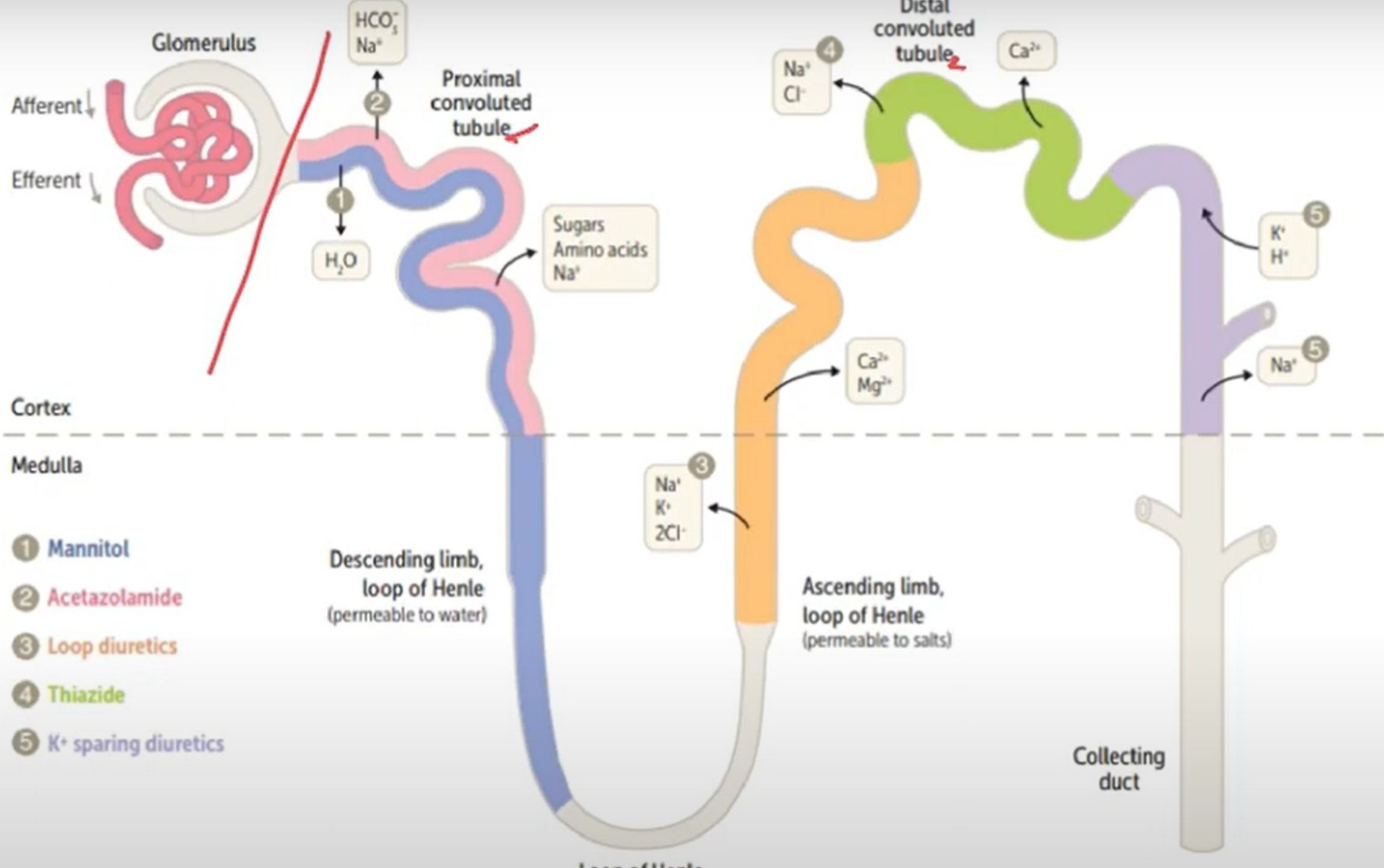


# Lec 1 – diarotic



## Thiazides (sulfonamide derivatives)

- **MOA:** inhibit Na/Cl cotransporter in ascending henle and distal tubule → decrease Na reabsorption → → increase excretion of Na, Cl, K and Mg... increase reabsorption of Ca...  
reduce peripheral vascular resistance
- **Uses:** Hypertension, heart failure, Hypercalciuria, Diabetes Insipidus
  - Chlorthalidone → Hypertension (long duration of action, once daily)
  - Metolazone → In renal failure
  - Indapamide → renal failure
- **Adverse effects:** Hypokalemia and hyponatremia, Hyperuricemia (risk of gout), volume depletion (orthostatic hypotension), Hypercalcemia, Hyperglycemia (esp.in DM patients)

## ▼ Loop diuretics (high ceiling)

- *Bumetanide*, *Furosemide*, *Torsemide*, *Ethacrynic acid*
- MOA: Inhibit Na/Cl/K cotransport in ascending Henle → decrease reabsorption of Na, Cl, K (Most efficacious, bcz ascending Henle reabsorbs 30% that can't be compensated for)
- Uses:
  - **Drug of choice for: Acute pulmonary edema in heart failure** (rapid onset → useful in emergency)
  - stimulate Ca excretion → treat Hypercalcemia
  - Hyperkalemia
- Pharmacokinetics: Oral or parenteral, 2-4 duration of action
- Adverse effects: **Ototoxicity**, Hyperuricemia, Acute hypovolemia, Hypokalemia, Hypomagnesemia



## ▼ Potassium-sparing diuretics

potassium sparing adverse effects عند ال  
hypo مش hyperkalemia لازم يكون

### 1. Aldosterone antagonist: Spironolactone

- MOA: Synthetic steroid that antagonizes aldosterone → inhibit synthesis of Na/K exchange proteins in collecting tubule → less Na reabsorption and K and H excretion
- Uses (orally): Diuretic, Secondary hyperaldosteronism, heart failure
  - Off the counter use: Hirsutism (in low dose to prevent diuretic effect)
- Adverse effects: Gastric upset and peptic ulcer, Gynecomastia, Menstrual irregularities!! (bcz of steroid action), hypokalemia, nausea, lethary, mental confusion

### 2. Epithelial Na channel blocker: *Triamterene* and *amiloride*

- MOA: Block Na channels → decrease Na/K exchange
- Used in combination with other diuretics because they are K-sparing (prevent loss of K that happens with thiazides and loop)
- Side effect: Leg cramps, may increase Urea nitrogen in blood + Uric acid and K retention

## ▼ Carbonic anhydrase inhibitors (*Acetazolamide*)

- MOA: inhibit carbonic anhydrase → less ability to exchange Na and H → less Na reabsorption → mild diuresis (not as efficacious as others)
- Uses: **Glaucoma** (reduce IOP in open-angle, decrease aques humor production)
- Pharmacokinetics: Orally or topically (eye drops) 1-4 times
- Adverse effects: Metabolic acidosis, K depletion, Renal stones, drowsiness, paresthesia (avoid in hepatic cirrhosis bcz decrease excretion of  $\text{NH}_4^+$ )

## ▼ Osmotic diuretics (Mannitol)

- MOA: increase osmolality of plasma and tubular fluid (bcz they are bulky) → retain water in lumen + increase rate of flow (flushing) → rapid powerful diuresis
  - Also help withdraw fluid from brain in cerebral edema and in acute glaucoma (bcz they increase plasma osmolality)
- Uses: **Decrease cerebral edema**, decrease IOP in acute narrow-angle glaucoma, increase excretion of drugs and heavy metals, **prevent renal failure**
- Contraindication: heart failure + established renal failure (may develop pulmonary edema)