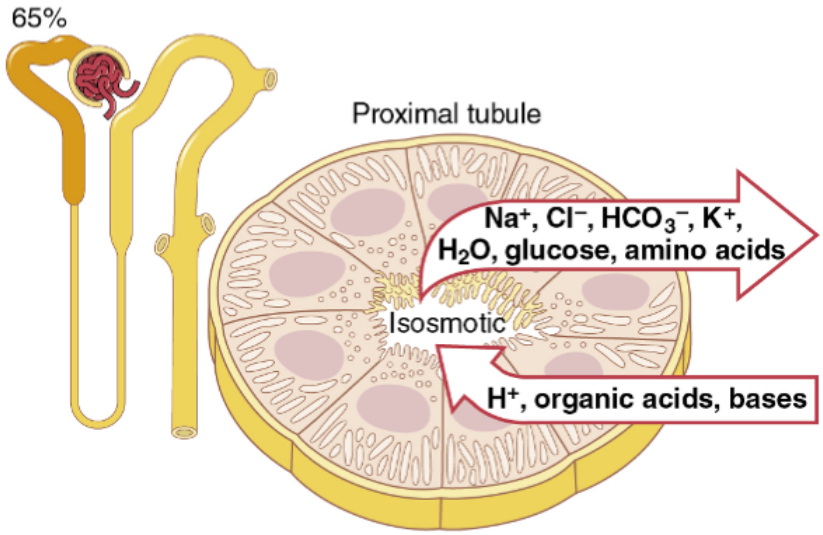
# Lecture 3- Renal physiology

# Transport Characteristics of Proximal Tubule (PT)

- **Proximal tubules**
- Extensive brush border on luminal side→ ↑ SA
- Extensive intercellular and basal channels
- High capacity for active (mitochondria) & passive reabsorption

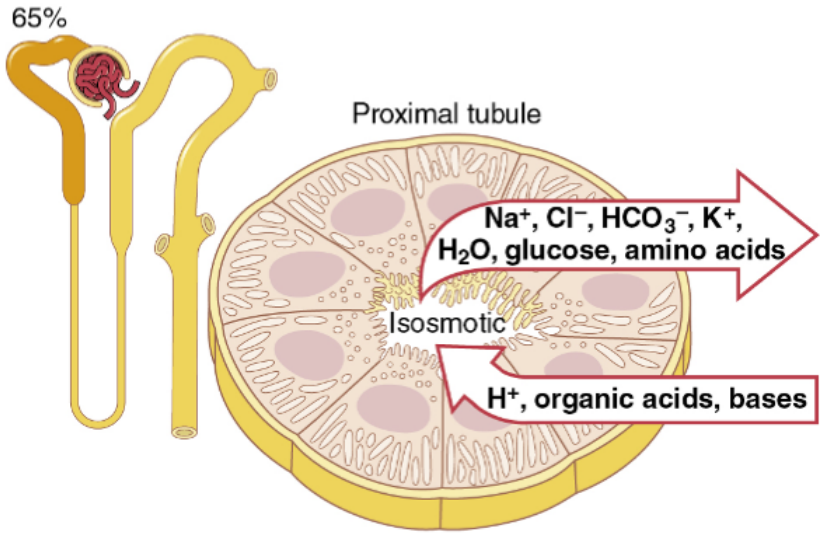


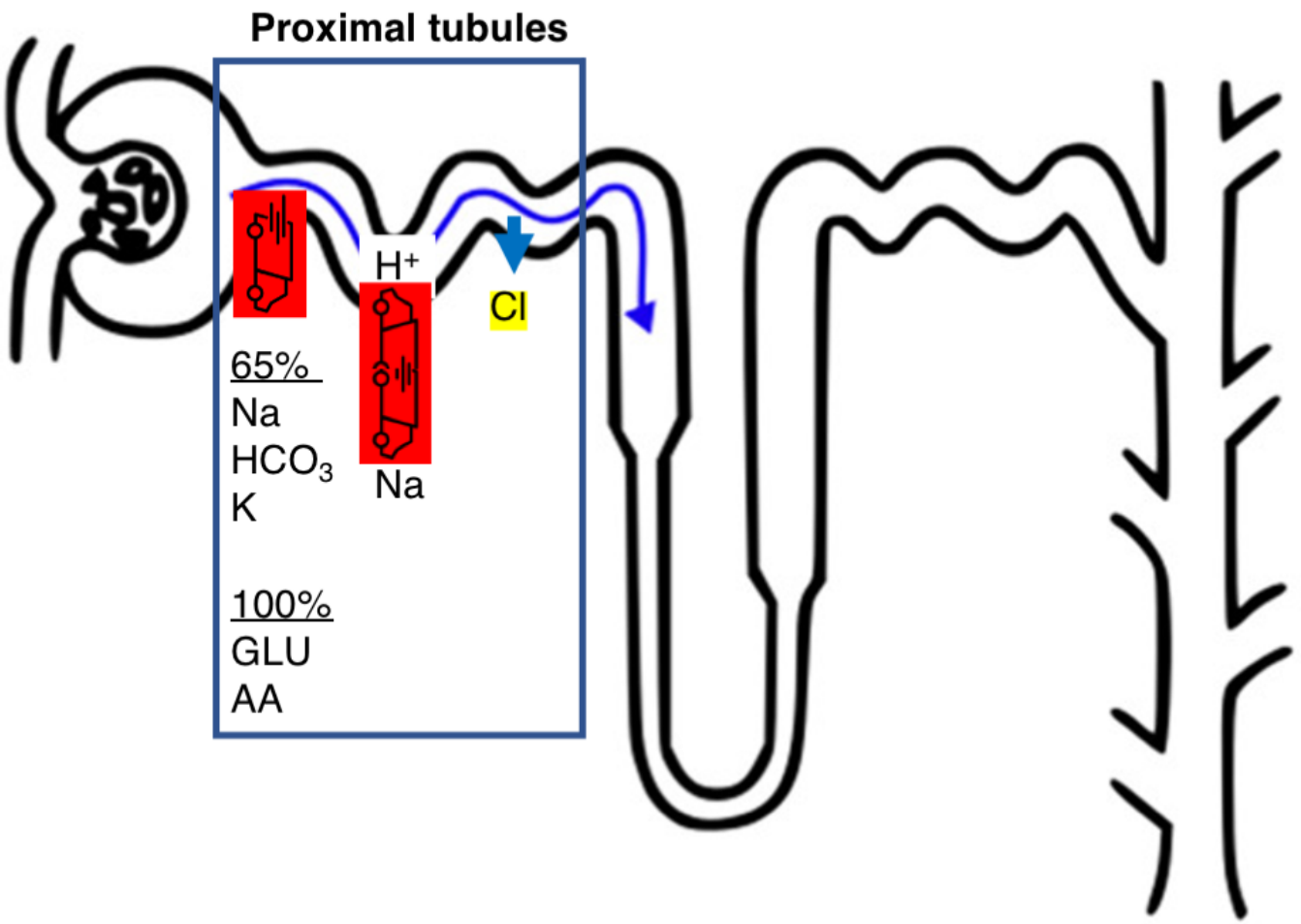

- **Reabsorption:**
- **65% of filtered Na, Cl, $HCO_3$ & K**
- *Na* is mainly reabsorbed by *primary transport*
- In 1st ½ of PT→ Na, GLU & AA → **COTRANSPORT**
- Reabsorb **all** filtered *glucose and amino acids*
- In 2nd ½ of PT → **high Cl** →diffusion through intercellular j.

