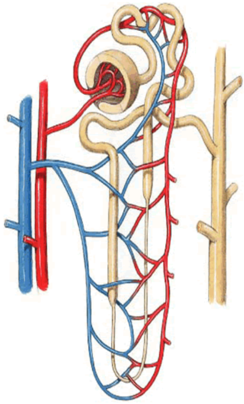

TUBULAR PROCESSING OF FILTRATE

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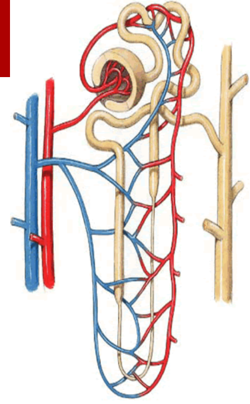


Contents

- The mechanisms of tubular transport through the different parts of the nephron.
- Tubular reabsorption and tubular secretion.
- Regulation of tubular processing.

Objectives

- Define tubular reabsorption and secretion.
- Identify the role of each tubular segment in glomerular filtrate modification and the types of substances being transported through each.
- Describe the hormonal/physiological factors regulating tubular function at each segment.
- Describe tubular reabsorption of sodium and water.
- Identify and describe mechanism involved in glucose reabsorption.
- Identify the tubular site and describe how amino acids and urea are reabsorbed.
- Identify and describe the characteristics of the loop of Henle, distal convoluted tubule and collecting ducts for reabsorption and secretion
- Describe the role of ADH in the reabsorption of water.
- Identify the site and describe the influence of aldosterone on reabsorption of Na+.
- List and explain the factors that control aldosterone and ADH release
- Identify and describe the juxtamedullary apparatus and its role in checking the filtrate.

Tubular Processing of Ultrafiltrate

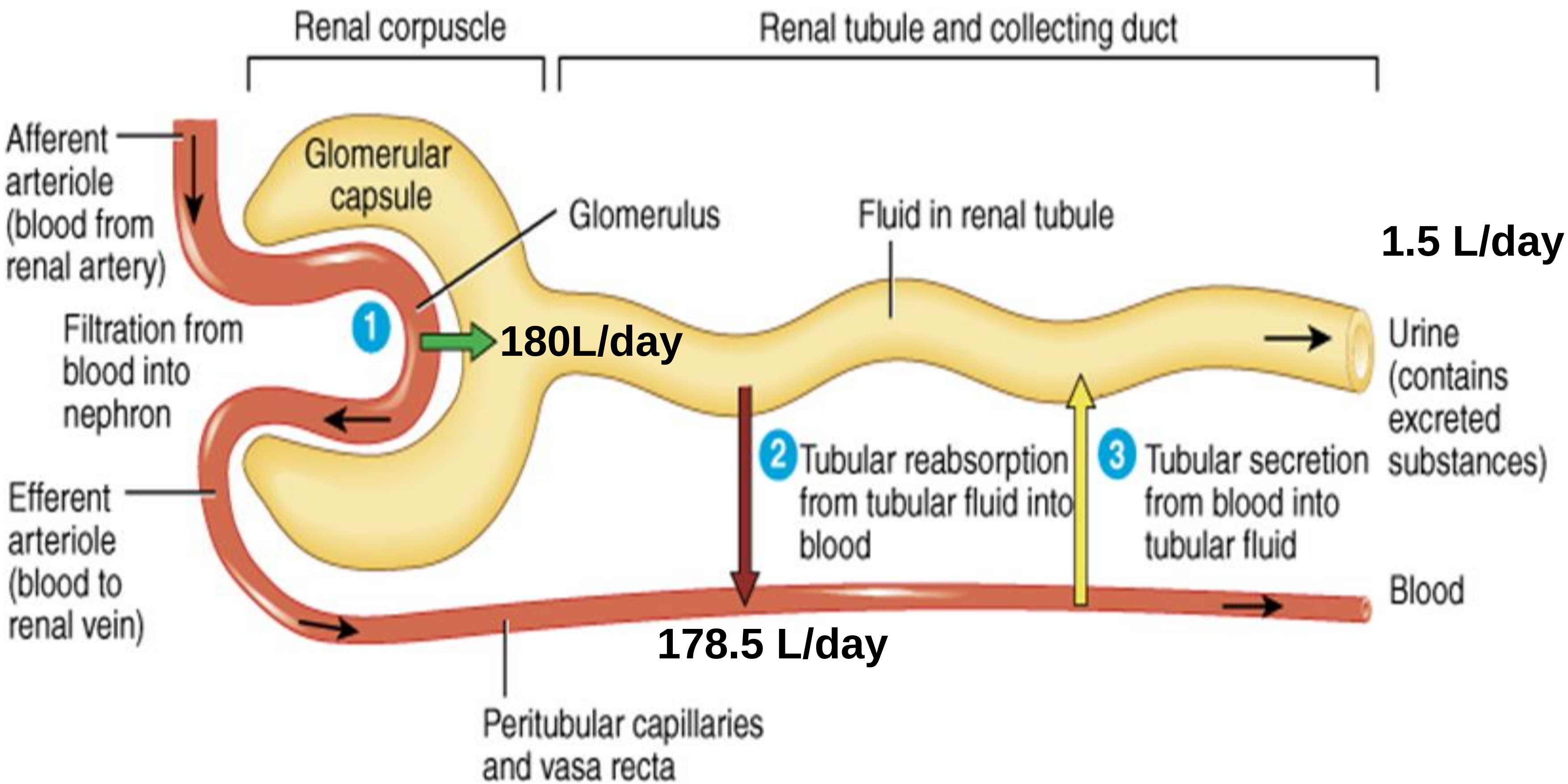
- After glomerular filtration the ultrafiltrate gets modified as it passes through the nephron tubule before it is finally excreted.

- **Tubular processing includes**:
  - ***Tubular reabsorption*** = reabsorption of substances from the glomerular filtrate into peritubular capillary blood.
  - ***Tubular secretion*** = secretion of substances from peritubular capillary blood into tubular fluid

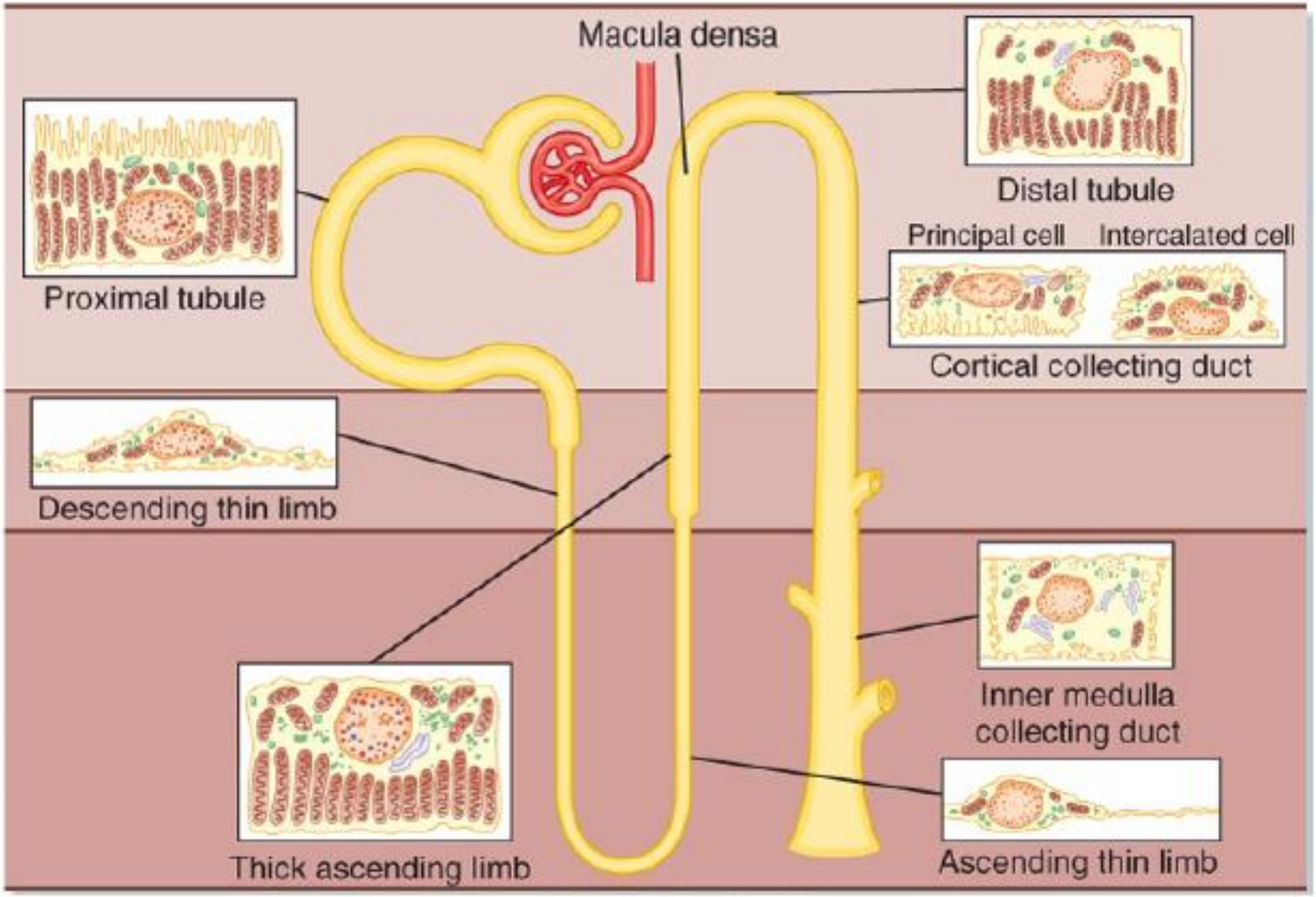
- ***What is the importance of tubular processing?***

Tubular Reabsorption

- Glomerular filtration and tubular reabsorption are quantitatively very large relative to the amount excreted!
- Glomerular filtration is non-selective whereas tubular reabsorption is highly selective.



Differences in Renal Tubular Cells Reflect Their Function in Tubular Processing



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

Figure 32-3 Diagram of a nephron, including the cellular ultra-structure.

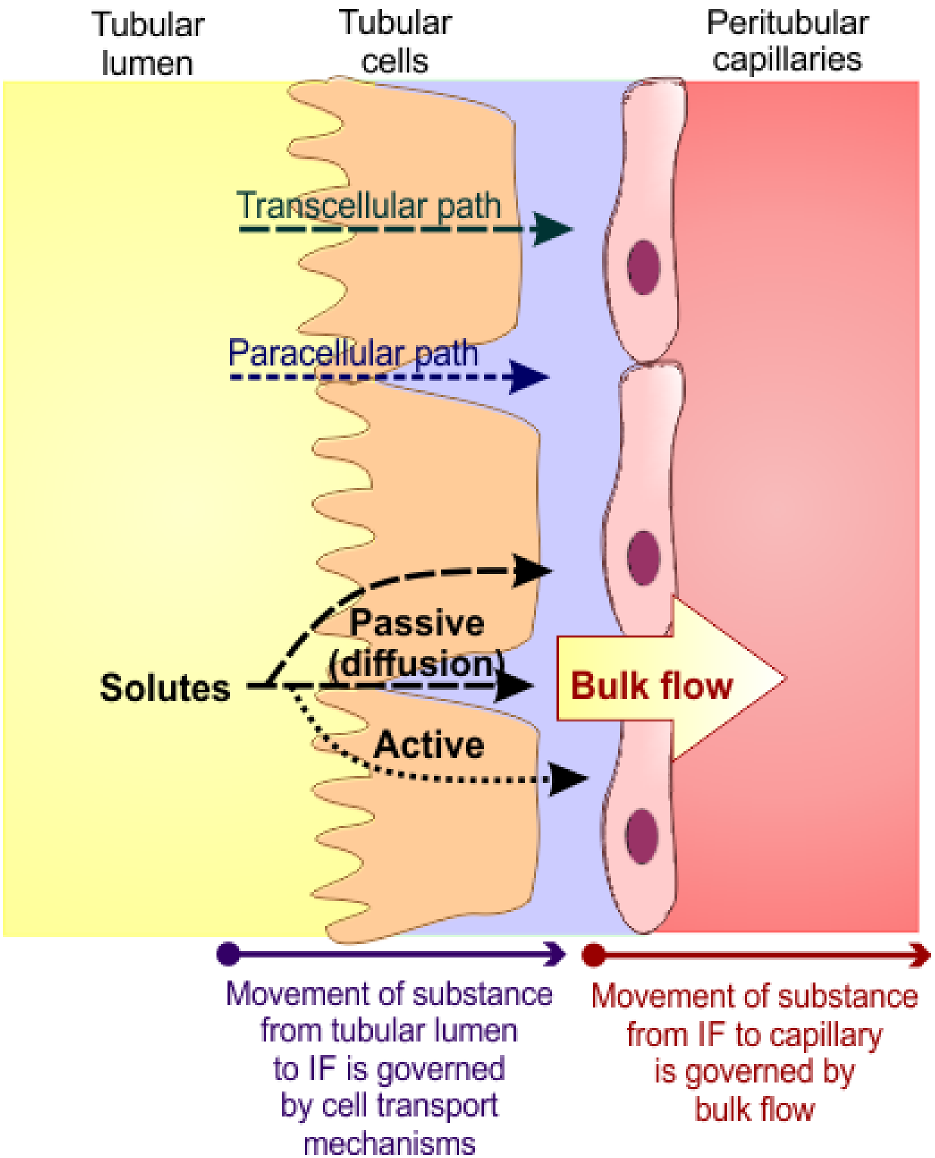
TUBULAR REABSORPTION

How does the nephron reabsorb substances

- ***Reabsorption is a 2 step process:***

1. Transport of substances from tubular lumen to IF.
2. Transport from IF to blood.

- From tubular lumen to IF;
  - Transport involves ***active*** & ***passive*** mechanisms.
  - Occur through ***paracellular*** and/or ***transcellular*** routes.
- From IF to blood:
  - By ultrafiltration (bulk flow).



