B.SC 4TH SEM
ZOOCC-409
UNIT-3

RENAL PHYSIOLOGY

BY

DR. AMRESH KUMAR

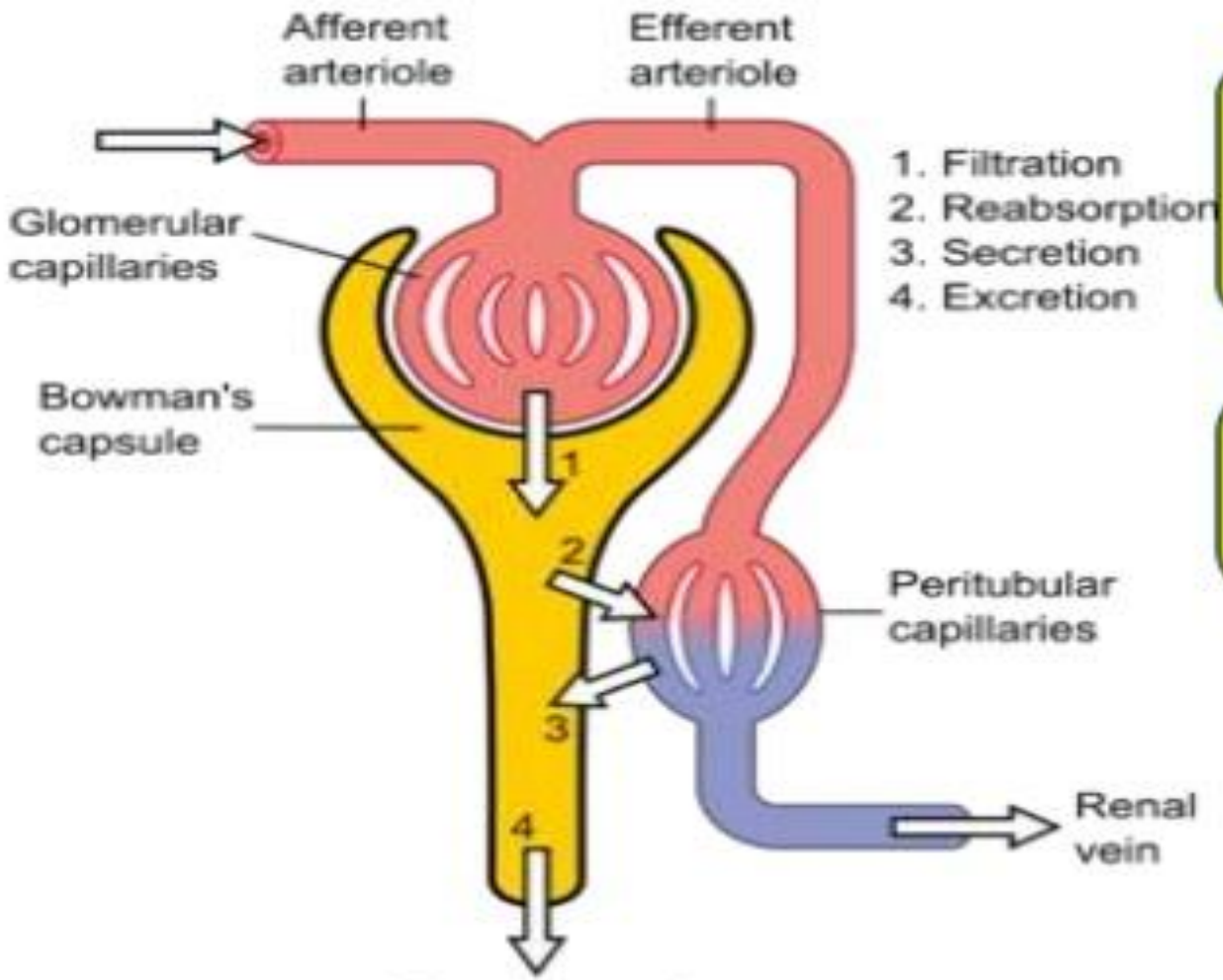
DEPT. OF ZOOLOGY, PWC, PATNA-01

amresh27@gmail.com

Overview

- Steps in urine formation
- Processing of glomerular filtrate by Reabsorption and secretion
- Substances reabsorbed in different parts of renal tubule and its mechanism
- Substances secreted in different parts of renal tubule and its mechanism
- Regulation of renal processing

Processes in Urine Formation



Excretion = Filtration – Reabsorption + Secretion

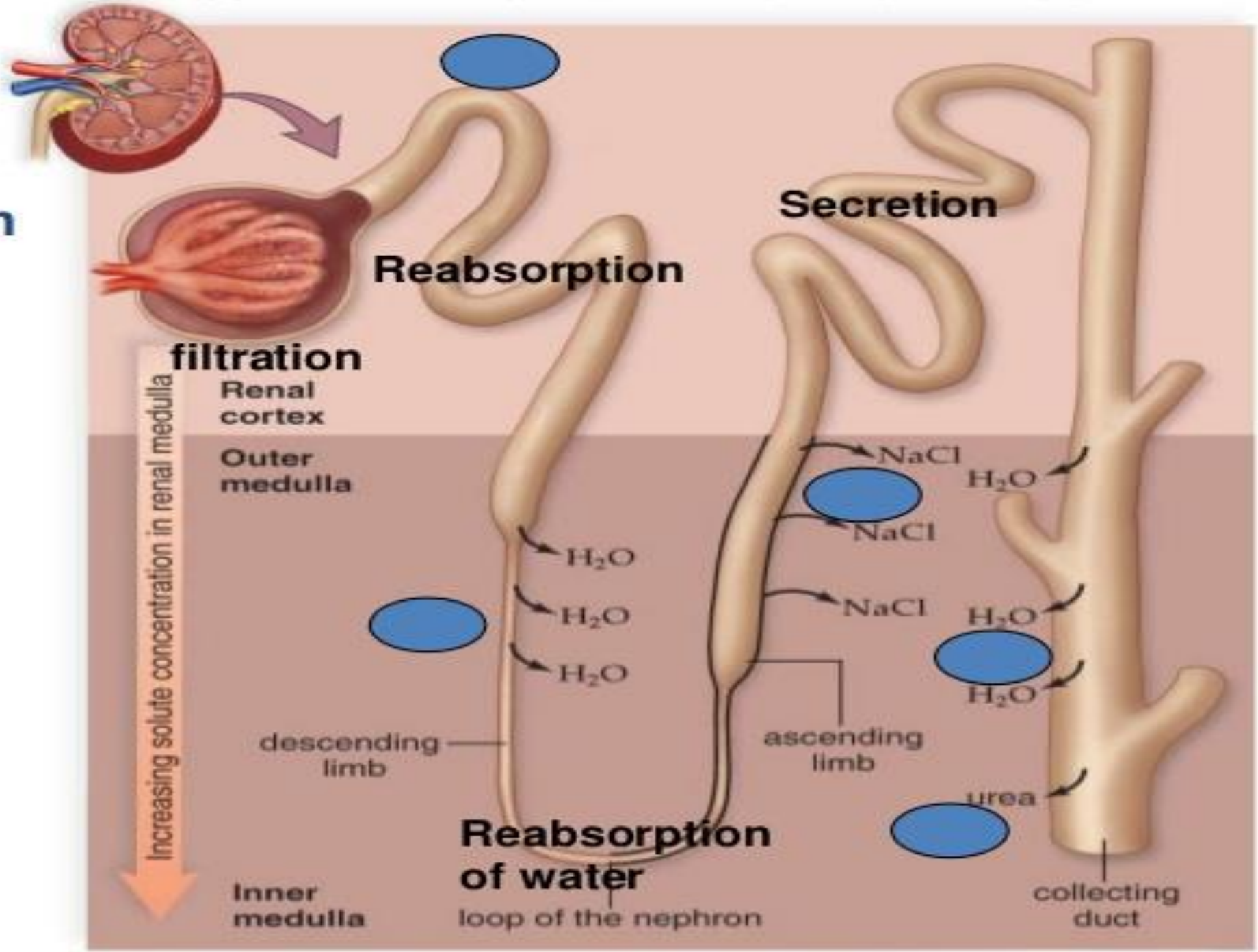
*Ultrafiltration

*Selective reabsorption

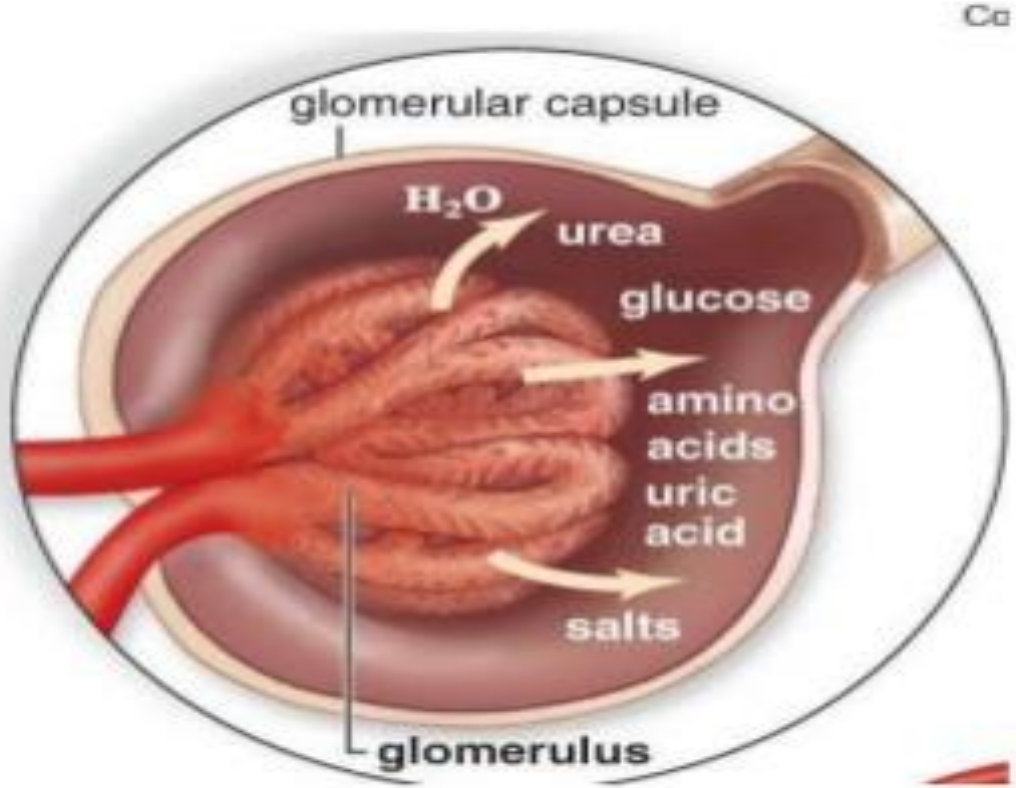
Secretion

Excretion

Nephron



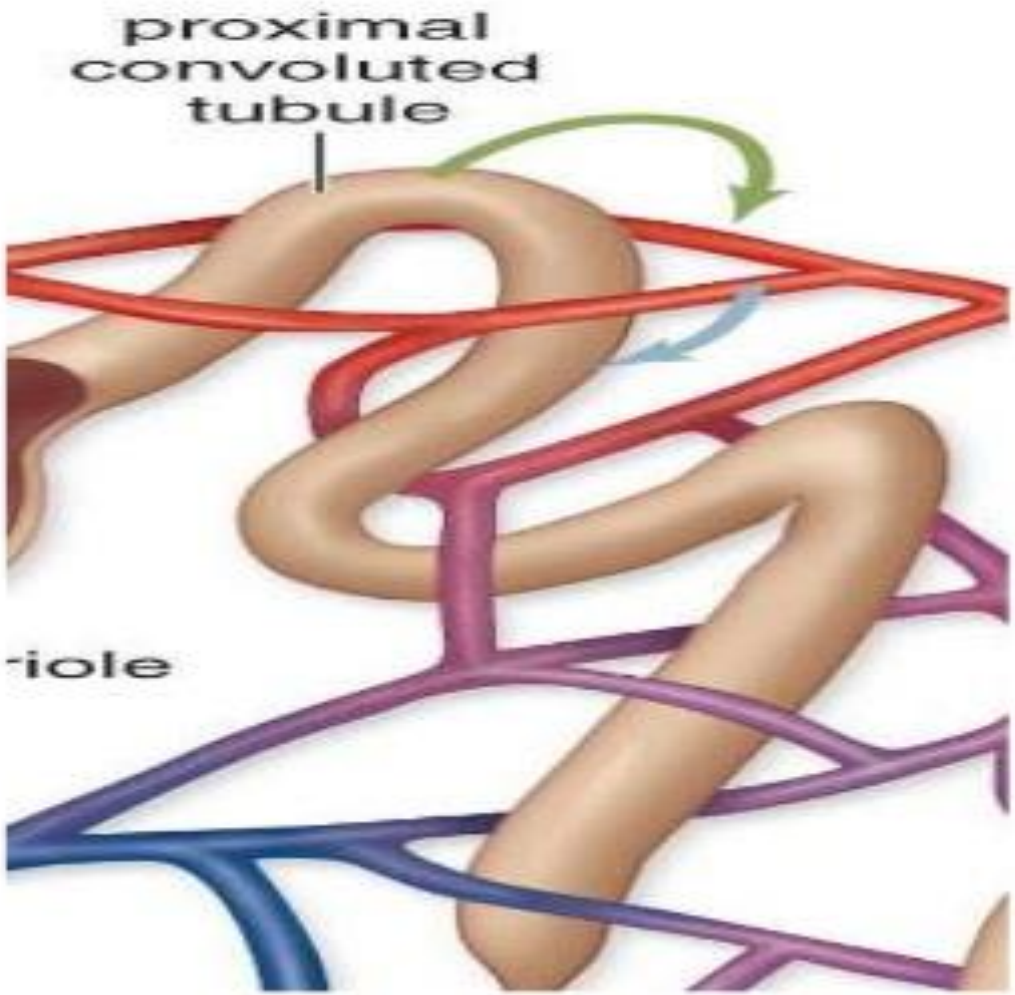
1. filtration



-blood pressure forces small molecules from the glomerulus to the capsule

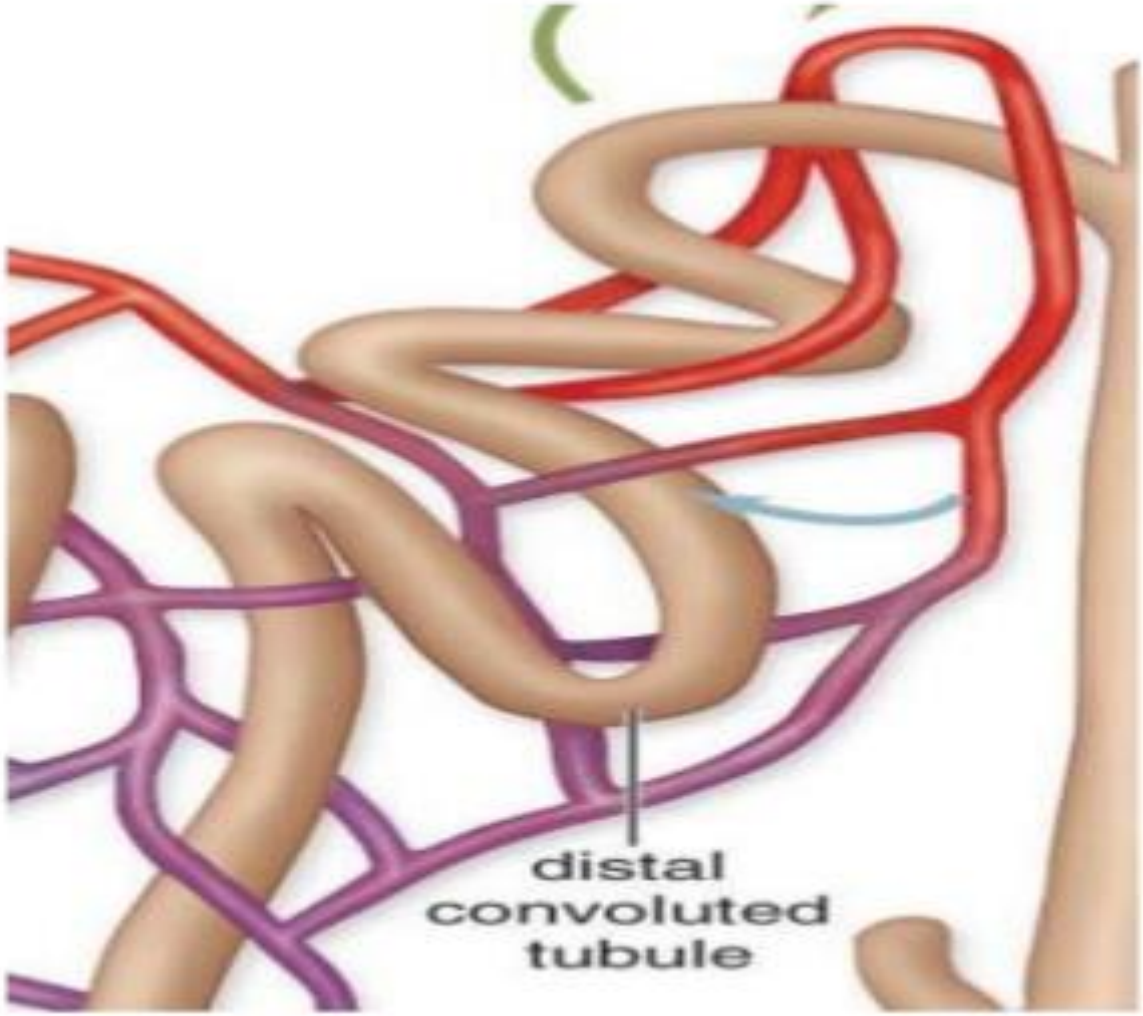
Filtrates:
glucose, amino acids
uric acid, urea

2. Tubular Reabsorption



-return of filtrates
from blood
at the proximal tubule
through diffusion
and active transport

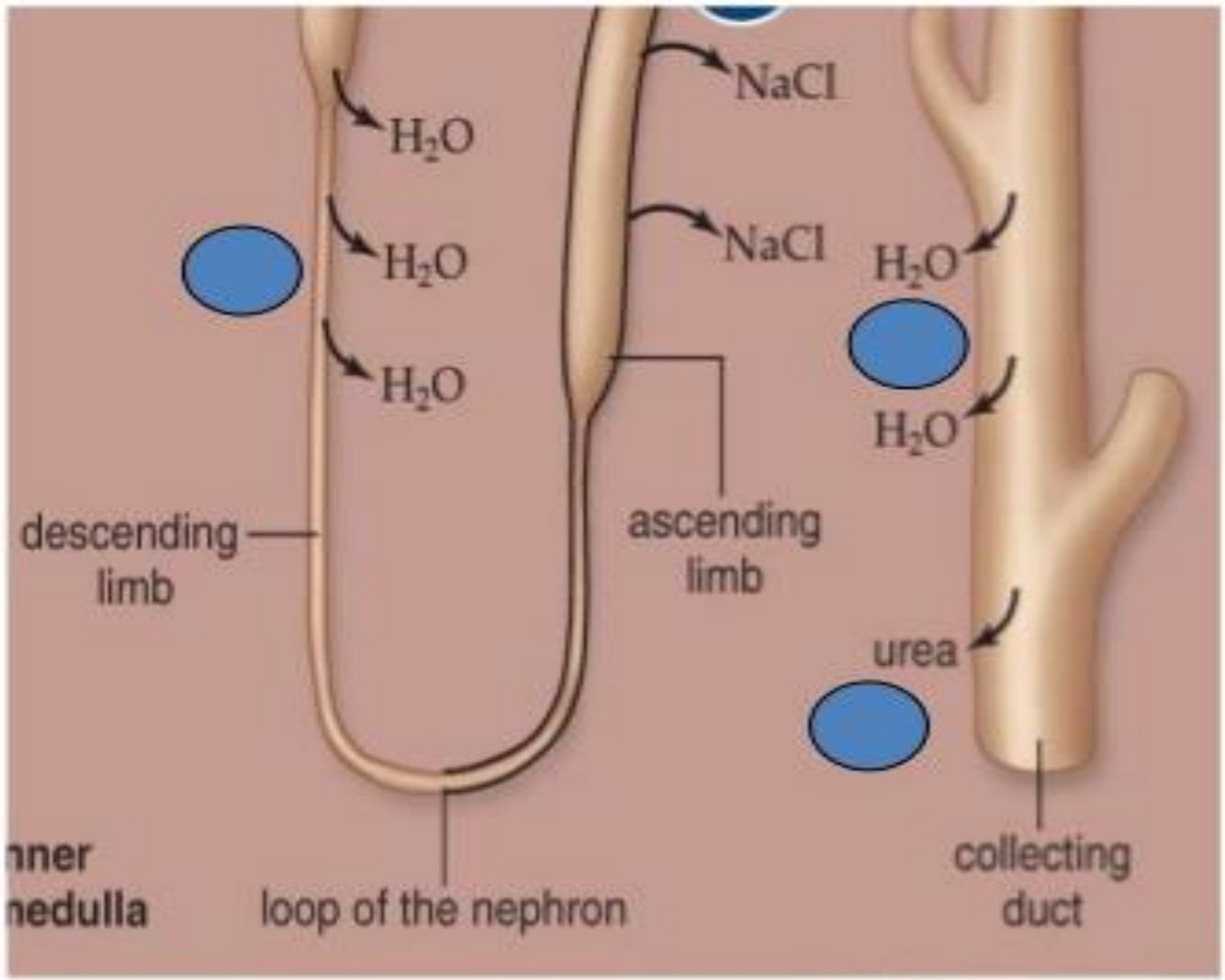
3. Tubular Secretion



-movement of molecules from blood into the distal convoluted tubule

Molecules: drugs and toxins

Reabsorption of water



-return of H_20 via osmosis along the loop of Henle and collecting duct

Processing of glomerular filtrate by Reabsorption and secretion

- **Reabsorption** is defined as movement of a substance from the tubular fluid to the blood, and this process occurs either via the tubular cells "the transcellular route" or between the cells" the paracellular route .

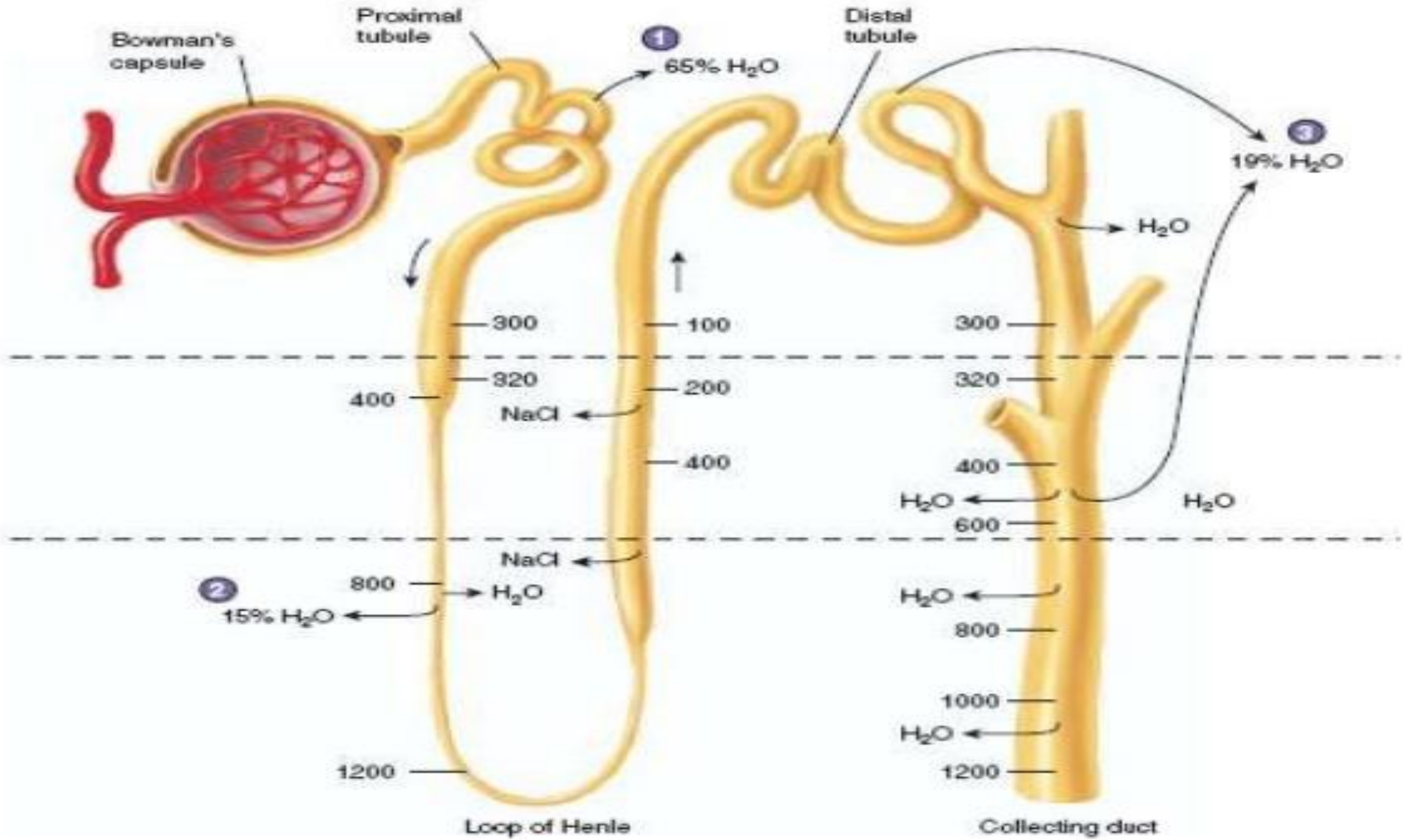
- **Tubular secretion** is defined as movement of a substance from the blood into the tubular fluid.

- The reabsorption and secretion that occur via **the transcellular route** are largely the result of secondary active transport of solutes by the tubular cells.

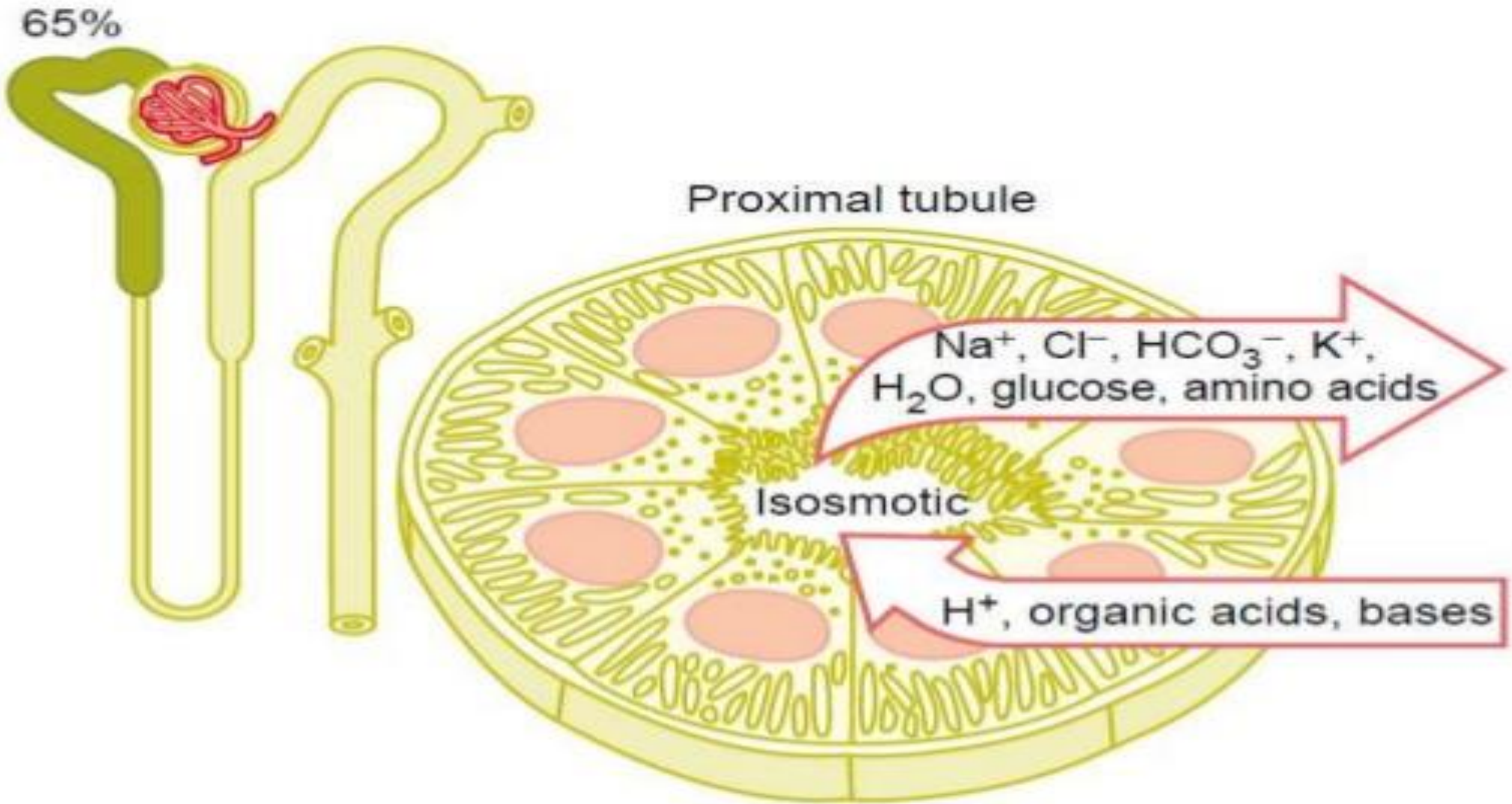
- **Paracellular** reabsorption occurs as a result of concentration or electrical gradients that favor movement of solutes out of the tubular fluid.