# Transport Characteristics of Proximal Tubule (PT)

- **Secretion:**

- Secretes organic acids, bases, & $H^+$ into lumen.
- $H^+$ secretion binds $HCO_3^-$ → $H_2CO_3$→$H_2O$ +$CO_2$
- Secretion of drugs (penicillin and salicylates), toxins, bile salts , ureat oxlate and catcholamines are secreted by the proximal tubule.




Proximal tubules
H+
Cl
65%
Na
HCO3
K
Na
100%
GLU
AA

# Glucose Transport Maximum

- In healthy adult, all filtered glucose is reabsorbed and **no** glucose will appear in urine.

- If plasma glucose ($P_G$) reaches 200 mg/dl, glucose appear in the urine – this level is the "Renal threshold"

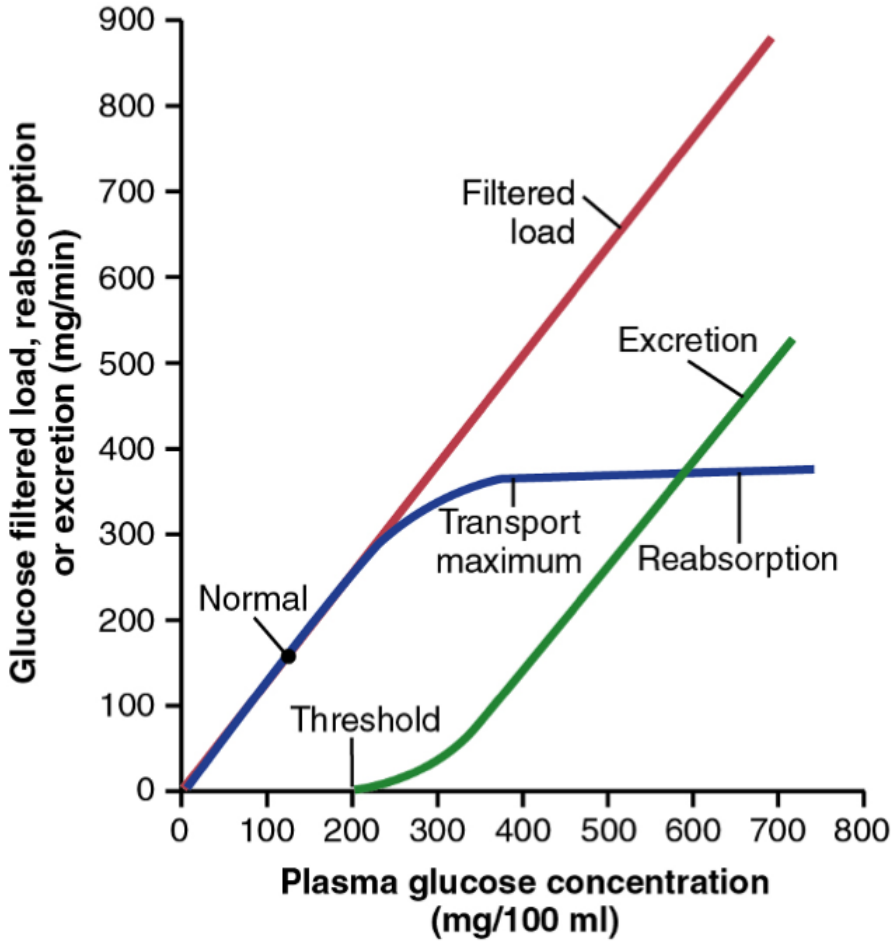
- The amount of reabsorbed glucose at very **high** filtered glucose, remains **constant**, this is called **glucose transport maximum** (TmG)= 375 mg/min

# Glucose Transport Maximum

- When filtered load > Tm →urinary excretion of glucose

- Appearance of glucose in urine (at the threshold) occurs before transport maximum is reached.!! Why?
- Not all nephrons have the same transport maximum for glucose→ some of nephrons begin to excrete glucose before others have reached their transport maximum.

- The overall transport maximum for the kidneys is reached when **all** nephrons have reached their maximal capacity to reabsorb glucose →no more glucose can be transported.



# Transport characteristics of loop of Henle

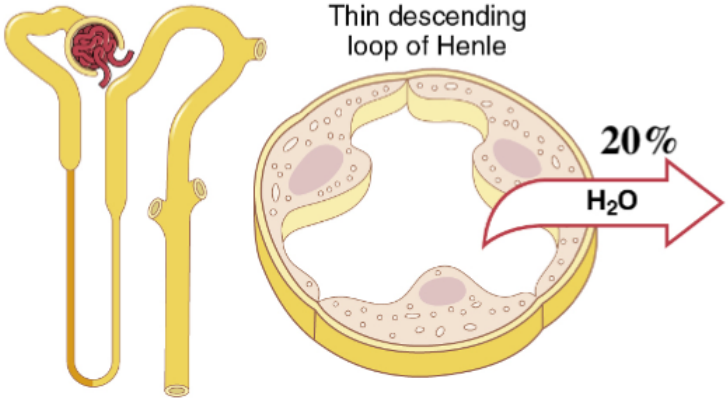
3 functionally segments:

1- Thin descending

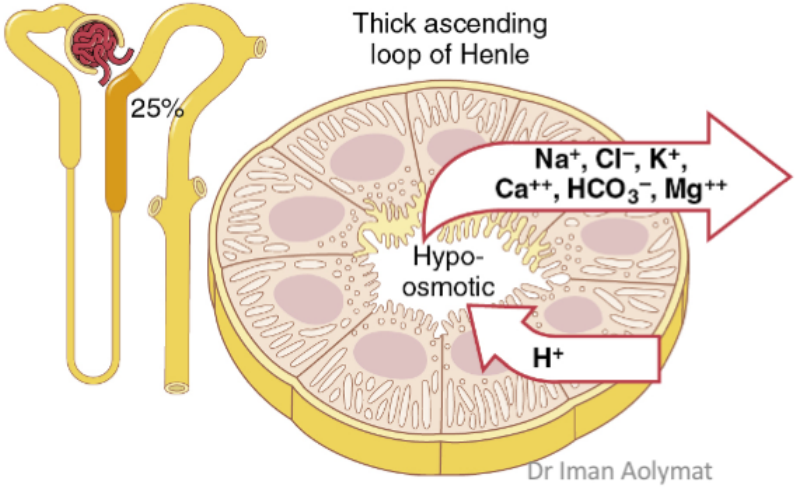
2- Thin ascending

3- Thick ascending

# Transport characteristics of loop of Henle




Thin epithelium
No brush borders
Few mitochondria
*Highly permeable* to H2O




- Reabsorption of
  $Na^+$, $Cl^-$, $K^+$, $HCO_3^-$,$Ca^{++}$, $Mg^{++}$
- <u>Secretion of $H^+$</u>
- **Not permeable to $H_2O$**