Transport Mechanisms Across the Tubule

Active Transport

- Requires energy.
- Moves substances against their electrochemical gradient.

Primary active

Directly coupled to energy source.

e.g. Na+-K+ ATPase.

Secondary active

Indirectly coupled to energy source.

Carrier protein.

e.g. Glucose & a.a.

Passive Transport

- Does not need energy.
- Moves substances down their electrochemical gradient.

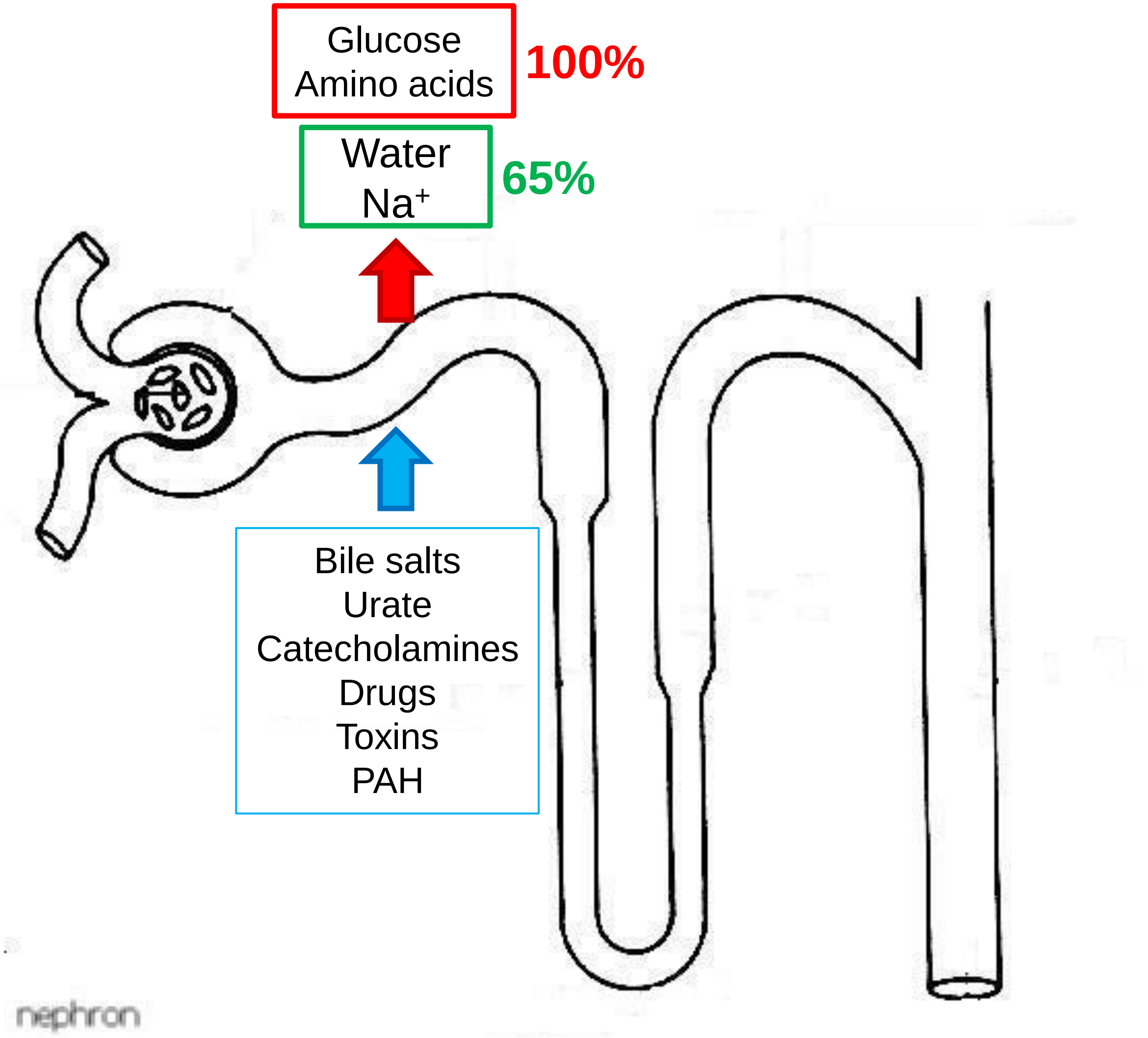
Passive diffusion Osmosis

Water
Solutes like Cl-
Urea

TUBULAR REABSORPTION IN EACH PART OF THE NEPHRON

Proximal Convoluted Tubule

- Most of the reabsorption occurs in the PCT.. ***Why***?
  - Highly metabolic cells.
  - Extensive brush border.
  - Lots of mitochondria.

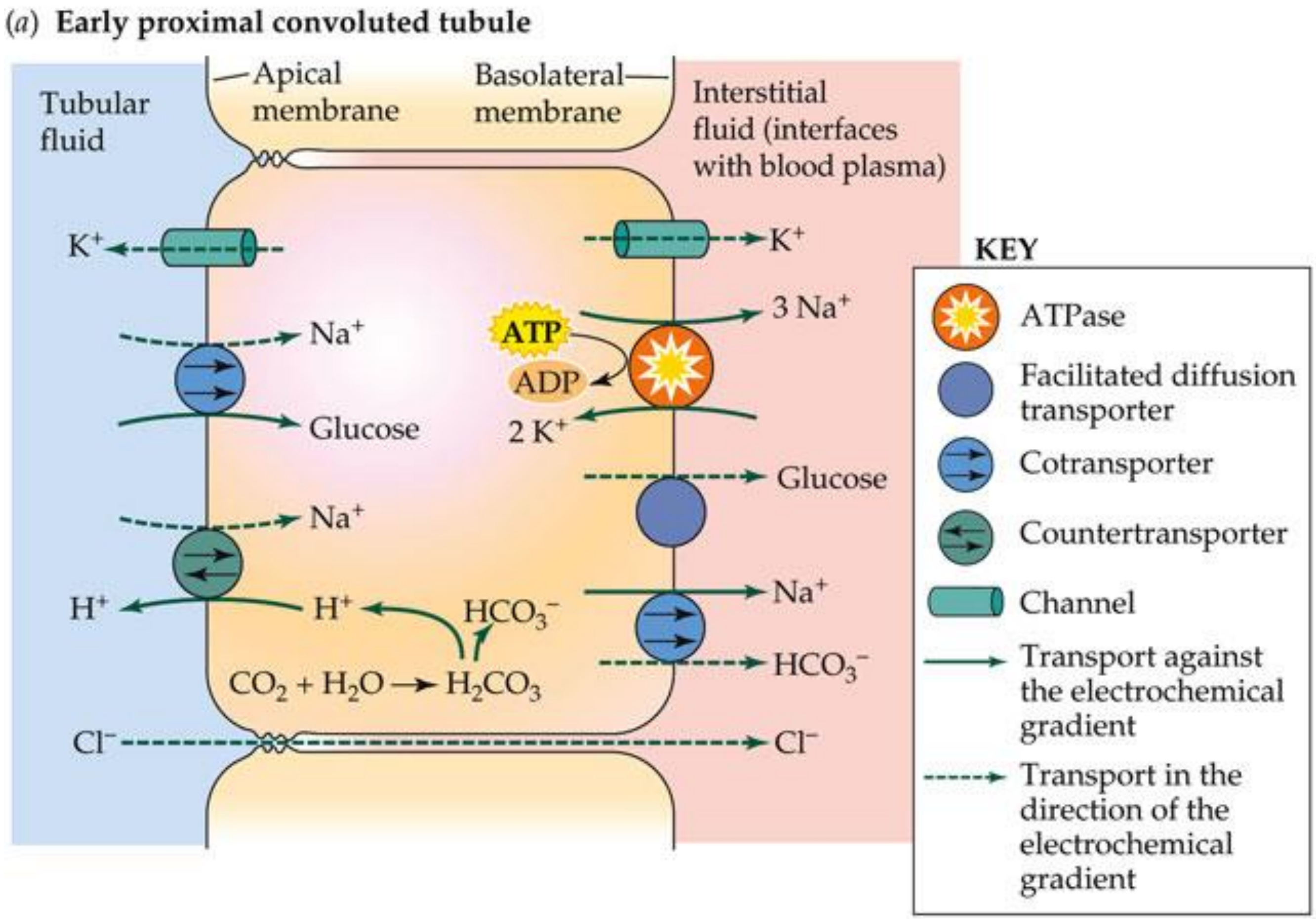


Sodium Reabsorption

Basolateral Na^+-K^+ ATPase pumps $3Na^+$ out and $2K^+$ into the cell

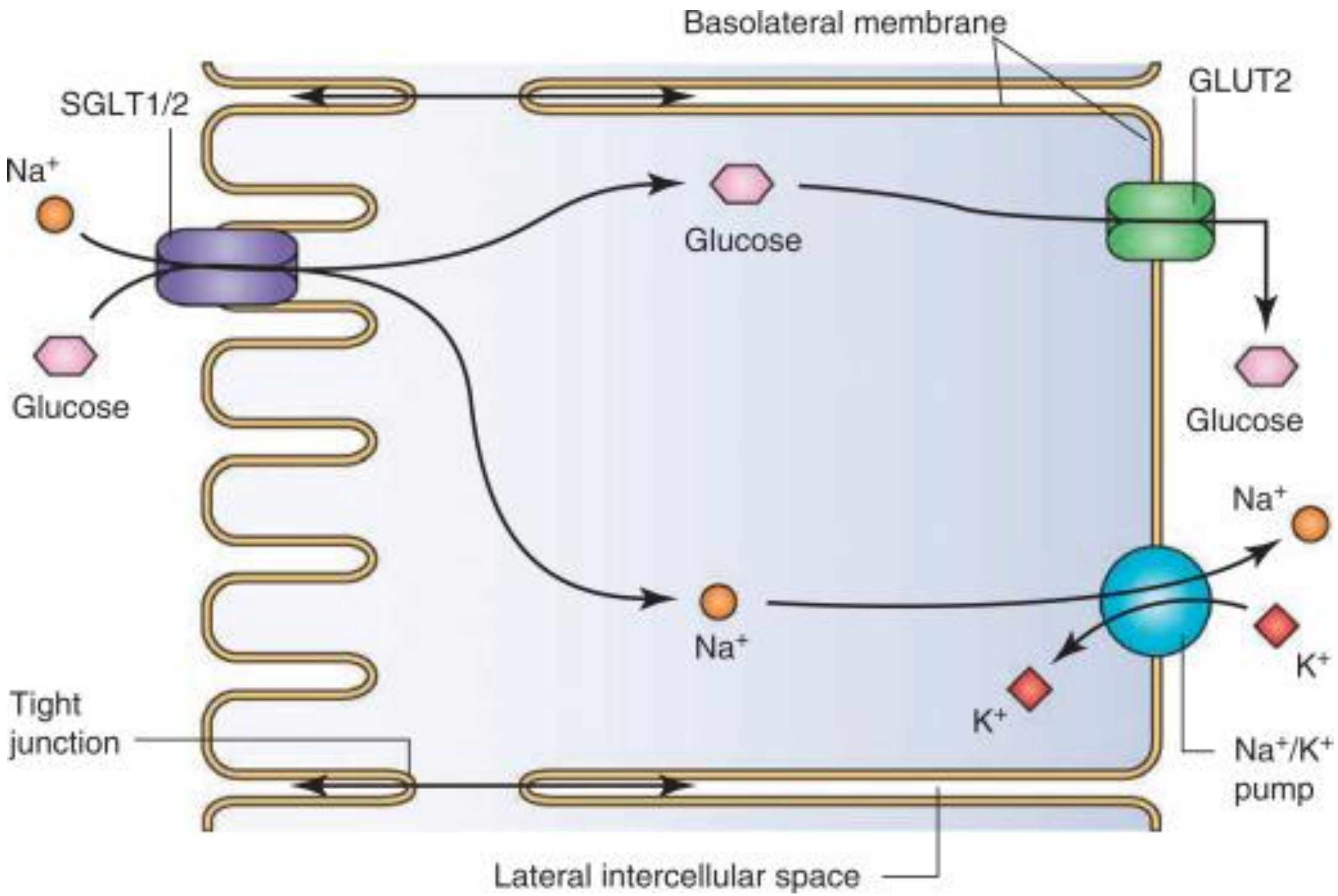
Results in low $[Na^+]i$

This gradient favours Na^+ entry across the apical membrane via transporter proteins



Animal Physiology 2e, Figure 28.16 (Part 1)

