PHYSIOLOGY TEAM 432

LECTURE : 6

Tubular secretion

Done By: Othman Al-Hekail
Reviewed By: Marwah Zummo – Khulood Al-Raddadi

OBJECTIVES

Absorption part in this lecture was removed to lecture 5

At the end of this lecture student should be able to describe:

- Mechanism of Bicarbonate reabsorption
- Mechanism of Phosphate reabsorption
- Urea reabsorption
- Mechanism of Tubular secretion of K & H

Mechanism of Tubular secretion of K & H

- ✓ **Secretion: From peritubular blood through peritubular space into renal tubular cell to tubular lumen.**
  - **Passive NH3 (ammonia) , salicylic acid.**
  - **Active:**
    - ➢ **Tubular maximum (Tm) : creatinine; PAH.**
    - ➢ **No Tm (no limit for secretion because they have to be tightly regulated) : K & H.**

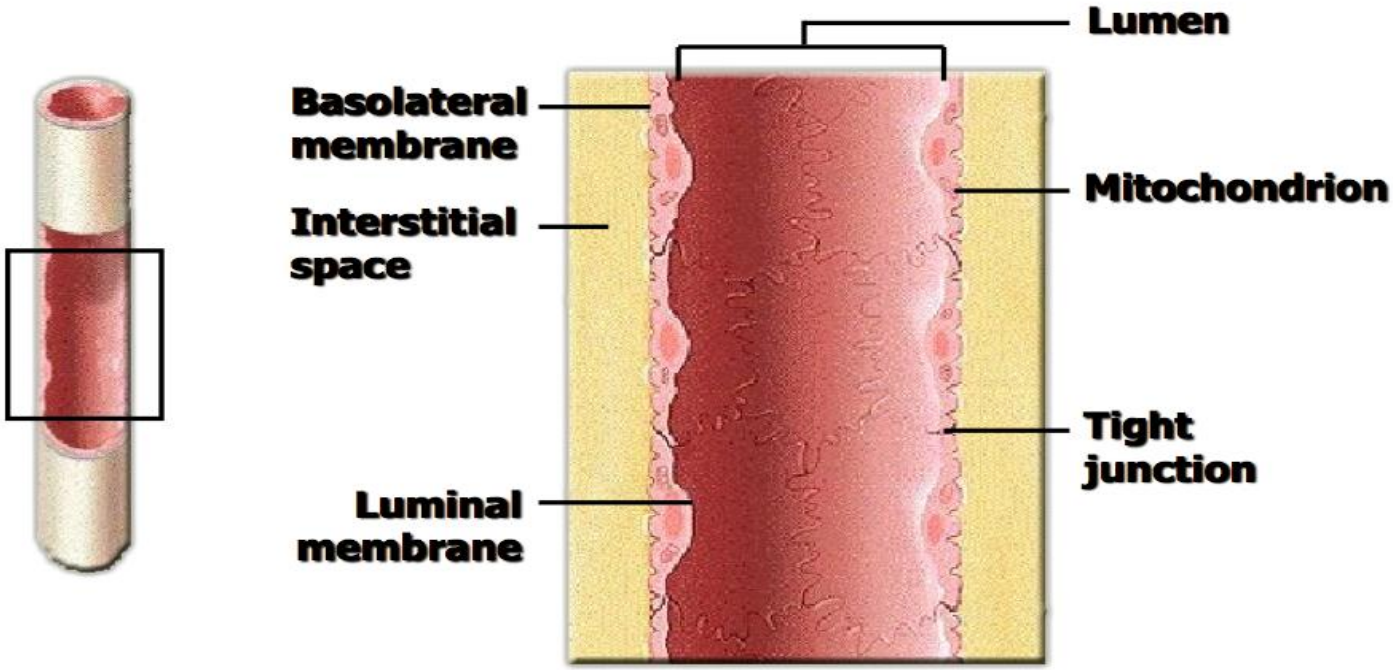
- ✓ **Potassium (normally in plasma between 3.5-5): (>5 toxic)**
  - **90% of filtered K is reabsorbed (PCT)**
  - **K is secreted in DCT passively in exchange for Na and under the control of Aldosterone hormone.**
  - **H and K compete together for exchange with Na.**

- ✓ **Hydrogen:**
  - **Excretion exchange for Na.**

LOOP OF HENLE

The Thin Loop of Henle:

- Cells simple squamous epithelial cells
- "Highly permeable to water **but** not to solutes"