# Transport characteristics of loop of Henle

## Cotransport

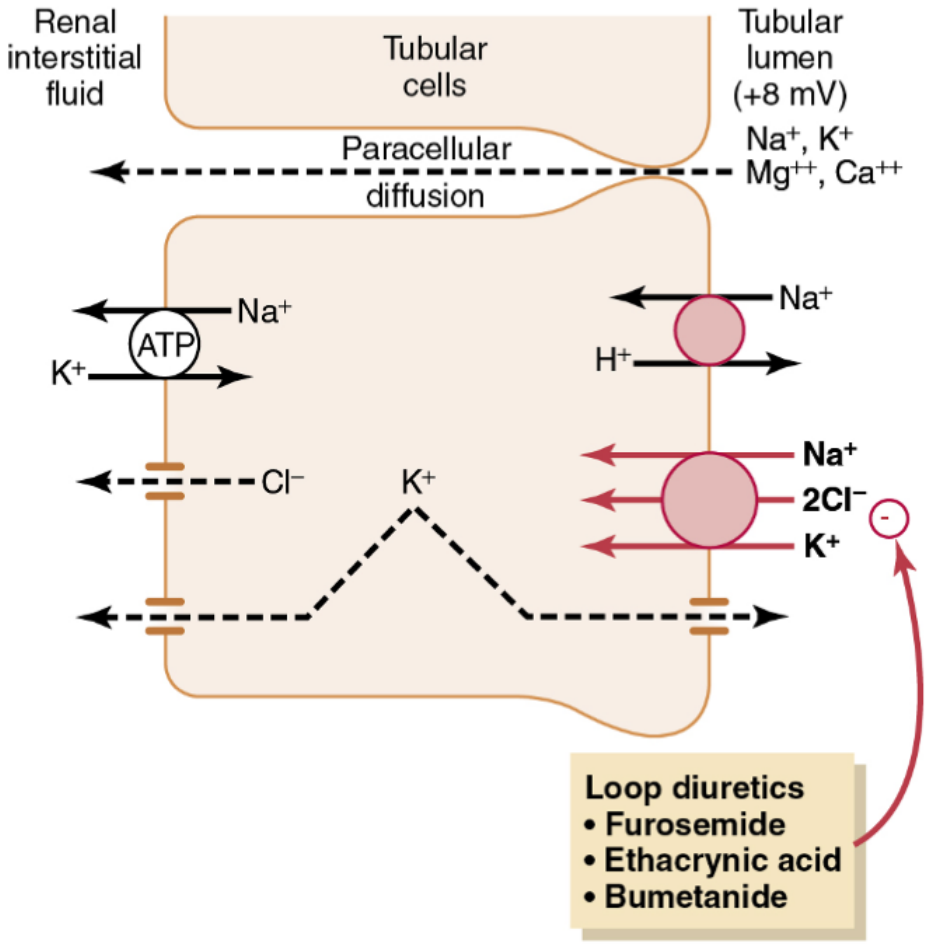
- NaCl & K transport in thick ALH
- DEPENDS on **Na+-K+ATPase** in basolateral membrane

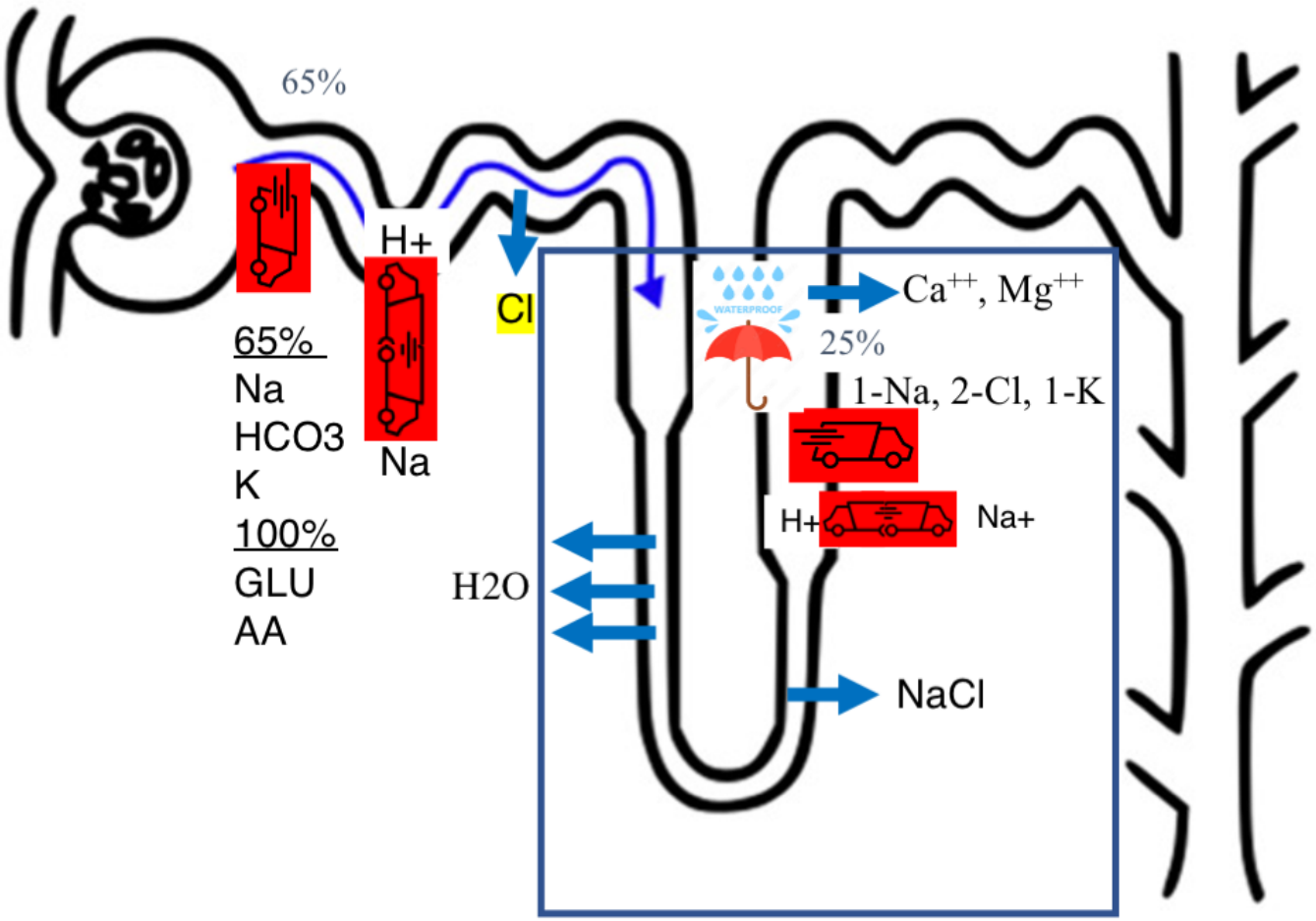
- Na+-K+ATPase →↓ intracellular Na→ Na diffusion from tubule to cell.