Glucose Reabsorption



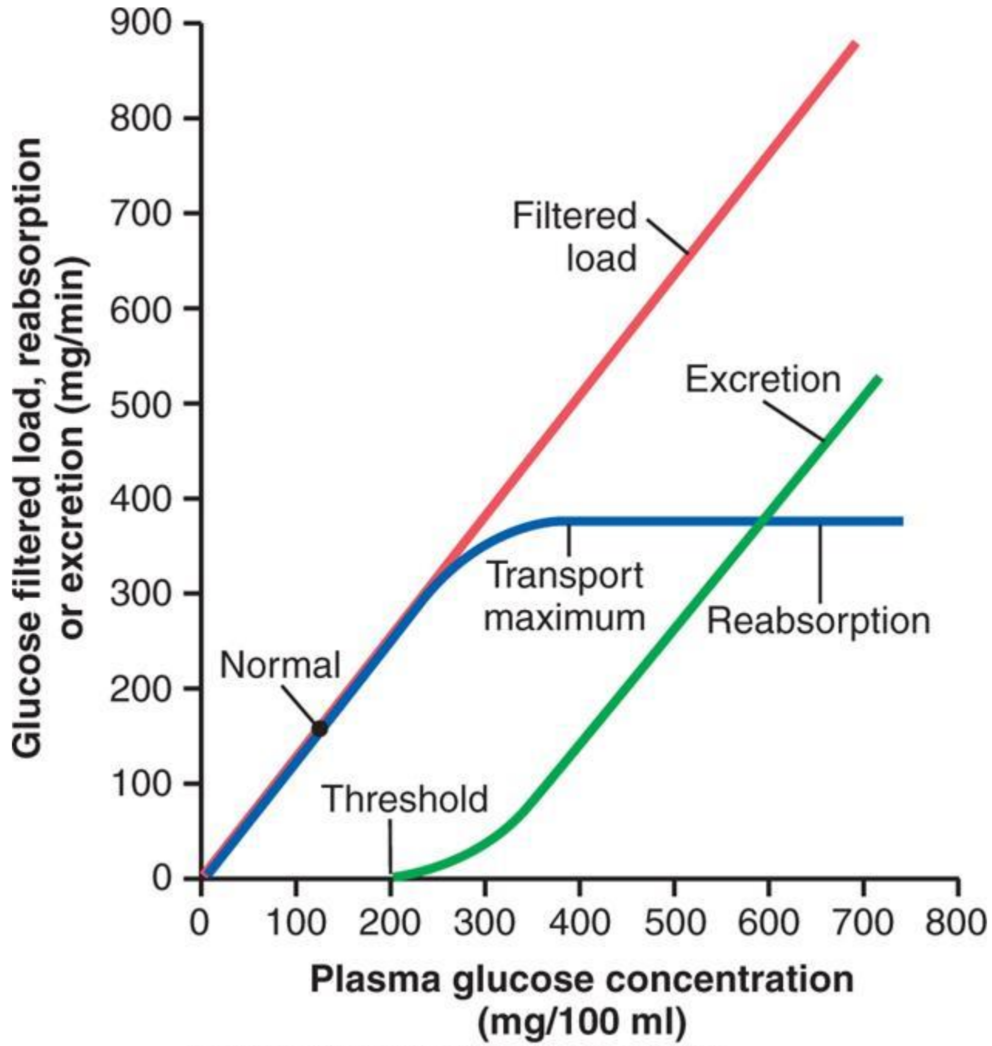
Transport Maximum for Glucose

What is meant by transport maximum?

Why does it occur?

What is the difference between transport maximum and threshold?

What happens if blood glucose level increased to 400mg/dl?



Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

Sodium Reabsorption

Early part of PCT	Late part of PCT

Early part of PCT

- Mainly coupled to;
  - Glucose.
  - Amino acids.
  - Lactate.
  - Phosphate

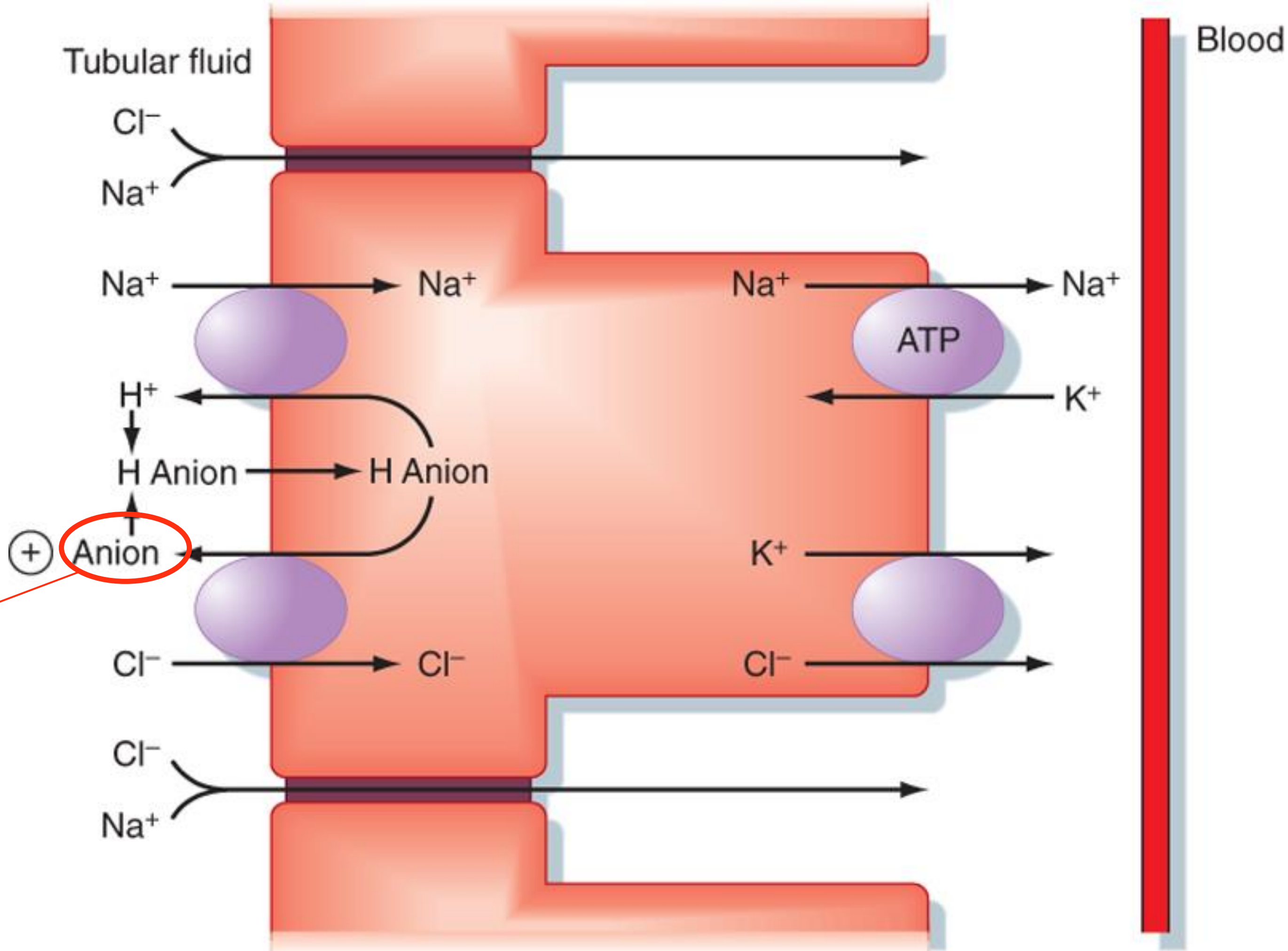
  } Symporters

  - Hydrogen → Antiporter

Late part of PCT

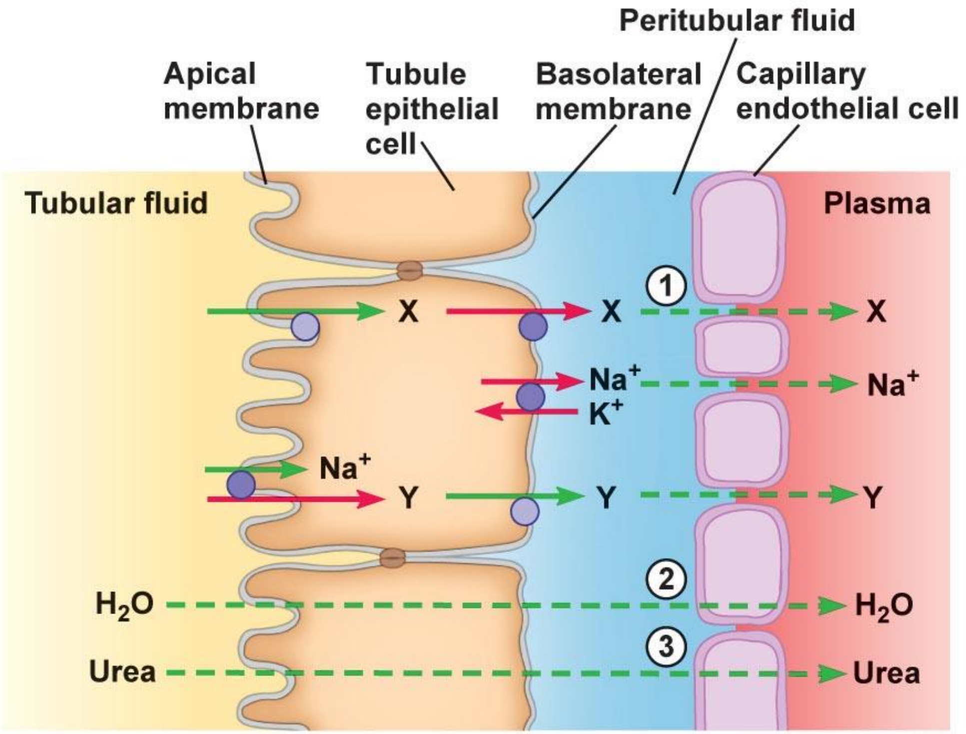
- Mainly coupled to Cl^-
- ***Why??***

Sodium Chloride Reabsorption in the 2nd half of the PCT



e.g.
Formate
Oxalate
Sulfate

Water Reabsorption in the PCT



Steps for water and urea reabsorption:

1. Solutes (Na^+, X, Y) are actively reabsorbed, increasing the osmolarity of peritubular fluid and plasma.
2. Water is reabsorbed by osmosis.
3. Urea (permeating solute) is reabsorbed passively.

Organic Anion/Cation Secretion

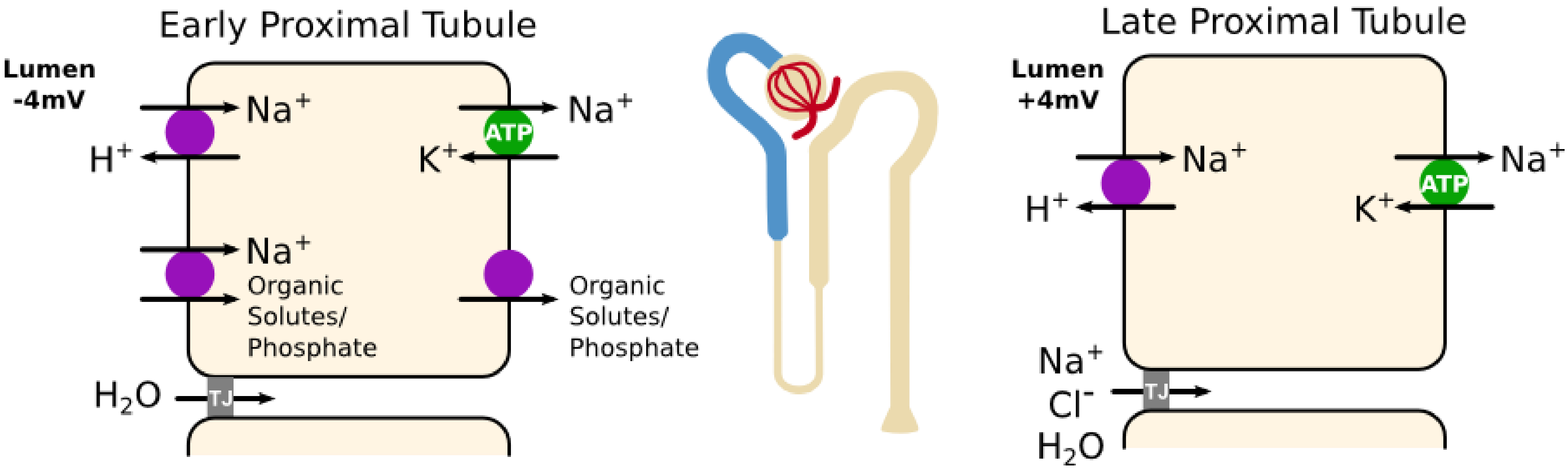
Organic Anions

- Endogenous:
  - Bile salts.
  - Oxalate.
  - Urate.
  - Vitamins (ascorbate, folate).
- Exogenous:
  - Acetazolamide.
  - Furosemide.
  - Salicylates.
  - Penicillin.

