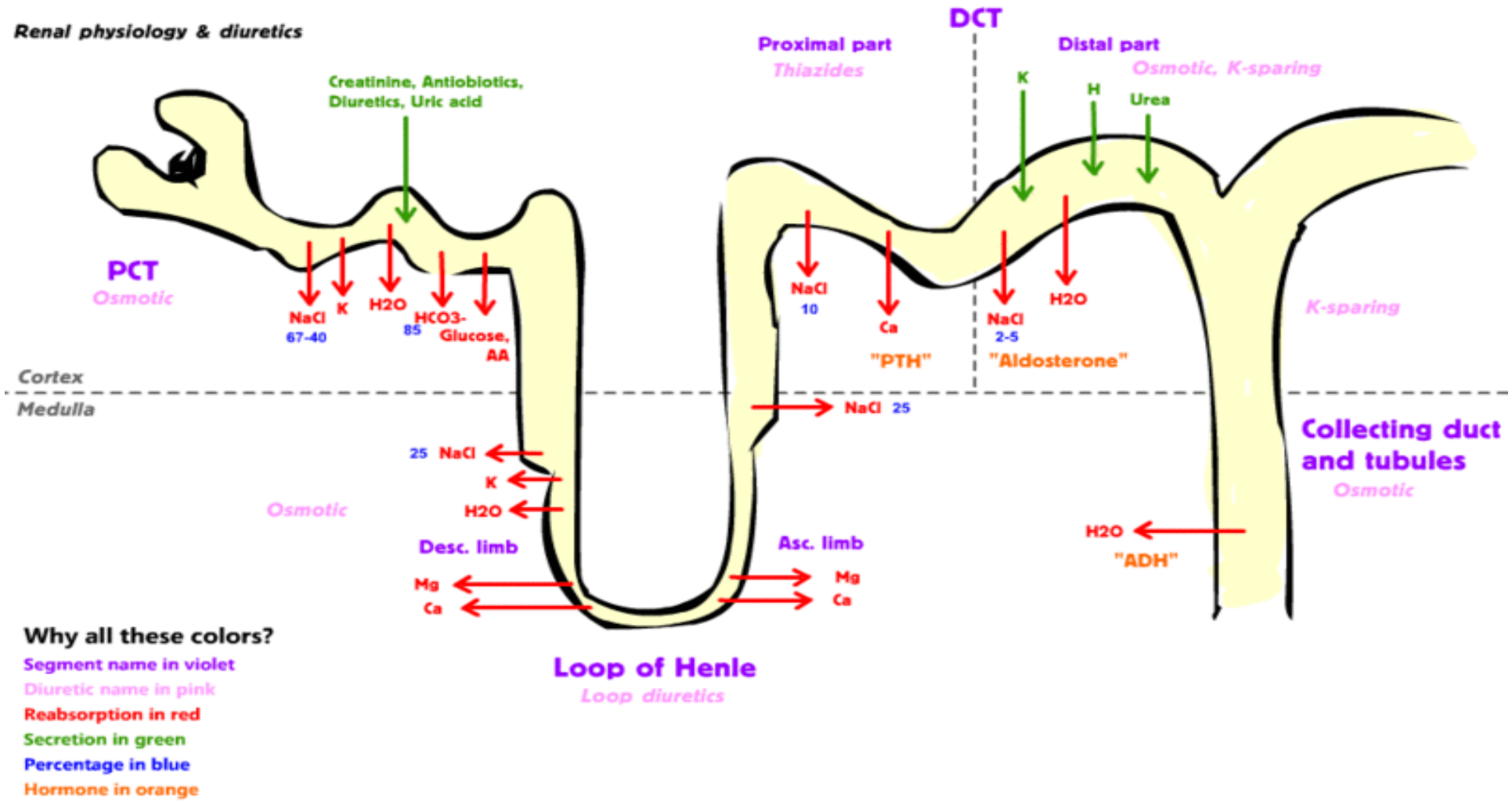
Specific Functions of Different Tubular Segments

Medical physiology department

Functions of Different Tubular Segments



1) Proximal Convoluted tubules(PCT)

The tubular epithelium of proximal tubules Are :

a) highly metabolic, having a large number of mitochondria.

b) large surface area on both luminal (brush border) and basal (extensive channels) borders.

Both a & b facilitate proximal tubular function.

Functions of Proximal Convoluted tubules(PCT)

[1] Reabsorption of :