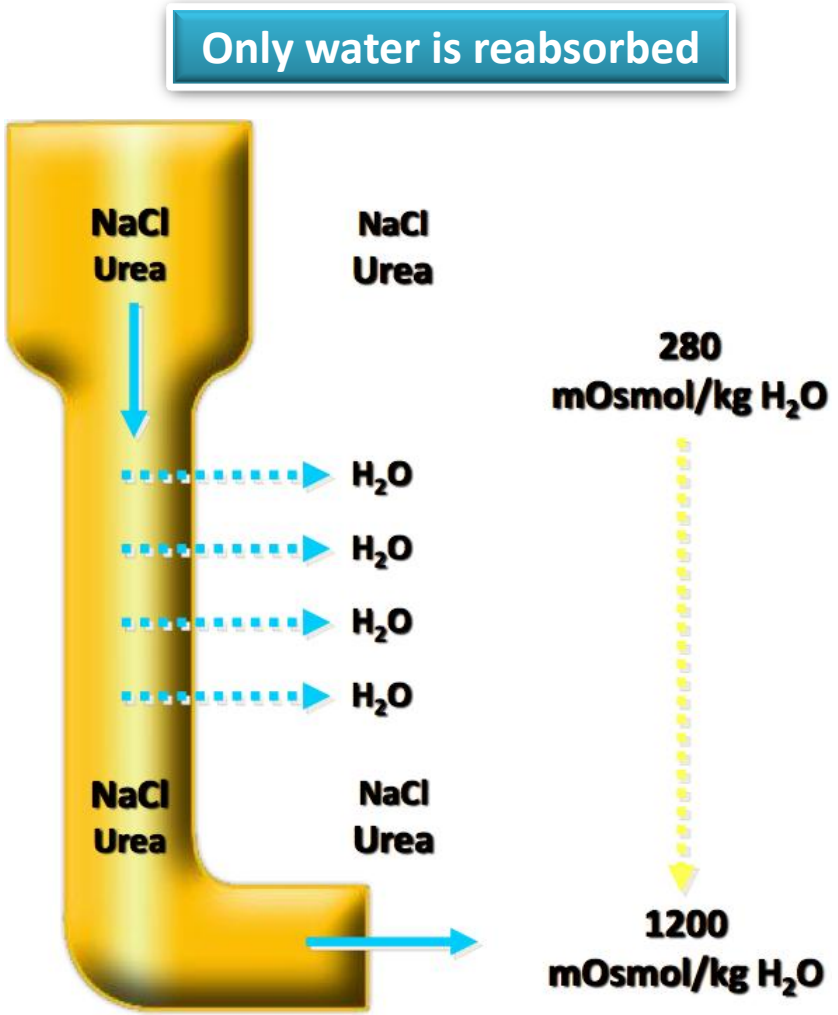


Dr Sitelbanat

11

THE DESCENDING LOOP

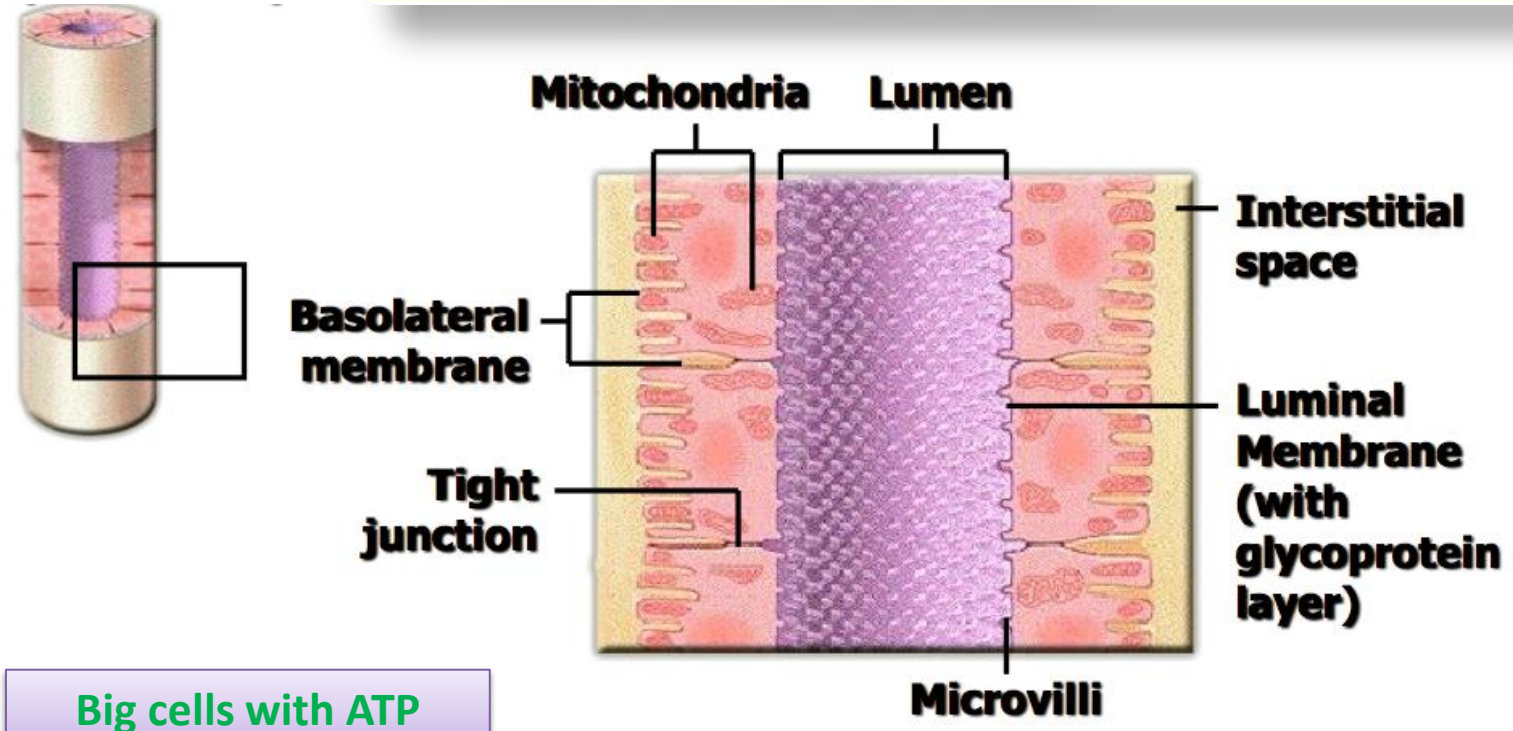
- ✓ Permeable to water **but** not for solute absorption.
- ✓ 20% of filtered water is reabsorbed.
- ✓ osmolality of filtrate increases from 290 (plasma) to 1200 mOsm/l at the tip of the loop.
- ✓ The **increasing osmolality** is due to only water reabsorption, ↑ **NaCl and ↑ Urea** concentration in filtrate.