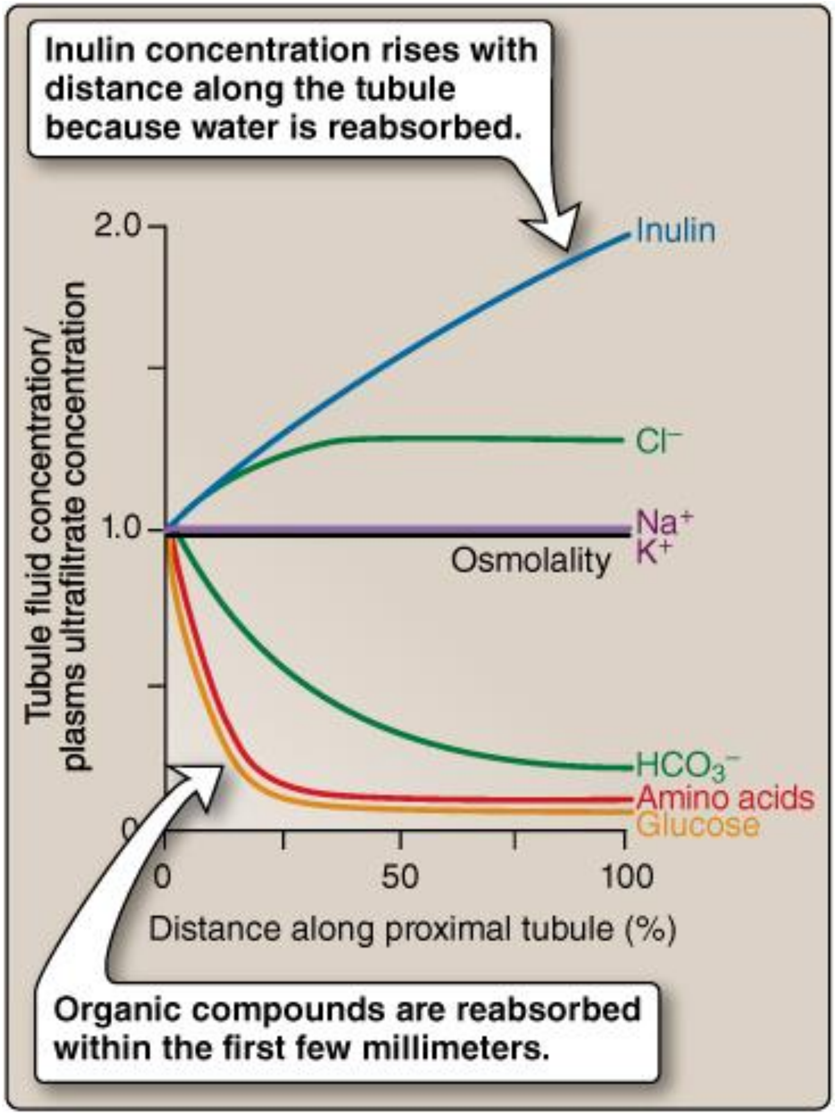
Organic cations

- Endogenous;
  - Creatinine.
  - Dopamine.
  - Epinephrine.
  - Norepinephrine.
- Exogenous;
  - Atropine.
  - Morphine.
  - Amiloride.
  - Procainamide.