Filtration, Reabsorption, and Secretion of Different Substances

- Nutritional substances, such as amino acids and glucose, are completely reabsorbed from the tubules and do not appear in the urine even though large amounts are filtered by the glomerular capillaries. Each of the processes - glomerular filtration, tubular reabsorption, and tubular secretion - is regulated according to the needs of the body.


Bowman's capsule
Proximal tubule
1
65% H_2O
Distal tubule
3
19% H_2O
H_2O
300
320
400
100
200
400
NaCl
NaCl
300
320
400
600
H_2O
H_2O
2
15% H_2O
800
H_2O
H_2O
800
1000
H_2O
1200
1200
Loop of Henle
Collecting duct

PCT – Major site of Reabsorption



Why is PCT, a major reabsorption site?

- PCT epithelial cells have extensive brush border.
- PCT epithelial cells have extensive numbers of carrier proteins.
- PCT epithelial cells have large numbers of mitochondria to support active transport.

PCT

- **Reabsorption**
  - 65 % filtered Na+ & Water and are reabsorbed by the PCT.
  - Most of the filtered Cl – is also are reabsorbed in PCT.
- **Secretion**
  - PCT is an important site for secretion of Organic acids and bases.
  - Eg: *Bile salts, oxalate, urate,* and *catecholamines*

A value of 1.0 indicates:

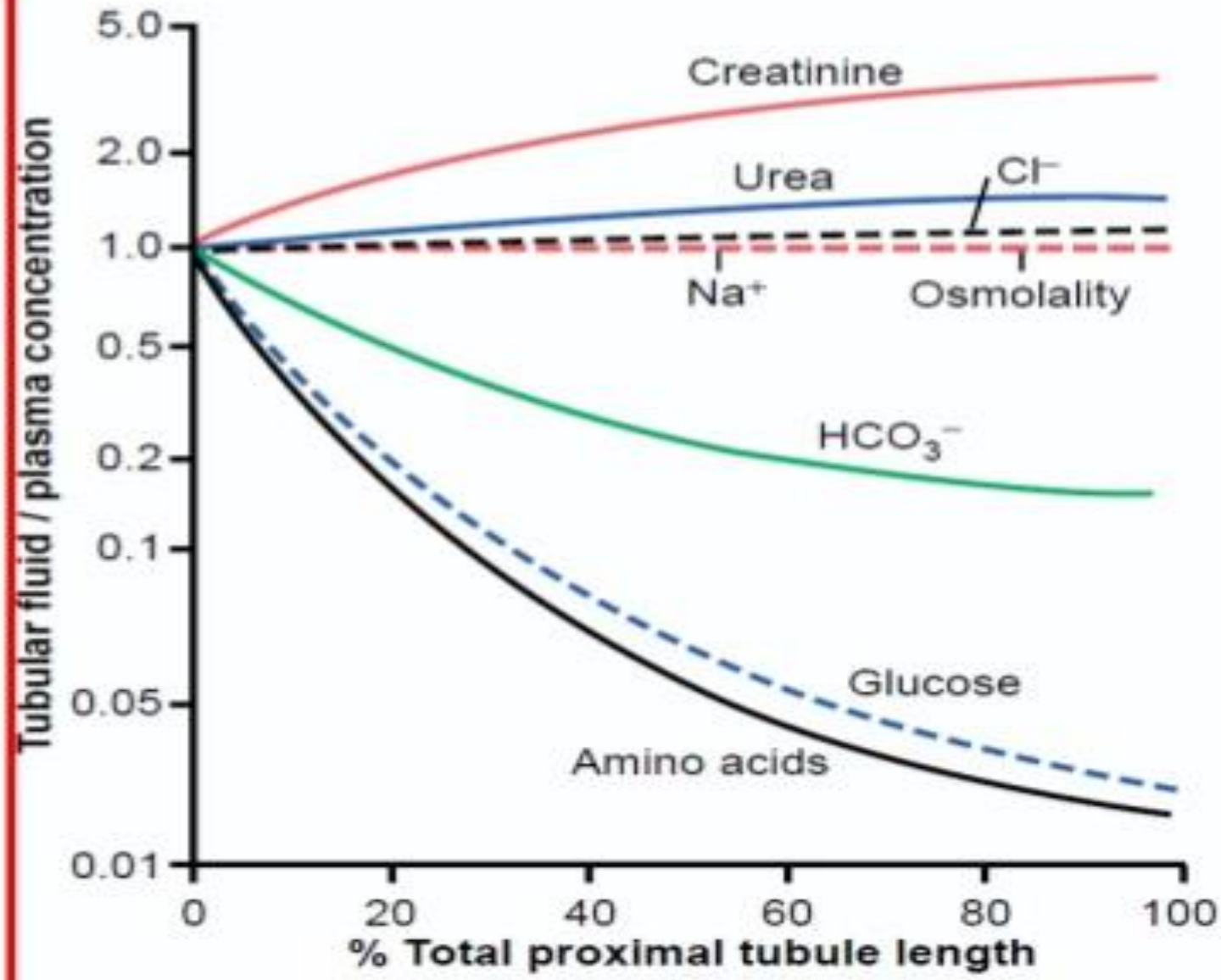
Concentration in the tubule is same as the concentration in the plasma.

Values below 1.0 indicates:

Substance is reabsorbed more avidly than water.

Values above 1.0 indicate:

Substance is reabsorbed to a lesser extent than water or is secreted into the tubules.



Concentration Changes of substances in tubule along the PCT relative to the concentrations in the plasma.

Tubular Reabsorption

- For reabsorbtion, substance must be transported :

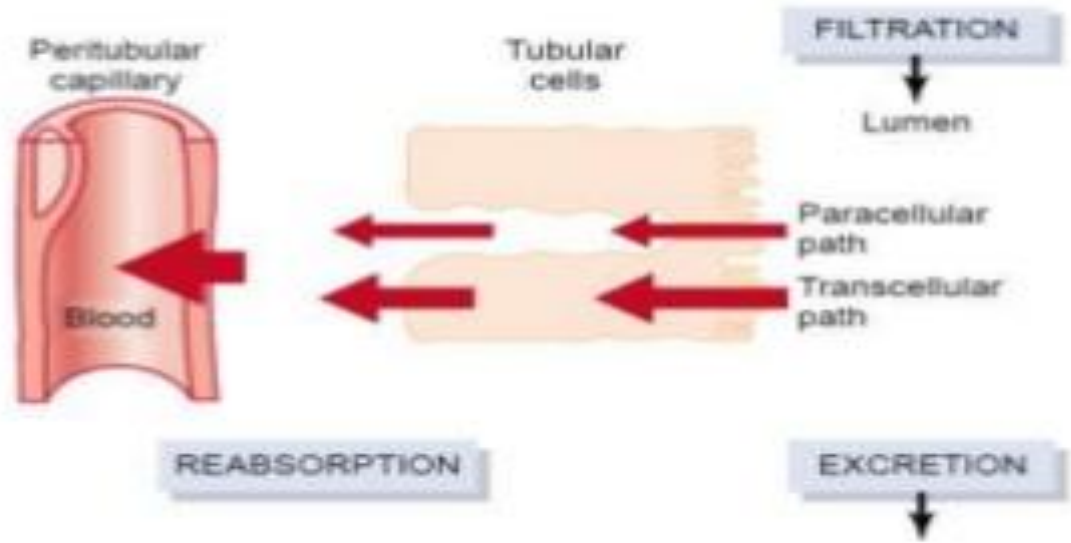
(1) Across the tubular epithelial membranes into interstitial fluid

Routes of transport :

- **Transcellular path**
  - Water and solutes can be transported through cell .
- **Paracellular path**
  - Through the junctional spaces between the cells

(2) Through the interstitium back into the blood .

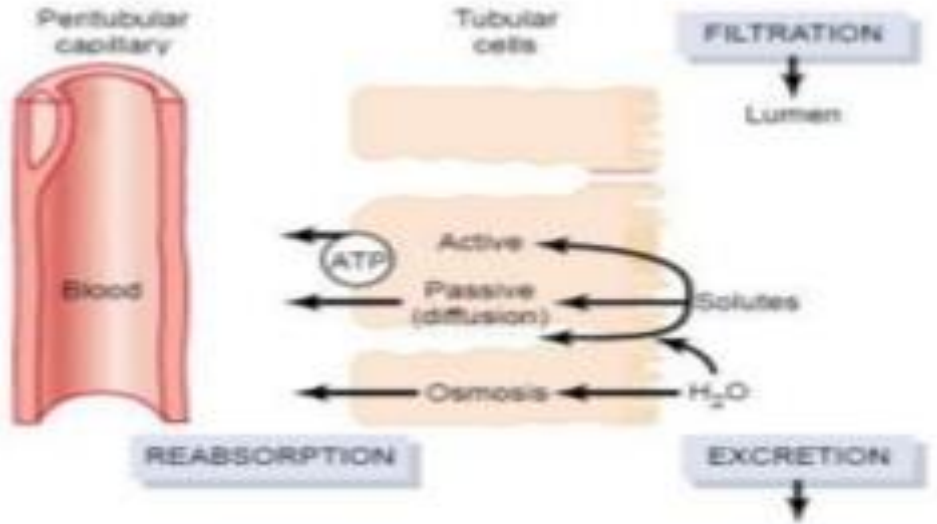
- Ultrafiltration (Bulk Flow)



Tubular Reabsorption

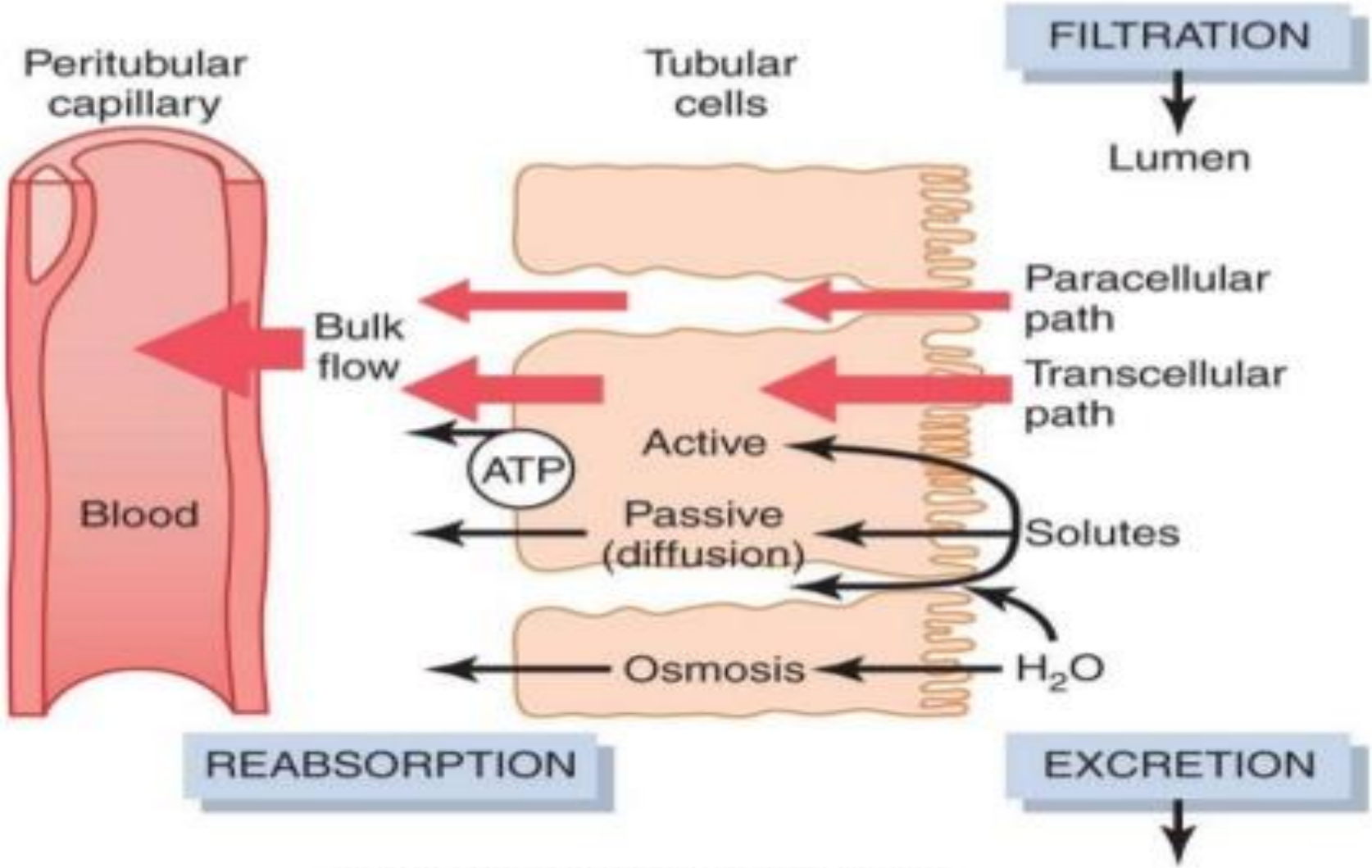
- Solutes are transported :
  - Through the cells (Transcellular route) by:
    - Diffusion or
    - Active transport

    or
  - Between the cells (Paracellular route) by:
    - Diffusion



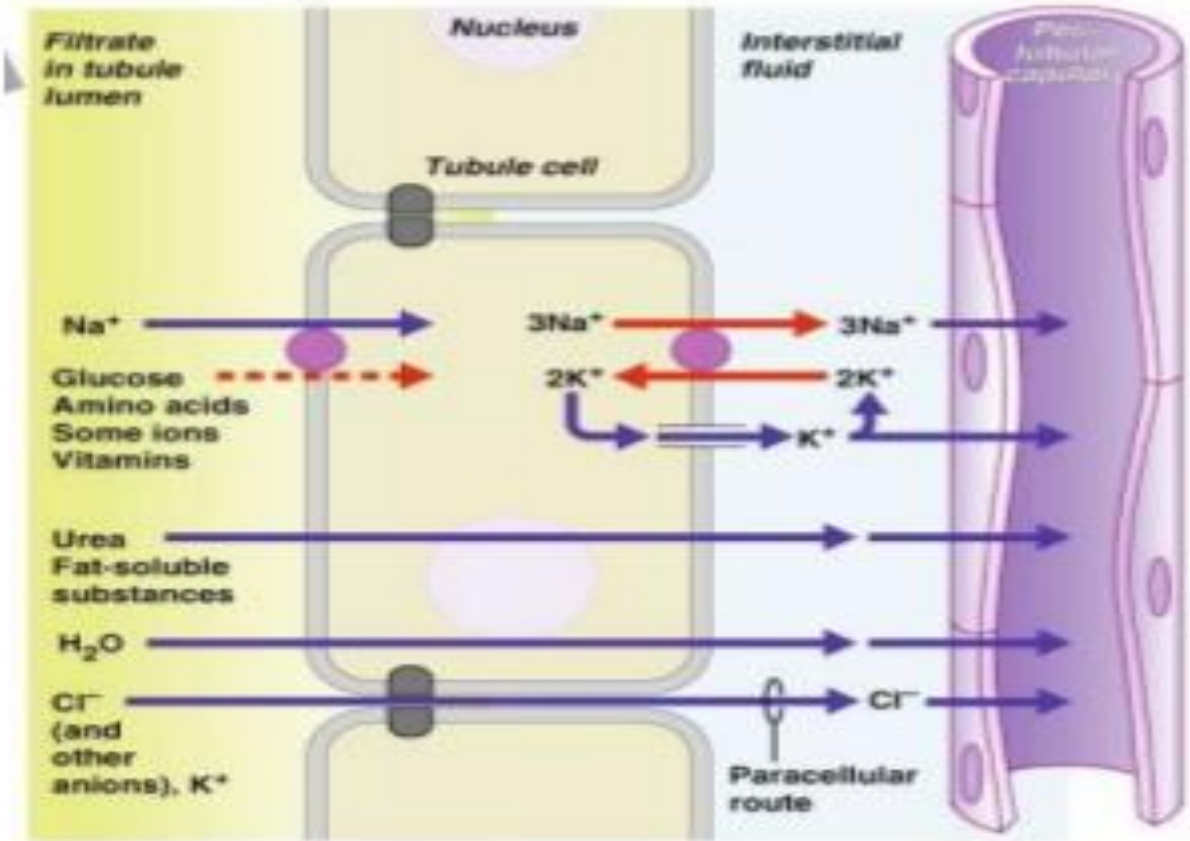
- Water is transported through the cells and between the tubular cells by osmosis.

Routes of Water and Solute Reabsorption



Proximal Convoluted Tubule (PCT); Reabsorption

- PCT is the most active in reabsorption
- <u>All</u> glucose, lactate, & amino acids
- Most Na^+, H_2O, HCO_3^- , CL^-
- and K^+
  - 65% Na^+ and H_2O
  - 90% HCO_3^-
  - 50% CL^-
  - 55% K^+

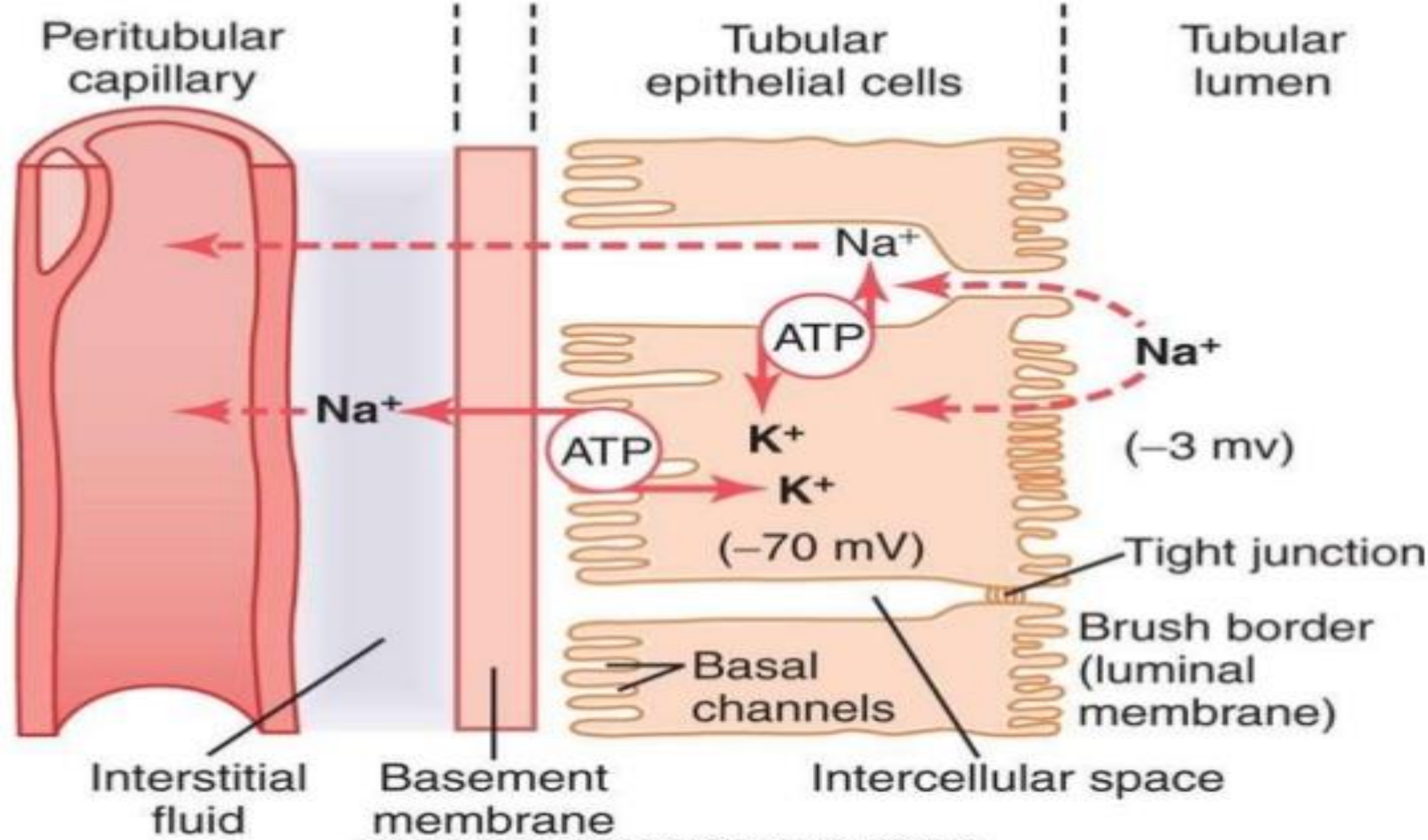


Data for a few plasma components that undergo filtration and reabsorption .

(Widmaire E. et al , 2008)

TABLE 16–2 Average Values for Several Components That Undergo Filtration and Reabsorption

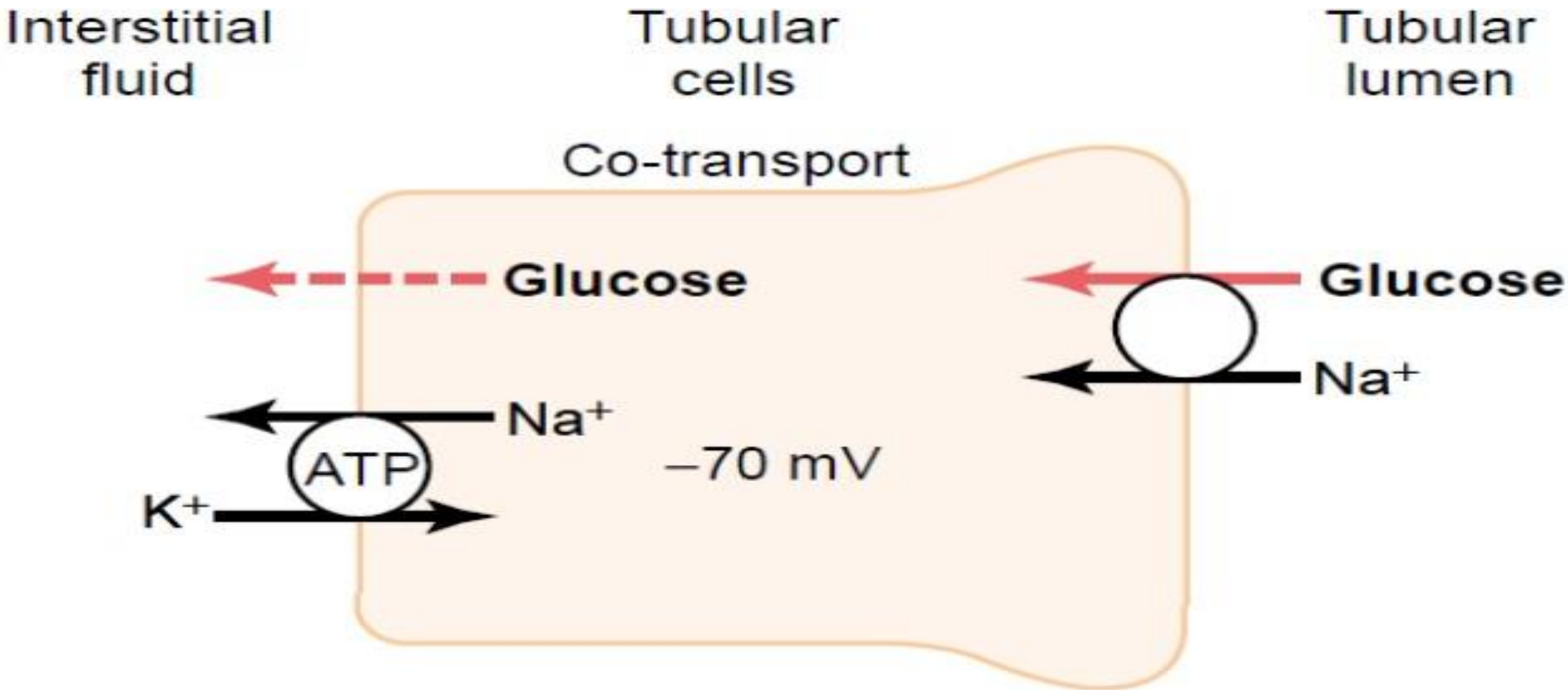
Substance	Amount Filtered per Day	Amount Excreted per Day	Percent Reabsorbed
Water, L	180	1.8	99
Sodium, g	630	3.2	99.5
Glucose, g	180	0	100
Urea, g	54	30	44

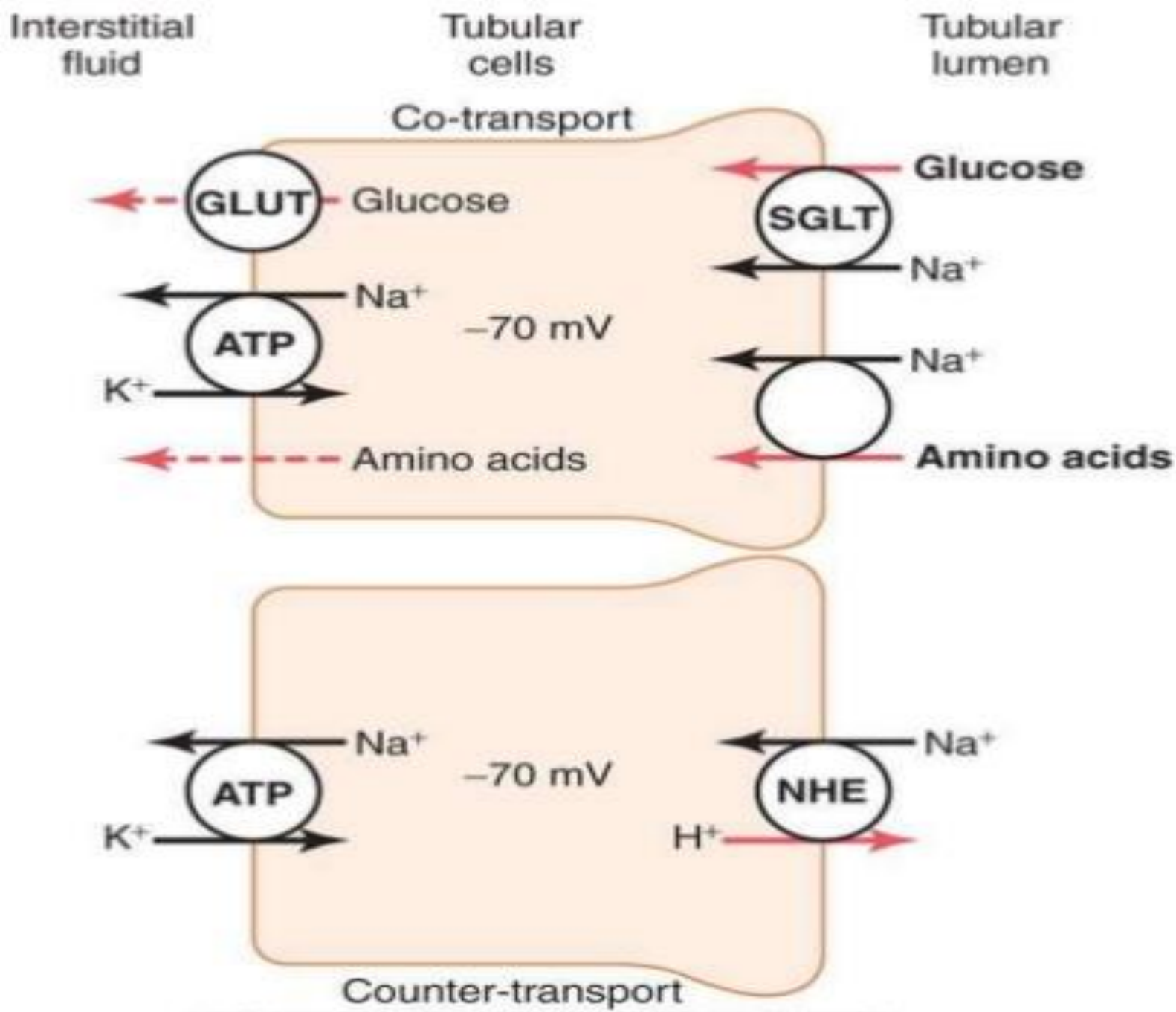


Reabsorption of Glucose

- By "Secondary active transport" in PCT.
- By "Sodium – Glucose co-transport "
- Sodium-potassium pump transports sodium from the interior of the cell across the basolateral membrane.
- It creates a low intracellular sodium concentration and a negative intracellular electrical potential.
- This drives sodium to inside the cell, which is co-transported with glucose.
- After entry into the cell, glucose exit across the basolateral membranes by facilitated diffusion.