THE ASCENDING LOOP OF HENLE AND EARLY DCT

Different physiology from descending because of different structures

Cells are cuboidal epithelial; Highly permeable to solutes, particularly NaCl, but not to water



Big cells with ATP

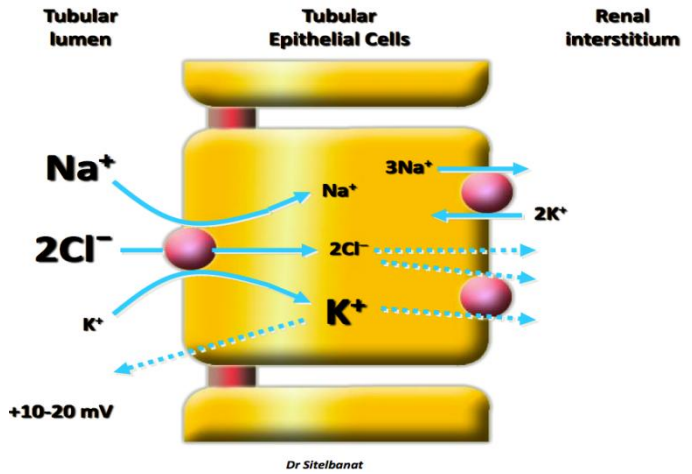
THE ASCENDING LIMB 1/3

No function so far

THICK ASCENDING LOOP 2/3

– Water impermeable
– Na/K/2Cl reabsorption by co-transport (luminar)
– Na/K ATPase in basolateral membrane

✓ Filtrate diluted due to solute reabsorption not water
✓ Osmolarity drop from 1200 to 200mosm/l



The thick ascending limb is very sensitive to diuretic drugs (Furosamide).

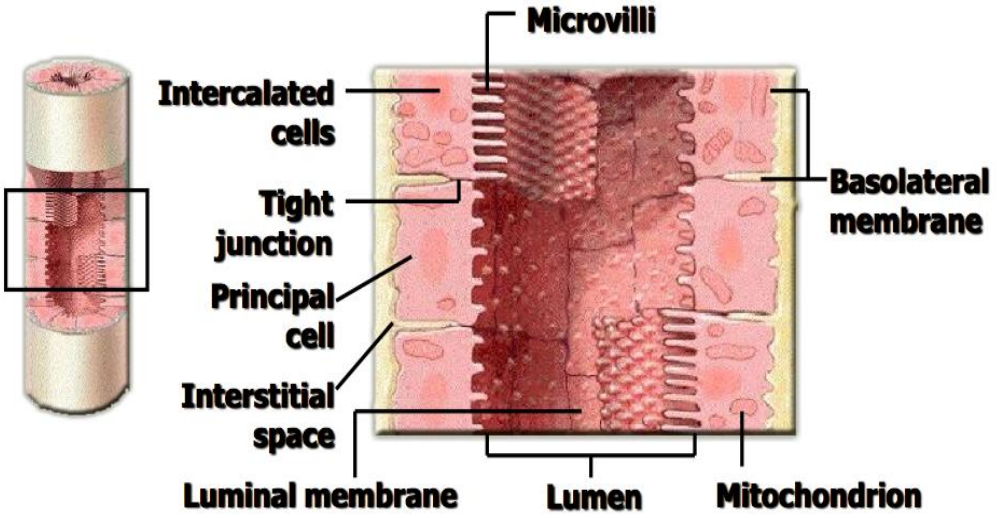
These diuretics (Lasix) block Na+ K+ 2Cl⁻ co-transporter:

