Lec 5

last lecture was about Reabsorption in PCT ... now we will talk about **Reabsorption in Loop of Henle (LOH)**

- each segment has different characteristics in terms of permiability & transport
- consists of thin descending & ascending, Thick ascending limbs

Thin Descending

- absorbs 15 % of water (osmosis) passively due to ...
  1) higher osmolarity in the interstitium than tubular fluid
  2) higher H_2O permiability due to aquaporins (paracellular rout)

Thin Ascending

- impermiable to H_2O
- passive transport of NaCl from tubular → interstitial until it reaches equilibrium

Thick Ascending * 2ndry active transport

- large cuboidal cells that use a lot of energy, & have large distribution of Na^+/K^+ ATPase, Na^+ channels, Cl^- channels.
- reabsorbs 25% of Na^+, K^+, Cl^-, HCO_3^-, Ca^{++}, Mg^{++} (electrolytes)
  - leads to hypoosmotic conc. at end of thick limb b/c it is impermiable to H_2O → so water is diluted, so this segment is called diluting segment

- the luminal side of this limb has multiple channels & is highly positively charged
  - Sodium chloride potassium channel takes Na, $2Cl^-$, K^+ from tubular fluid → into cell
  - Na^+/H^+ exchange channel reabsorbes Na^+ & secretes H^+
  - transcellular rout due to Na^+ gradient of Na^+/K^+ ATPase

* when H^+ is secreted, HCO_3^- is reabsorbed

- due to high positive charge of luminal side → it repels (+) charged ions through paracellular rout to be reabsorbed
  - * the more (+) charge = the more repulsion (Mg^{++}, Ca^{++})
  - this is called voltage Drag *

* NaCl reabsorption 50% transcellular, 50% paracellular (by voltage drag)

Clinically

- furosemide is called a loop diuretic b/c it blocks Na - K - Cl channel → inhibiting reabsorption of them
- the conc. of these ions will ↑ in tubular fluid, & b/c water follows the solute, we will have diuresis → ↑ in urine fluid volume .... ↓ blood volume, ↓ BP

Early Distal Tubule

- Reabsorbs Na^+ & Cl^- through Na^+/Cl^- channel using the Na^+ gradient
- impermiable to water
- Thiazide blocks these channels → diuresis

- this segment is functionally similar to thick ascending limb
- contains macula densa, & also called diluting segment

Late Distal Tubule & Collecting Duct

- paired together due to similar characteristics
- permiability to H_2O is variable & depends on ADH
- water was diluted in earlier segments = low osmolarity of tubular fluid
- If ADH is present, it activates aquaporins → high H_2O reabsorption
- So ADH prevents high urine volume, ↑ extracellular fluid & BP
- divided in 2 parts

Principal Cells

- contain epithelial sodium potassium channels (ENac) → they reabsorb Na^+ but secrete K^+ *
- aldosterone works on principal cells to ↑ ENac activity → useful in the case of hyperkalemia b/c more K^+ is eliminated
- Amiloride drug acts as a diuretic b/c it blocks ENac → potassium sparing diuretic b/c K^+ will not be secreted, & Na^+ is not reabsorbed → diuresis w/out changing K^+ conc. in blood
- Aldosterone antagonist (spironolactone) blocks aldosterone

function → so also a diuretic

Intercalated Cells

- function in **acid base balance**, mainly secreting H^+ b/c our body makes more acids than bases, & reabsorbs bicarbinate back into blood to neutrilize acids in the body

* **prevents acidosis**

- has the ability to **oppose direction of transport** in the case of alkalosis

notes

- PCT → reabsorbs 65% of Na
- thick ascending → 25% Na
- early distal → 5% Na
- late distal & collecting duct → 2% Na
- .6 % of Na^+ excreted
- Conc. of solutes in different parts of tubule depends on reabsorption of solutes compared to water
  - if more H_2O reabsorbed → tubular fluid solute conc. ↑ (creatine & inulin)
  - if less H_2O reabsorbed → solute conc. ↓ (glucose, AA)

Diuretic type	Channel involved	Present in	Mechanism summary
Loop-acting Ex. Furosemide (Lasix)	Blocks sodium chloride potassium (Na-K-Cl) channel	Thick ascending limb of Henle (PCT)	Inhibits Na+ reabsorption → water follows solute so H2O reabs. ↓ = diuresis
Thiazide	Blocks Na+/Cl- channel	Early distal tubule	Inhibits Na+ and Cl- reabs. → solute remains in tubular fluid → water follows solute = diuresis
Potassium-sparing Ex. Amiloride Triamterene	Blocks epithelial sodium potassium channel (ENac)	Principal cells in late distal tubules and collecting ducts	Inhibits Na+ reabs.... = diuresis Blocks K+ secretion into tubular fluid so K+ is spared from excretion
Aldosterone antagonists Ex. Spironolactone Eplerenone	ENac Note: aldosterone stimulates ENac, aldosterone antagonists inhibit aldosterone	Principal cells in late distal tubules and collecting ducts	Aldosterone stimulates ENac→ inc. Na+ reabs., inc. K+ secretion into tubular fluid = prevent diuresis. Antagonist inhibits this (does the opposite).
Antidiuretic Hormone (ADH)	Inserts aquaporins into	membranes of late distal tubules and collecting ducts	Inc. H2O permeability → inc. H2O reabs. = *prevents* diuresis

Changes in Concentration of Substances in tubules

- measured as tubular fluid conc. / Plasma conc.
- different segments have different conc. percentages
- loop of henle has poor reabsorption of inulin, urea, creatine, & PAH, so their conc. is high
- After thin descending part → ↑ conc. of PAH, creatine, urea, inulin, Cl^-, Na^+, K^+ → b/c of passive reabsorption of water
- at thick ascending → ↓ conc. of Cl^-, Na^+, K^+ b/c of extensive active reabsorption
- early distal → ↓ conc. of Na, K^+, Cl^-
- Collecting tubule → ↑ solute conc. b/c of H_2O reabsorption from ADH

* higher water reabsorption = higher conc. of tubular fluid