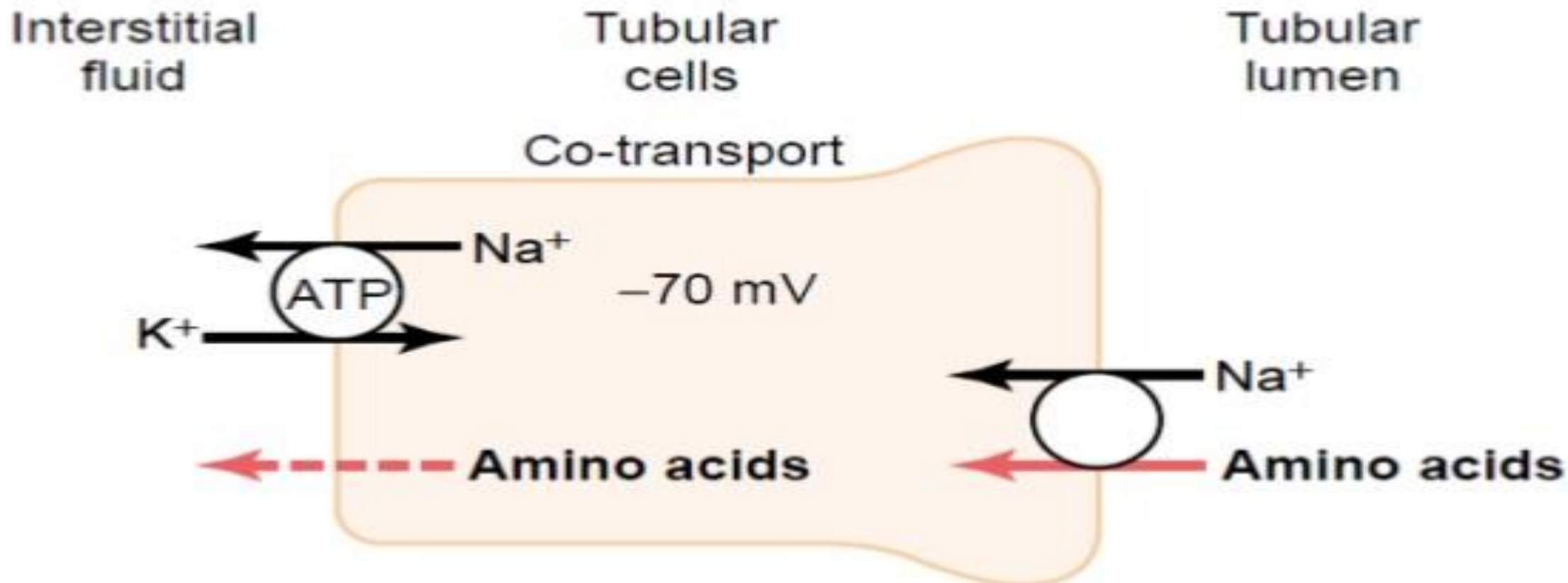
Reabsorption of Glucose





Reabsorption of Amino Acid

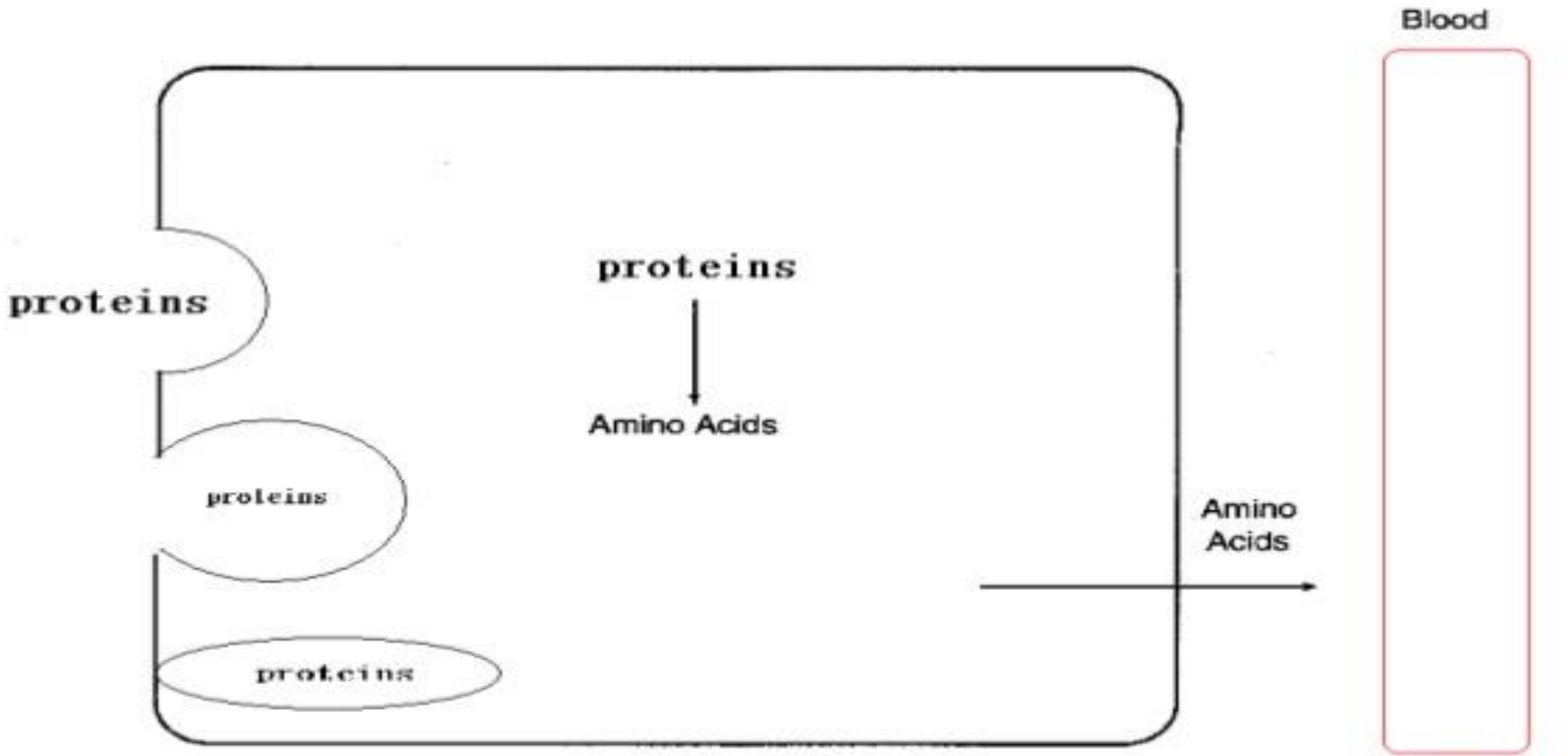
- With the same mechanism as “Glucose” i.e. by sodium co-transport.



Reabsorption of Proteins

- PCT, reabsorbs large proteins by **Pinocytosis**.
- Once inside the cell, the protein is digested into its constituent amino acids, which are reabsorbed through the basolateral membrane into the interstitial fluid.

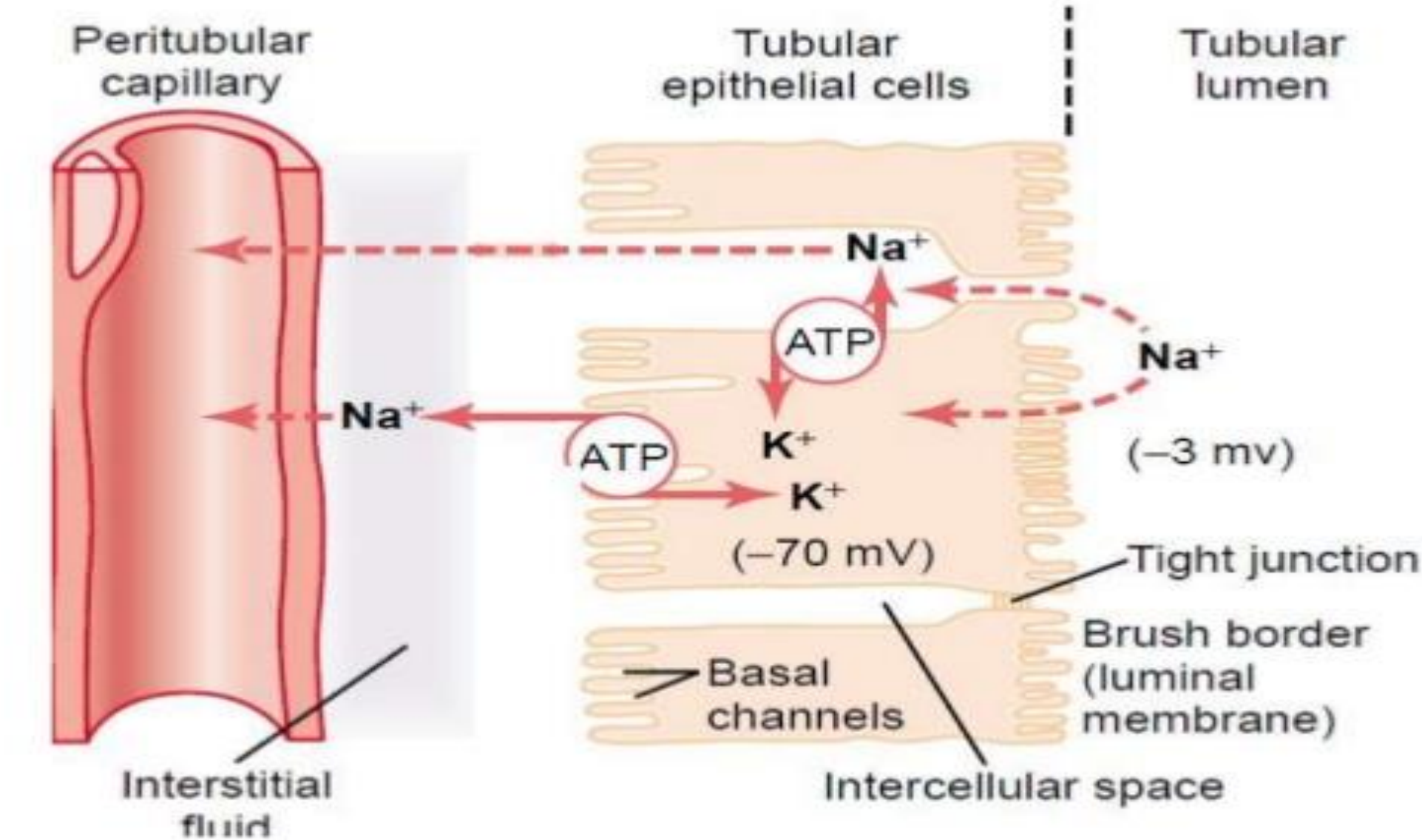
Pinocytosis for proteins

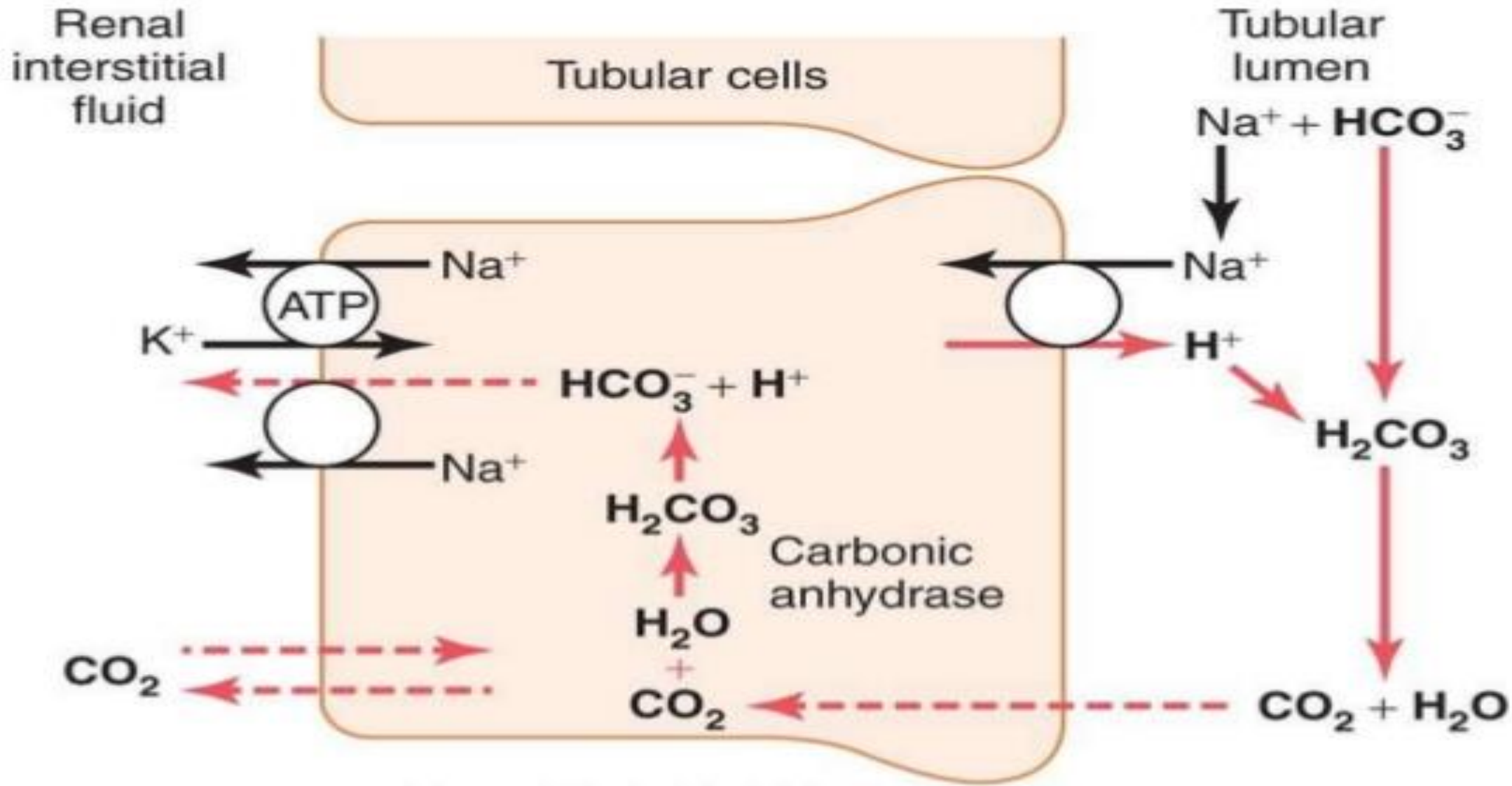


Reabsorption of Sodium

- Sodium-potassium pump transports sodium from the interior of the cell across the basolateral membrane.
- It creates a low intracellular sodium concentration and a negative intracellular electrical potential.
- It causes:
  - Sodium ions to diffuse into the cell.
  - Activation of sodium co-transport with many different substances.

Reabsorption of Sodium





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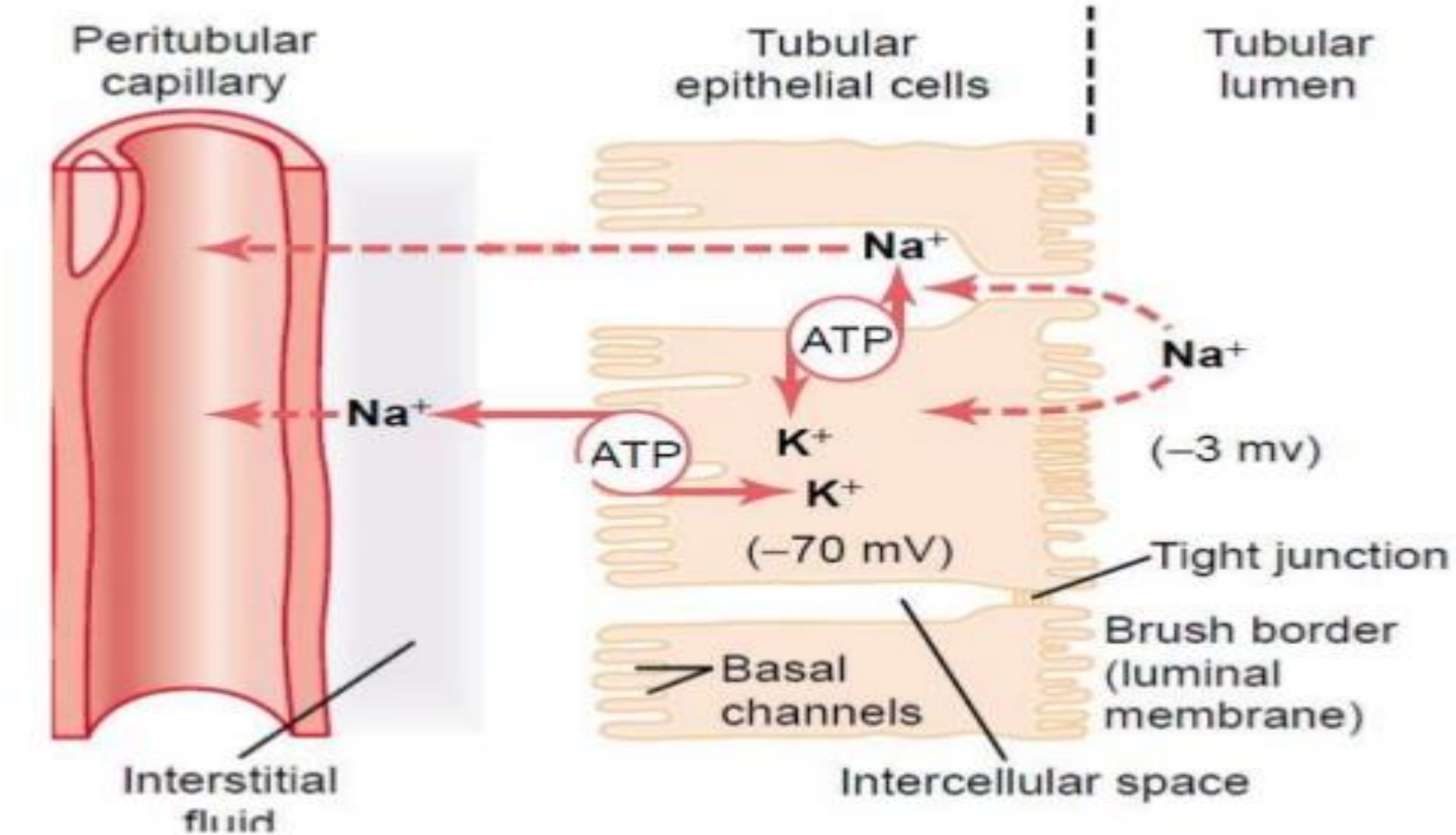
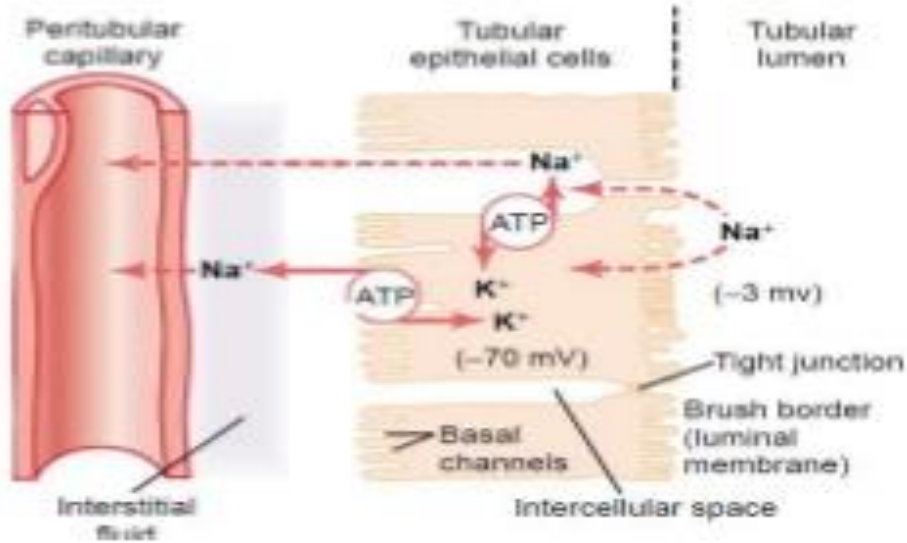
Reabsorption of Sodium



Reabsorption of Sodium

Involves three steps:

1. Na+ is transported into the cell down an electrochemical gradient established by the Na+/K+ pump on the basolateral side of the membrane.

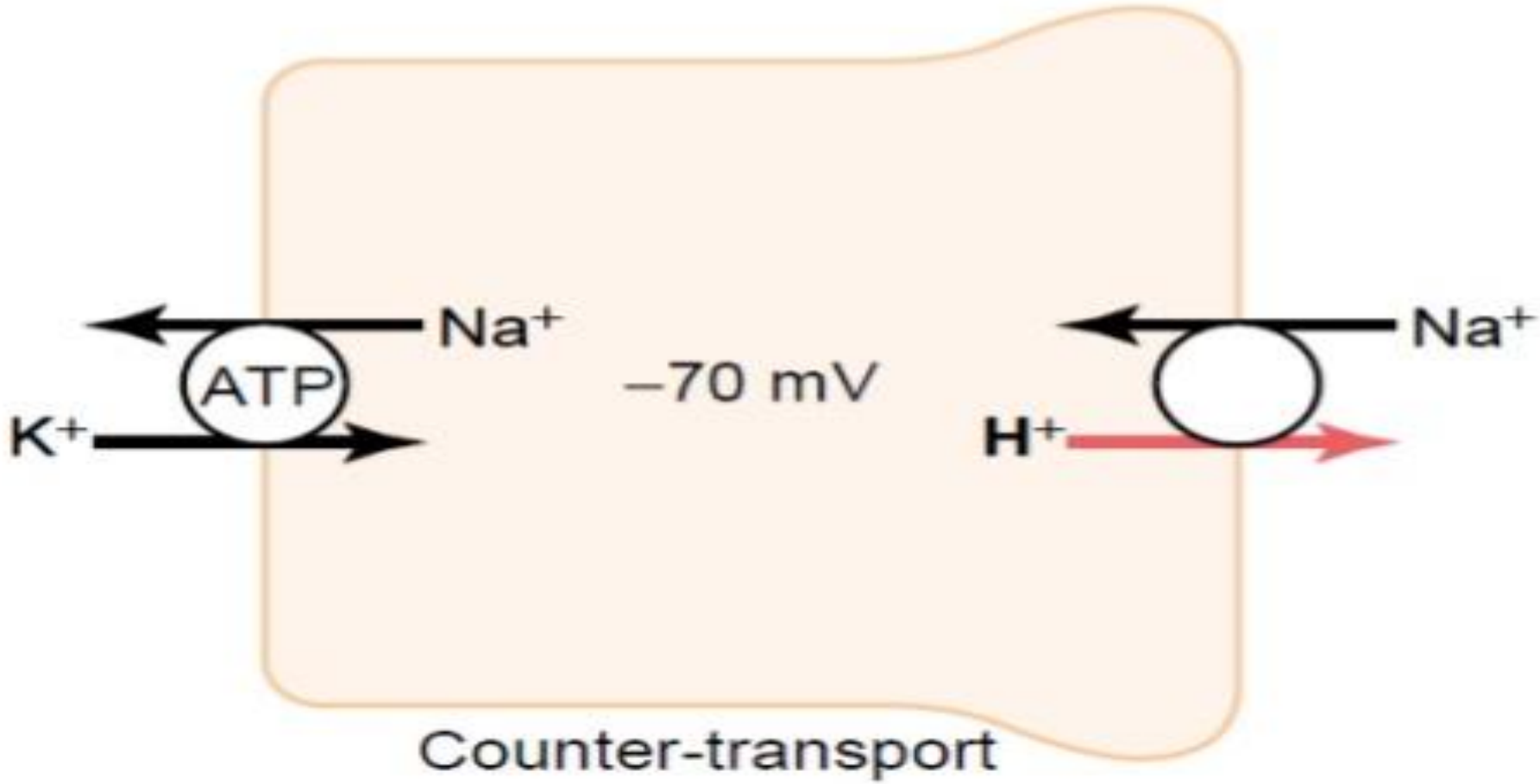


2. Sodium is transported across the basolateral membrane by the sodium-potassium ATPase pump.

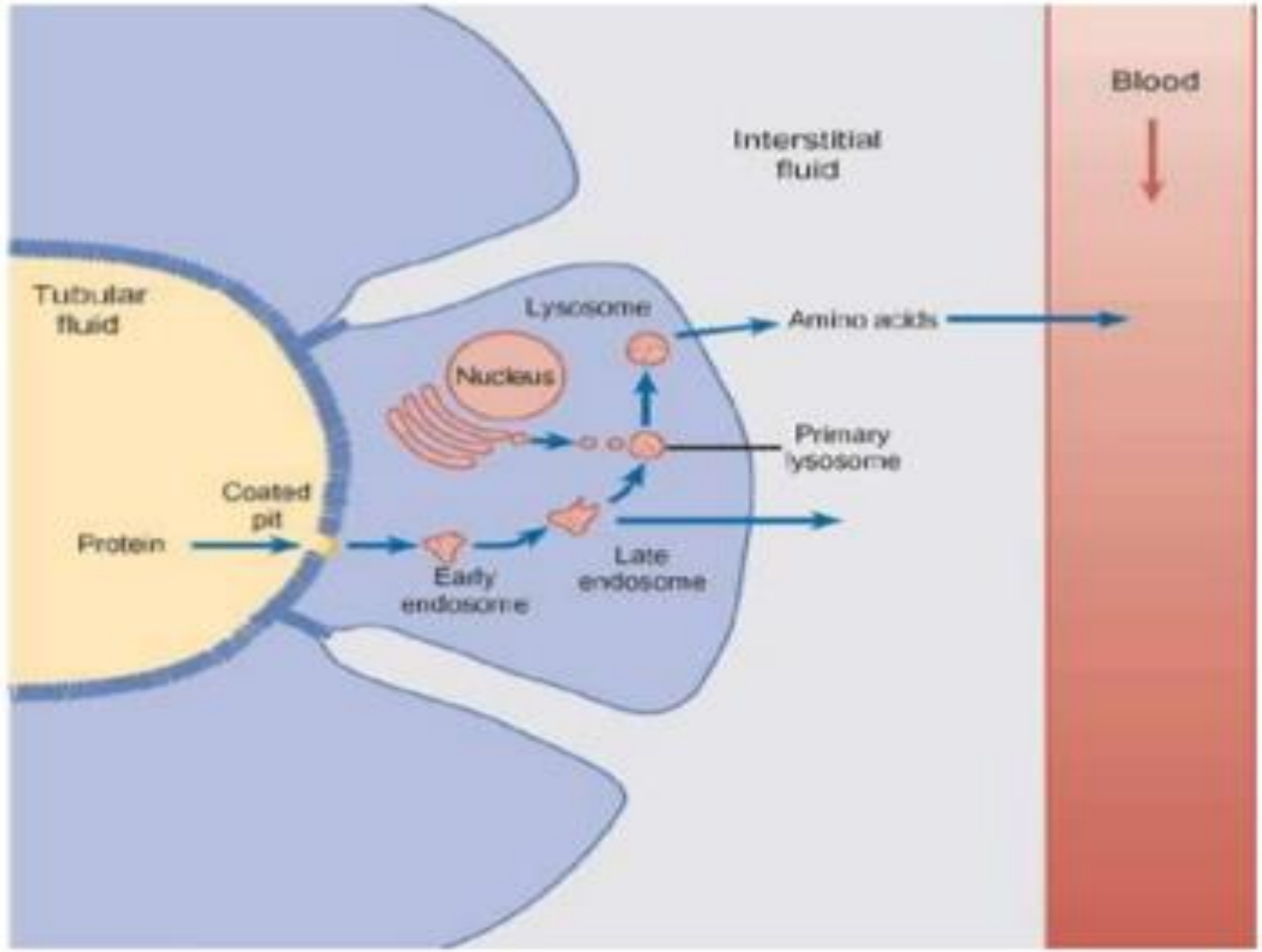
3. Sodium is reabsorbed from the interstitial fluid into the peritubular capillaries by ultrafiltration.