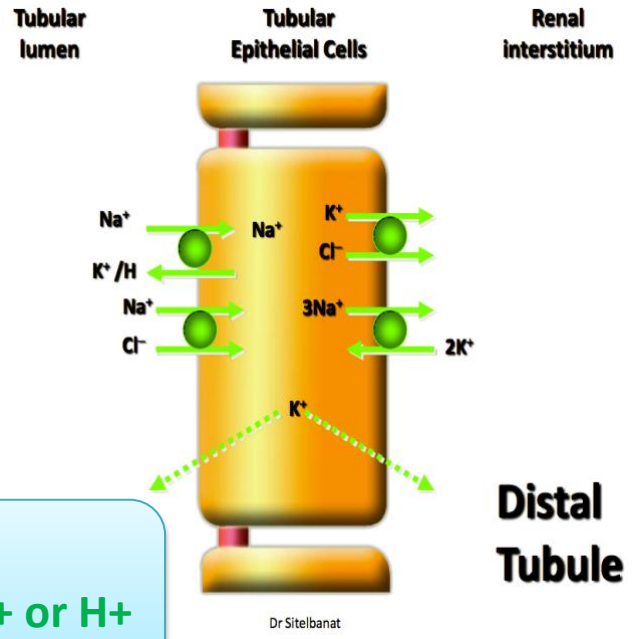
✓ Decreased NaCl reabsorption
✓ Isotonic fluid delivered to distal tubule instead of a hypotonic fluid
✓ Increased fluid excretion – "diuresis"
✓ These drugs are called "Loop" diuretics

THE LATE DCT AND CORTICAL COLLECTING DUCT

Cuboidal cells are of two distinct functional types principal and intercalated cells.

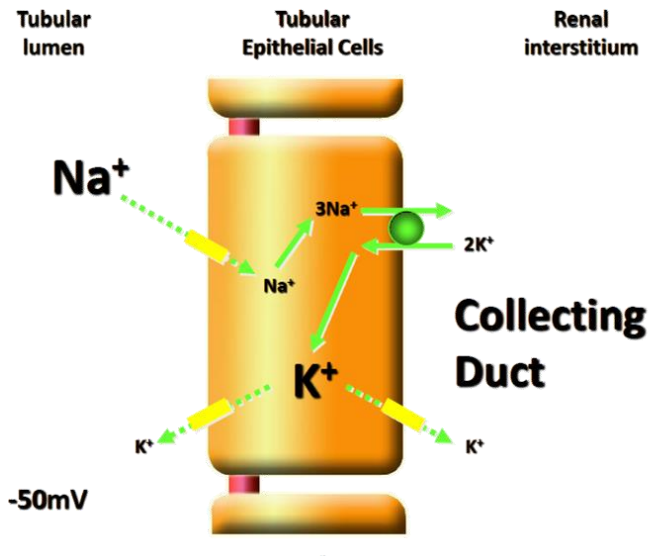
- Principal cells permeability to water and solutes is regulated by hormones (ADH & aldosterone).
- Intercalated cells secretion of hydrogen ions for acid/base balancing .





- 19% of filtered H_2O is reabsorbed
- 0.9% of filtered Na+ is reabsorbed in exchange of K+ or H+
- Cl^- also reabsorbed