- Movement of Na is mediated primarily by a 1-Na, 2-Cl, 1-K co-transporter

## Counter transport

Na-H counter-transport mechanism

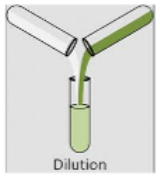


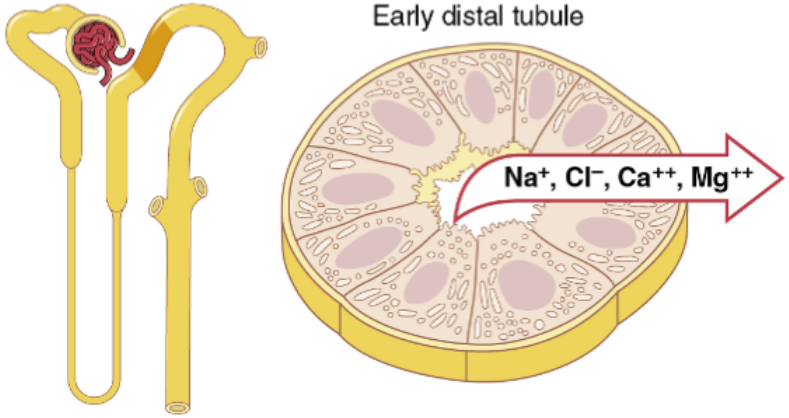

65%
H+
Cl
65%
Na
HCO3
K
100%
GLU
AA
Na
Ca++, Mg++
25%
1-Na, 2-Cl, 1-K
H+
Na+
H2O
NaCl
loop of Henle