Summary of PCT Transport Mechanisms

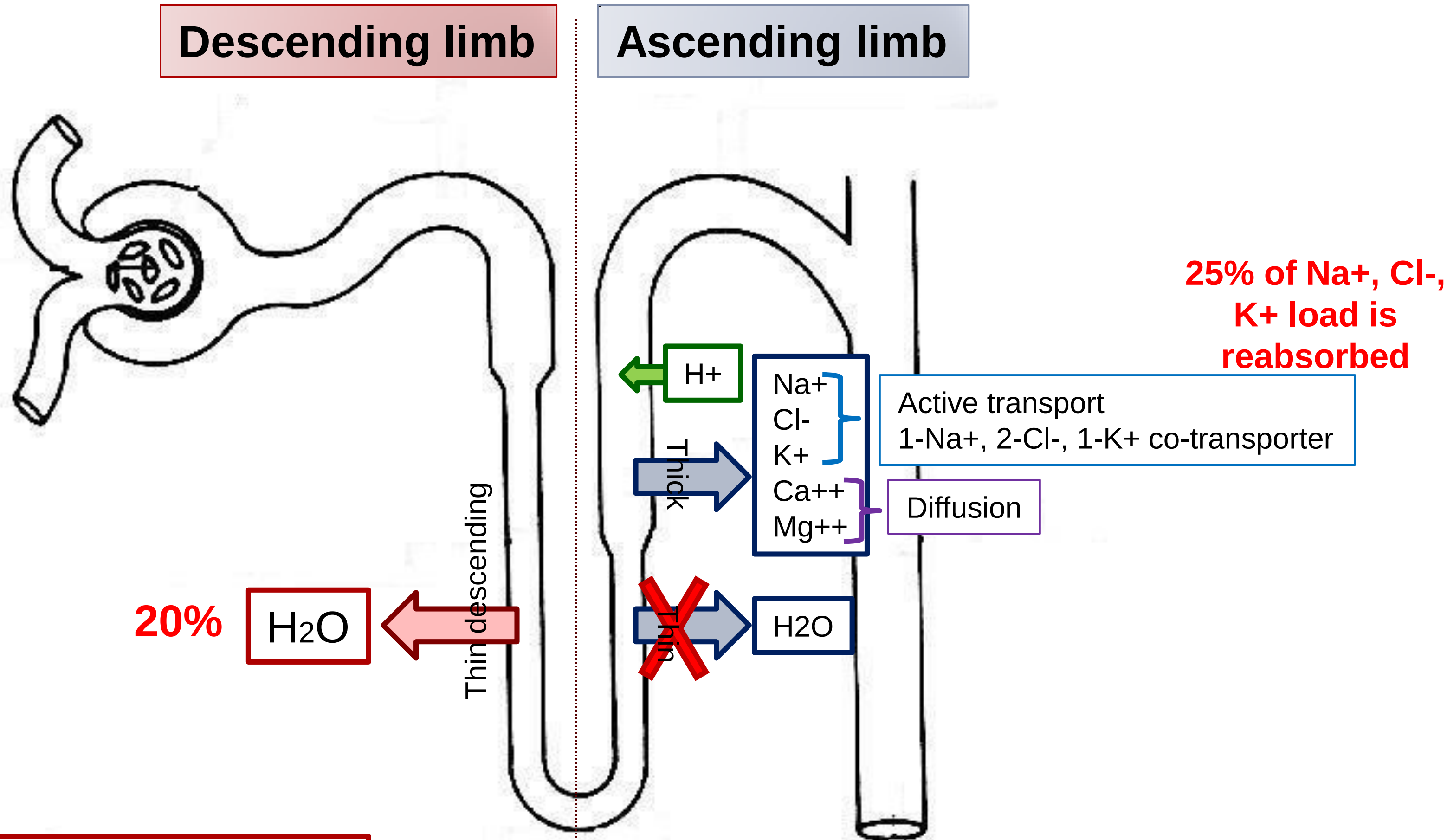


Summary of PCT Filtrate Modification



LOOP OF HENLE

Loop of Henle

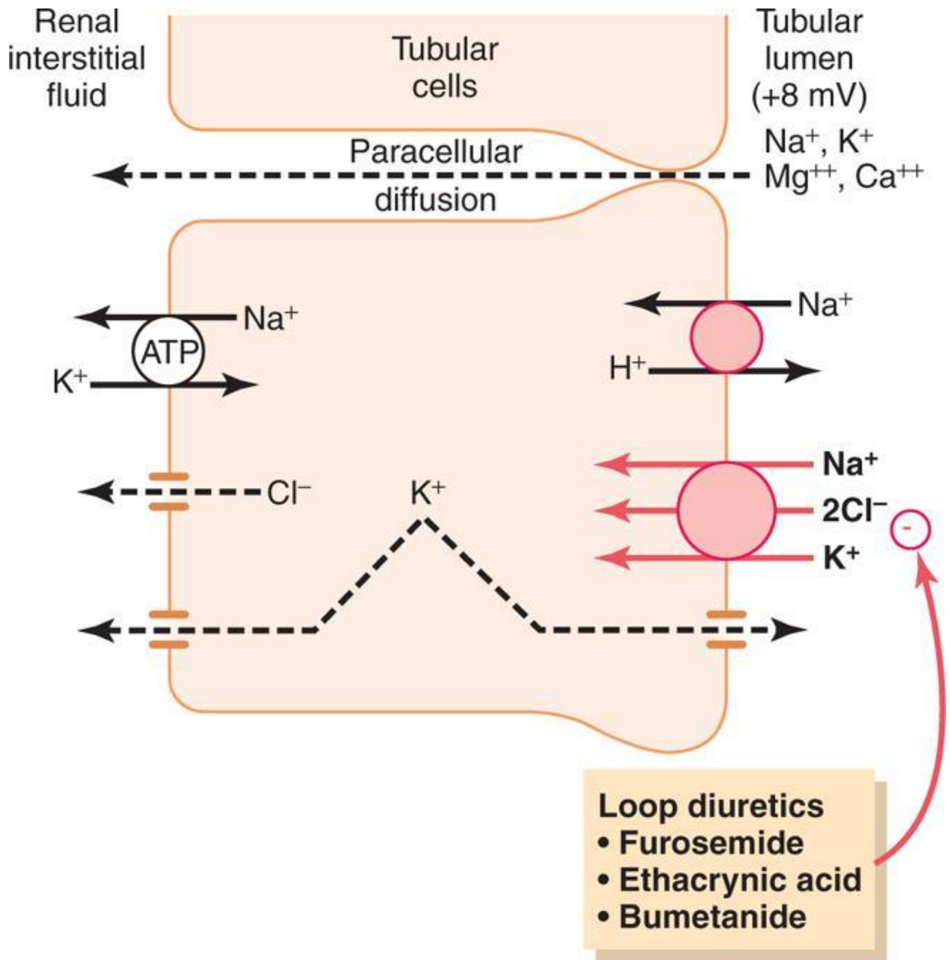


- Highly permeable to water
- Moderate permeability to solutes

- ***Impermeable*** to water
- Reabsorption of solutes in the thick segment

Loop of Henle

Mechanism of transport in the thick ascending loop of Henle



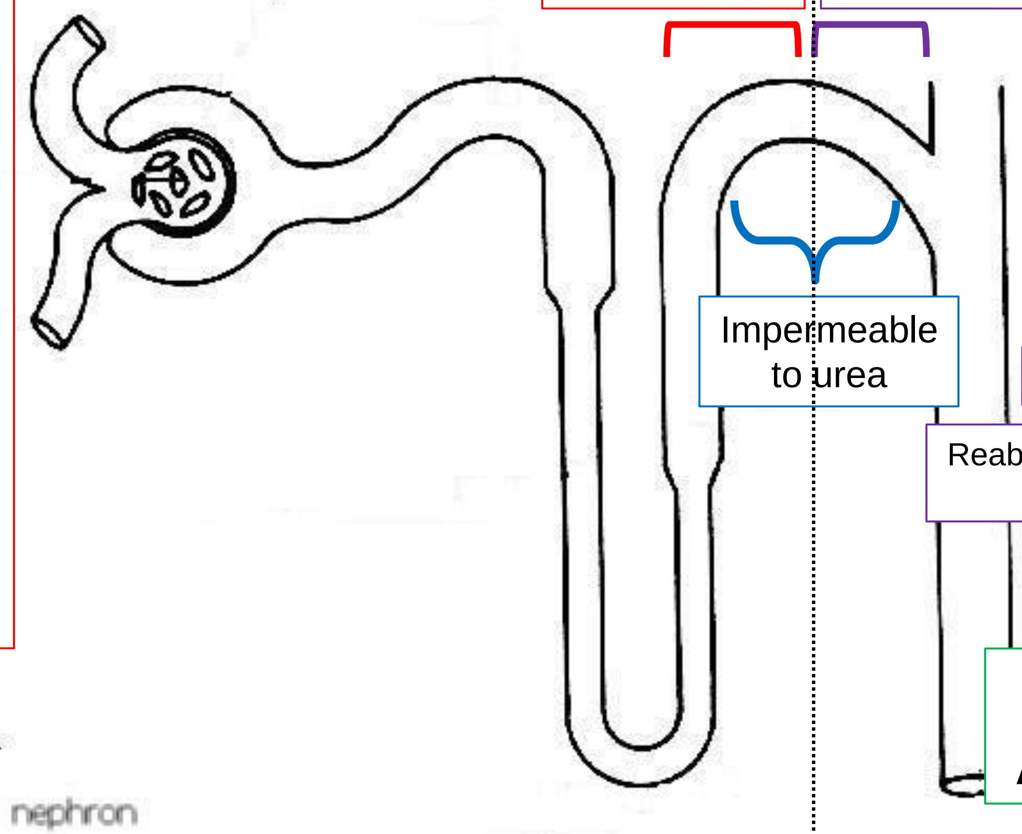
Distal Convoluted Tubule

Resembles the thick ascending loop of Henle

Known as *the diluting segment*

Reabsorbs 5% of NaCl

Early part | **Late part**



Impermeable to urea

Resembles the cortical collecting tubule

Principal cells

Reabsorb Na+ & H_2O
Secrete K+

Controlled by Aldosterone

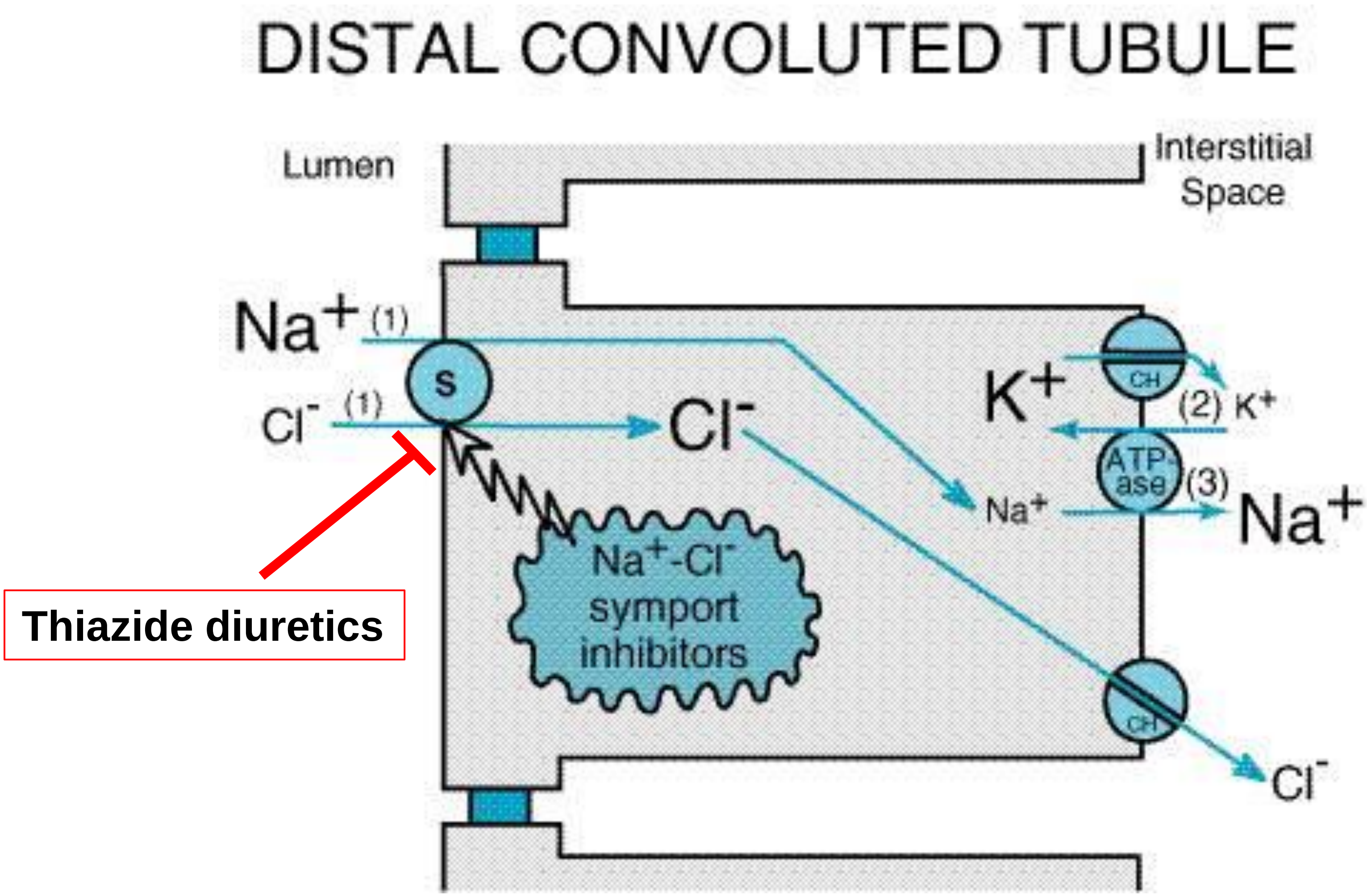
Intercalated cells Type A

Reabsorb K+
Secrete H+

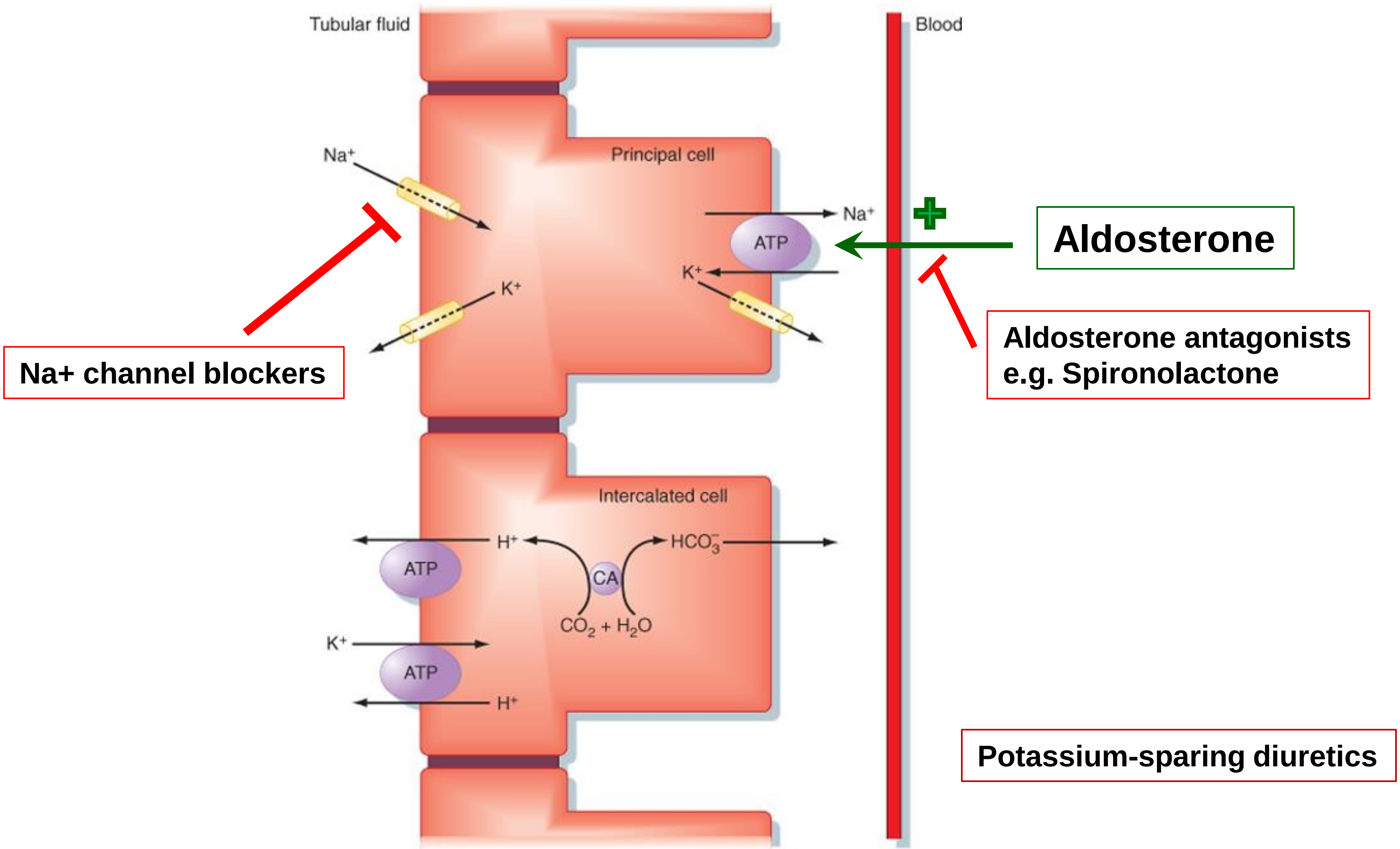
Acid-base regulation

Permeability to H_2O depends on *ADH*

Early Distal Tubule

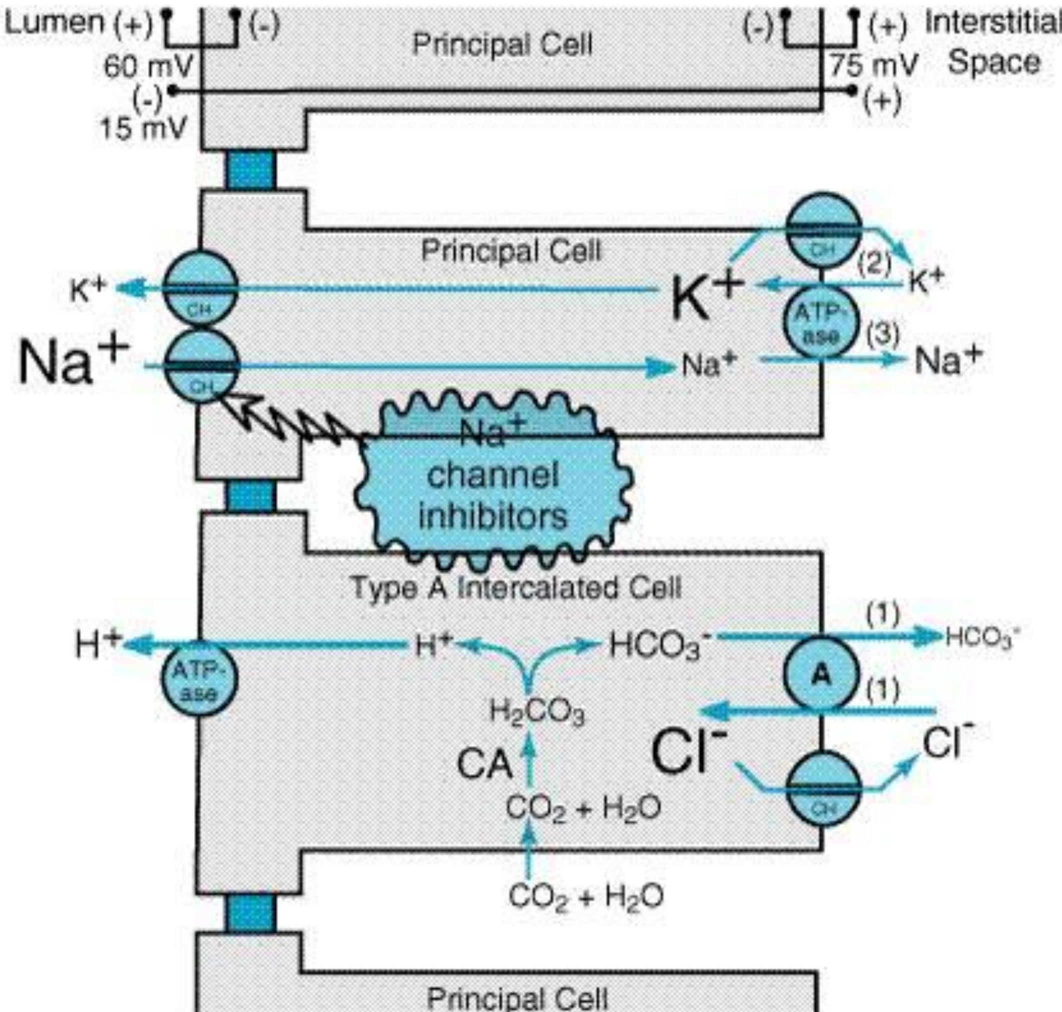


Late Distal Tubule & Collecting Tubule

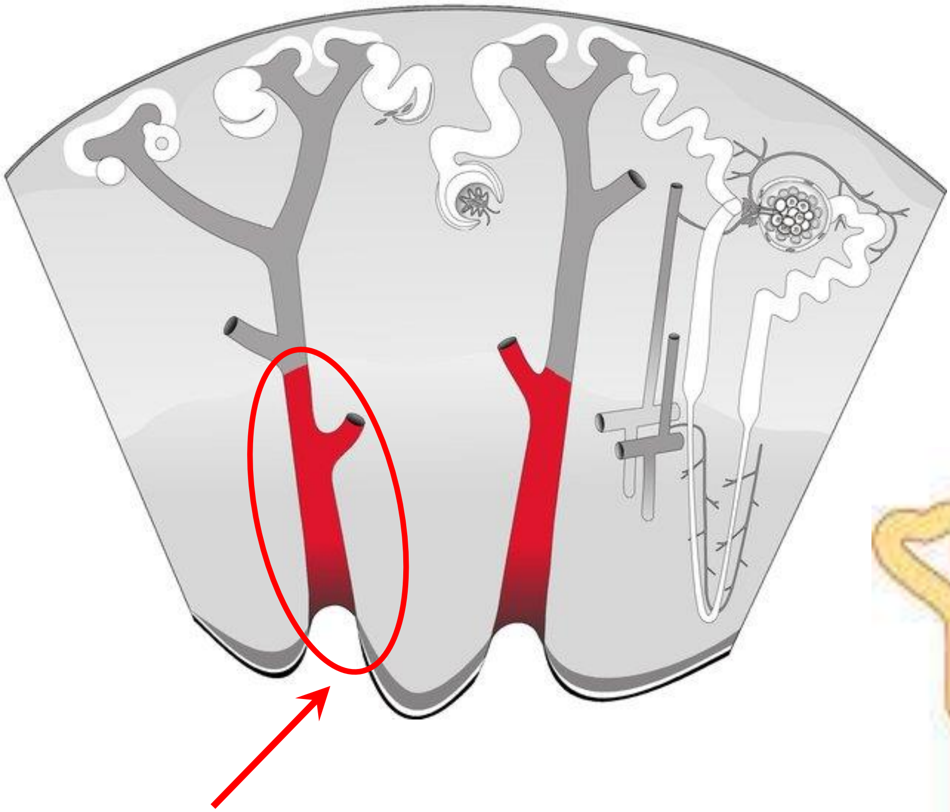


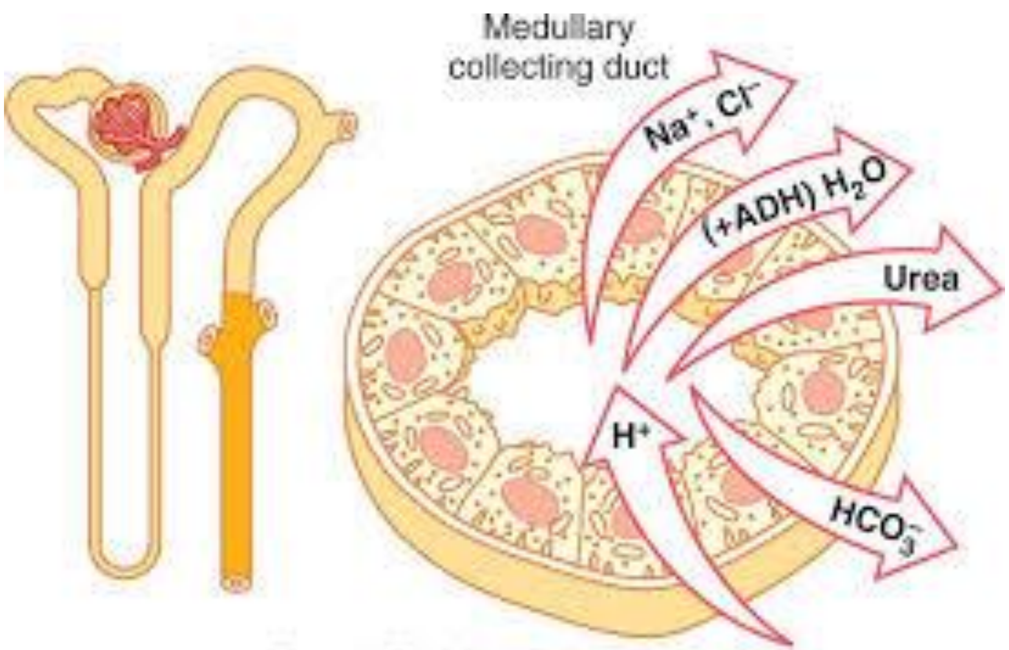
Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