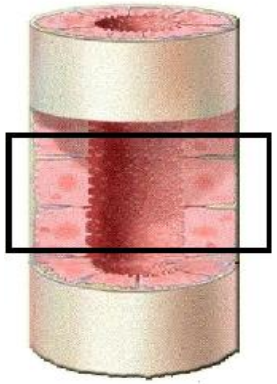
CELLS OF THE MEDULLARY COLLECTING

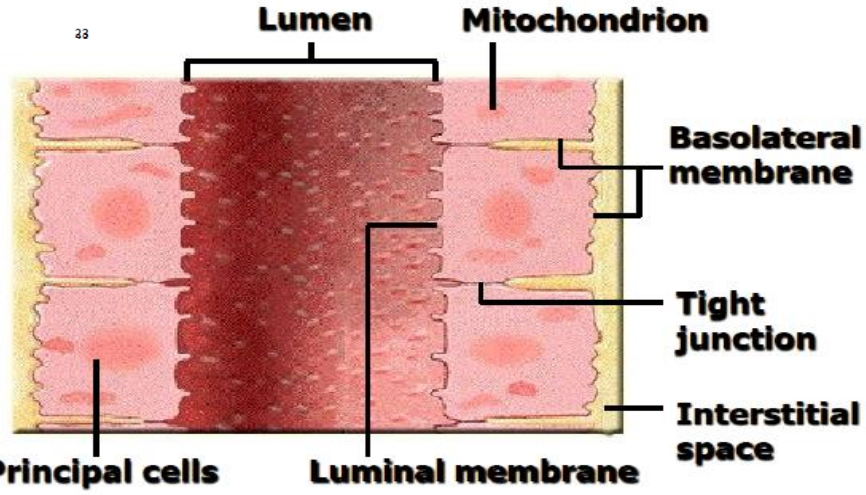


Collecting duct

- Cells are mainly principal cells.
- Water permeable only under ADH only.
- Urea is reabsorbed in the presence of ADH.
- Na reabsorbed in exchange for K under the influence of aldosterone.

Dr Sitelbanat





Hormonally regulated permeability to water and urea.

Dr Sitelbanat

UREA RECIRCULATION

- Urea is passively reabsorbed in proximal tubule.
- In the presence of ADH, water is reabsorbed in distal and collecting tubules, concentrating urea in these parts of the nephron.
- The inner medullary collecting tubule is highly permeable to urea, which diffuses into the medullary interstitium.
- ADH increases urea permeability of medullary collecting tubule.

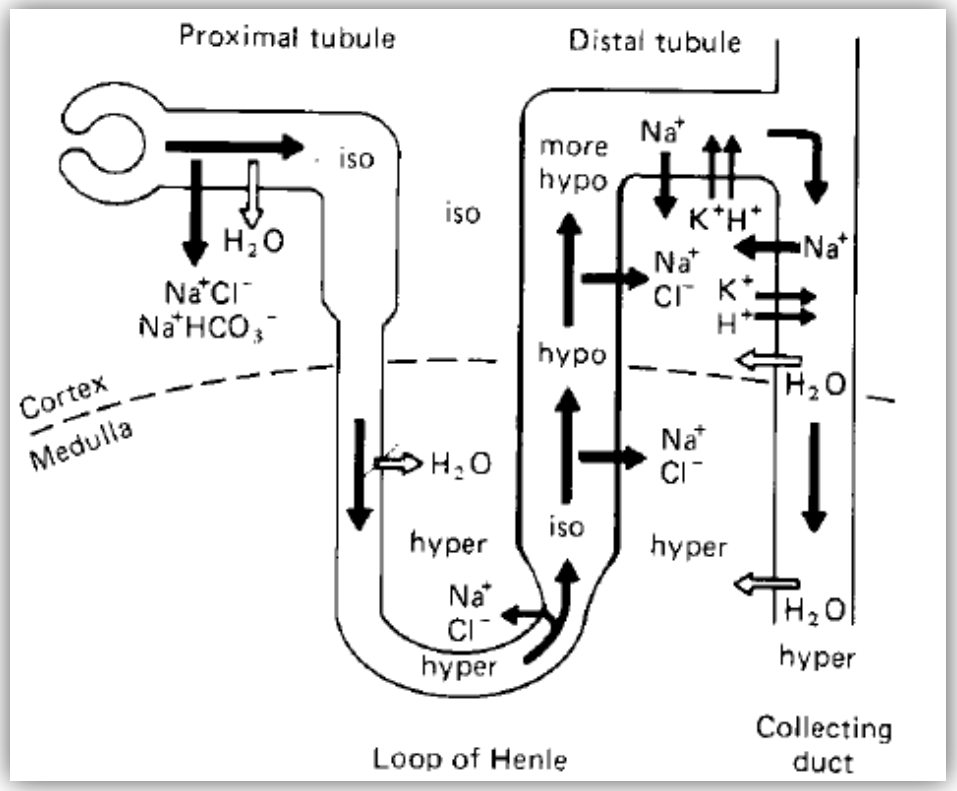
Urea is filtered → 40-50% reabsorbed in PCT → reabsorbed in collecting duct in the presence of water.