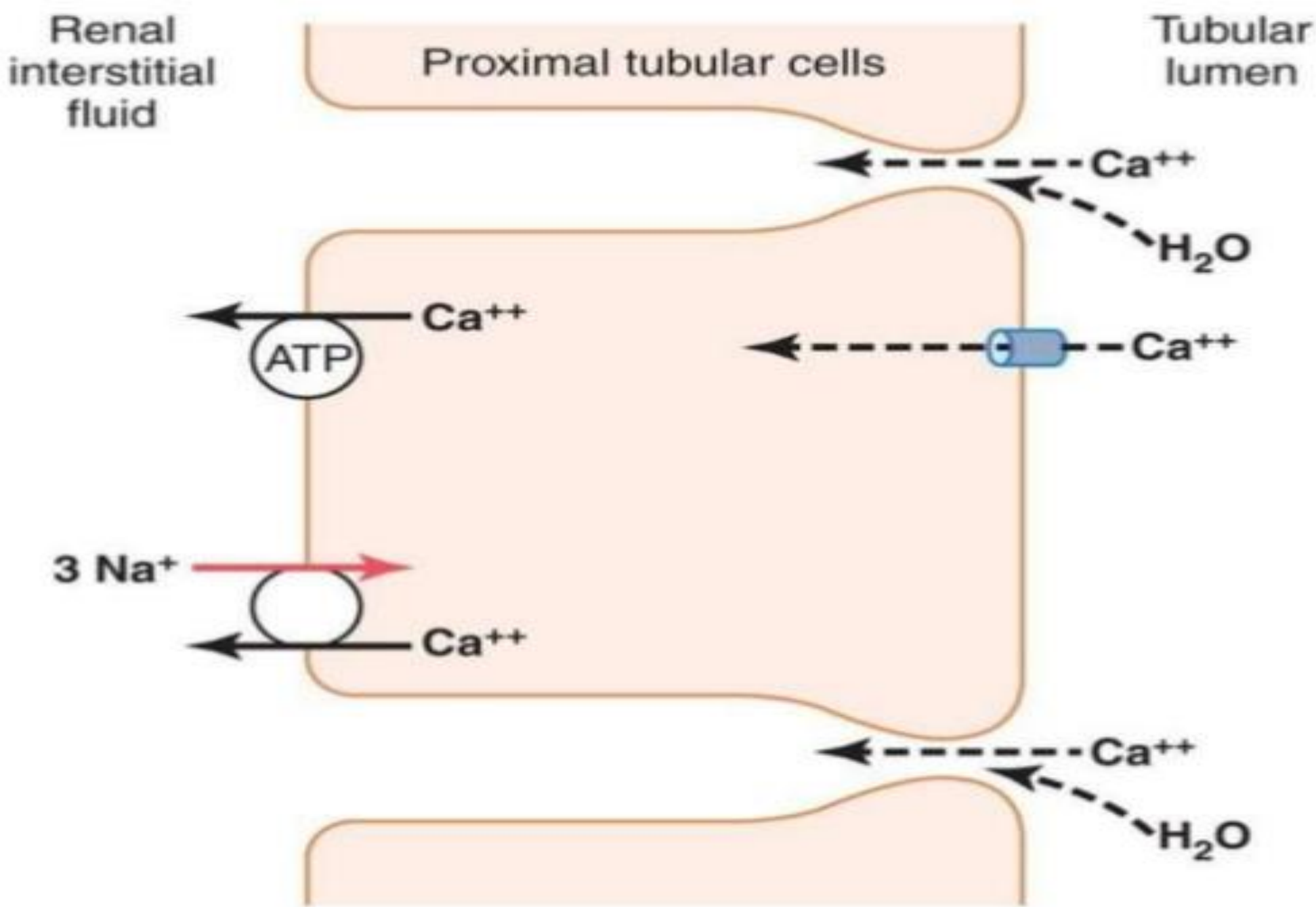
Reabsorption of Sodium

- It is also antiported with "Secretion of H+"



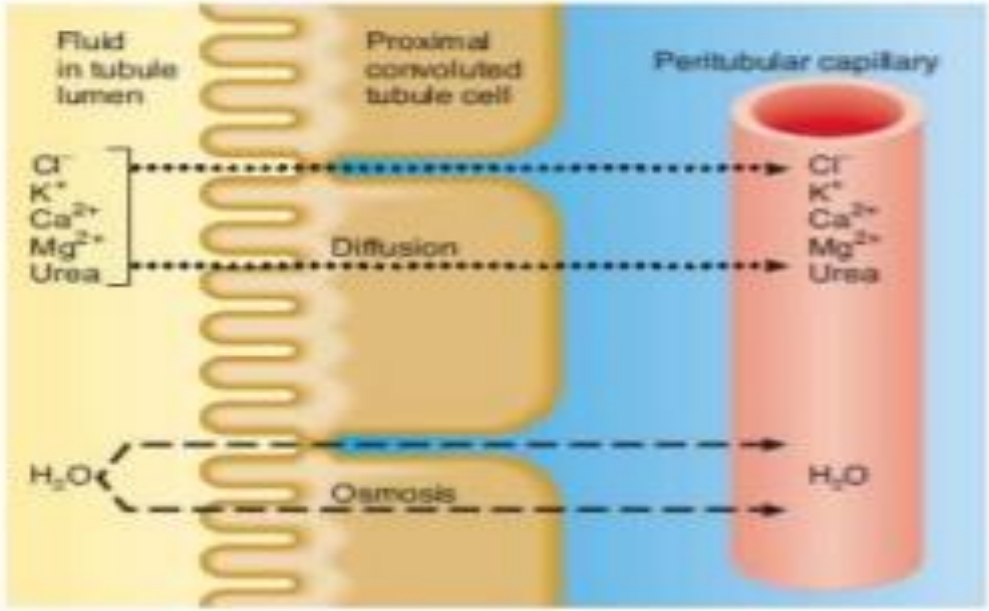
Protein absorption





Reabsorption of water / ions / nutrients

- Passive tubular reabsorption:
  - Na^+ ions establish an electro-chemical gradient favoring anions (Cl & HCO_3^-)
  - Na^+ establishes an osmotic gradient allowing water (via aquaporins) to leave water permeable region (PCT & Loop)



As water leaves the tubules the remaining solutes become more concentrated & follow their diffusion gradient out of the filtrate (cations, fatty acids, urea)

Water Reabsorption

- When solutes are transported out of the tubule, it increases the osmotic pressure on the other side.
- And this drags the water to the hyperosmolar side.
- PCT is highly permeable to water.
- Distal parts of the nephron, like; loop of Henle to the collecting tubule, become less permeable to water and solutes.
- However, Anti-Diuretic Hormone (ADH) greatly increases the water permeability in the distal and collecting tubules.

Water Reabsorption

- Thus, water movement across the tubular epithelium can occur only if the membrane is permeable to water, no matter how large the osmotic gradient.

- In the proximal tubule, the water permeability is always high, and water is reabsorbed as rapidly as the solutes.

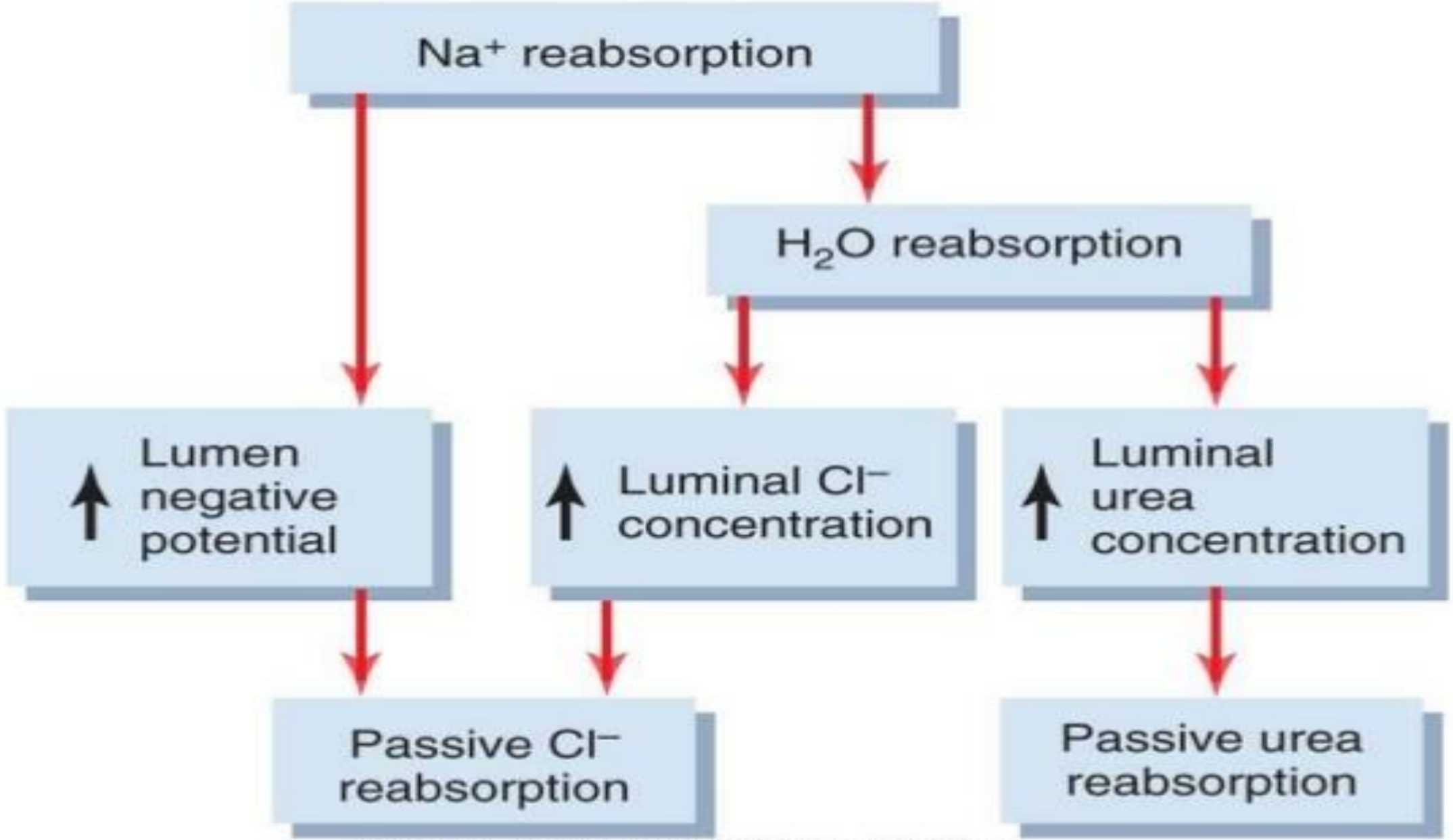
- In the ascending loop of Henle, water permeability is always low, so that almost no water is reabsorbed,despite a large osmotic gradient.

- Water permeability in the last parts of the tubules—the distal tubules, collecting tubules, and collecting ducts—can be high or low, depending on the presence or absence of ADH.

Reabsorption of Chloride

Happens in three different manners:

- By Secondary active transport
  - Co-transport of chloride with sodium across the luminal membrane.
- By concentration gradient
  - When water is reabsorbed from the tubule by osmosis, it concentrates the chloride ions in the tubular lumen & thus causes diffusion of Cl –
- By electrical gradient
  - When Na+ is reabsorbed it leaves the inside of the lumen negatively charged, compared with the interstitial fluid.
  - This causes chloride ions to diffuse *passively* through the *paracellular pathway by electric gradient*.



Reabsorption of Urea

- Only half of the urea that is filtered is reabsorbed, remaining urea passes into the urine.
- Reabsorption happens in following manners:
  - By concentration gradient
    - When water is reabsorbed from the tubule by osmosis, it concentrates the Urea in the tubular lumen & thus causes diffusion.
  - By urea transporters
    - We know urea is not permeable in the tubule as readily as water.
    - In some parts of the nephron, especially the inner medullary collecting duct, passive urea reabsorption is facilitated by specific *urea transporters*.

Reabsorption of Creatinine

- Creatinine, is a large molecule and is essentially impermeant to the tubular membrane.

- Therefore, almost none of the creatinine that is filtered is reabsorbed, so that virtually all the creatinine filtered by the glomerulus is excreted in the urine.

Transport Maximum

- Substances that use carrier protein to be *secreted* also exhibit transport maximum.

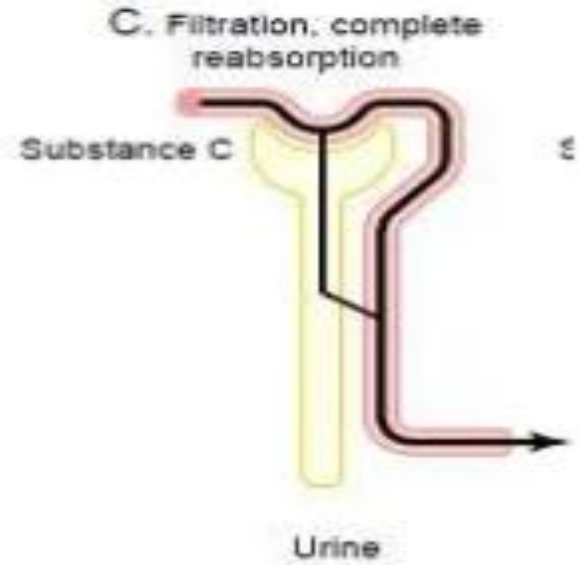
Substance	Transport Maximum
Creatinine	16 mg/min
Para-aminohippuric acid	80 mg/min

Transport Maximum

- For substances that are actively transported, there is a limit to the rate at which the solute can be transported, called as **Transport maximum**.

- This limit is due to saturation of the specific transport systems involved when the amount of solute delivered to the tubule (*tubular load*) exceeds the capacity of the carrier proteins.

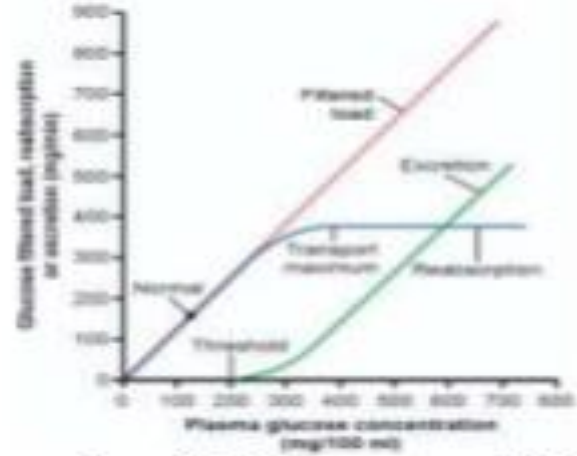
Transport Maximum



Example

- We know that Normally, all the filtered glucose is reabsorbed in PCT
- So glucose does not appear in the urine
- However, when the filtered load exceeds the capability of the tubules to reabsorb glucose, urinary excretion of glucose does occur.

Transport Maximum



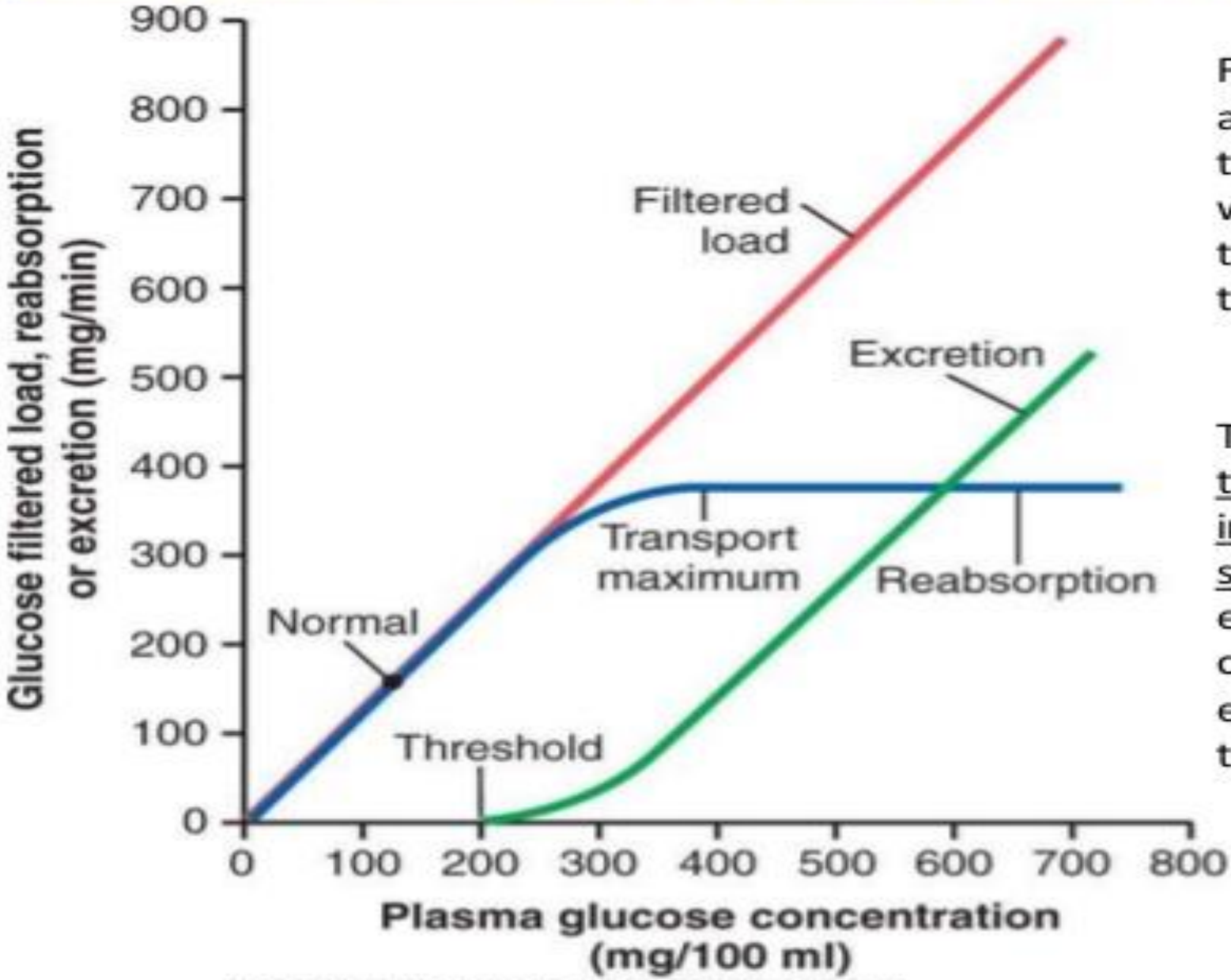
Example

- When the plasma glucose concentration is 100 mg/100 mL and the filtered load is at its normal level, 125 mg/min, there is no loss of glucose in the urine.

- However, when the plasma concentration of glucose rises above about 200 mg/100 ml, increasing the filtered load to about 250 mg/min, a small amount of glucose begins to appear in the urine.

- This point is termed the *threshold* for glucose.

Transport maximum for substances that are actively reabsorbed

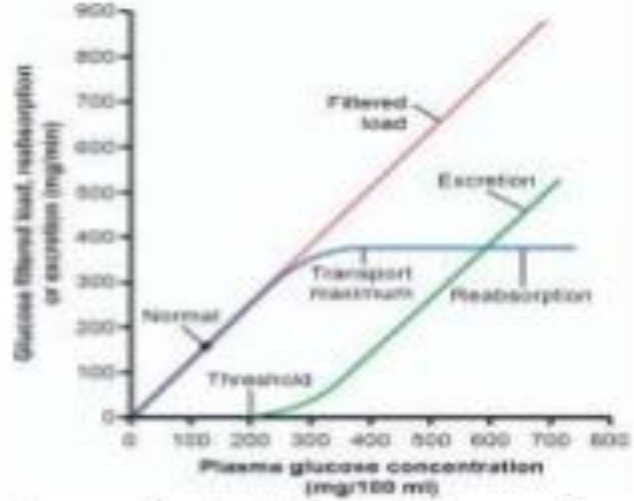


Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

For most substances that are actively reabsorbed or secreted, there is a limit to the rate at which the solute can be transported, often referred to as the ***transport maximum***.

This limit is due to **saturation** of the specific transport systems involved when the amount of solute delivered to the tubule exceeds the capacity of the carrier proteins and specific enzymes involved in the transport process.

Transport Maximum



Example

- *Note that this appearance of glucose in the urine (at the threshold) occurs before the transport maximum is reached.*

- Reason for the difference between threshold and transport maximum is that not all nephrons have the same transport maximum for glucose, and some of the nephrons excrete glucose before others have reached their transport maximum.

- *The overall transport maximum for the kidneys, which is normally about 375 mg/min, is reached when all nephrons have reached their maximal capacity to reabsorb glucose.*

Transport Maximum for some substances

Substance	Transport Maximum
Glucose	375 mg/min
Phosphate	0.10 mM/min
Sulfate	0.06 mM/min
Amino acids	1.5 mM/min
Urate	15 mg/min
Lactate	75 mg/min
Plasma protein	30 mg/min

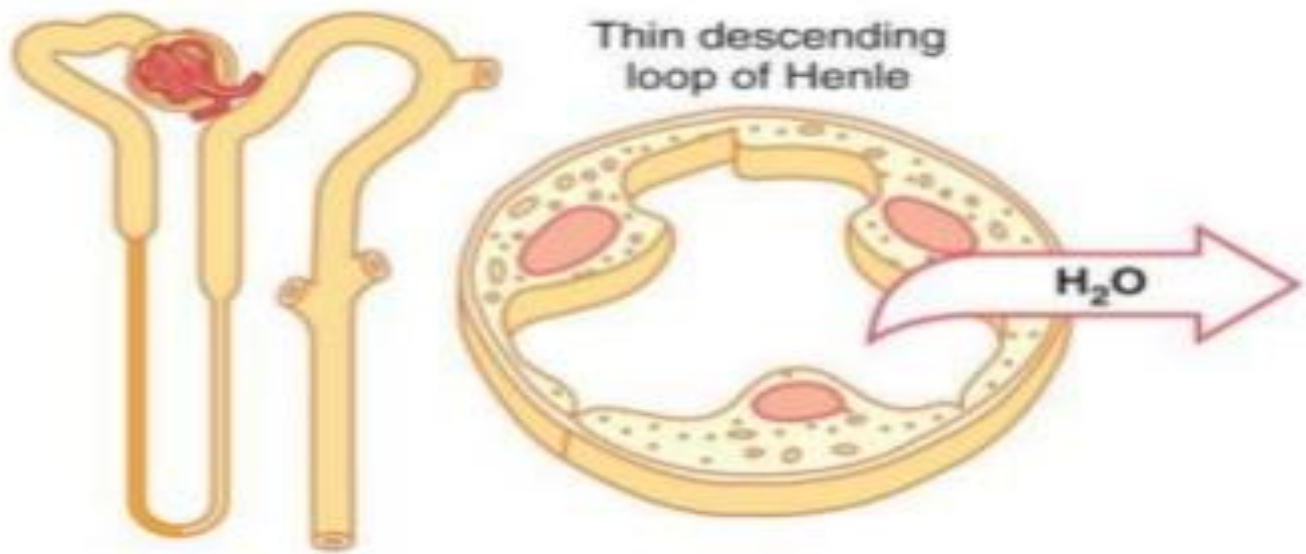
Transport Maximum

Na+ Reabsorption in PCT does Not Exhibit a Transport Maximum

- The maximum transport capacity of the basolateral sodium-potassium ATPase pump is usually far greater than the actual rate of net sodium reabsorption.
- Other factors limit the reabsorption rate besides the maximum rate of active transport.
- The "Tight Junction" of PCT despite the name is not impermeable to sodium.
- So that significant amount of sodium transported out of the cell leaks back.

Loop of Henle: Reabsorption

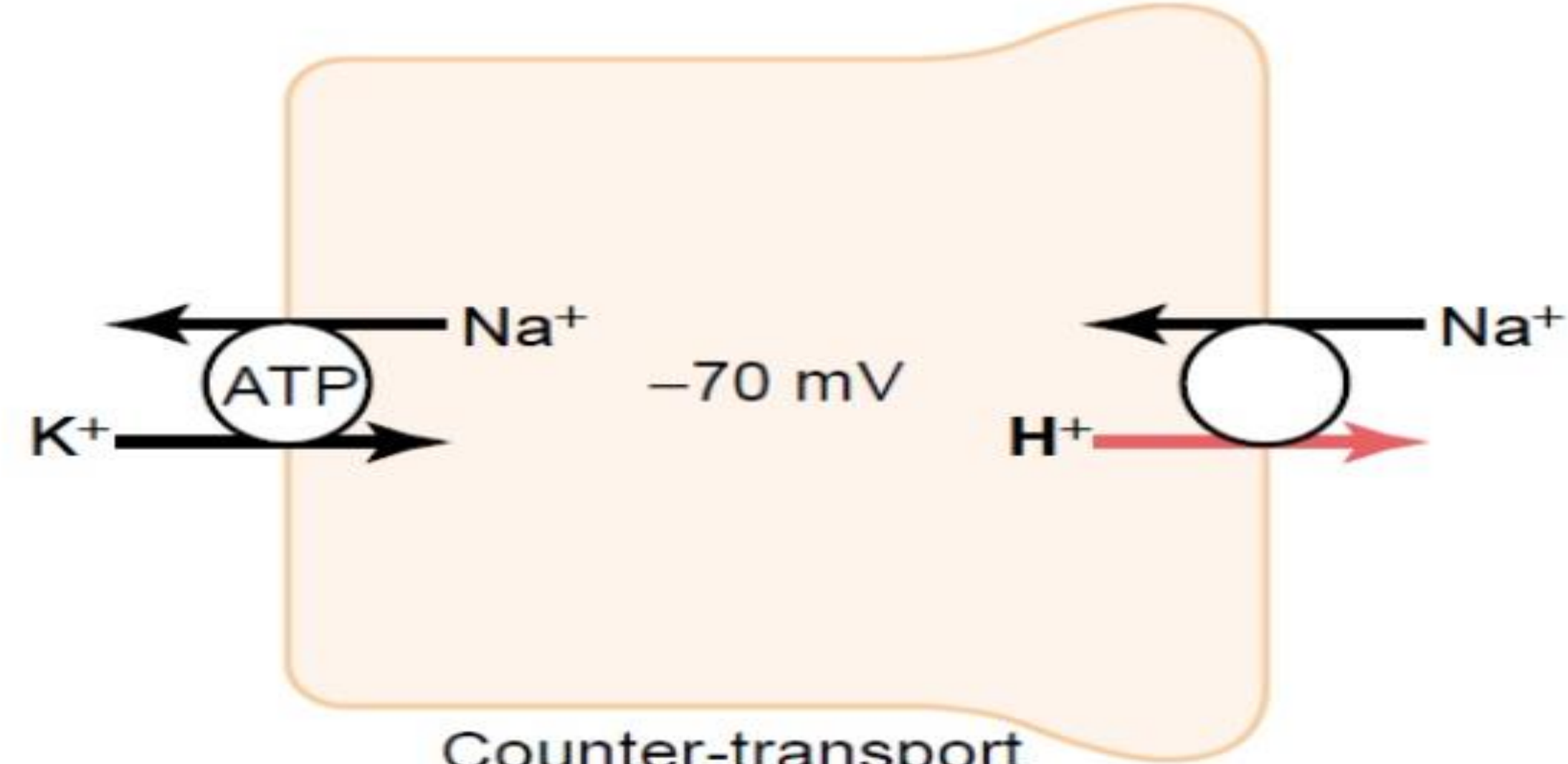
- Descending limb:
  - H_2O reabsorbed by osmosis



Secretion of H+

- By "secondary active transport"
- Antiported against sodium.
- By, Na+/K+ pump, Na+ is thrown out of cell.
- Which causes enotropic energy to be created in cell.
- This energy causes drive of Na+ inside while antiported with H+ in lumen.