LATE DISTAL TUBULE AND COLLECTING DUCT



Medullary Collecting Duct



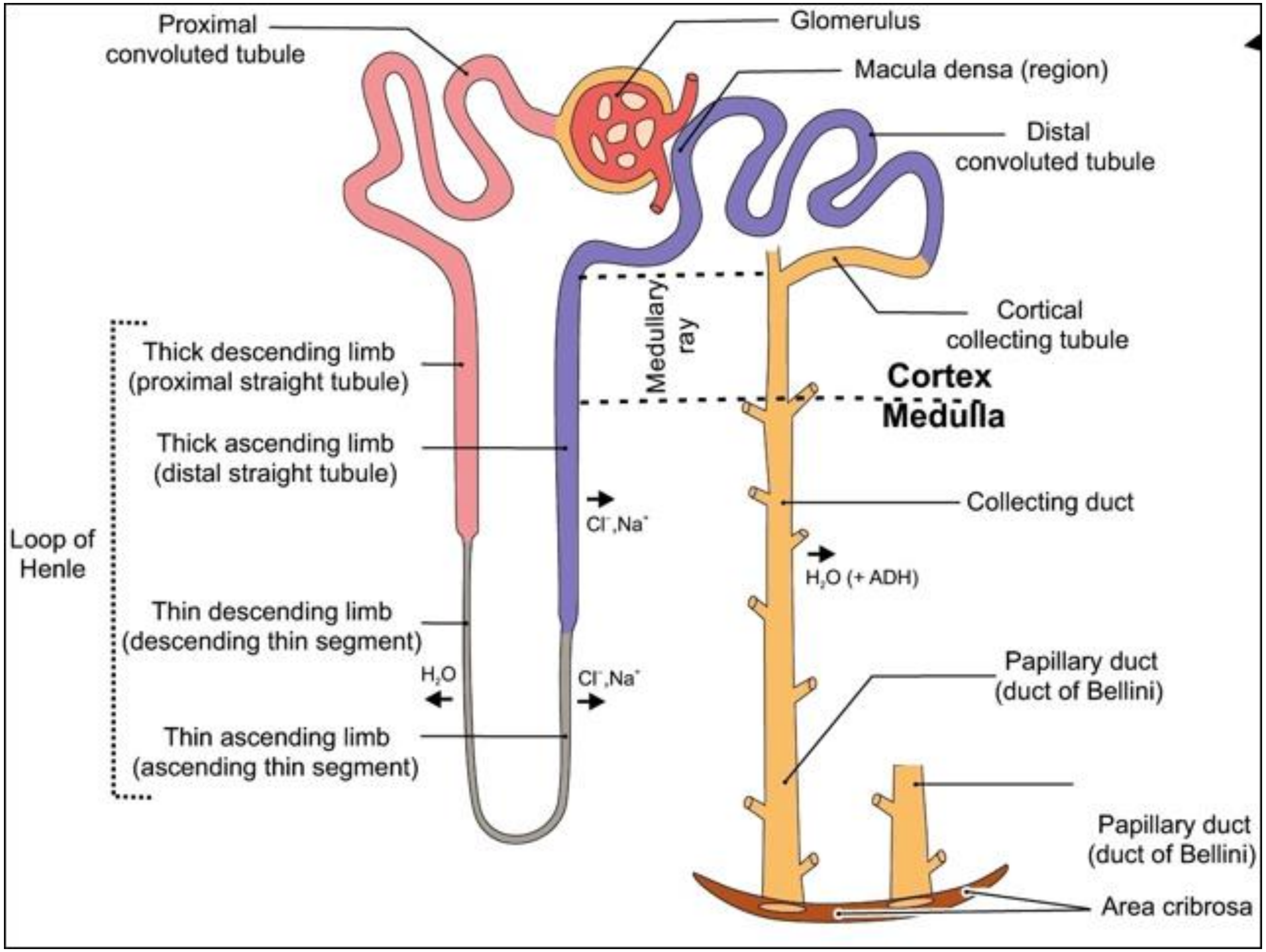


Medullary Collecting Ducts

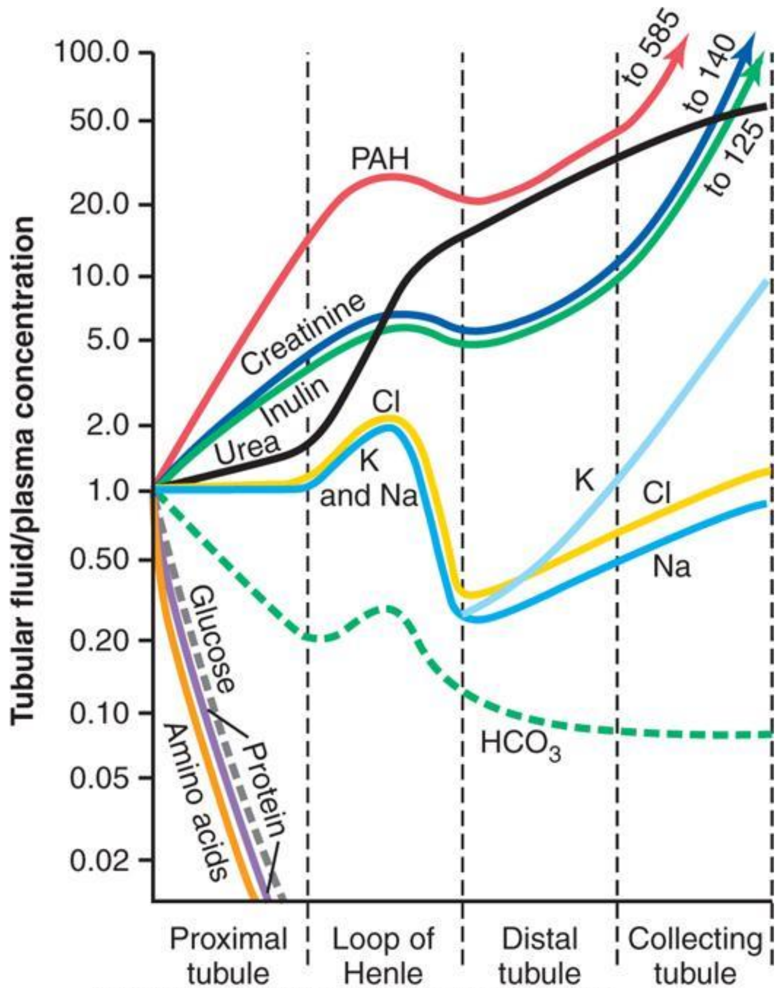
Permeability to water is under ADH control

Permeable to urea

Secrete H+



Summary of the Concentrations of the different Solutes in the Different Tubular Segments



Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

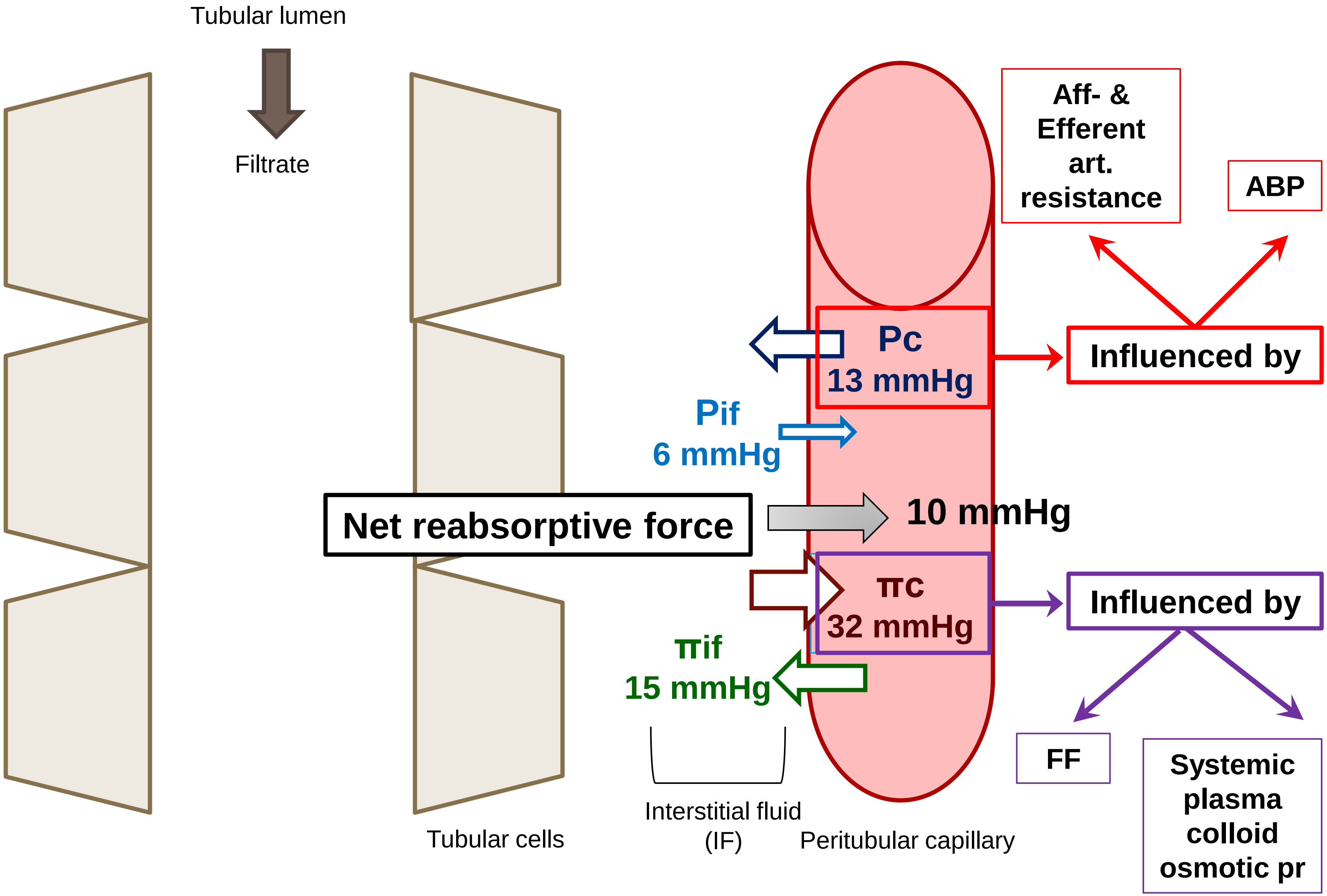
Regulation of Tubular Reabsorption

- ***Regulation of tubular reabsorption depends on***:
  1. Physical forces that govern reabsorption.
  2. Hormonal and neural mechanisms.

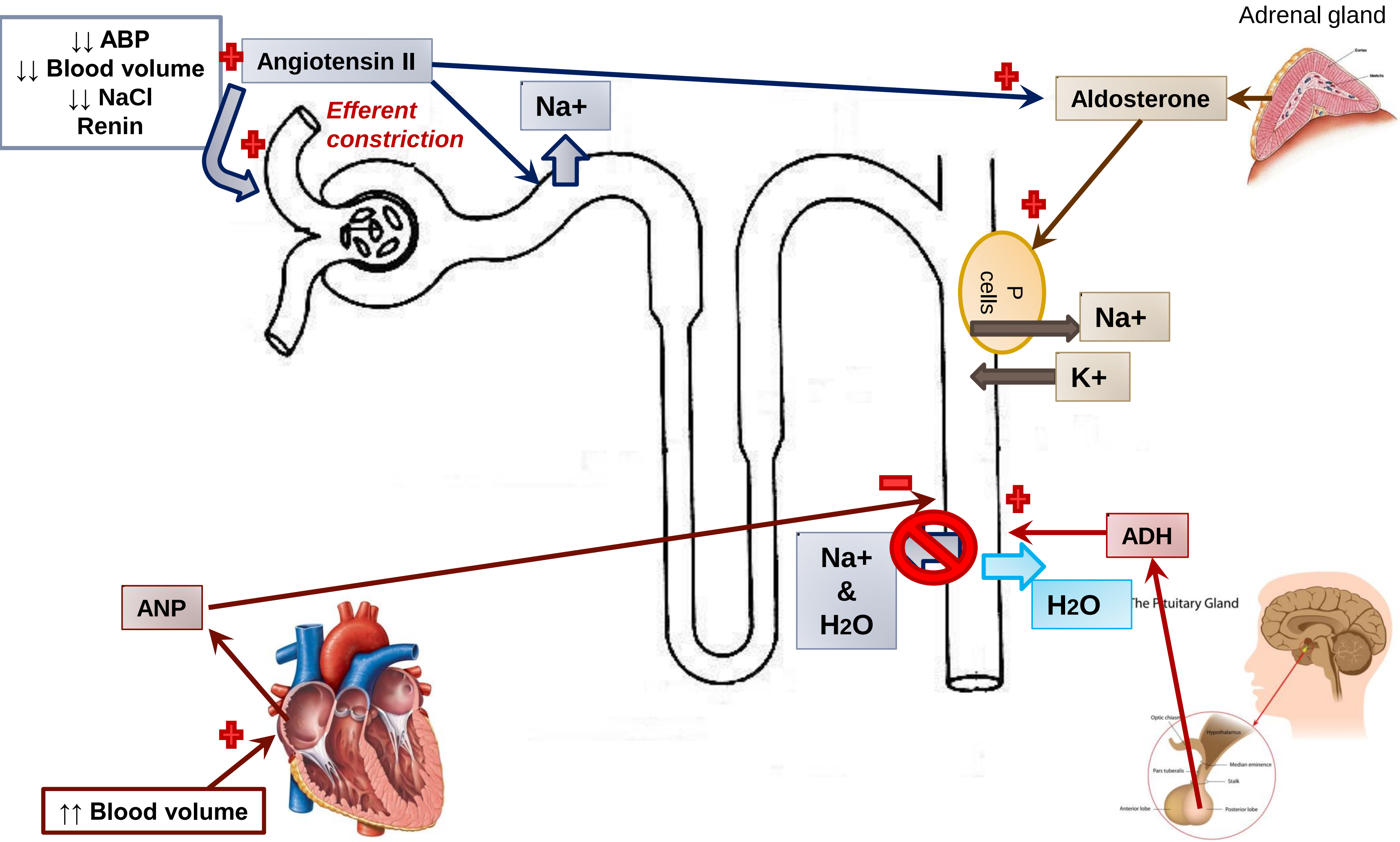
- Tubules can increase their reabsorption in response to increased tubular load → ***glomerulotubular balance.***

- ***What are the physical forces that govern tubular reabsorption?***

Physical Forces that Govern Tubular Reabsorption

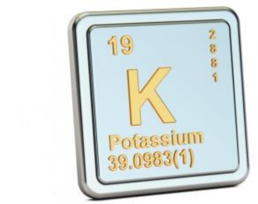


Hormonal Regulation of Tubular Reabsorption



REGULATION OF POTASSIUM

Potassium



- One of the most abundant cations in the body.
- $[K^+]_I > [K^+]_o \rightarrow$ 150 mEq/L > 3.5-5 mEq/L.
- ***Why is K^+ important?***
  - ✓ Cell volume regulation.
  - ✓ Cell pH regulation.
  - ✓ Resting membrane potential.
  - ✓ Cardiac and neuronal activity.