OSMOLALITY OF THE FILTRATE ALONG THE NEPHRON

Briefly

Filtrate compared to plasma in different parts:

- **PCT: Iso**
- **DL: Hyper (1200 at the tip)**
- **AL: Iso or even Hypo (reduced again) "diluted segment of nephron".**
- **The rest of the parts depend on ADH.**



OSMOLALITY OF THE FILTRATE ALONG THE NEPHRON

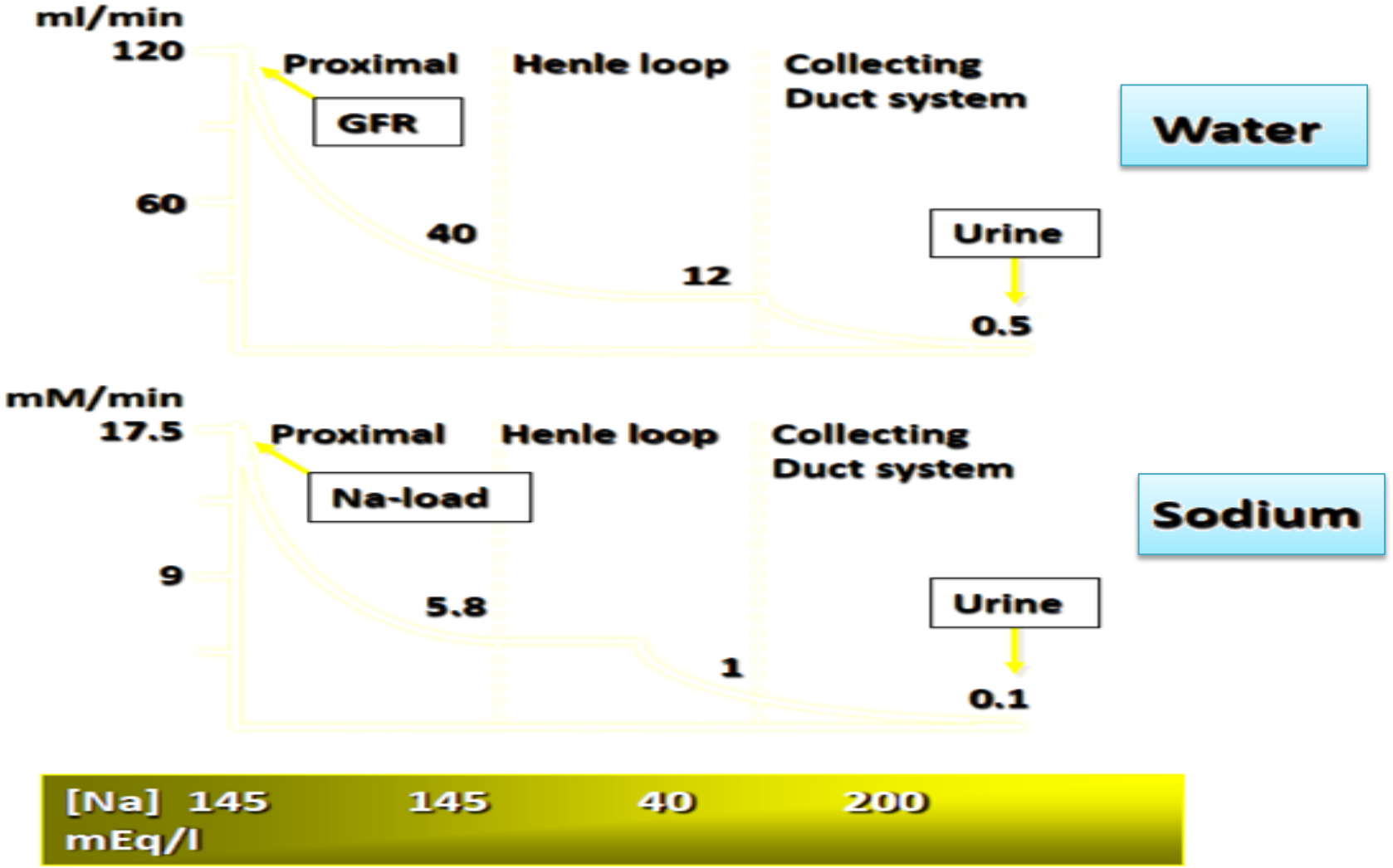
Details

- **Osmolality of filtrate in PCT:**
  - Similar to plasma ~ 290 mosm
  - Due to reabsorption of equal portion of solute & water
- **Osmolality of filtrate in Descending Loop:**
  - Graded ↑in osmolality from 300 mosm. To maximum of 1200 mos. at the tip of loop
  - Due to only water reabsorption
- **Osmolality of filtrate in Ascending Loop:**
  - Graded ↓in osmolality1200-150
  - Due to only solute reabsorption
- **Osmolality of filtrate in Collecting D:**
  - Osmolality depend on ADH
  - ↑ADH →↑water reabsorption → concentrate urine 1200 mosm
  - No ADH →no water reabsorption → dilute urine 50mosm