Secretion of H+

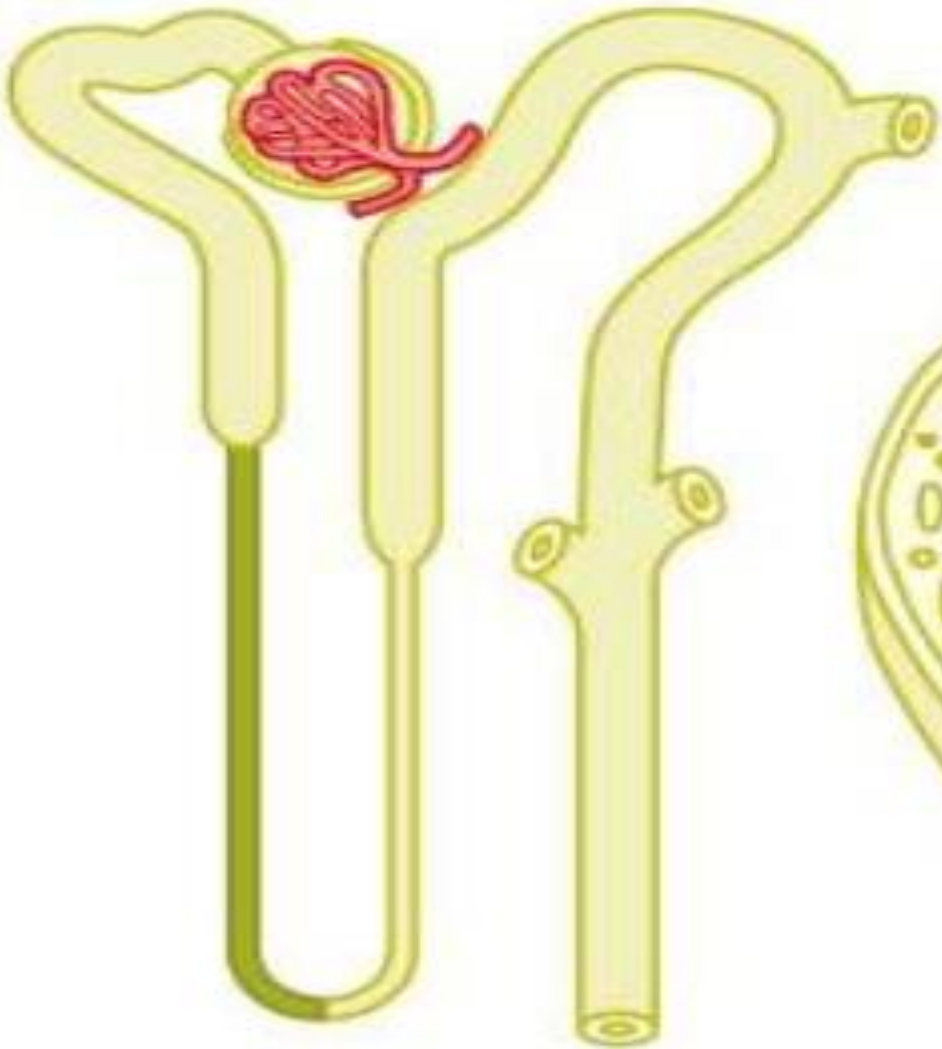


Secretion of H+

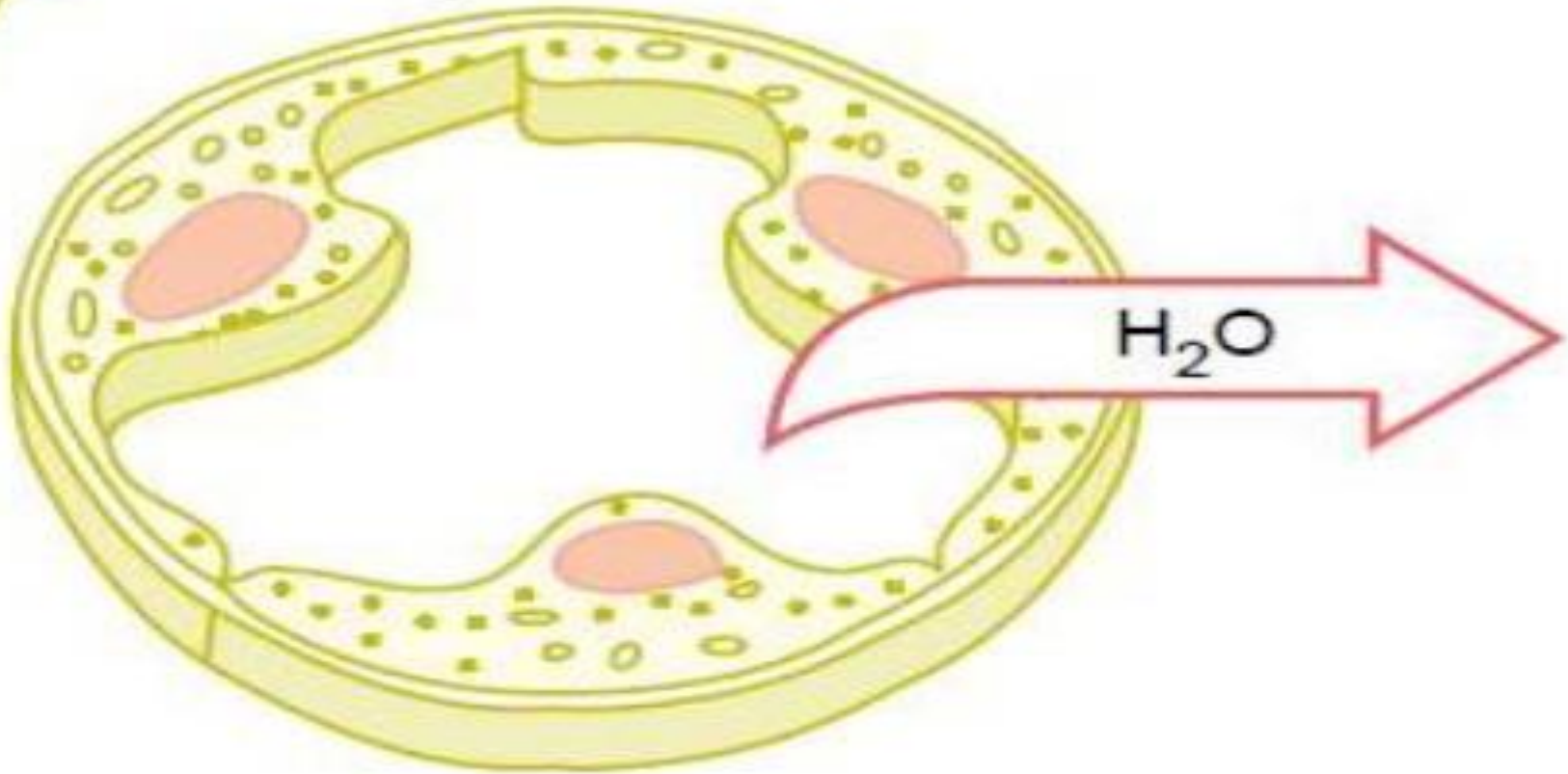
- H+ is also secreted through a H+ pump in late DCT or cortical collecting tubule

Para-aminohippuric acid (PAH)

- It is an amide derivative of the Glycine and Para-aminobenzoic acid.
- It is not naturally found in human.
- PAH is secreted very rapidly.
- An average person can clear about 90 % of the PAH from the plasma flowing through the kidneys and excrete it in the urine.
- It is a diagnostic agent useful in measurement of RPF.
- It needs to be IV infused before use diagnostically.



Thin descending
loop of Henle



Reabsorption in Loop of Henle

Descending thin segment

- Highly permeable to water and
- Moderately permeable to most solutes, including urea and sodium.

- About 20 percent of the filtered water is reabsorbed in the loop of Henle, and almost all of this occurs in the thin descending limb.

- This property is important for concentrating the urine.

Reabsorption in Loop of Henle

Ascending limb

- Both thick and thin ascending loop is virtually impermeable to water.

- The thick ascending loop of Henle, has thick epithelial cells that have high metabolic activity and are capable of active reabsorption of sodium, chloride, and potassium .

- About 25 per cent of the filtered loads of sodium, chloride, and potassium are reabsorbed in the loop of Henle, mostly in the thick ascending limb.

- Considerable amounts of other ions, such as calcium, bicarbonate, and magnesium, are also reabsorbed in the thick ascending loop of Henle.

- The ascending limb is also called the diluting segment.

Reabsorption in Loop of Henle

Ascending limb

- Thick ascending limb also has a Na+/H+ Antiport.
- That mediates sodium reabsorption and hydrogen secretion in this segment.

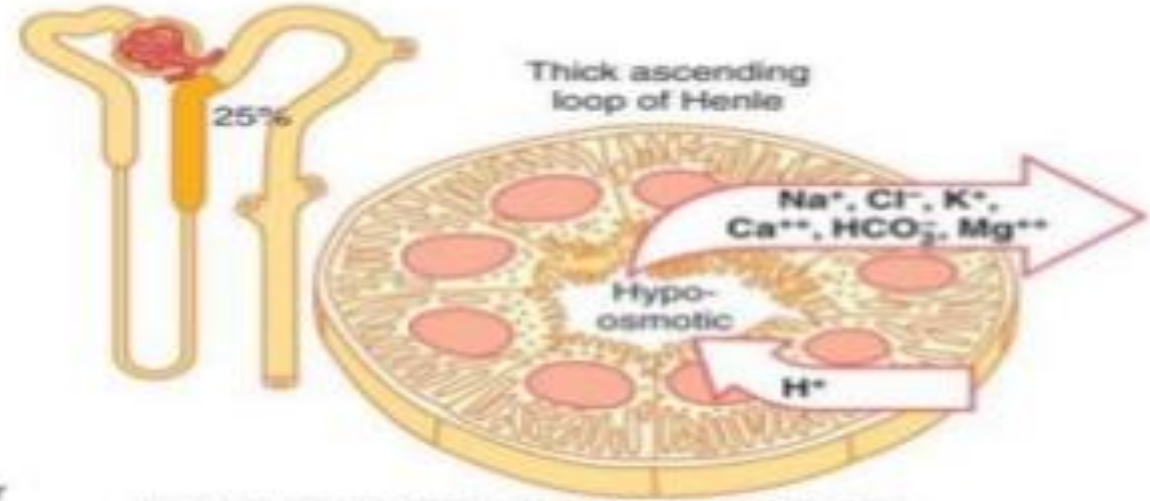
Loop of Henle: Reabsorption

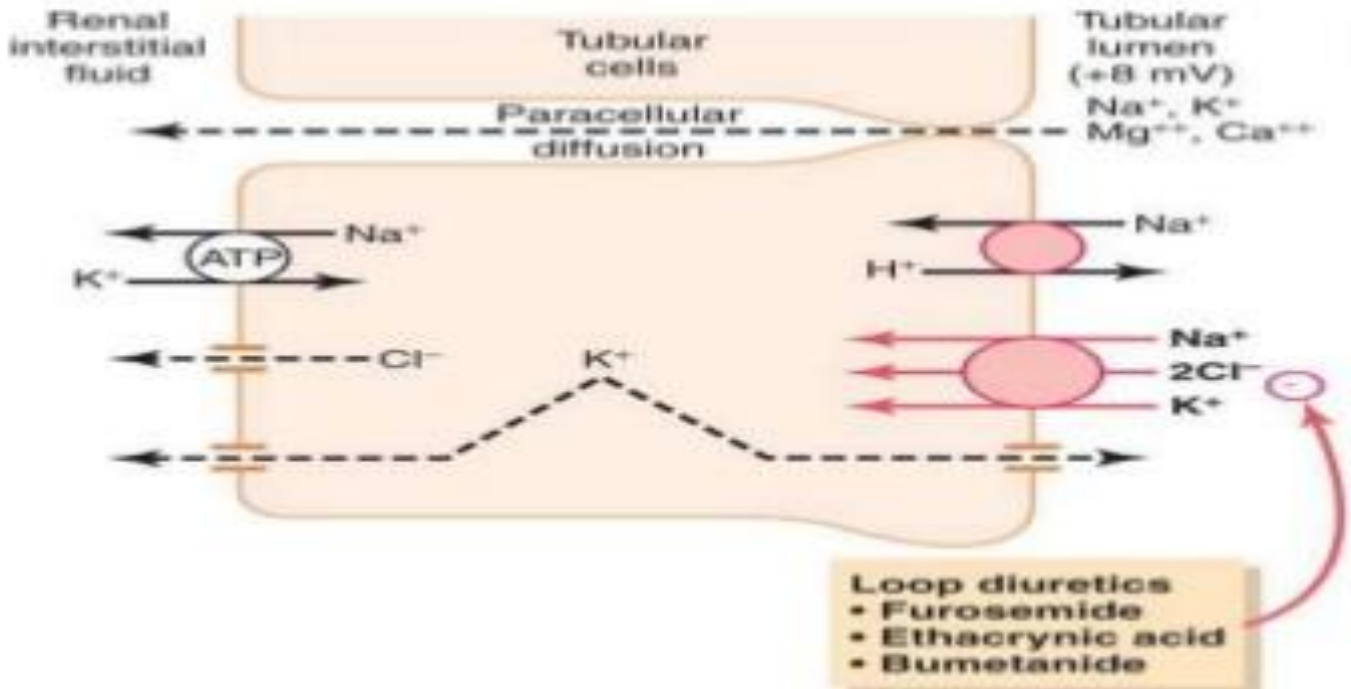
Ascending limb:

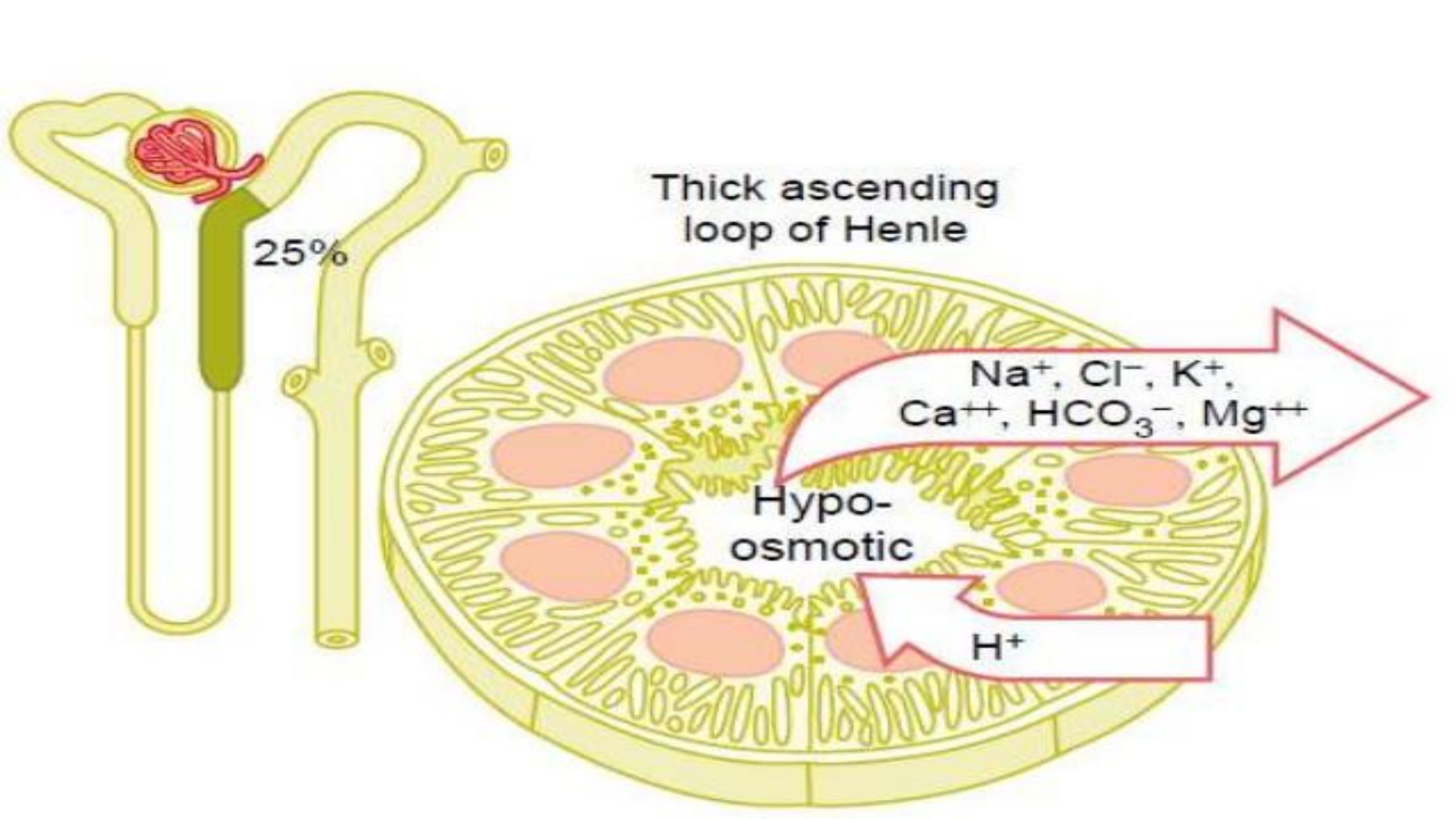
Na^+, Cl^-, K^+ active transport

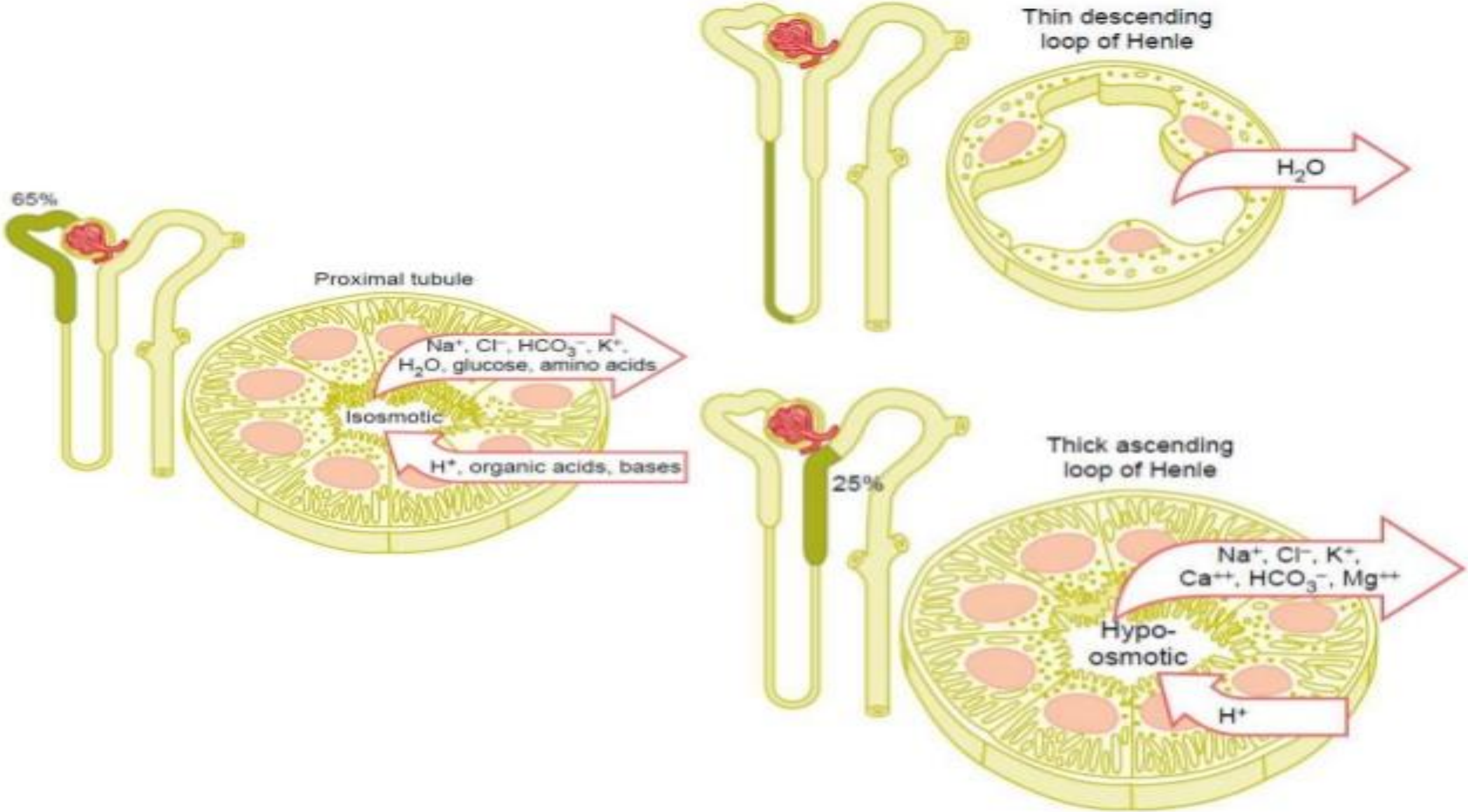
Ca^{2+}, Mg^{2+} passive transport

H2O : impermeable






Thick ascending
loop of Henle
25%
Na+, Cl−, K+,
Ca++, HCO3−, Mg++
Hypo-
osmotic
H+


65%
Proximal tubule
Na^+, Cl^-, HCO_3^-, K^+,
H_2O, glucose, amino acids
Isosmotic
H^+, organic acids, bases
Thin descending
loop of Henle
H_2O
25%
Thick ascending
loop of Henle
Na^+, Cl^-, K^+,
Ca^{++}, HCO_3^-, Mg^{++}
Hypo-
osmotic
H^+

Late Distal Tubule and Cortical Collecting Tubule

- The second half of the distal tubule and the subsequent cortical collecting tubule have similar functional characteristics.

- Anatomically, they are composed of two distinct cell types:

  — *Principal cells and*

  — *Intercalated cells*

Late Distal Tubule and Cortical Collecting Tubule

Principal cells

- **Reabsorb Sodium and Secrete Potassium.**
- Na+/K+ pump in basolateral membrane maintains a low Na+ concentration inside the cell.
- Therefore, favors sodium diffusion into the cell through special channels.
- The secretion of potassium by these cells from the blood into the tubular lumen involves two steps:

(1)Potassium enters the cell because of the sodium-potassium ATPase pump, which maintains a high intracellular potassium concentration, and then

(2)Once in the cell, potassium diffuses down its concentration gradient across the luminal membrane into the tubular fluid.

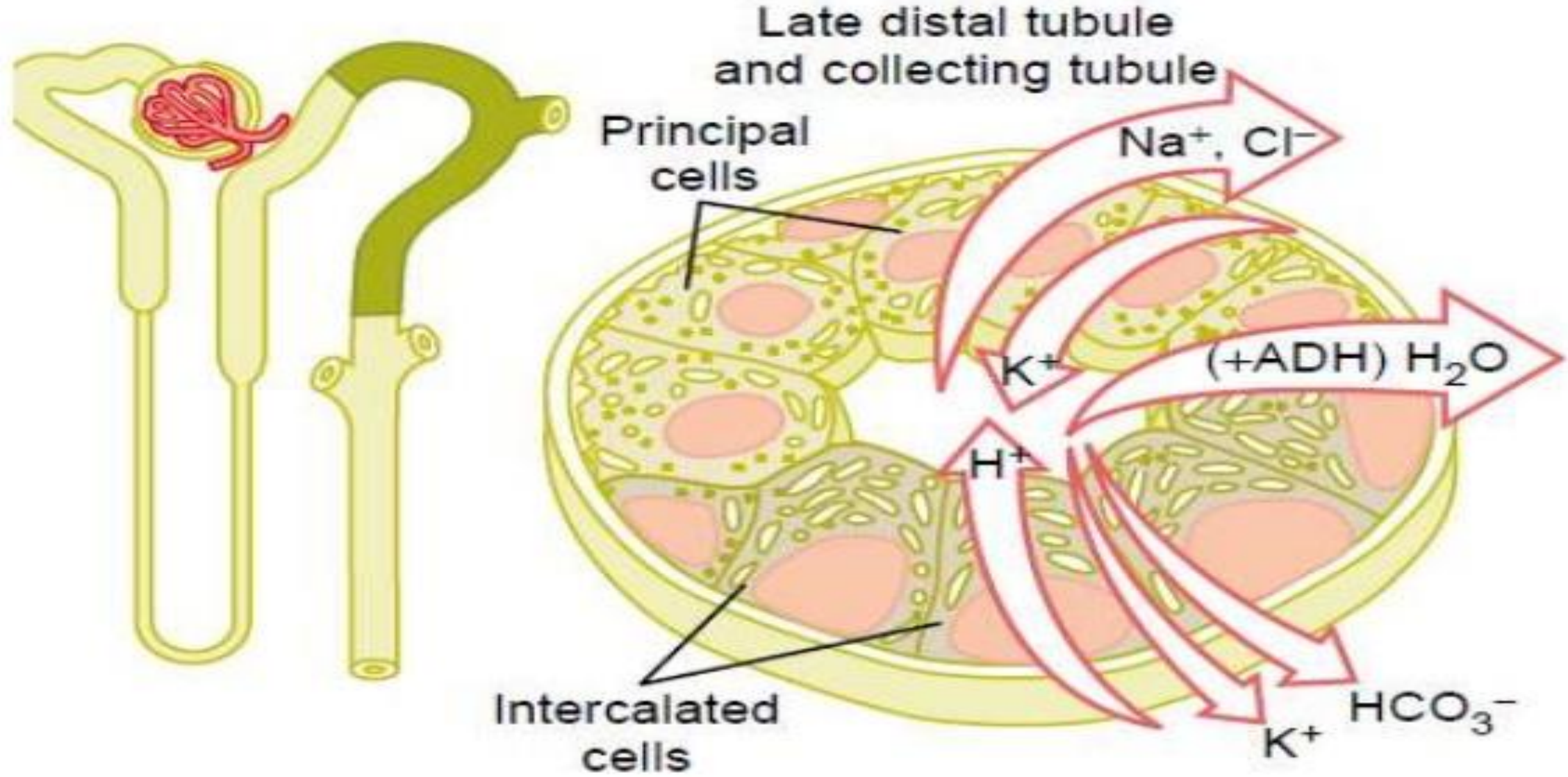
Late Distal Tubule and Cortical Collecting Tubule

Intercalated cells

- The intercalated cells
  - Secrete hydrogen &
  - Reabsorb potassium & Bicarbonate

- H+ is generated in this cell by the action of carbonic anhydrase on water and carbon dioxide to form carbonic acid, which then dissociates into hydrogen ions and bicarbonate ions.