# Early Distal Tubule

- ***Not permeable to water***

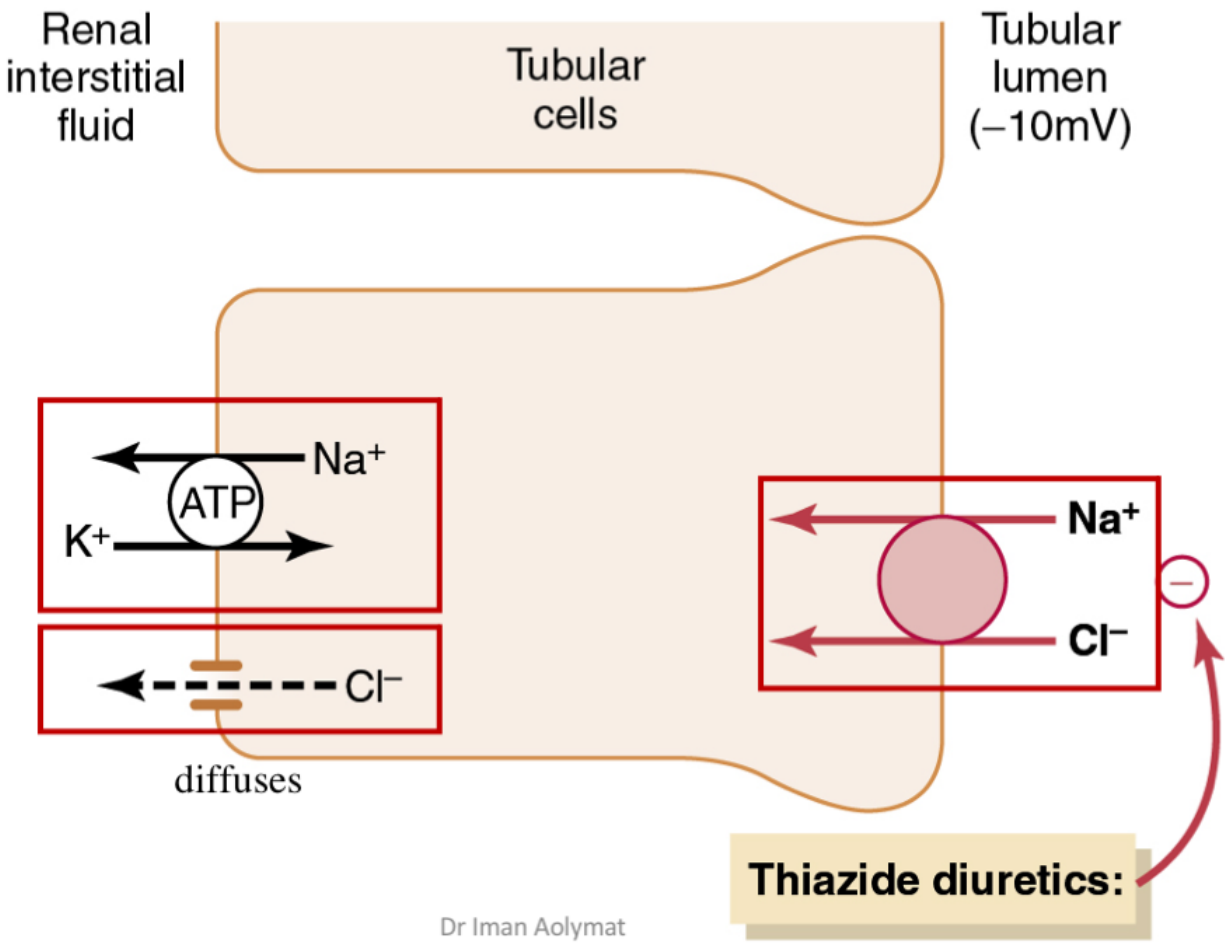

- ***Impermeable urea.***
- Called *diluting segment*

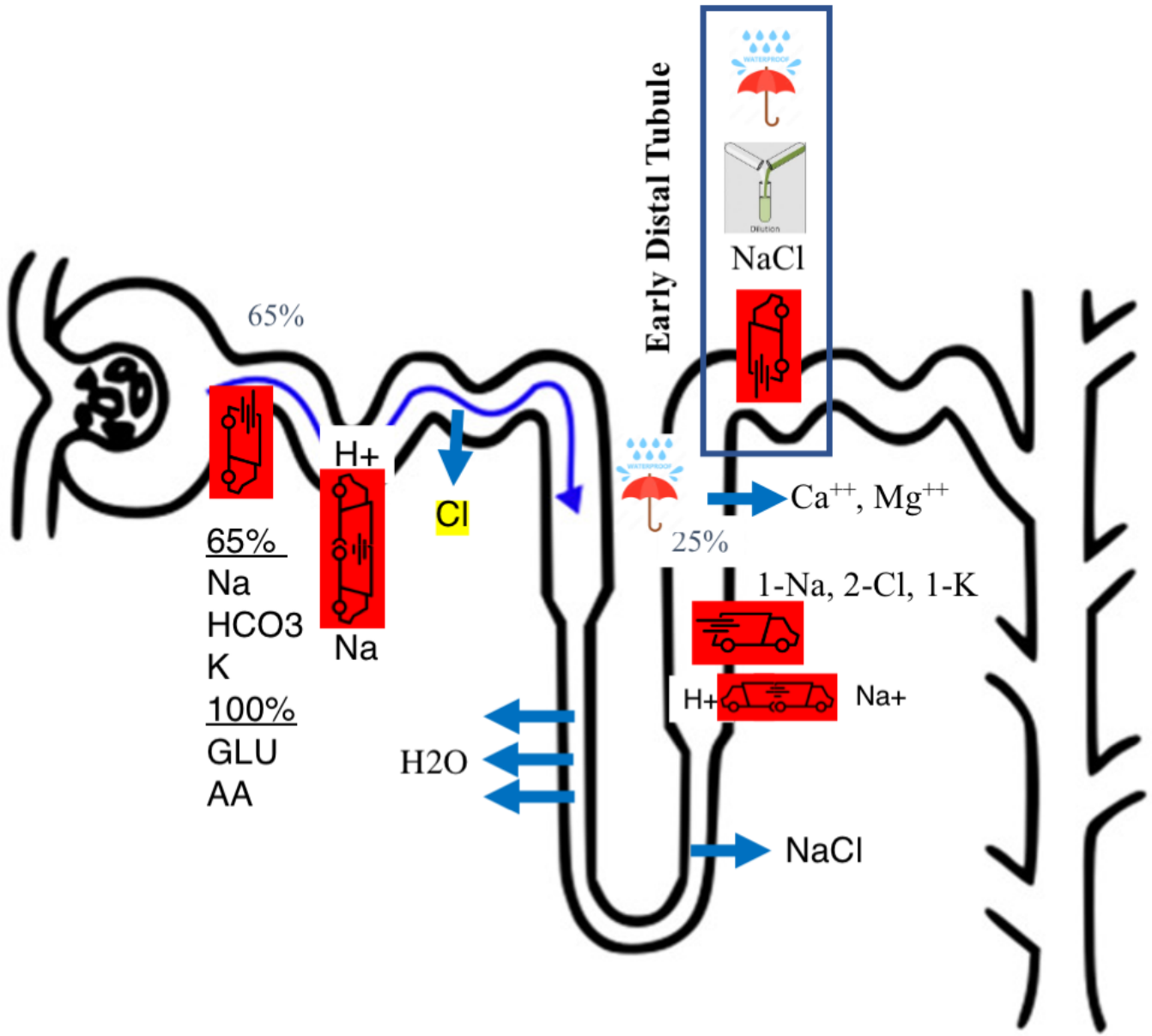


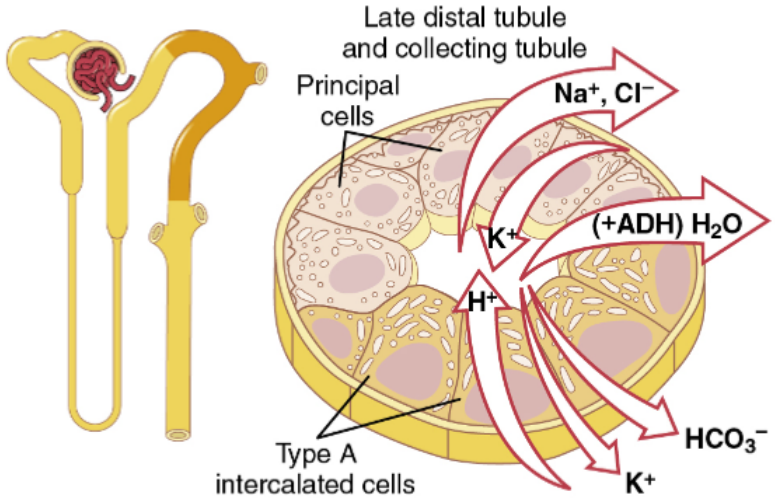

- **Active** reabsorption of $Na^+$, $Cl^-$, $K^+$, $Mg^{++}$

# Early Distal Tubule




Early Distal Tubule
NaCl
65%
H+
Cl
65%
Na
HCO3
K
100%
GLU
AA
Na
H2O
Ca++, Mg++
25%
1-Na, 2-Cl, 1-K
H+
Na+
NaCl

# Late Distal Tubules and Collecting Tubules.




- Control dilution or concentration of urine
- Permeability to $H_2O$ depends on **ADH**

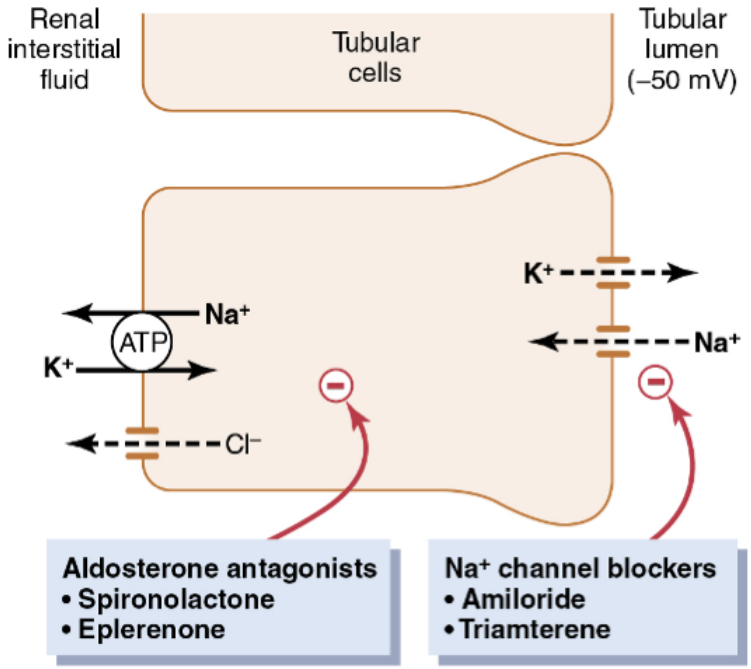
↑ ADH → ↑ permeability

↓ADH → ↓ permeability

- ***Not very permeable to urea***

# Principal Cells

- Na+-K+ATPase pump basolateral membrane.
- Low Na & High K intracellular →Na diffusion IN & K diffusion OUT
- **Aldosterone** ++Na reabsorption & K excretion
- Sites of action of the K-sparing diuretics.
- Aldosterone antagonists
- Na channel blockers