SUMMARY

Segment	% filtered load reabsorbed	Mechanism of H_2O reabsorption	Hormones that regulate H_2O permeability
Proximal tubule	67	Passive	None
D Henle's loop	15	DL only; passive	None
Distal tubule	0 Water impermeable	No water reabsorption	None
Late distal tubule & collecting duct	~8-17	Passive	ADH

SUMMARY


ml/min
120
Proximal
Henle loop
Collecting
Duct system
GFR
Water
60
40
Urine
12
0.5
mM/min
17.5
Proximal
Henle loop
Collecting
Duct system
Na-load
Sodium
9
5.8
Urine
1
0.1
[Na] 145
mEq/l
145
40
200

SUMMARY

Male

Transport of substances from peritubular capillaries to tubular lumen:

Primary active secretion:

- For H^+
- In late distal & collecting tubules
- H^+ -ATPase pump at luminal membrane

Secondary active secretion (depends on primary active secretion):

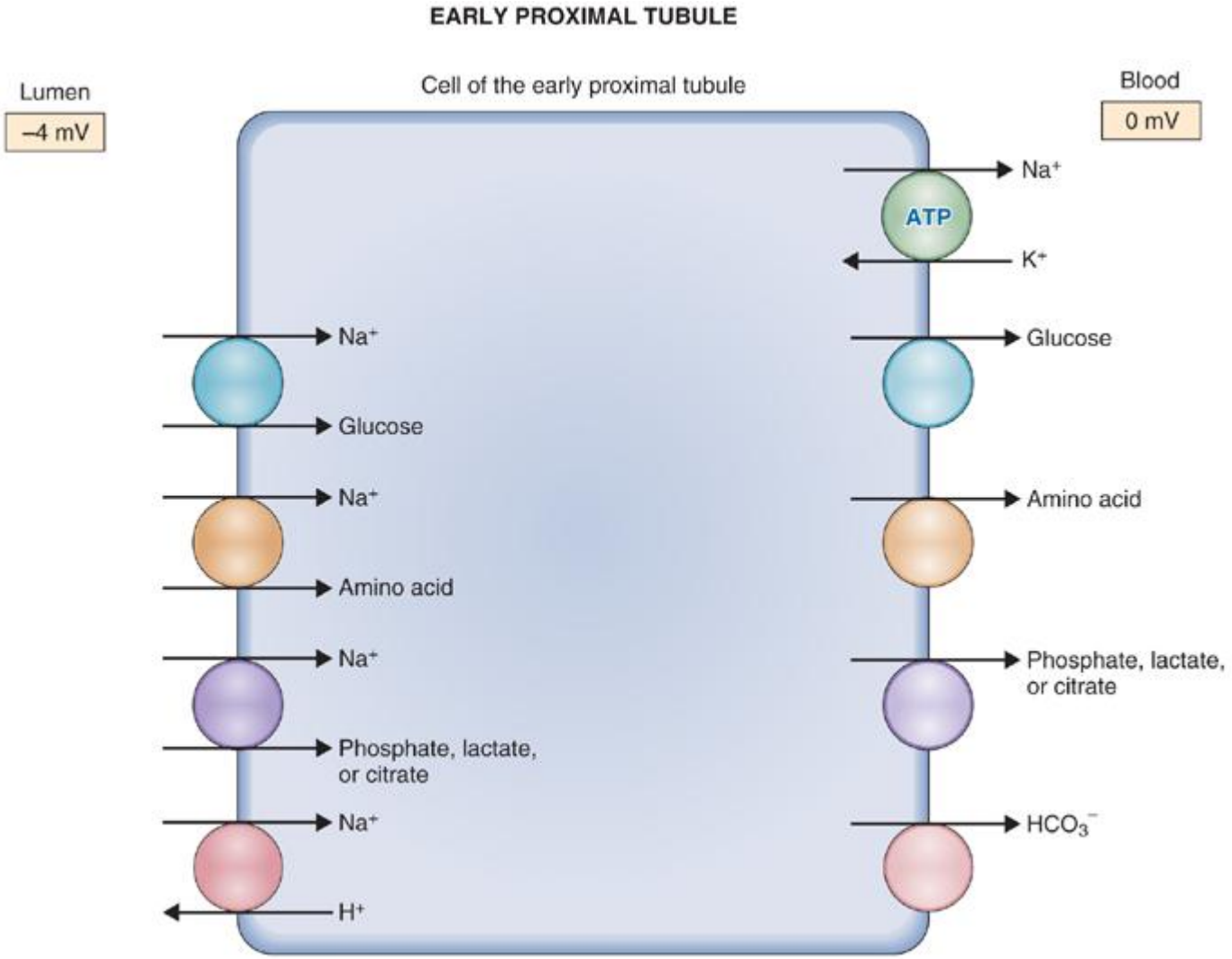
- H^+ in PCT (counter-transport)
- K^+, urate in distal tubules