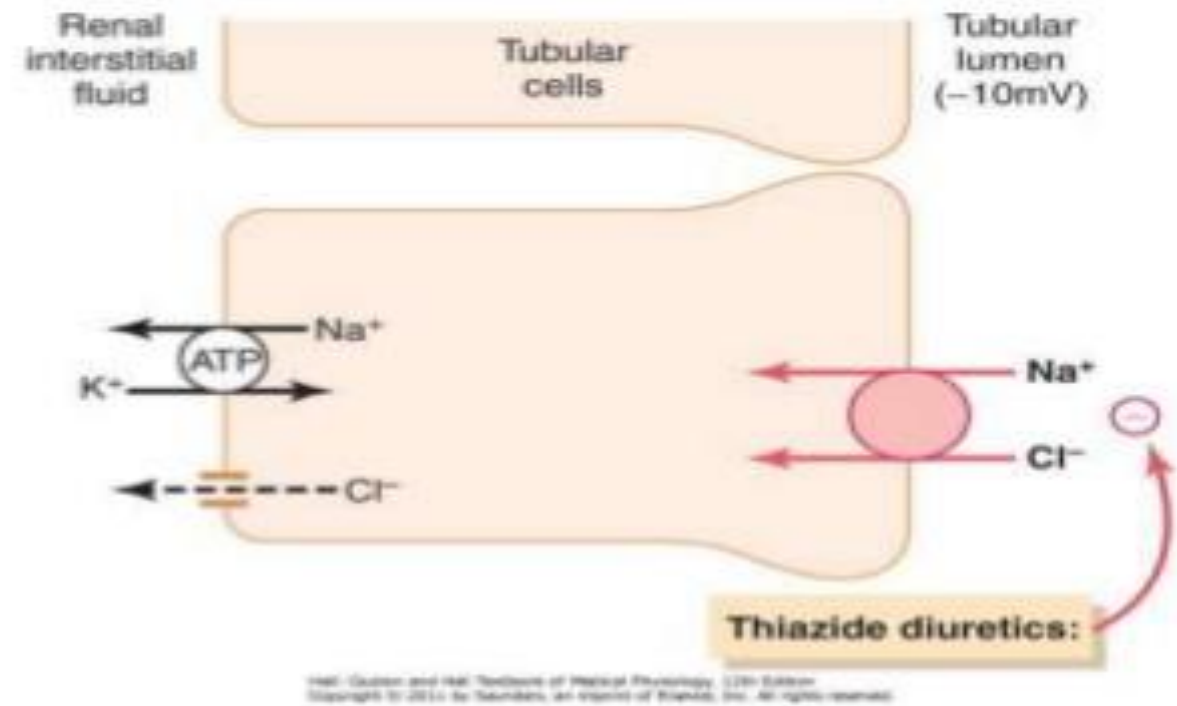
- H+ is thrown to lumen by H+ Pump, a different mechanism than in PCT where H+ is Antiported with Na+.

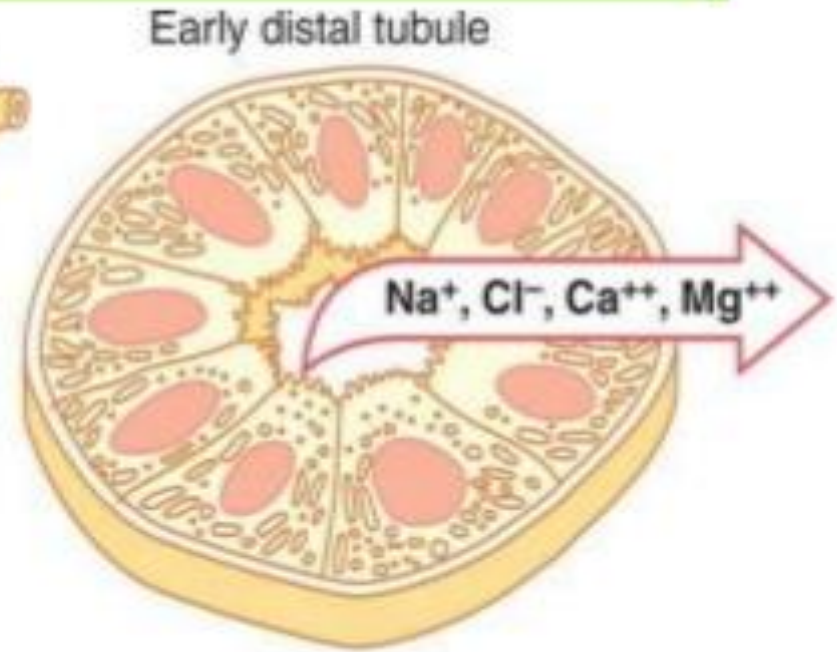

Late distal tubule
and collecting tubule
Principal
cells
Na+, Cl−
K+
(+ADH) H2O
H+
Intercalated
cells
K+
HCO3−

Distal Convoluted Tubule: Reabsorption

Early tubule:

- Na^+ : symporter mediated
- Ca^{2+} : PTH mediated
- Cl^- : diffusion
- H_2O : impermeable





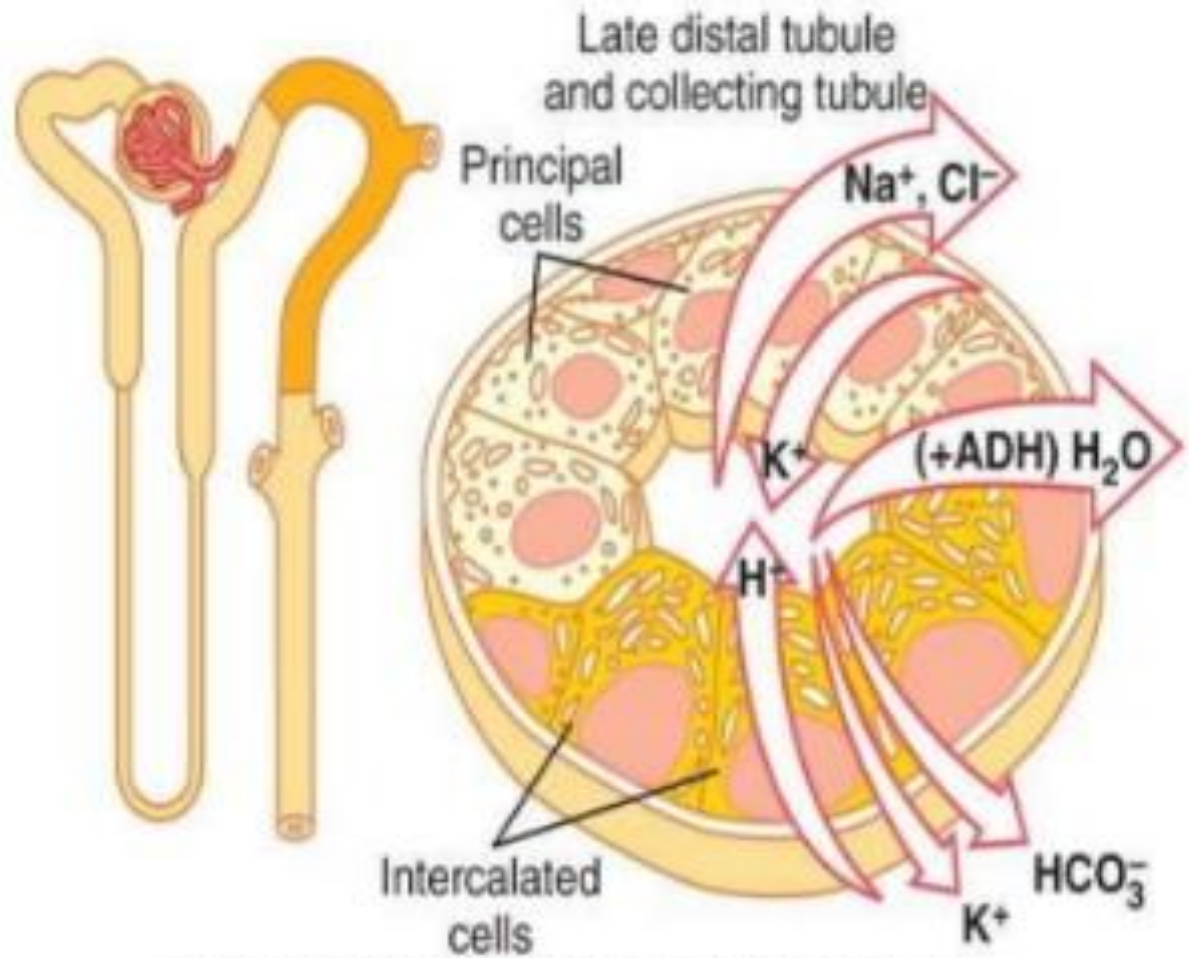
Distal Convoluted Tubule & Collecting Tubule : Reabsorption

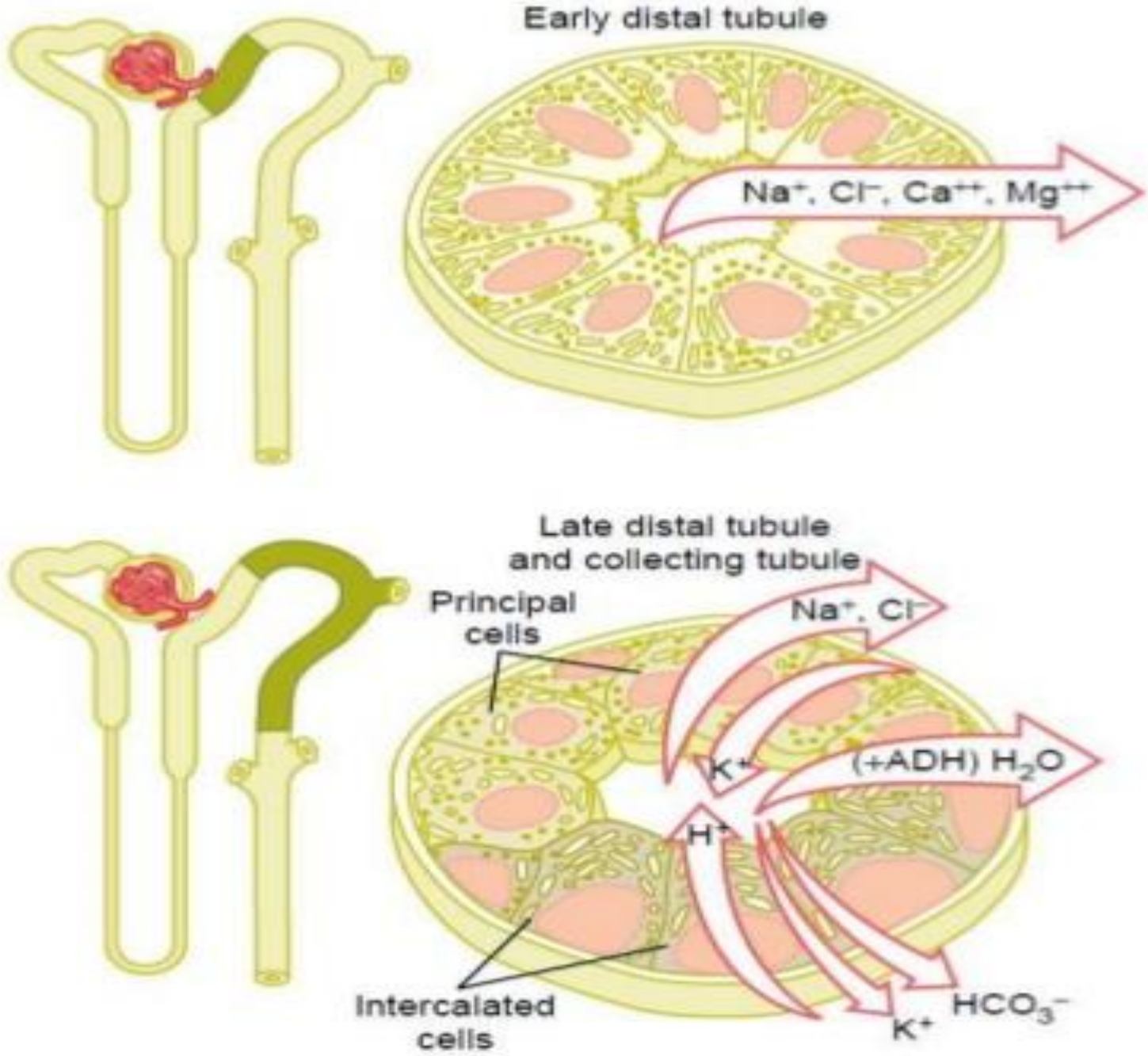
Principal cells:

- Na^+ : Aldosterone mediated
- Ca^{2+} : PTH mediated
- H_2O : ADH mediated

Intercalated cells

- H_2CO_3




Early distal tubule
Na+, Cl−, Ca++, Mg++
Late distal tubule
and collecting tubule
Principal
cells
Na+, Cl−
K+
(+ADH) H2O
H+
Intercalated
cells
K+
HCO3−

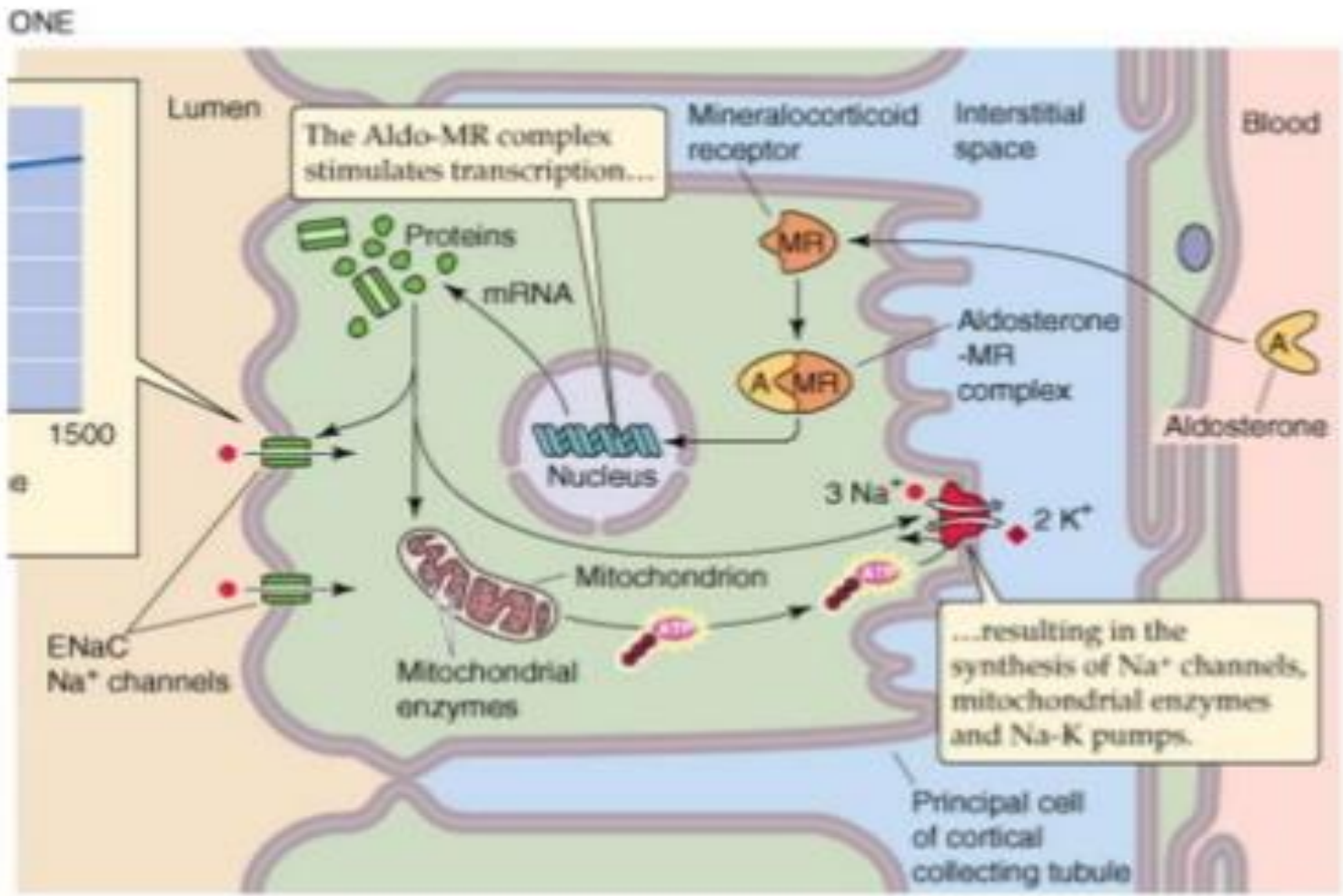
Late Distal Tubule and Cortical Collecting Tubule

- The intercalated cells play a key role in acid-base regulation of the body fluids.

- The permeability of the late distal tubule and cortical collecting duct to water is controlled by the concentration of *ADH*.

- This special characteristic provides an important mechanism for controlling the degree of dilution or concentration of the urine.

Mechanism of Action of Aldosterone



& Boulpaep: Medical Physiology, Updated Edition www.studentconsult.com

Medullary Collecting Duct

- Although the medullary collecting ducts reabsorb less than 10 per cent of the filtered water and sodium, they are the final site for processing the urine and, therefore, play an extremely important role in determining the final urine output of water and solutes.

- The epithelial cells of the collecting ducts are nearly cuboidal in shape with smooth surfaces and relatively few mitochondria.

Special characteristics of this Medullary Collecting Duct

1. The permeability of the medullary collecting duct to water is controlled by the level of ADH.With high levels of ADH, water is avidly reabsorbed into the medullary interstitium, thereby reducing the urine volume and concentrating most of the solutes in the urine.

2. Unlike the cortical collecting tubule, the medullary collecting duct is permeable to urea. Therefore, some of the tubular urea is reabsorbed into the 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.

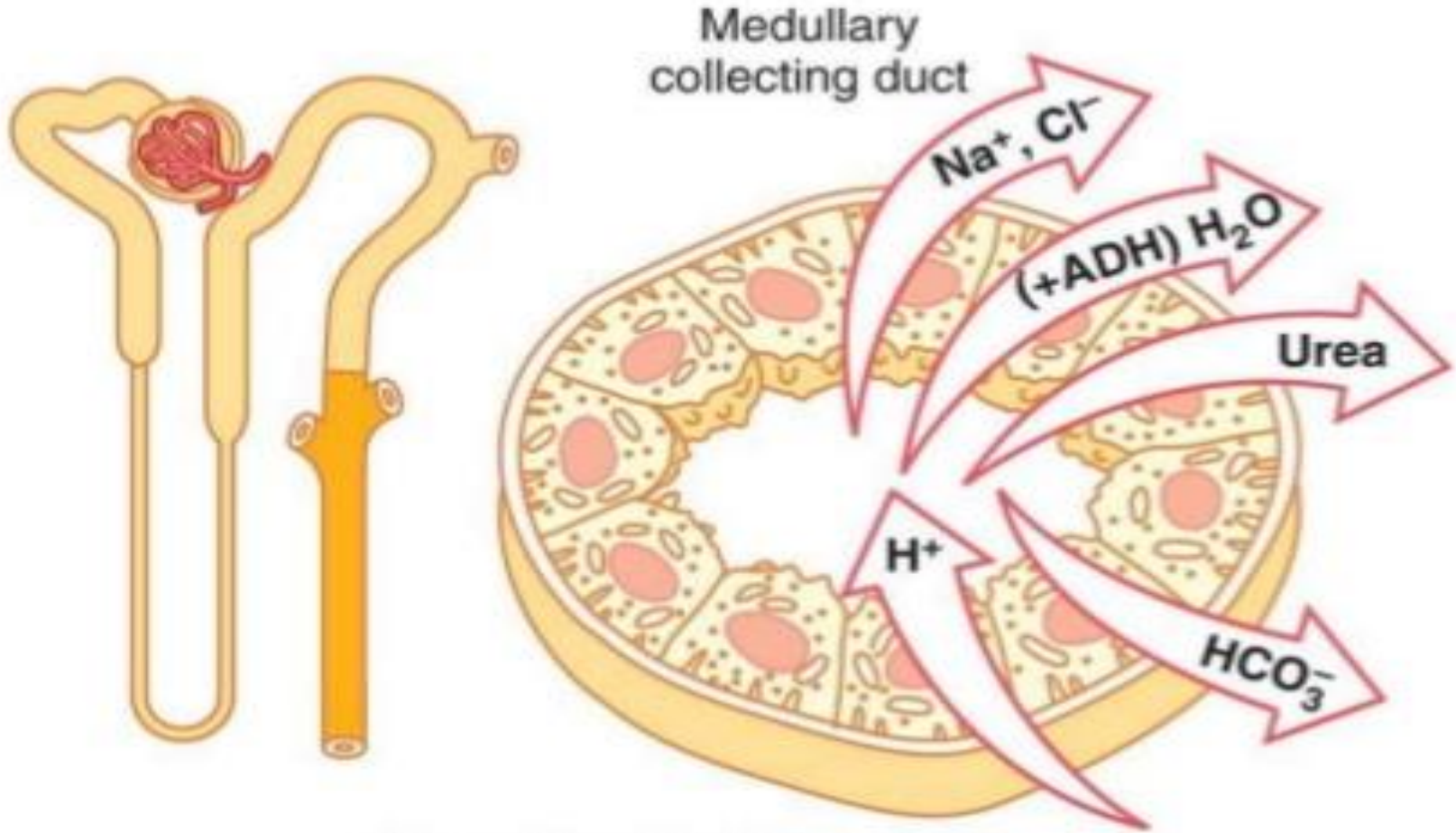
3. The medullary collecting duct is capable of secreting hydrogen ions against a large concentration gradient, as also occurs in the cortical collecting tubule. Thus, the medullary collecting duct also plays a key role in regulating acid-base balance.

Medullary Collecting Duct: Reabsorption

HCO_3^-

H_2O : ADH dependent

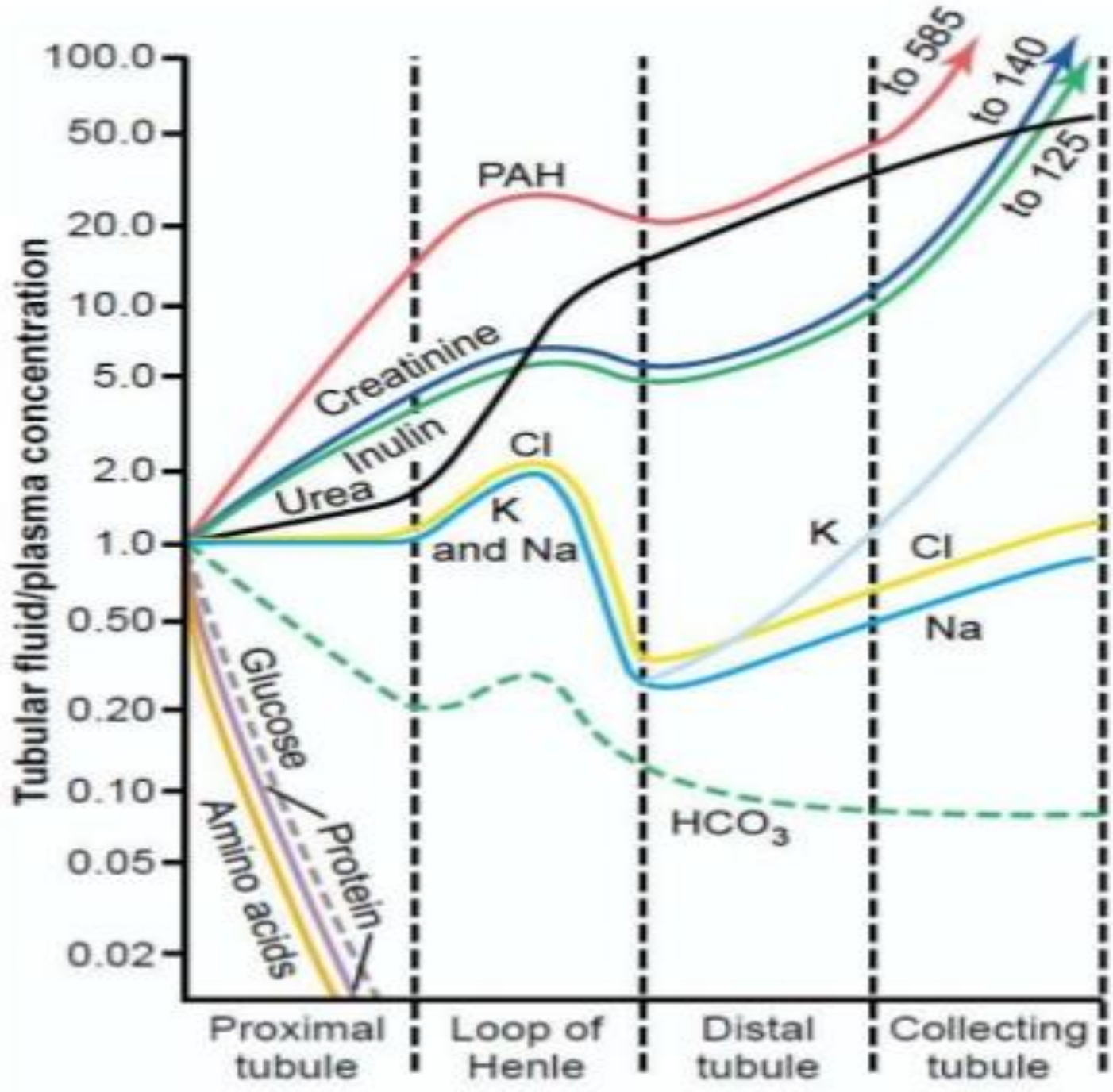
Urea: facilitated diffusion



Tubular Secretion

- Tubules also secrete substances into the filtrate.
- H^+, K^+, NH_4^+, creatinine
- Important functions:
  - Disposes of substances not in original filtrate (certain drugs and toxins)
  - Bile salts, oxalate, urate and catecholamines
  - Disposes of excess K^+

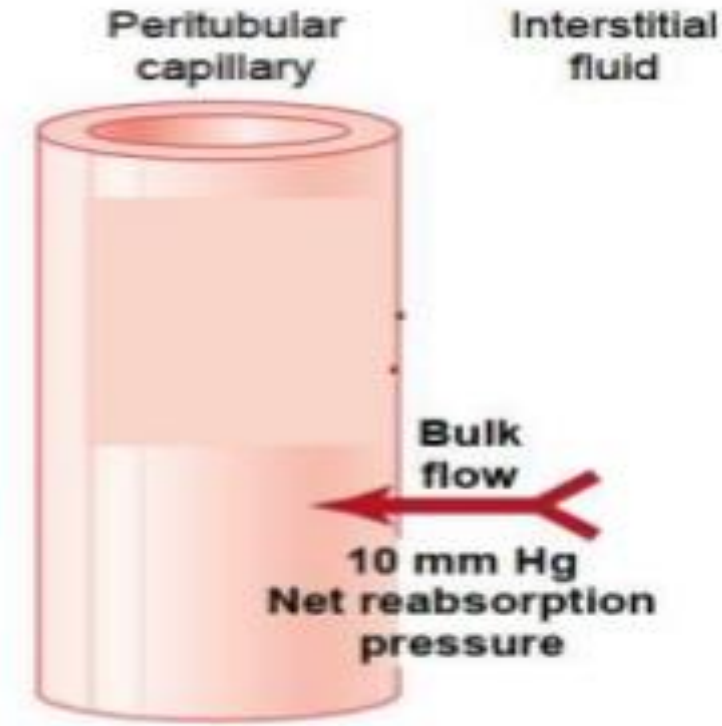
- Urine consists of filtered & secreted substances


Tubular fluid/plasma concentration
100.0
50.0
20.0
10.0
5.0
2.0
1.0
0.50
0.20
0.10
0.05
0.02
PAH
Creatinine
Inulin
Urea
Cl
K
and Na
Glucose
Amino acids
Protein
HCO_3
to 585
to 140
to 125
K
Cl
Na
Proximal tubule
Loop of Henle
Distal tubule
Collecting tubule

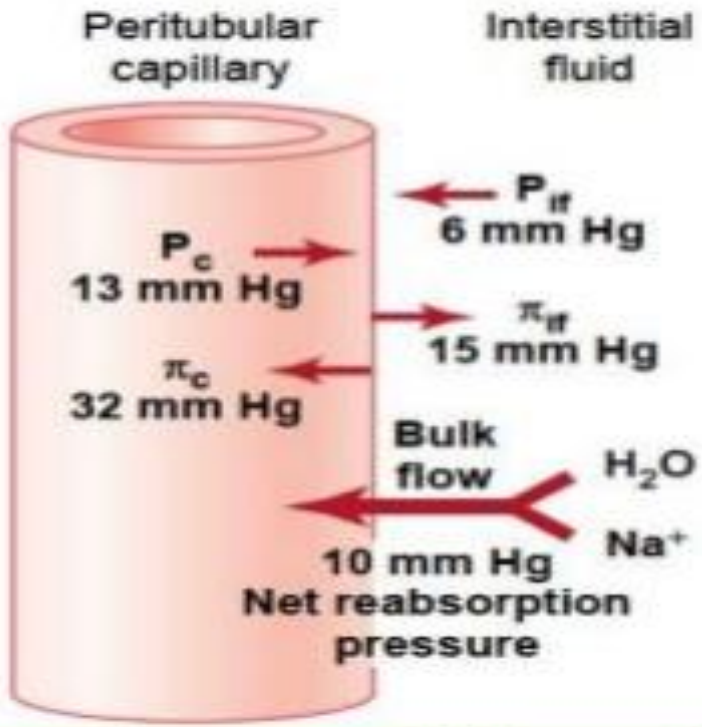
Regulation Of Reabsorption

Reabsorption Rate

- It is the rate at which Filtrates are reabsorbed per unit time.
- More than 99 per cent of the filtrate are normally reabsorbed.
- It is normally 124 ml/min.