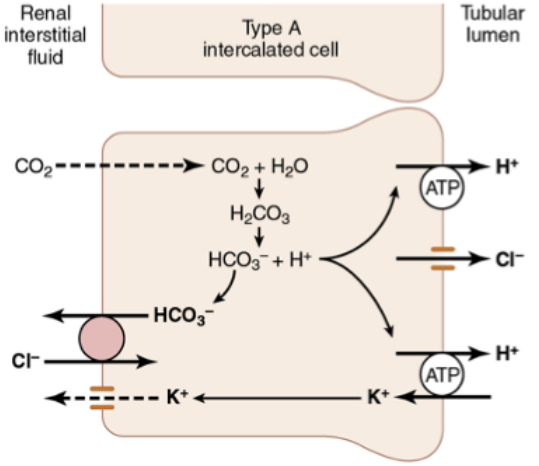



# **Intercalated Cells**- in acid-base regulation

**BEAR (Beta cells excrete HCO3, Alpha cells reabsorb it)**

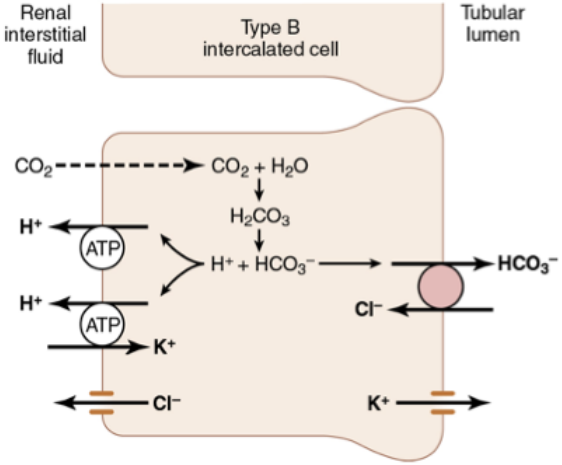
## Type A intercalated cells

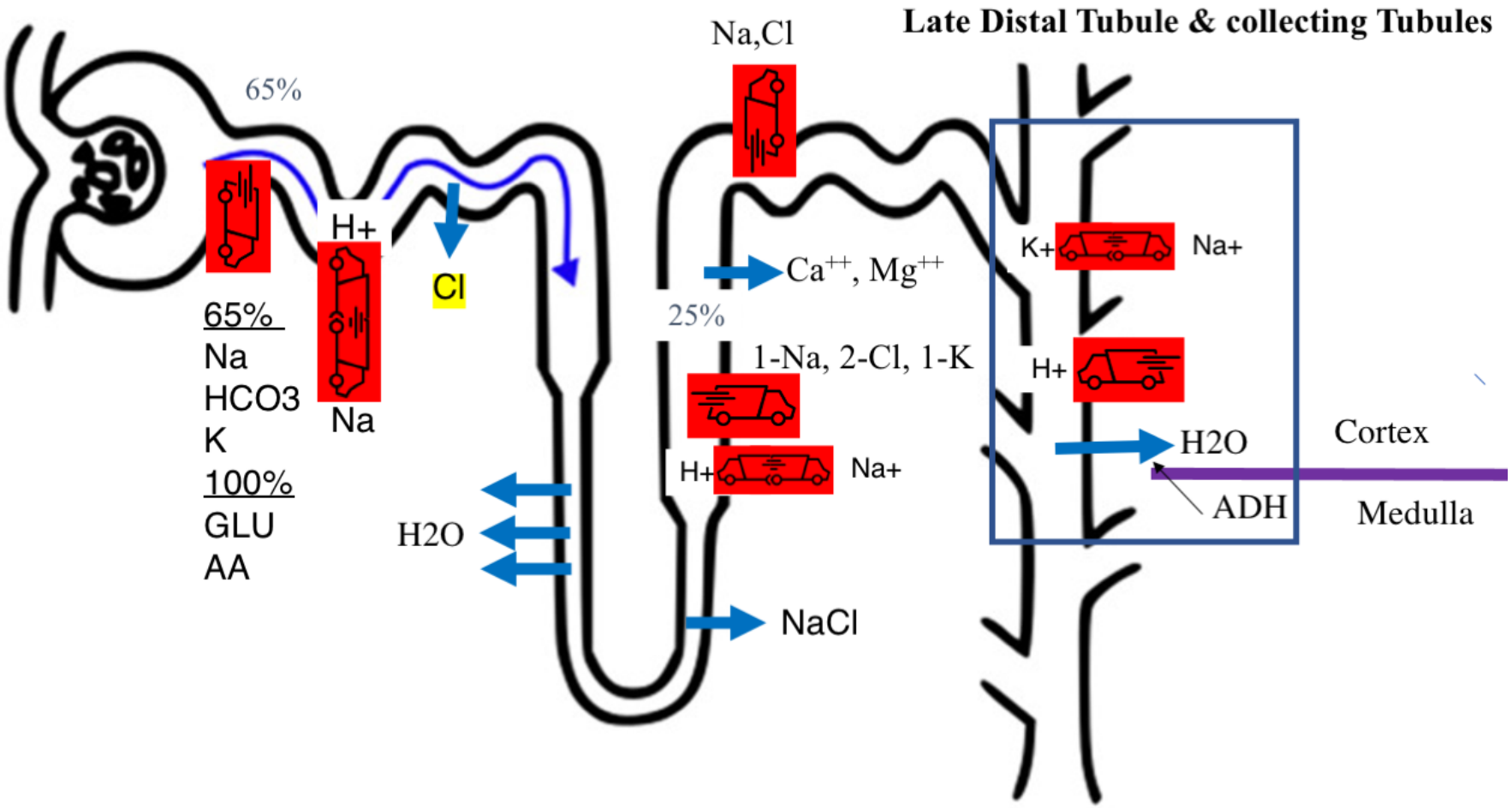
- $H^+$ secretion is mediated by a H-ATPase
- $H^+$ source?
- Reabsorb K
- for each $H^+$ secreted, $HCO_3$ reabsorbed across **the basolateral membrane**.




## Type B intercalated cells

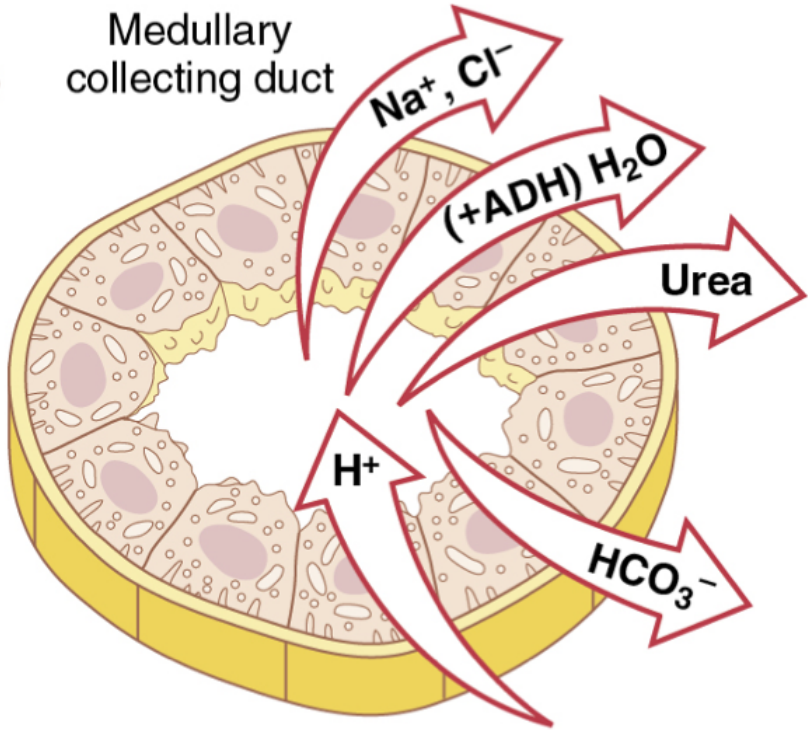
- Functions is opposite to those of type A cells (**in alkalosis**)
- $HCO_3$ to lumen
- $H^+$ reabsorption via H-ATPase
- Secrete K




Late Distal Tubule & collecting Tubules
Na,Cl
65%
H+
Cl
65%
Na
HCO3
K
100%
GLU
AA
Na
25%
Ca++, Mg++
1-Na, 2-Cl, 1-K
H+
Na+
H2O
NaCl
K+
Na+
H+
H2O
ADH
Cortex
Medulla