SUMMARY

- Substances that become absorbed are more than substances that are secreted.
- Absorption is in different direction with secretion:
  - Absorption: from tubular lumen into renal tubular cell to peritubular space to peritubular blood .
  - Secretion: From peritubular blood through peritubular space into renal tubular cell to tubular lumen.
- If a patient has hyperkalemia (↑K), he will present with acidosis, WHY ?? Because K and H compete together but the "K" has the priority to get rid from the body so the H is left inside the cells which causes Acidosis.
- The diluted segment of the nephron is " thick ascending limb", WHY ?? Because it helps in filtrate diluting after passing the descending limb "concentrated filtrate".
- H is secreted in PCT by 2nd active secretion (counter-transport) in exchange for Na but under hormonal control (aldosterone) in DCT.
- Diuretic drugs will block Na/K/2Cl co-trasporter in the ascending limb.

SUMMARY

From Linda



SUMMARY

From quizlet

1. **Reabsorbed in Ascending Limb**	Na, Cl, K. Cuboidal to columnar cells.
2. **Reabsorbed in Collecting Duct**	H_2O, Na, H, HCO_3, urea. Intercalated cells (cuboidal w/microvilli) & Principal cells (cuboidal w/out microvilli).
3. **Reabsorbed in DCT**	Na (aldosterone reg.), Ca (PTH reg.), Cl (cotransported with Na). Cuboidal cells with very few microvilli.
4. **Reabsorbed in Descending Limb**	H_2O. Simple squamous epithelium.
5. **Reabsorbed in PCT**	Na, glucose, amino acids, H_2O, many ions, & HCO_3. Cuboidal cells with dense microvilli & large mitochondria.
6. **Secreted in Ascending Limb**	Urea. Cuboidal to columnar cells.
7. **Secreted in Collecting Duct**	K, H, HCO_3, NH_4. Intercalated cells (cuboidal w/microvilli) & Principal cells (cuboidal w/out microvilli).
8. **Secreted in PCT**	H, NH_4, & some drugs. Cuboidal cells with dense microvilli & large mitochondria.

SUMMARY

From Linda

Segment/Cell Type	Major Functions	Cellular Mechanisms	Hormone Actions	Diuretic Actions
Early Proximal Tubule	Isosmotic reabsorption of solute and water	Na^+-glucose, Na^+–amino acid, Na^+-phosphate cotransport	PTH inhibits Na^+-phosphate cotransport	Osmotic diuretics
		Na^+-H^+ exchange	Angiotensin II stimulates Na^+-H^+ exchange	Carbonic anhydrase inhibitors
Late Proximal Tubule	Isosmotic reabsorption of solute and water	NaCl reabsorption driven by Cl^- gradient	—	Osmotic diuretics
Thick Ascending Limb of the Loop of Henle	Reabsorption of NaCl without water Dilution of tubular fluid Single effect of countercurrent multiplication Reabsorption of Ca^{2+} and Mg^{2+} driven by lumen-positive potential	Na^+-K^+-$2Cl^-$ cotransport	ADH stimulates Na^+-K^+-$2Cl^-$ cotransport	Loop diuretics

SUMMARY

From Linda

Early Distal Tubule	Reabsorption of NaCl without water Dilution of tubular fluid	Na^+-Cl^- cotransport	PTH stimulates Ca^{2+} reabsorption	Thiazide diuretics
Late Distal Tubule and Collecting Ducts (principal cells)	Reabsorption of NaCl	Na^+ channels (ENaC)	Aldosterone stimulates Na^+ reabsorption	K^+-sparing diuretics
	K^+ secretion	K^+ channels	Aldosterone stimulates K^+ secretion	
	Variable water reabsorption	Water channels	ADH stimulates water reabsorption	
Late Distal Tubule and Collecting Ducts (α-intercalated cells)	Reabsorption of K^+ Secretion of H^+	H^+-K^+ ATPase H^+ ATPase	— Aldosterone simulates H^+ secretion	— K^+-sparing diuretics

ADH, Antidiuretic hormone; PTH, parathyroid hormone; ENaC, epithelial Na^+ channel.

THE END

If there are any problems or suggestions
Feel free to contact:

Physiology Team Leaders
Mohammed Jameel & Khulood Al-Raddadi

432100187@student.ksu.edu.sa
432200235@student.ksu.edu.sa

THANK YOU

Actions speak louder than Words