Reabsorption Rate (Fluid Dynamic)

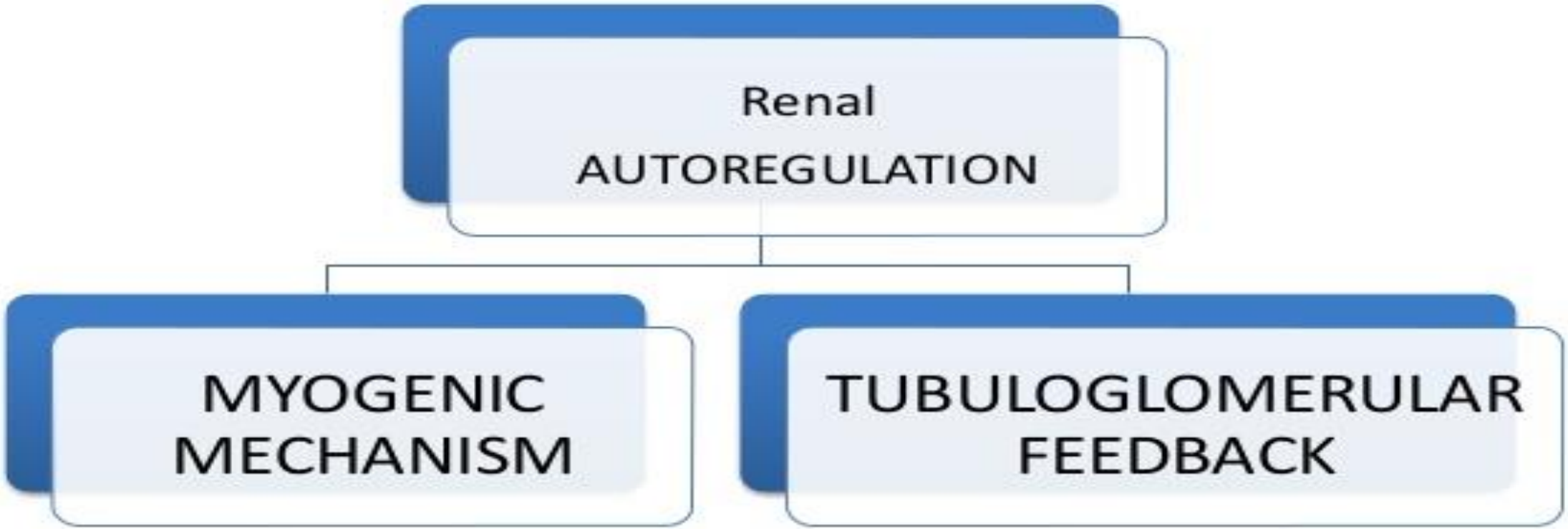


Pc = Capillary hydrostatic pressure
Pif = Interstitial hydrostatic pressure
Πc = Capillary osmotic Pressure
Πif = Interstitial osmotic pressure

$K_f = 12.4$

$$\text{Reabsorption} = K_f \times \text{Net reabsorptive force}$$

$$\text{Reabsorption} = K_f \times (P_{if} - P_c + \pi_c - \pi_{if})$$



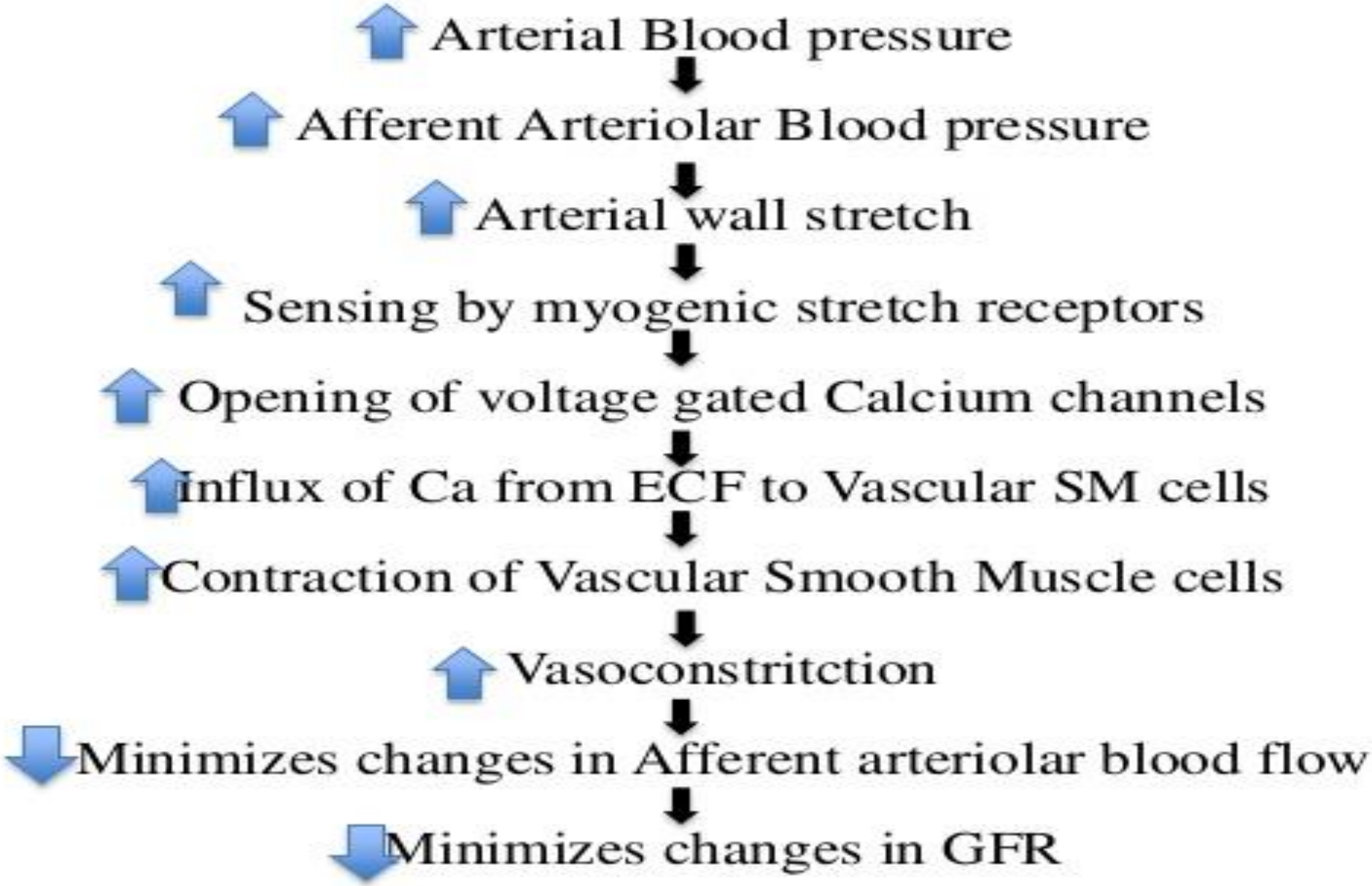
➢ Other Factors involved in Autoregulation

- Neural
- Hormonal
- Vasoactive Substances

Myogenic Mechanism

- Arterial smooth muscle contracts and relaxes in response to increases and decreases in vascular wall tension.
- It contributes upto 50% of total autoregulatory response
- Occurs very rapidly, reaching a full response in 3-10 seconds
- It is a property of the preglomerular resistance vessels – arcuate, interlobular and the afferent
- It is not seen in efferent arterioles, probably because of lack of voltage gated Ca channels

Mechanism of Myogenic Autoregulation



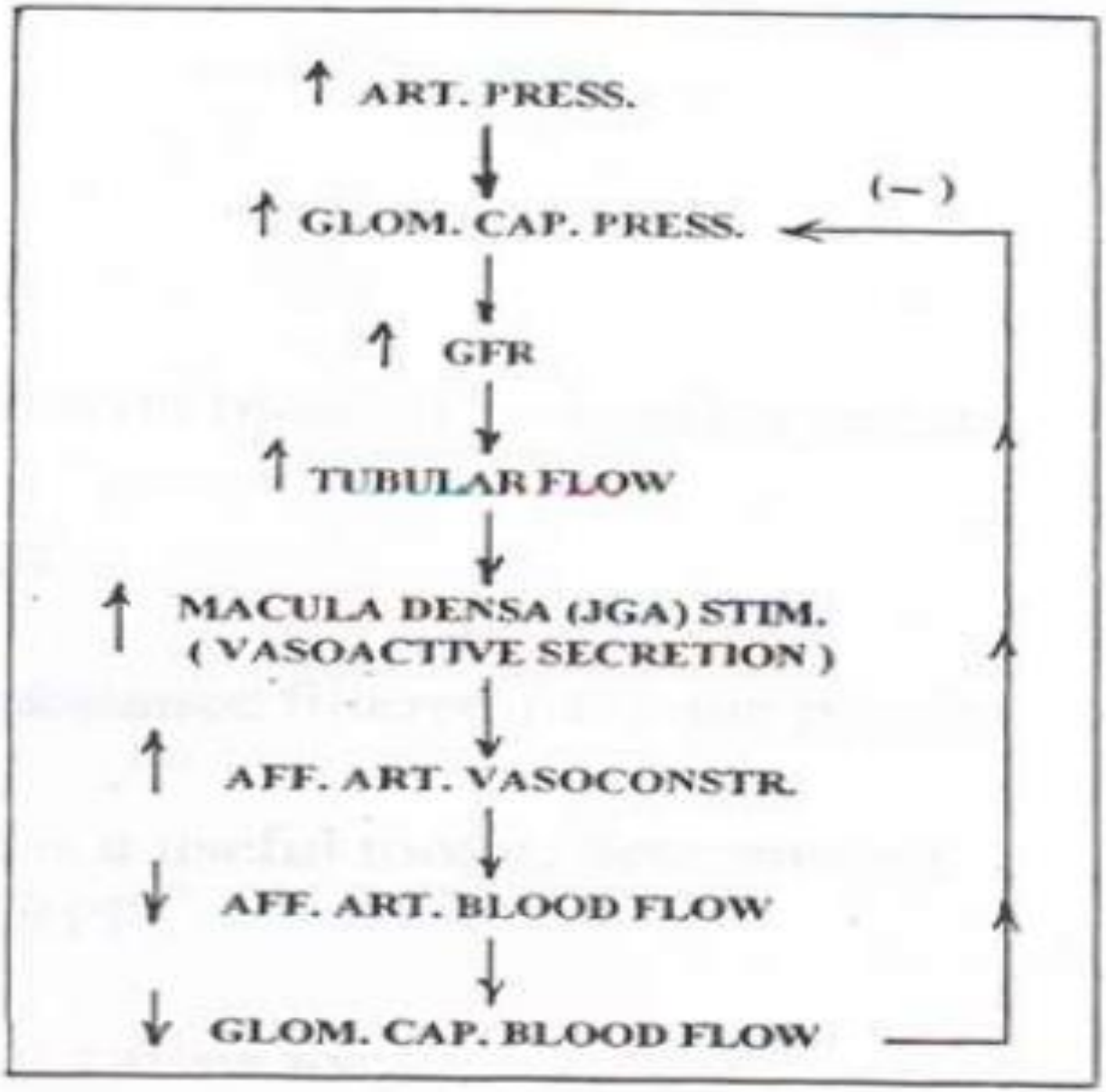
Glomerulotubular Balance

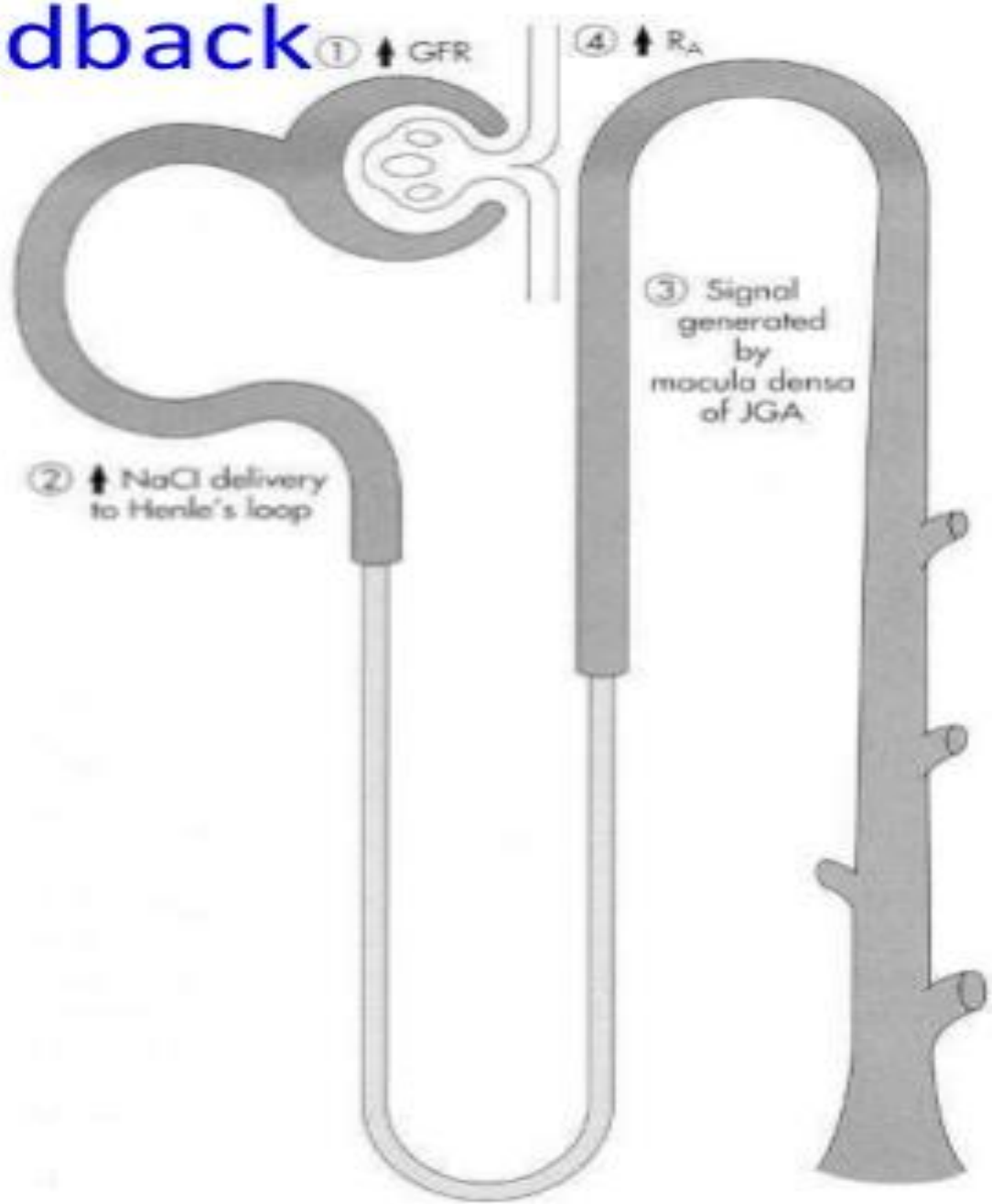
- It is an intrinsic ability of the tubules to increase their reabsorption rate in response to increased tubular load.

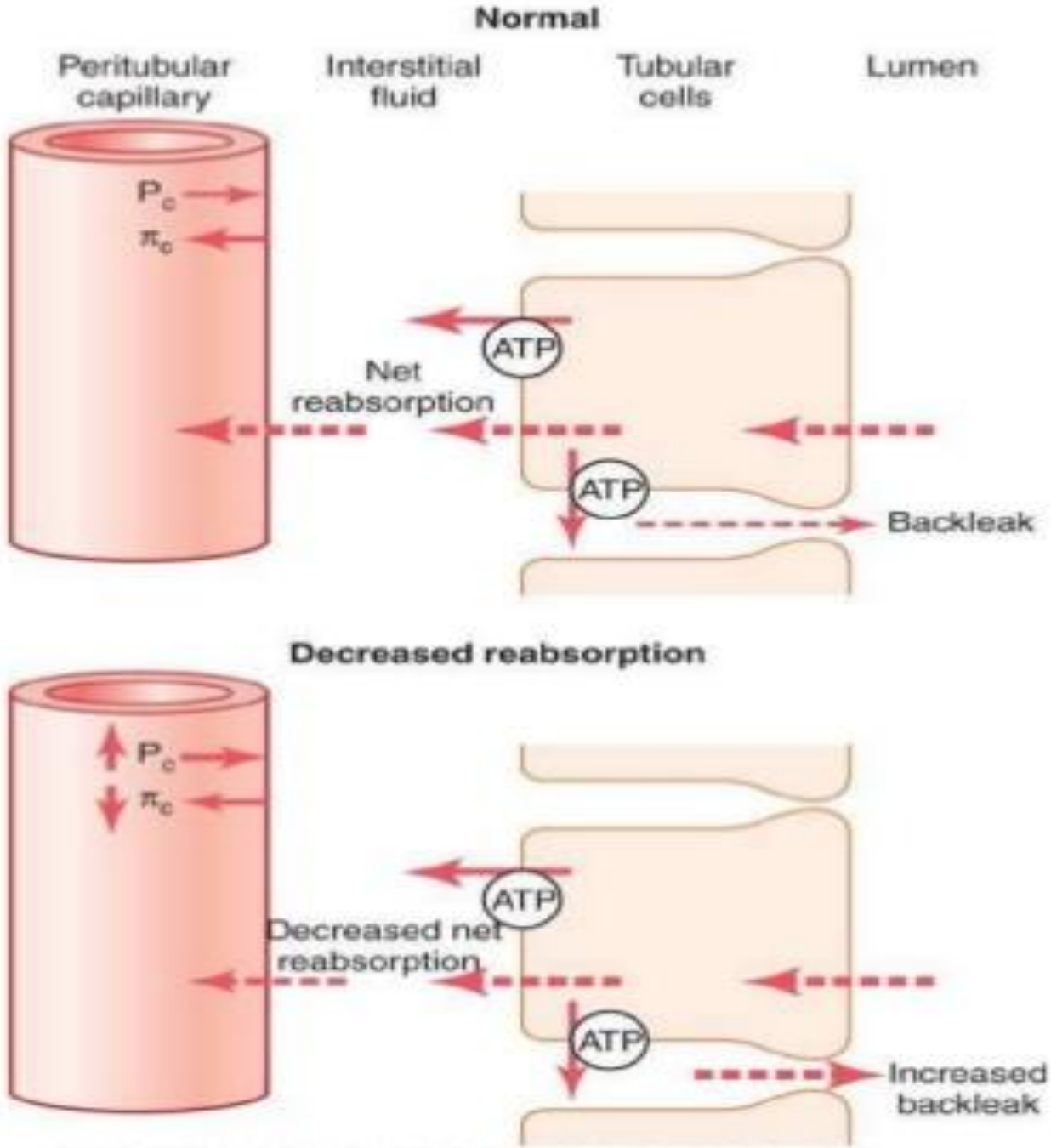
- Mainly observed in PCT.

- Due to changes in physical forces in the tubule and surrounding renal interstitium.

2) Tubuloglomerular feedback







Neural regulation of GFR

- Sympathetic nerve fibers innervate afferent and efferent arteriole
- Normally sympathetic stimulation is low nd has no effect on GFR
- During excessive Sympathetic stimulation (Defense, Brain Ischemia, Severe Hemorrhage) lastin from few minutes to few hours can stimulate the Renal vessels
- Vasoconstriction occurs as a result which conserves blood volume(hemorrhage)and causes a fall in GFR.
- Parasympathetic Nervous System – Acetylcholine causes release of NO from the Endothelial cells, hence Vasodilation.

Natriuresis

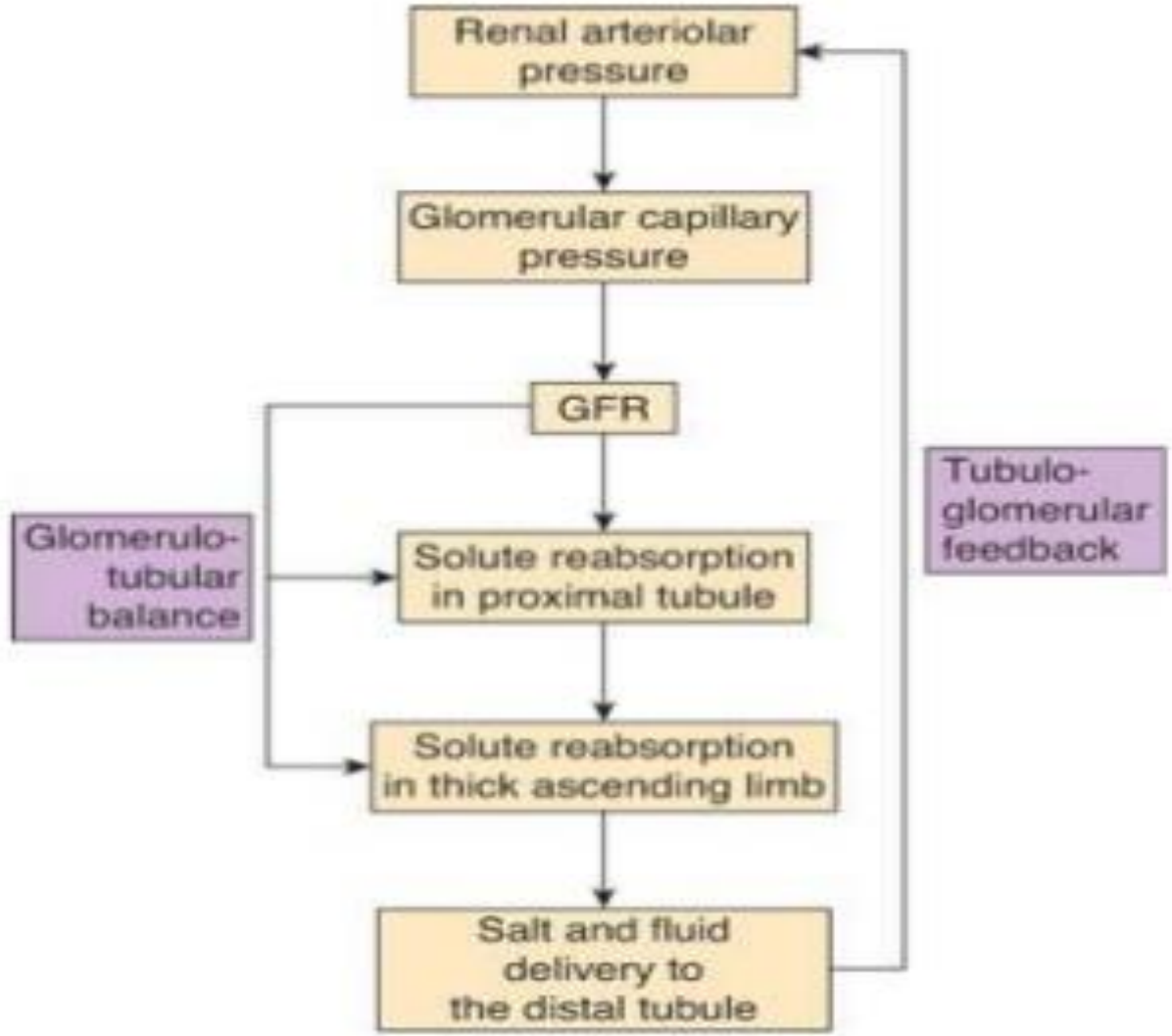
- It is the process of excretion of sodium in the urine.
- If "Back – leak" of Sodium increases, more sodium is excreted in urine.
- And, if, this condition is due to increase in Hydrostatic pressure of interstitium; we call it "Pressure Natriuresis"
- Hydrostatic pressure of interstitium can rise due to over-accumulation of fluid as a consequence of decreased "Bulk Flow"

Pressure-Diuresis

- Hydrostatic pressure of interstitium can rise due to over-accumulation of fluid as a consequence of decreased “Bulk Flow”.

- Which increases “Back-Leak” and subsequently causes the water to be more in tubule; causing more urine excretion (Diuresis).

Regulation of renal processing



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

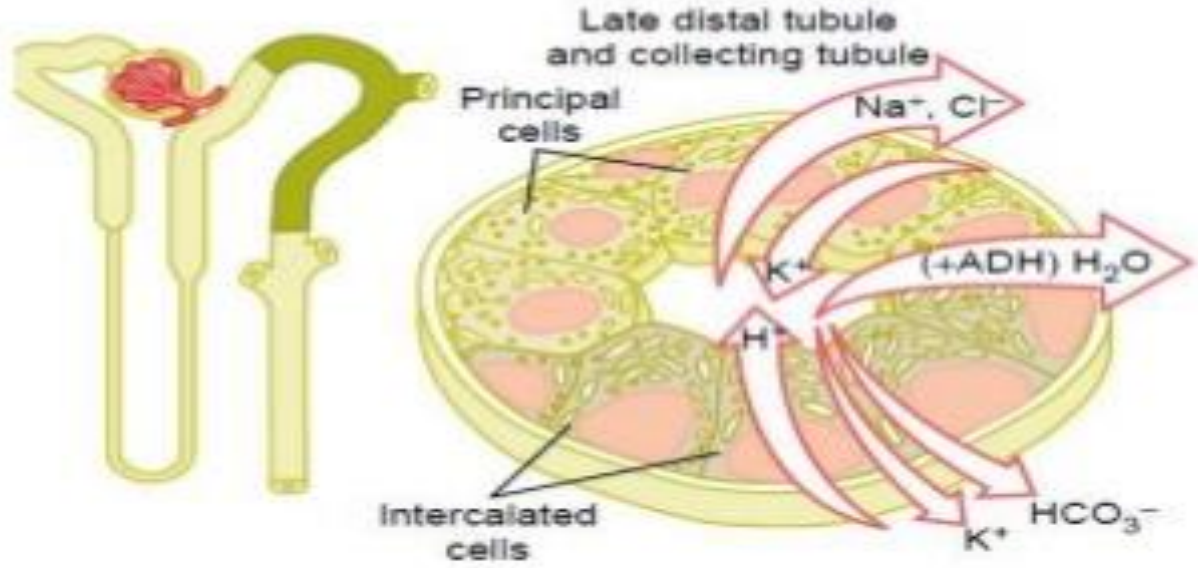
Hormonal Control of Reabsorption

- Hormones provide specificity of tubular reabsorption for different electrolytes and water.

Hormones	Effect
Aldosterone	• Increases Na+ Reabsorption • Increases K+ Secretion
Angiotensin II	•Increases Na+ Reabsorption • Increases Water Reabsorption
ADH	• Increases Water Reabsorption
ANP	•Decreases Na+ Reabsorption. •Decreases Water Reabsorption.
PTH	•Increases Calcium Reabsorption.
SNS	•Increases Sodium Reabsorption.