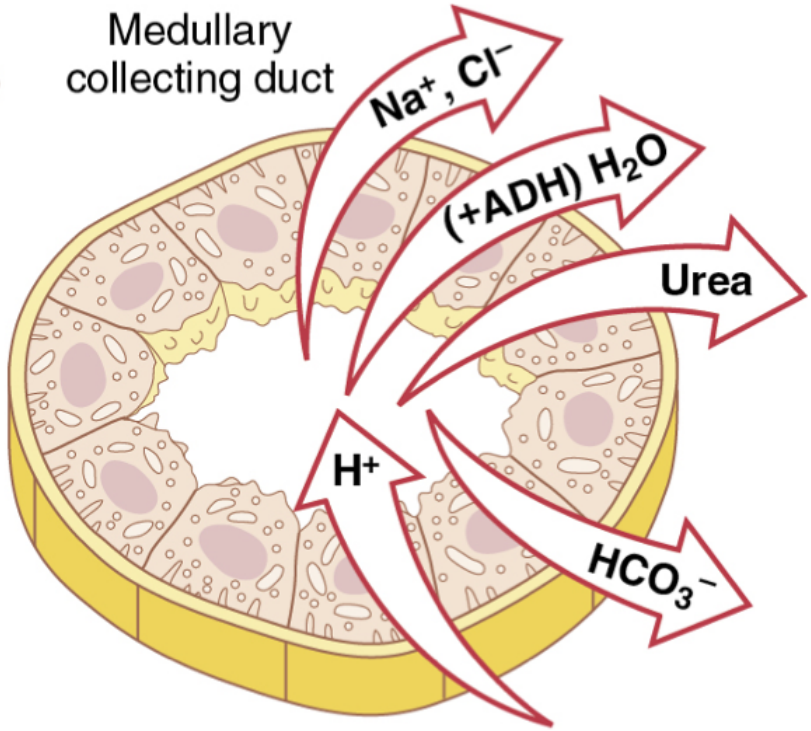
# Medullary collecting ducts

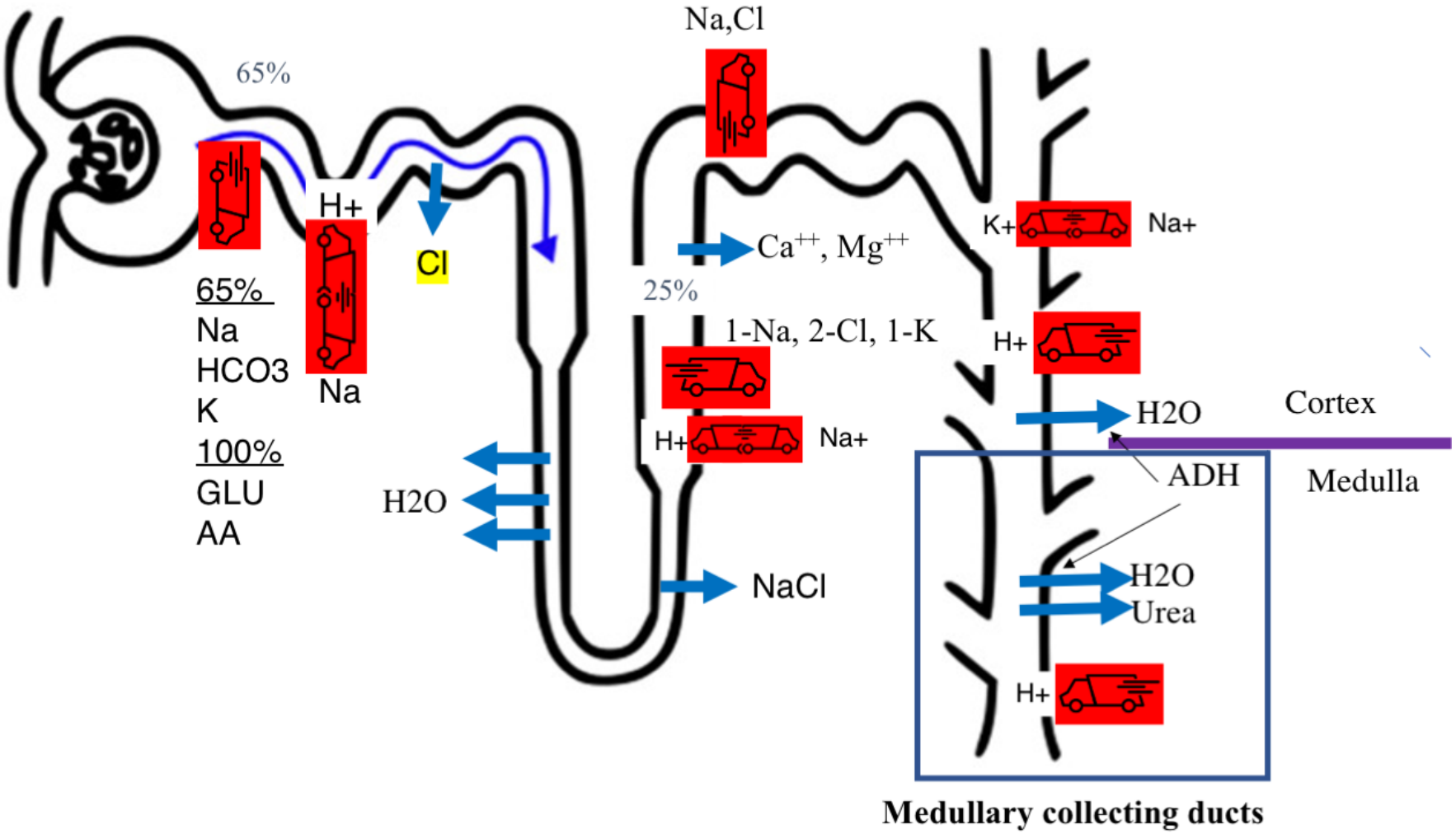
- Reabsorb <10% of filtered $H_2O$ & Na.
- Play an extremely important role in <u>determining the final urine output of water and solutes</u>.
- **Secretes H+** against a large concentration gradient→ plays a key role in regulating **acid-base balance**.



# Medullary collecting ducts

- $H_2O$ permeability → controlled by **ADH**.
- **Permeable to urea**→urea is reabsorbed into **medullary interstitium** → helping to raise the **osmolality** in this region of the kidneys and contributing to the kidneys' overall ability to form a **concentrated** urine.