The Importance of Regulating K^+

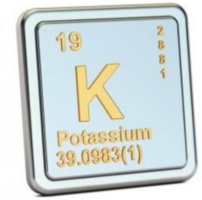
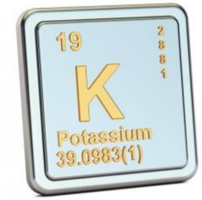


Table 37-1 Physiological Role of K^+ Ions

A. Roles of Intracellular K^+	
Cell-volume maintenance	Net loss of $K^+ \rightarrow$ cell shrinkage Net gain of $K^+ \rightarrow$ cell swelling
Intracellular pH regulation	Net loss of $K^+ \rightarrow$ cell acidosis Net gain of $K^+ \rightarrow$ cell alkalosis
Cell enzyme functions	K^+ dependence of enzymes (e.g., some ATPases, succinic dehydrogenase)
DNA/protein synthesis, growth	Lack of $K^+ \rightarrow$ reduction of protein synthesis, stunted growth
B. Roles of Transmembrane $[K^+]$ Ratio	
Resting cell membrane potential	Reduced $[K^+]_i/[K^+]_o \rightarrow$ membrane depolarization Increased $[K^+]_i/[K^+]_o \rightarrow$ membrane hyperpolarization
Neuromuscular activity	Low plasma K^+: muscle weakness, muscle paralysis, intestinal distention, respiratory failure High plasma K^+: increased muscle excitability; later, muscle weakness (paralysis)
Cardiac activity	Low plasma K^+: slowed conduction of pacemaker activity, arrhythmias High plasma K^+: conduction disturbances, ventricular arrhythmias, and ventricular fibrillation

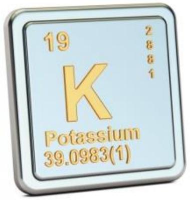
(Boron & Boulpaep. Medical Physiology)

Potassium Homeostasis



- Dietary intake of potassium = 80-120 mEq/day.
- Absorption of 40 mEq into ECF can ↑ $[K^+]$ in ECF ≈ 2 mEq/L!!
- ***How does the body protect against this risk of hyperkalemia following each meal?***

Body Defense Against K^+ Abnormalitie



1st line of defence

Cellular shift

Redistribution of K^+ between ICF and ECF.

↑↑ ECF [K^+] → shift K^+ into the cells
↓↓ ECF [K^+] → shift K^+ out of the cells.

What are the factors altering K^+ distribution between both compartments?

Renal excretion

Depending on K^+ body status, the kidney may;

↑↑ excretion of K^+
↓↓ excretion of K^+

How does the kidney achieve that?

Factors Affecting K^+ Distribution Between ICF and ECF

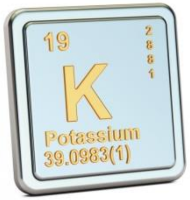


Table 35-1. Major Factors, Hormones, and Drugs Influencing the Distribution of K^+ between the Intracellular and Extracellular Fluid Compartments

Physiological: Keep Plasma [K^+] Constant
Epinephrine
Insulin
Aldosterone
Pathophysiological: Displace Plasma [K^+] from Normal
Acid-base balance
Plasma osmolality
Cell lysis
Exercise
Drugs That Induce Hyperkalemia
Dietary K^+ supplements
ACE inhibitors
K^+-sparing diuretics
Heparin

(Koeppen & Stanton. Berne & Levy Physiology, 6th ed)

Physiologic factors affecting K⁺ distribution between ICF and ECF:

- Help regulate plasma [K^+]: keep plasma [K^+] constant.
  - Aldosterone.
  - Insulin.
  - Epinephrine.

(Boron & Boulpaep Medical Physiology-updated edition)

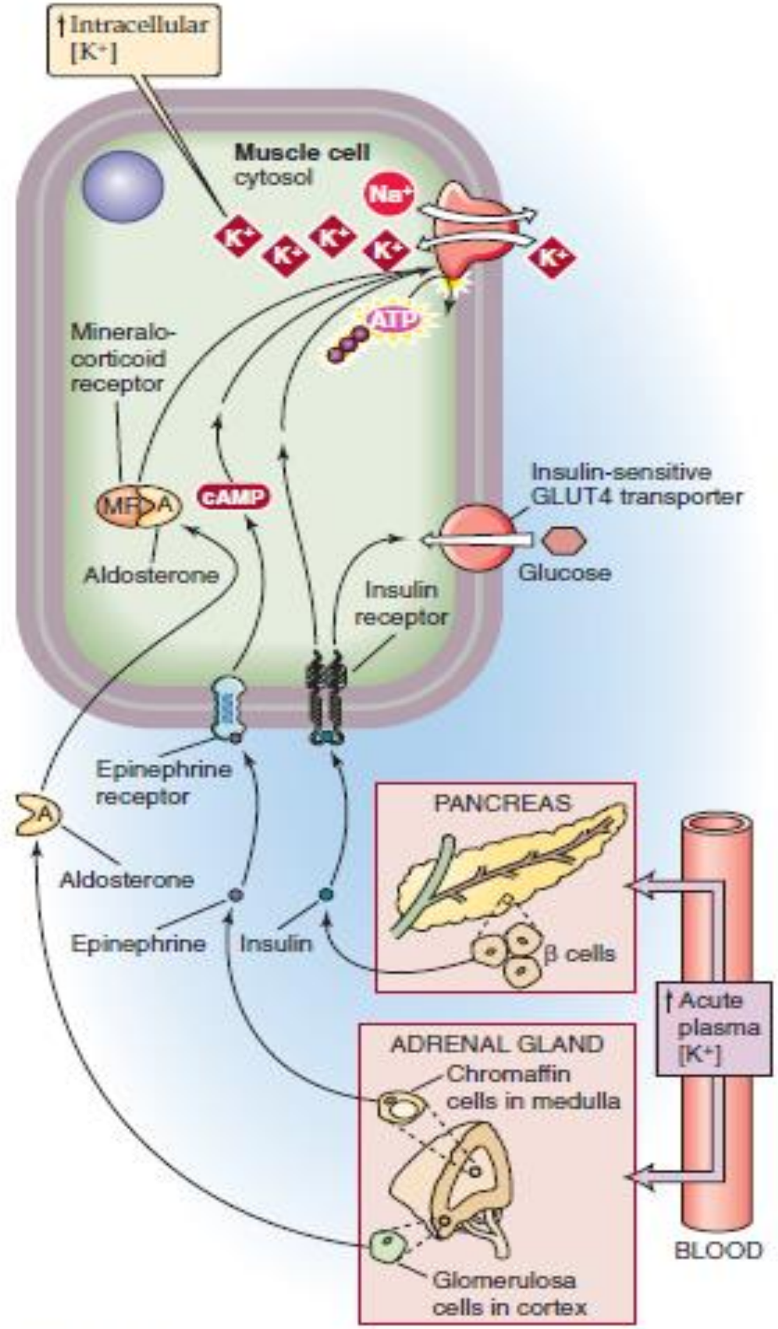
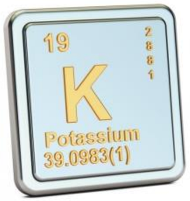


Figure 37-3 K⁺ uptake into cells in response to high plasma [K⁺].

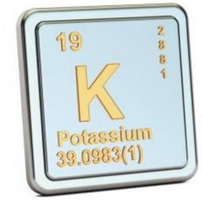
Pathophysiologic Factors Affecting K^+ Distribution Between ICF and ECF



- Acid base disturbance.
- Change in plasma osmolality.
- Cell lysis.
- Exercise.

How do these factors affect K^+ distribution between ICF and ECF compartments?

Renal Excretion of Potassium



Potassium leaves the body through;

1. GI loss ≈ 5-10%
2. Renal excretion ≈ 90-95%.

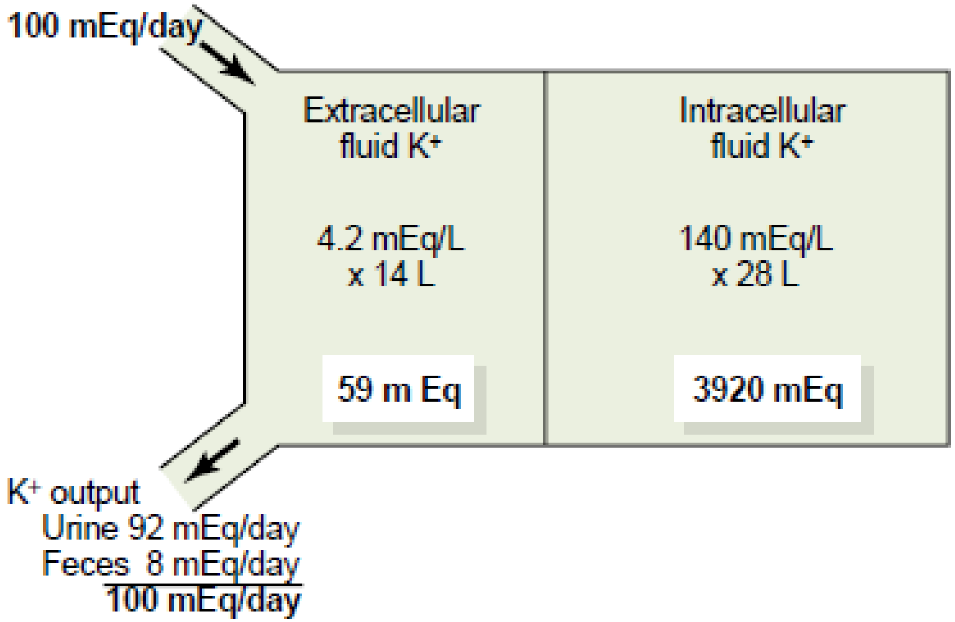
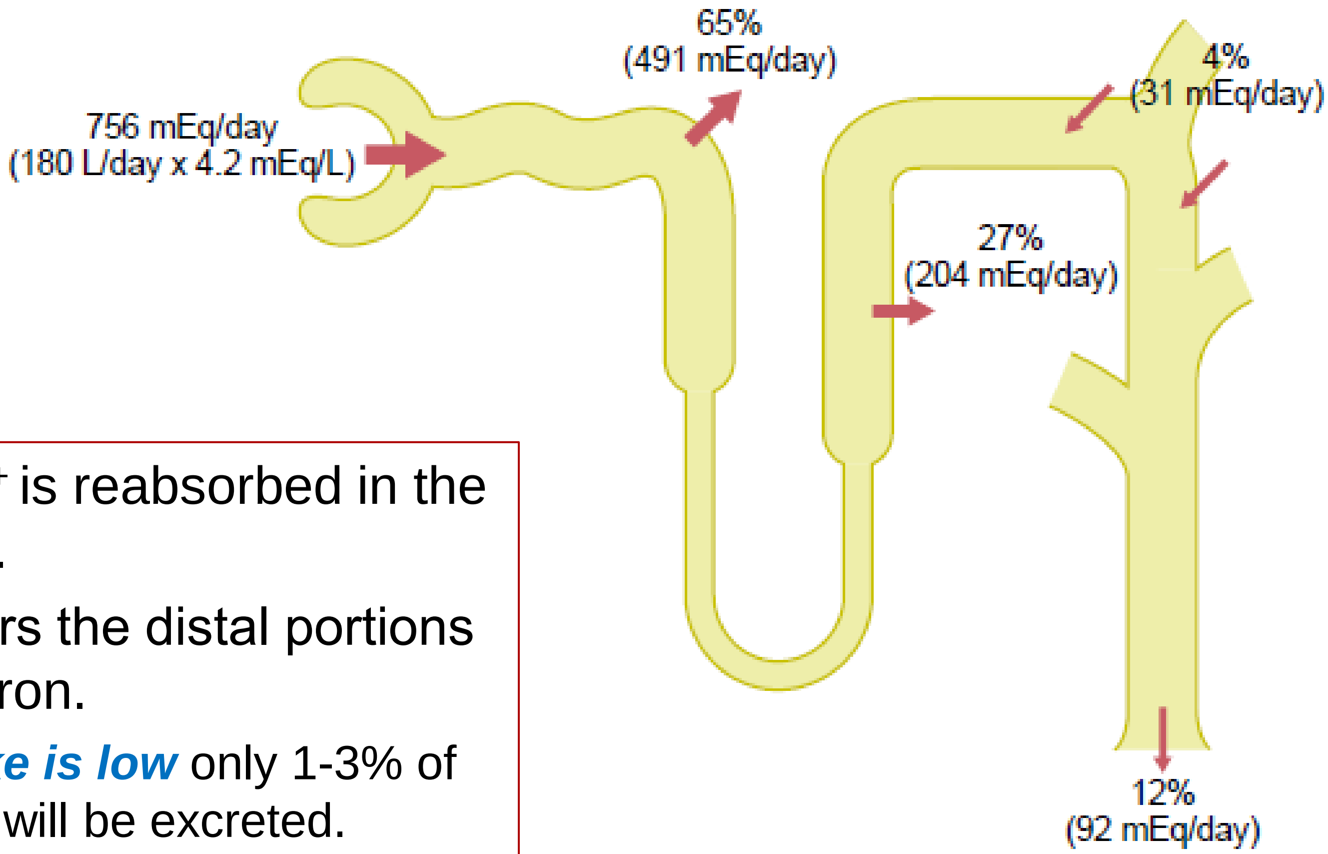


Figure 29–1

Normal potassium intake, distribution of potassium in the body fluids, and potassium output from the body.