Aldosterone

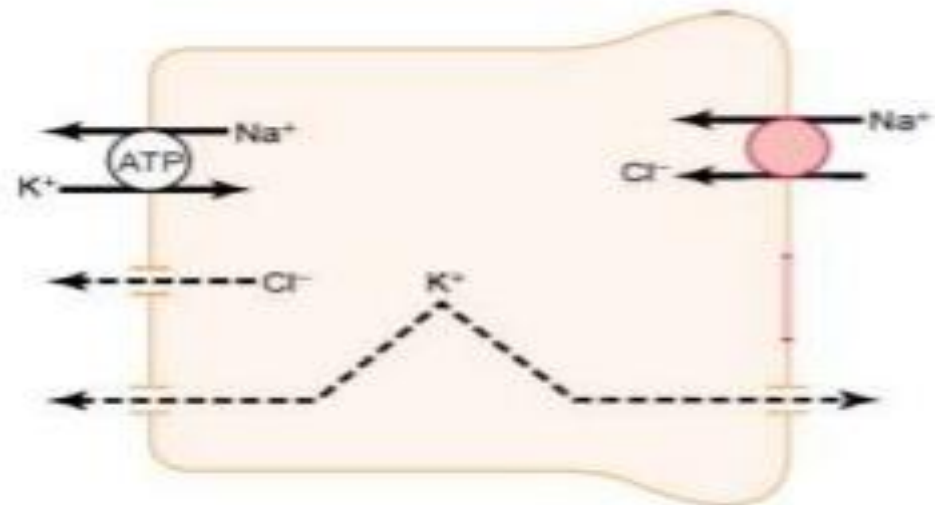
- Secreted by the zona glomerulosa cells of the adrenal cortex.
- The primary site of aldosterone action is on the principal cells of the cortical collecting tubule.



Aldosterone

Mechanism

- It stimulates Sodium-potassium ATPase pump on the basolateral side of the cortical collecting tubule membrane.



- Aldosterone also increases the sodium permeability of the luminal side of the membrane.

Adrenal Gland Disease

- **Addison's disease** :
  - Absence of aldosterone
  - Causes marked loss of sodium (Hyponatremia)
  - Causes accumulation of potassium (Hyperkalemia)
- **Conn's syndrome** :
  - Excess aldosterone
  - Causes Sodium retention (Hypernatremia)
  - Causes Potassium depletion (Hypokalemia)

Angiotensin II

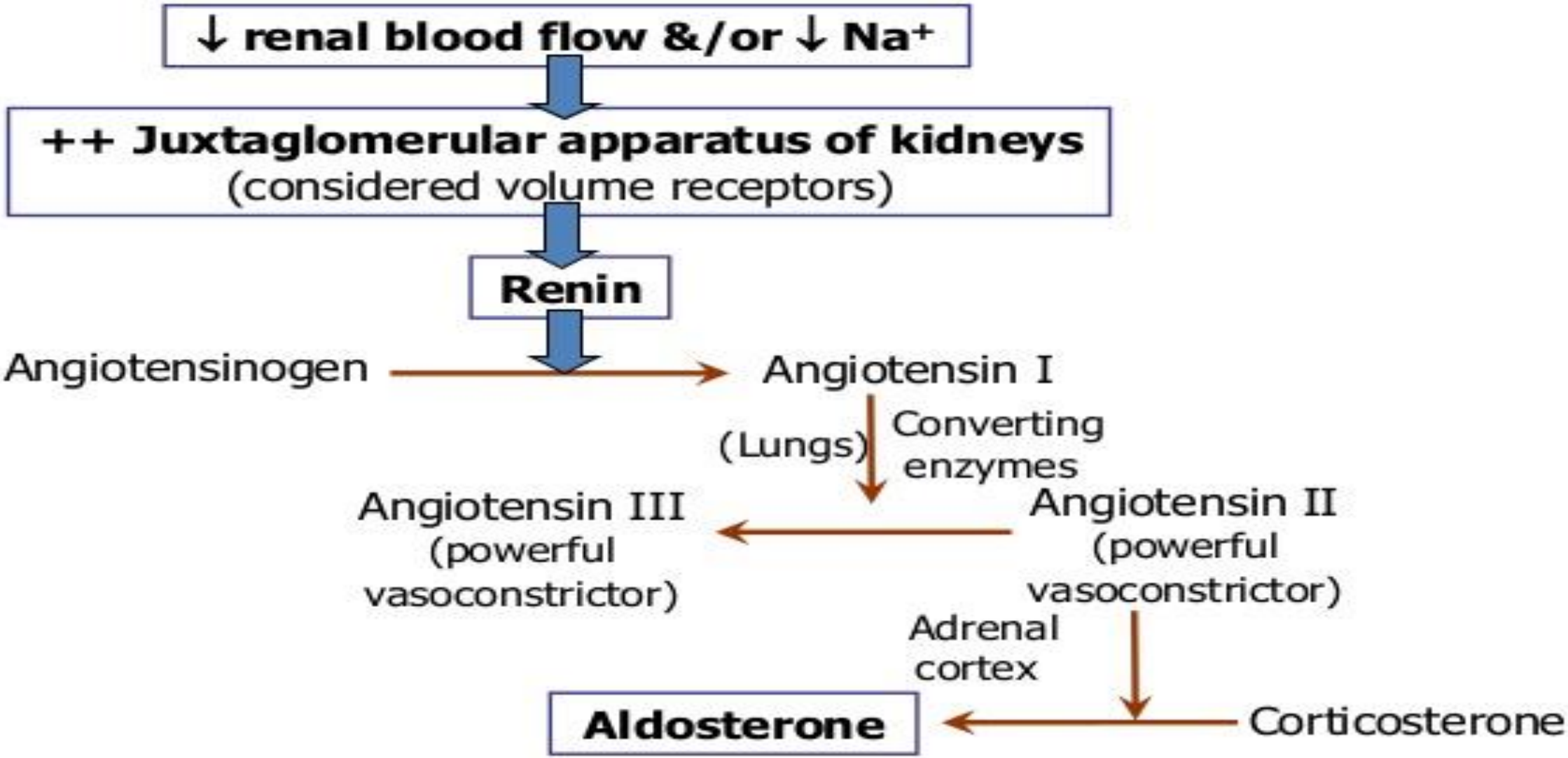
- It is the most powerful sodium-retaining hormone in human body.
- It also increases Water Reabsorption.
- Stimulated when a person has low arterial pressure.

Angiotensin II

Mechanism

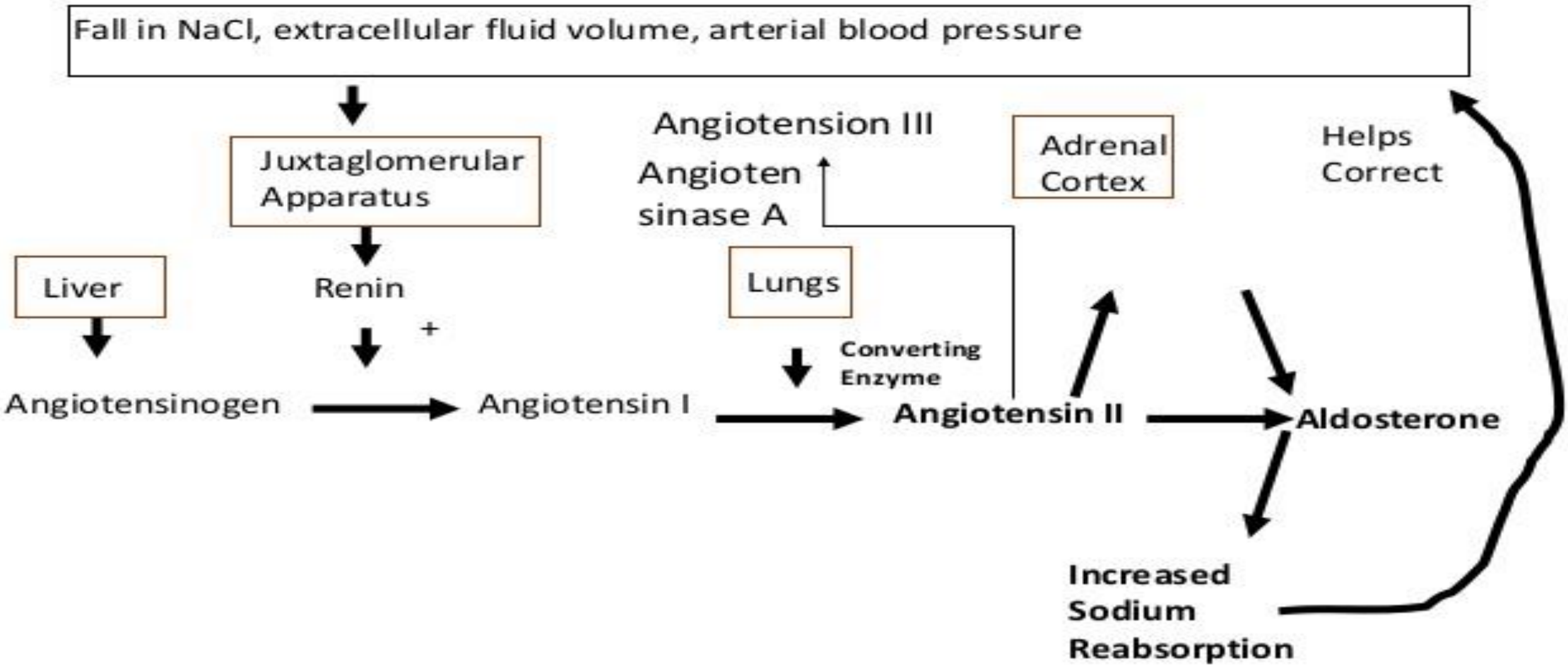
1. Stimulates aldosterone.
2. Constricts efferent arterioles.
   - Efferent arteriolar constriction reduces peritubular capillary hydrostatic pressure, which increases net tubular reabsorption.
   - Efferent arteriolar constriction, increases the time for plasma to stay in glomerulus , raises filtration fraction, & increases osmotic pressure in the peritubular capillaries; this increases the reabsorption of sodium and water.
3. Stimulates Na+/K+ pump on basolateral membrane.
4. Stimulates Na+/H+ exchange in the luminal membrane.

Renin-Angiotensin System:



- N.B. Aldosterone is the main regulator of Na^+ retention.

Rennin-Angiotensin-Aldosterone System



ADH

- Anti Diuretic Hormone (AKA Vasopressin).
- Produced by pituitary
- Increases the water permeability of the distal tubule, collecting tubule, and collecting duct.

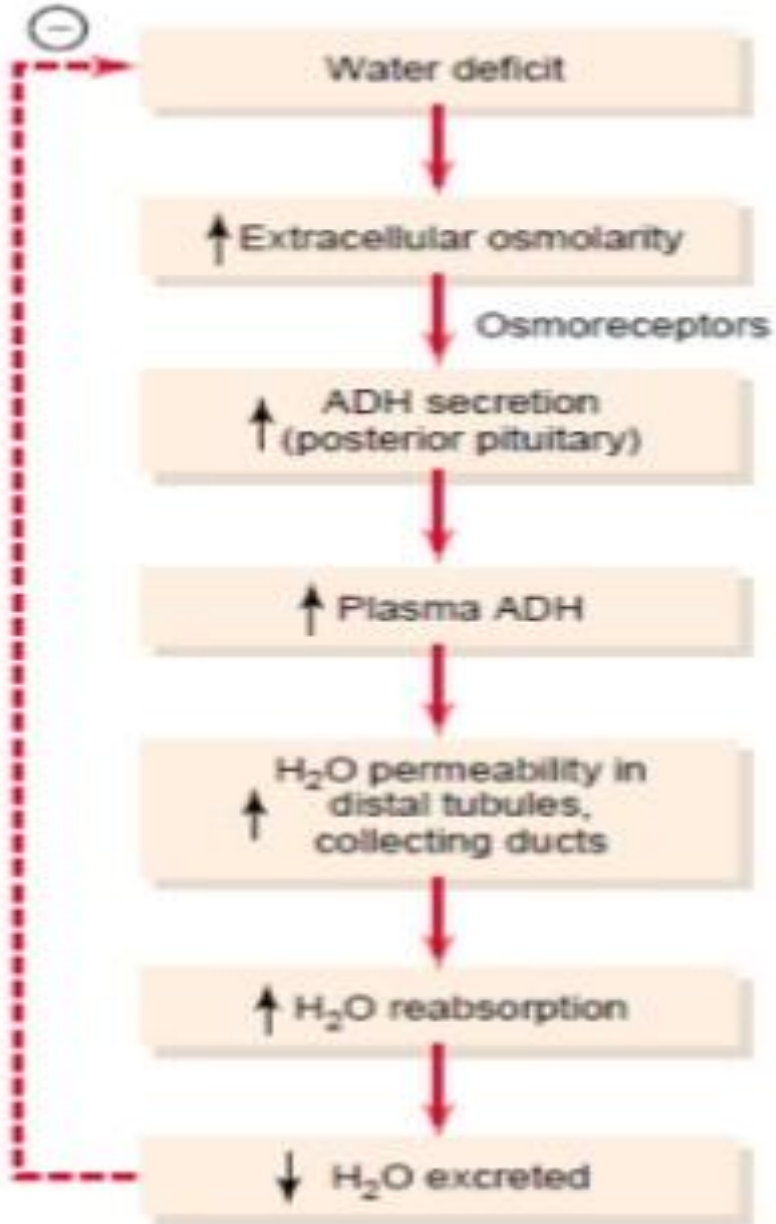
ADH

Mechanism

- ADH binds to *V2 receptors* in the late distal tubules, collecting tubules, and collecting ducts, increasing the formation of cyclic AMP and activating protein kinases.

- This, in turn, stimulates the movement of an intracellular protein, called *aquaporin-2 (AQP- 2)*, to the luminal side of the cell membranes.

- The molecules of AQP-2 cluster together and fuse with the cell membrane to form *water channels* that permit rapid diffusion of water through the cells.


Water deficit
↑ Extracellular osmolarity
Osmoreceptors
↑ ADH secretion (posterior pituitary)
↑ Plasma ADH
↑ H_2O permeability in distal tubules, collecting ducts
↑ H_2O reabsorption
↓ H_2O excreted

Atrial Natriuretic Peptide

Mechanism

- Increased plasma volume stretches cardiac atria which secretes ANP.

- Increased levels of ANP,
  - Inhibit the reabsorption of sodium and water by the renal tubules,especially in the collecting ducts.
  - Increases urinary excretion.

Parathyroid Hormone

- **Increases Calcium Reabsorption.**
- Decreases phosphate reabsorption
- Stimulation of magnesium reabsorption

Sympathetic Nervous System

- **Activation Increases Sodium Reabsorption.**
- Constricts renal arterioles, thereby reducing GFR.
- Increases sodium reabsorption in the PCT, the thick ascending limb of the loop of Henle, and perhaps in more distal parts of the renal tubule.
- It also stimulates RAAS which adds to the overall effect to increase tubular reabsorption.

Decreased Macula Densa Sodium Chloride Causes Dilation of Afferent Arterioles and Increased Renin Release.

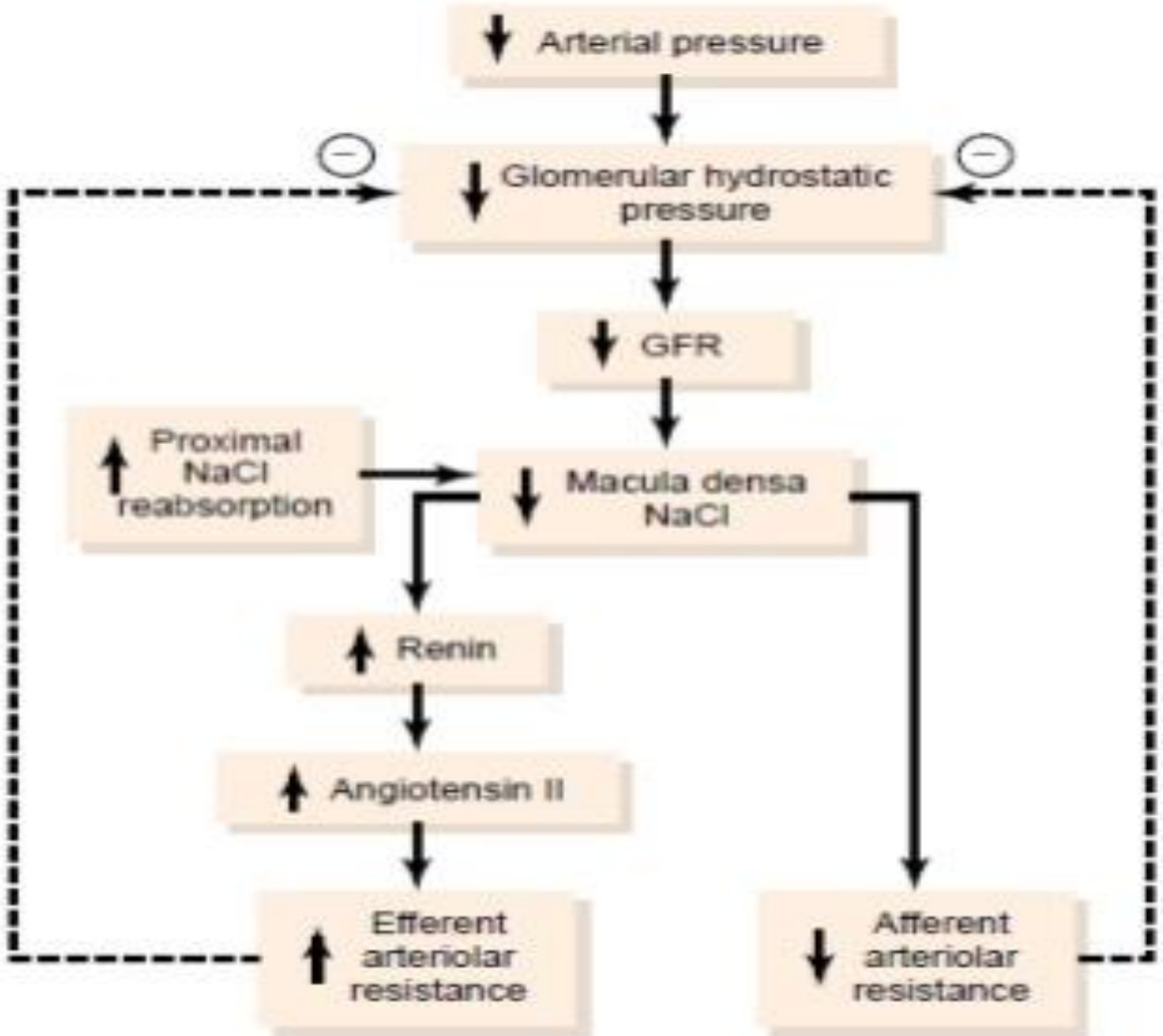


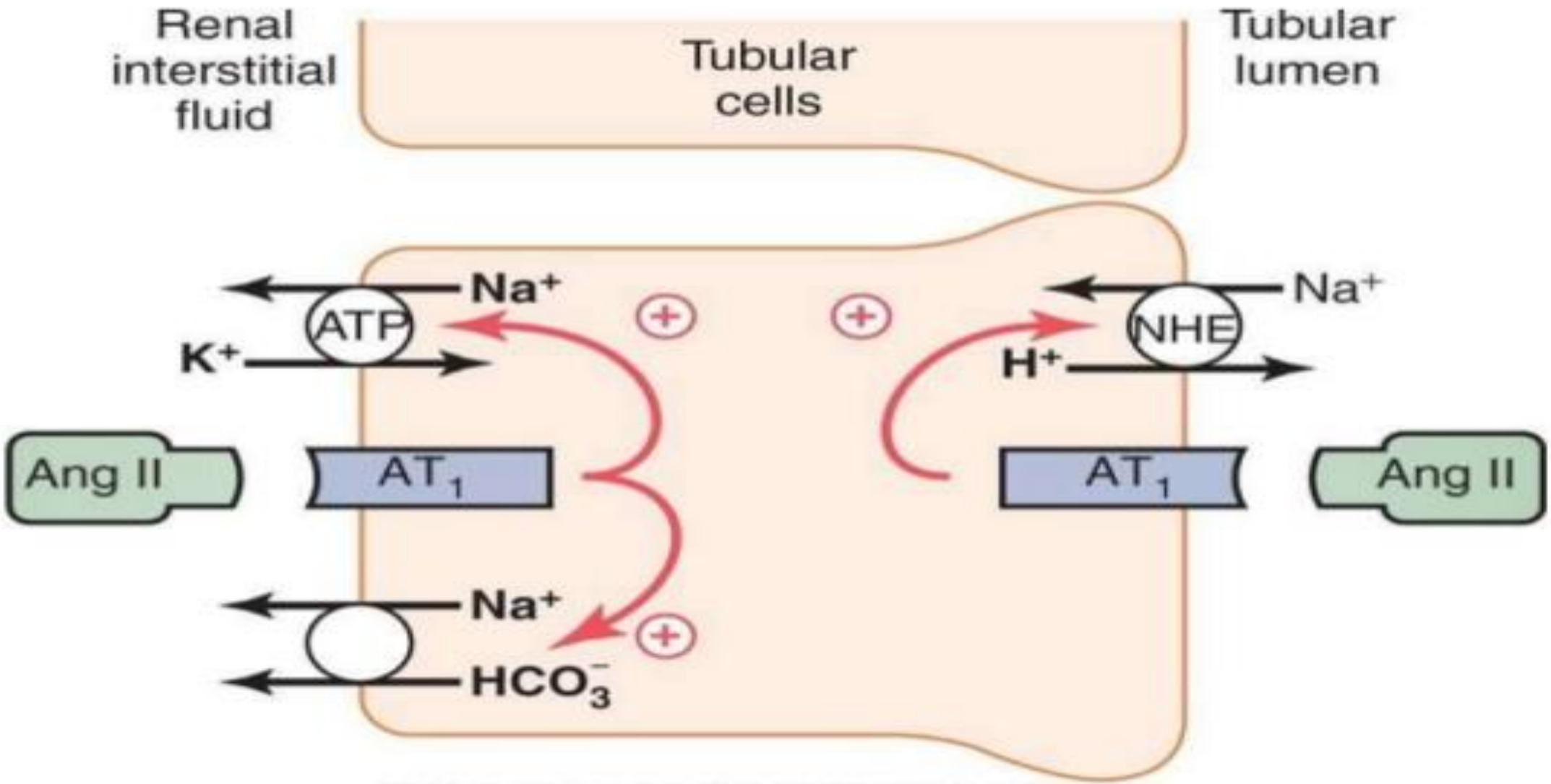
Figure:
Macula densa feedback mechanism for autoregulation of glomerular hydrostatic pressure and glomerular filtration rate (GFR) during decreased renal arterial pressure.

Regulation of renal processing

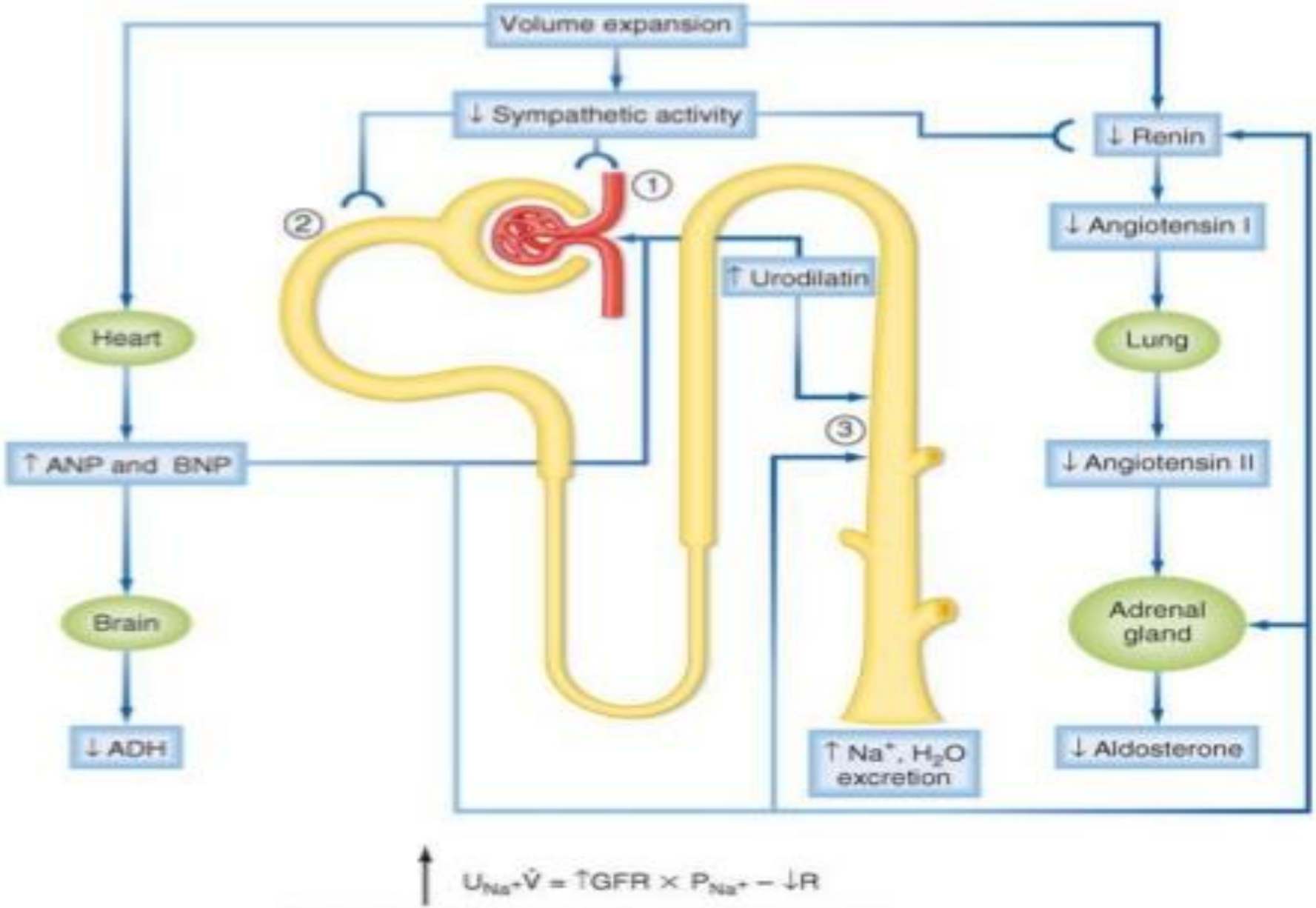
Hormonal Regulation of Tubular Reabsorption and Tubular Secretion

HORMONE	MAJOR STIMULI THAT TRIGGER RELEASE	MECHANISM AND SITE OF ACTION	EFFECTS
Angiotensin II	Low blood volume or low blood pressure stimulates renin-induced production of angiotensin II.	Stimulates activity of Na^+/H^+ antiporters in proximal tubule cells.	Increases reabsorption of Na^+, other solutes, and water, which increases blood volume and blood pressure.
Aldosterone	Increased angiotensin II level and increased level of plasma K^+ promote release of aldosterone by adrenal cortex.	Enhances activity of sodium–potassium pumps in basolateral membrane and Na^+ channels in apical membrane of principal cells in collecting duct.	Increases secretion of K^+ and reabsorption of Na^+, Cl^-; increases reabsorption of water, which increases blood volume and blood pressure.
Antidiuretic hormone (ADH) or vasopressin	Increased osmolarity of extracellular fluid or decreased blood volume promotes release of ADH from posterior pituitary gland.	Stimulates insertion of water channel proteins (aquaporin-2) into apical membranes of principal cells.	Increases facultative reabsorption of water, which decreases osmolarity of body fluids.
Atrial natriuretic peptide (ANP)	Stretching of atria of heart stimulates ANP secretion.	Suppresses reabsorption of Na^+ and water in proximal tubule and collecting duct; inhibits secretion of aldosterone and ADH.	Increases excretion of Na^+ in urine (natriuresis); increases urine output (diuresis) and thus decreases blood volume and blood pressure.
Parathyroid hormone (PTH)	Decreased level of plasma Ca^{2+} promotes release of PTH from parathyroid glands.	Stimulates opening of Ca^{2+} channels in apical membranes of early distal tubule cells.	Increases reabsorption of Ca^{2+}.

Mechanism of Action of Angiotensin II



Mechanism of Action of Atrial Natriuretic Peptide



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3. Textbook of Physiology-6th edition(Berne and Levy)
4. Textbook of Medical Physiology-2nd edition(Walter F. Boron, Emile L. Boulpaep)

Thank you!!!