitol

Generic name : OSMOTIC DIURETICS

Mechanism of action:

It increases the renal excretion of water by exerting high osmotic pressure within tubular lumen without Na loss.

- **Therapeutic uses:**

✓ **Increased intracranial pressure (cerebral edema & cerebral tumors).**

✓ **Glaucoma: In cases of acute glaucoma and before eye surgery, it reduce IOP.**

✓ **They are used to maintain urine flow in cases acute toxicity induced acute renal failure**

- **side effect**

- Dehydration and extracellular water expansion


Thank You!