Renal Potassium Handling



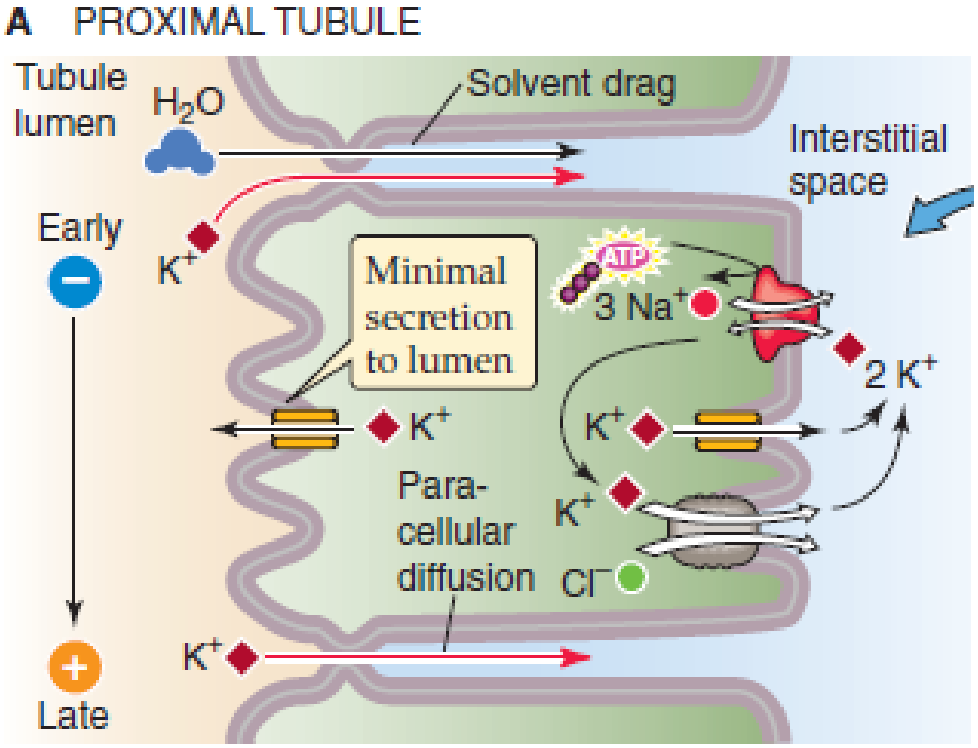
- ≈ 90% of K^+ is reabsorbed in the PCT & TAL.
- ≈ 10% enters the distal portions of the nephron.
  - ***If K^+ intake is low*** only 1-3% of filtered K^+ will be excreted.
  - ***If K^+ intake is normal/high***, 10-15% of filtered K^+ will be excreted

Potassium Handling by the kidney

It is the sum of filtration – reabsorption + secretion

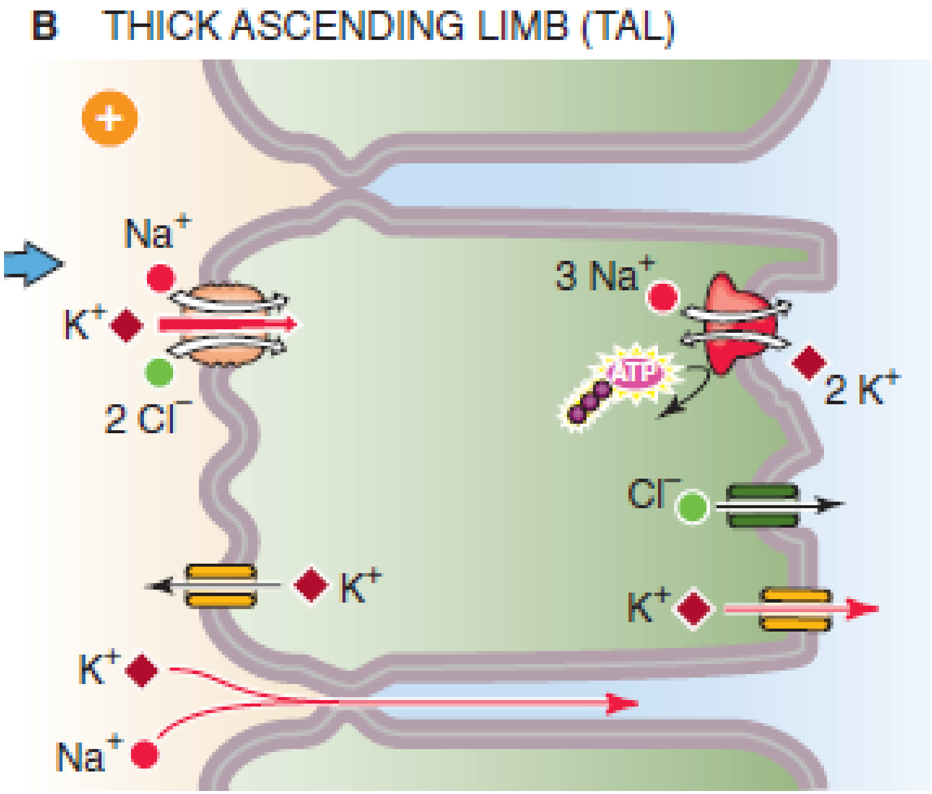
In the PCT → K^+ reabsorption is a passive process.. ***How?***

Water reabsorption through the paracellular route drags K^+ with it (***solvent drag***).



Potassium Handling by the TAL

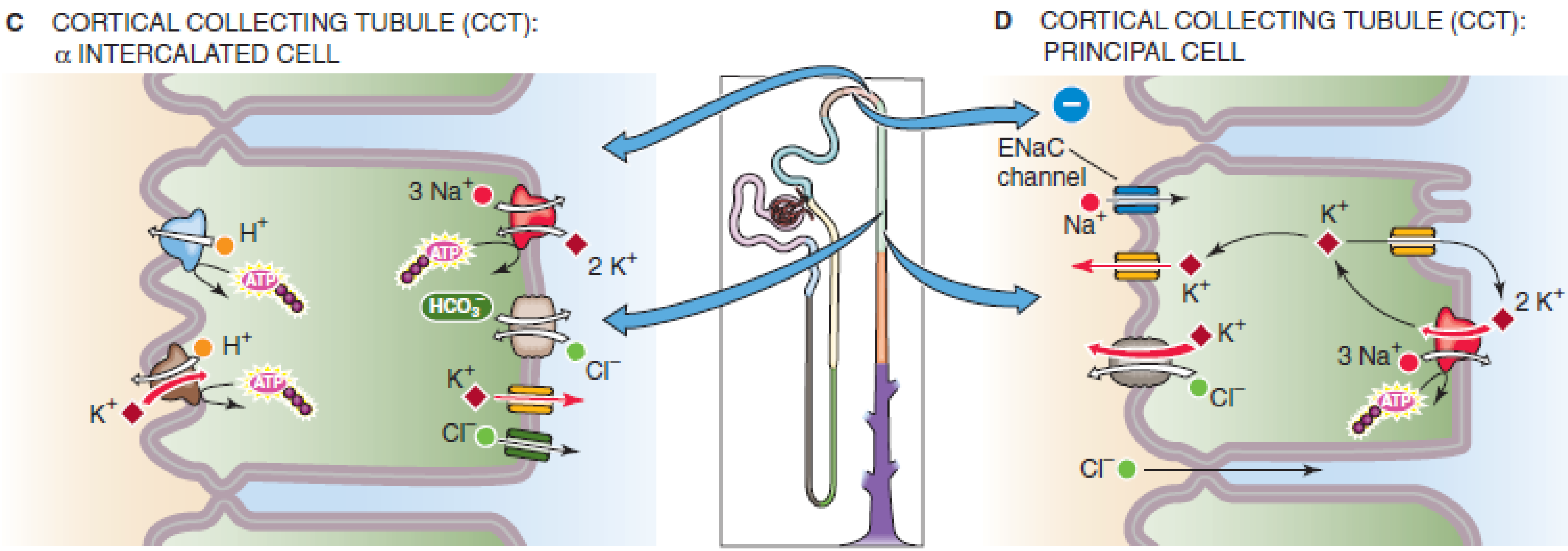
By secondary active transport using the apical triple transporter (NKCC2).



Potassium Handling by the CT

Alpha-Intercalated cells

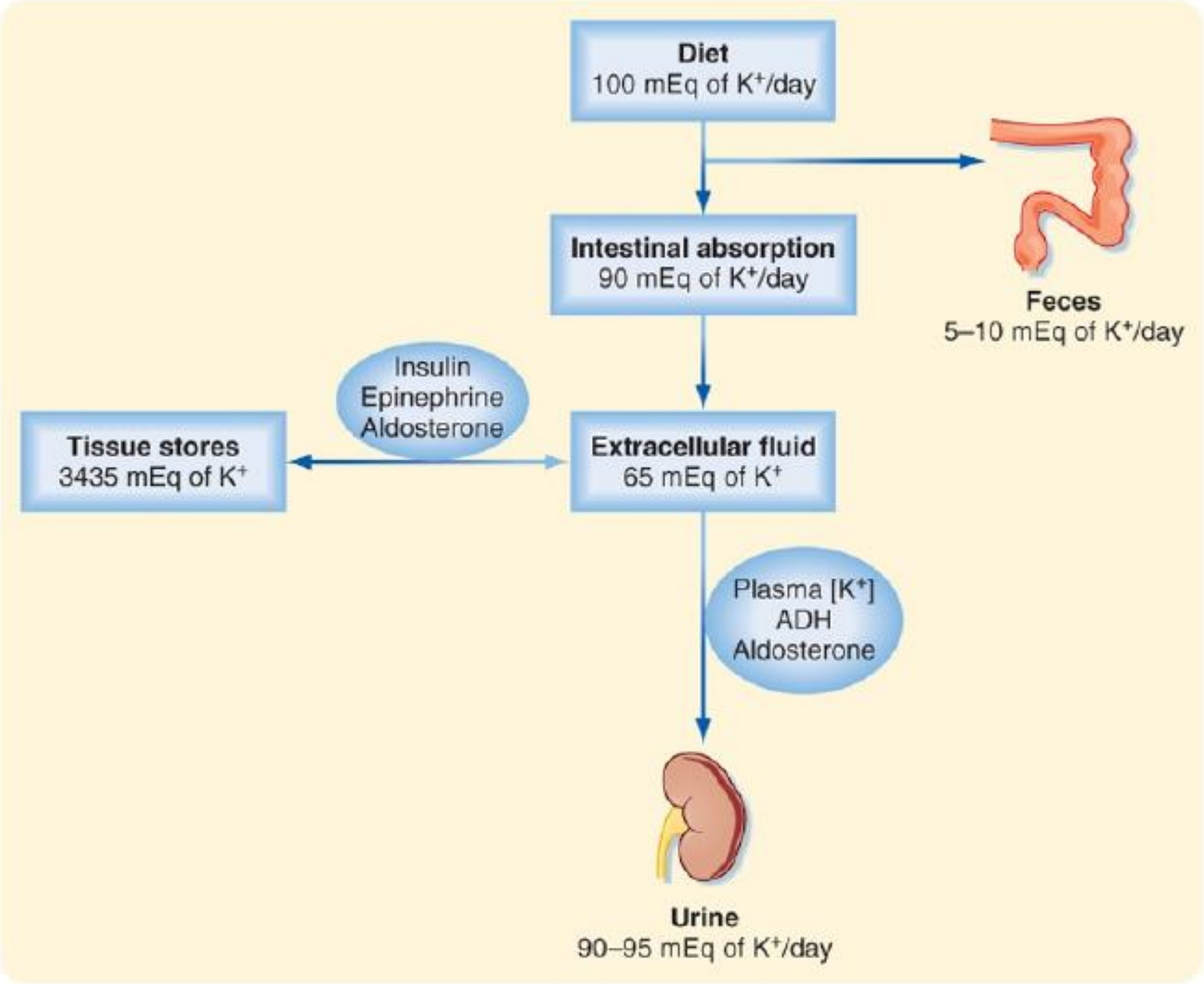
Principal cells



Secrete H^+ and reabsorb K^+

Reabsorb Na^+ and water & secrete K^+

Overview of Potassium Homeostasis



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

THANK YOU