65%
H+
Na
Cl
65%
Na
HCO3
K
100%
GLU
AA
H2O
Na,Cl
Ca++, Mg++
25%
1-Na, 2-Cl, 1-K
H+
Na+
NaCl
K+
Na+
H+
H2O
Cortex
Medulla
ADH
H2O
Urea
H+
Medullary collecting ducts

# Antidiuretic Hormone (ADH)

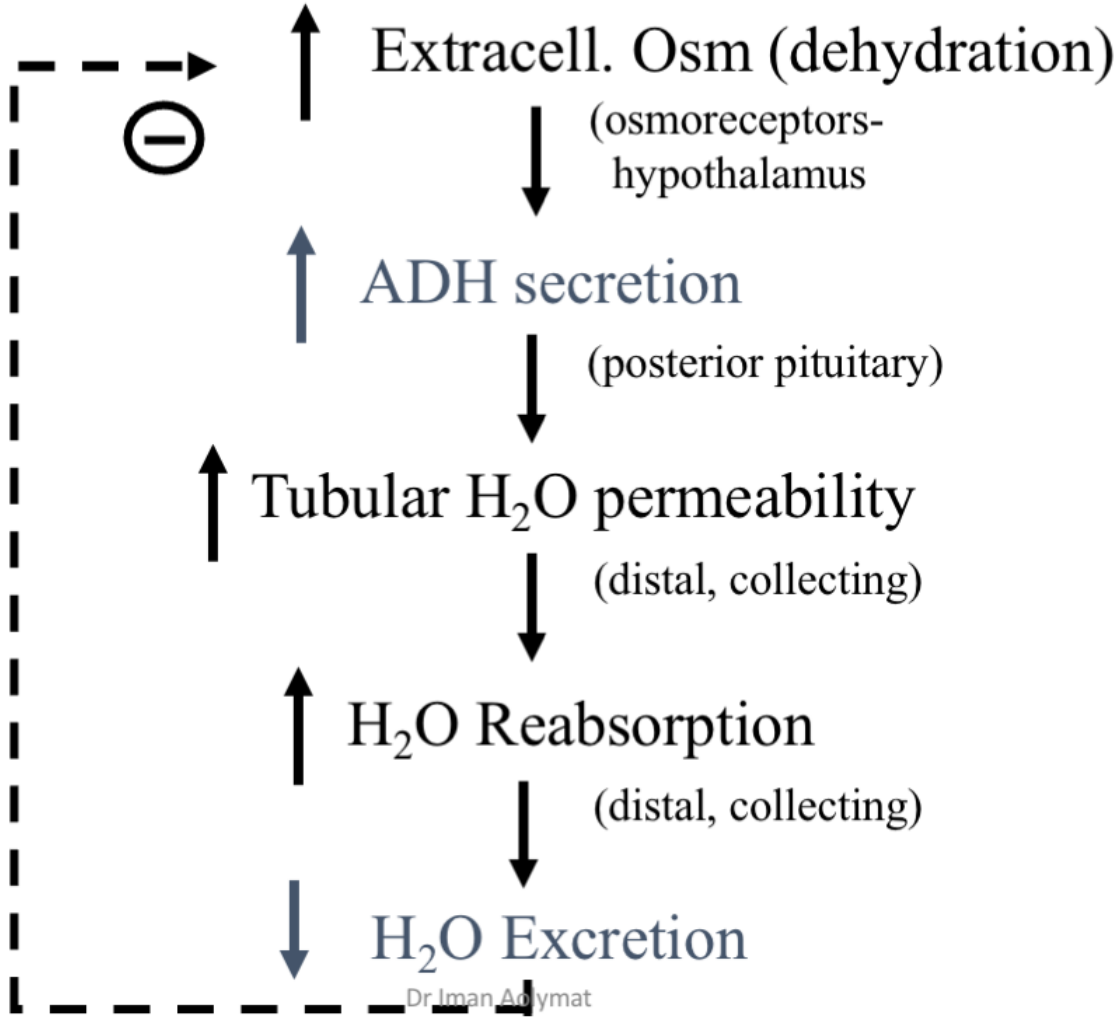
- Increases $H_2O$ permeability and reabsorption in **distal and collecting tubules**→ control of extracellular fluid *osmolarity*

- Inducing vasoconstriction- Vasopressin

# Stimuli for ADH Secretion

- ++ osmolarity
- -- blood volume/ P
- Other stimuli :
  - input from cerebral cortex (e.g. fear)
  - angiotensin II
  - nausea
  - nicotine
  - morphine

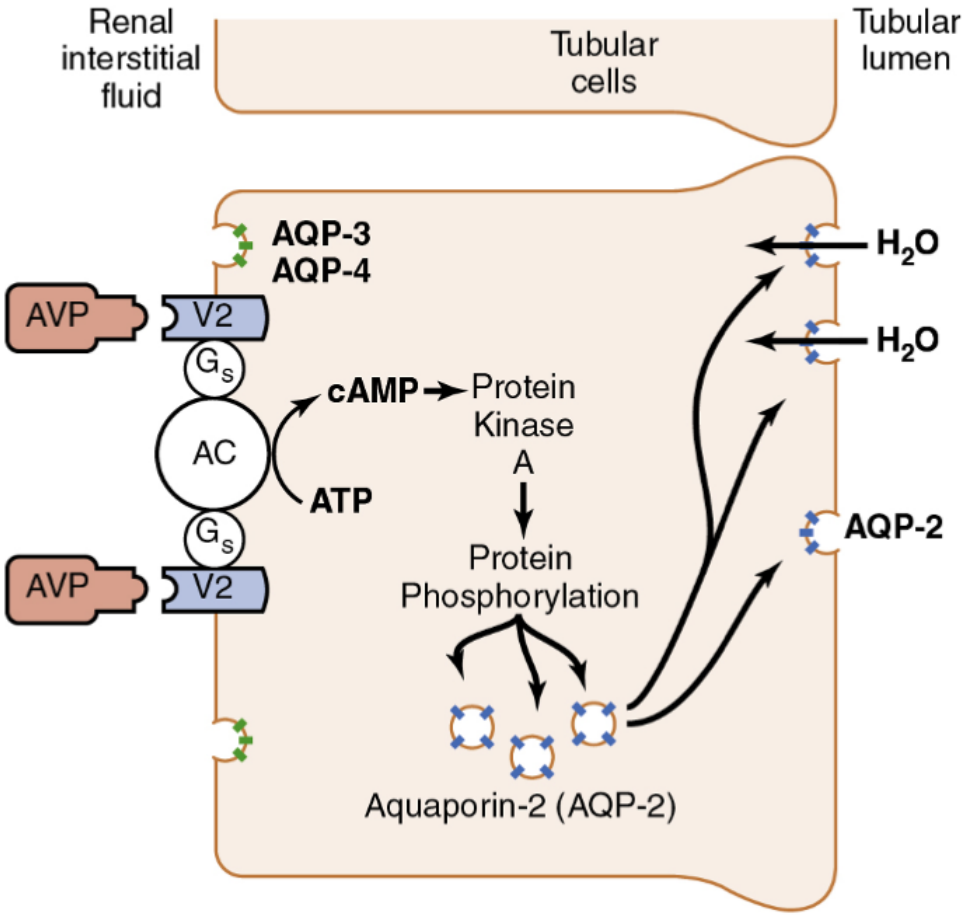
## Feedback Control of Extracellular Fluid Osmolarity by ADH



# Mechanism of action of ADH in distal and collecting tubules

Binds V2 receptors→ form cyclic AMP →++ AQP

- When ADH decreased → AQP back to cytoplasm



## Factors That Decrease ADH Secretion

- -- osmolarity
- ++ blood volume/ P

- Other factors :
  - alcohol
  - clonidine (antihypertensive drug)
  - haloperidol (antipsychotic)

**ADH is considerably more sensitive to small changes in osmolarity than to changes in blood volume**

# The End
# Thank you