* 65 % of filtered Na^+, H_2O, cl, ca+2 , HCO_3 , K^+

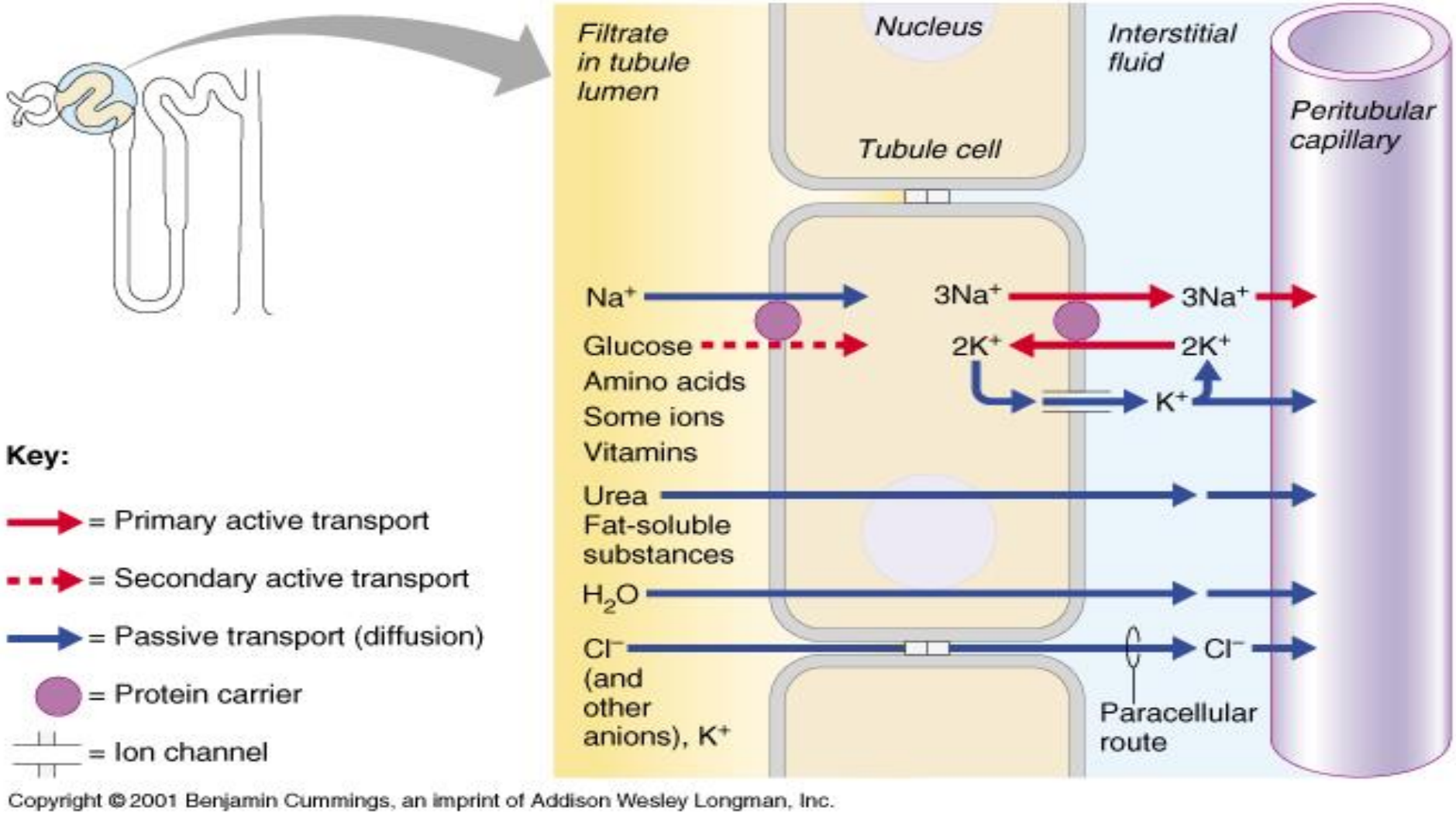
- Na^+ :primary active transport: (In upper half of PCT: with glucose, amino acids (a.a.).In lower half of PCT: is accompanied by passive diffusion of cl)
- Cl^-, H_2O : Passive reabsorption secondary to Na^+
- Partial reabsorption of urea : back diffusion secondary to H_2O

[2] Secretion of :

- H^+: Counter transported with Na^+ at luminal border. (NA+/H+ CT)
- Organic substances: as bile salts, oxalate, urate, catecholamine
- Drugs: as penicillin, salicylate & PAH acid.
- Uric acid & creatinine

[3] Ammonium Synthesis from glutamine.

PCT



2) Functions of loop of Henle:

1]Thin descending limb

- Reabsorption of 20% of filtered water
- So, fluid reaching the tip is hypertonic.

2]Thick ascending limb:

- Reabsorption of 25% of filtered Na, K, cl, some Ca & Mg & few HCO_3
- Secretion of H so, the fluid entering the tubule is hypotonic

3)Functions of Distal convoluted tubules (DCT) & cortical collecting tubules (CT):

[1] First half of DCT(diluting segment) :

a) Absorption of Na^+, K^+, cl^-

b) Impermeable to H_2O , Urea (like thick ascending limb)

c) H+ secretion

[2] Second half of DCT & cortical CT:

(a) Absorption of Na^+ with K^+ secretion(active transport) under effect of aldosterone (**principal** cells)

(b) Secrete H^+ & reabsorb HCO_3 (active transport) **intercalated** cells (I cells).

- Impermeable to urea.

(c) Facultative H_2O reabsorption under effect of ADH (5%).

(d) Ca++ reabsorption by primary active transport (under Parathormone effect).

(e) Ammonium synthesis from glutamine.

4)Functions of Medullary collecting duct:

1]Concentration of urine : by facultative H_2O reabsorption under effect of ADH.

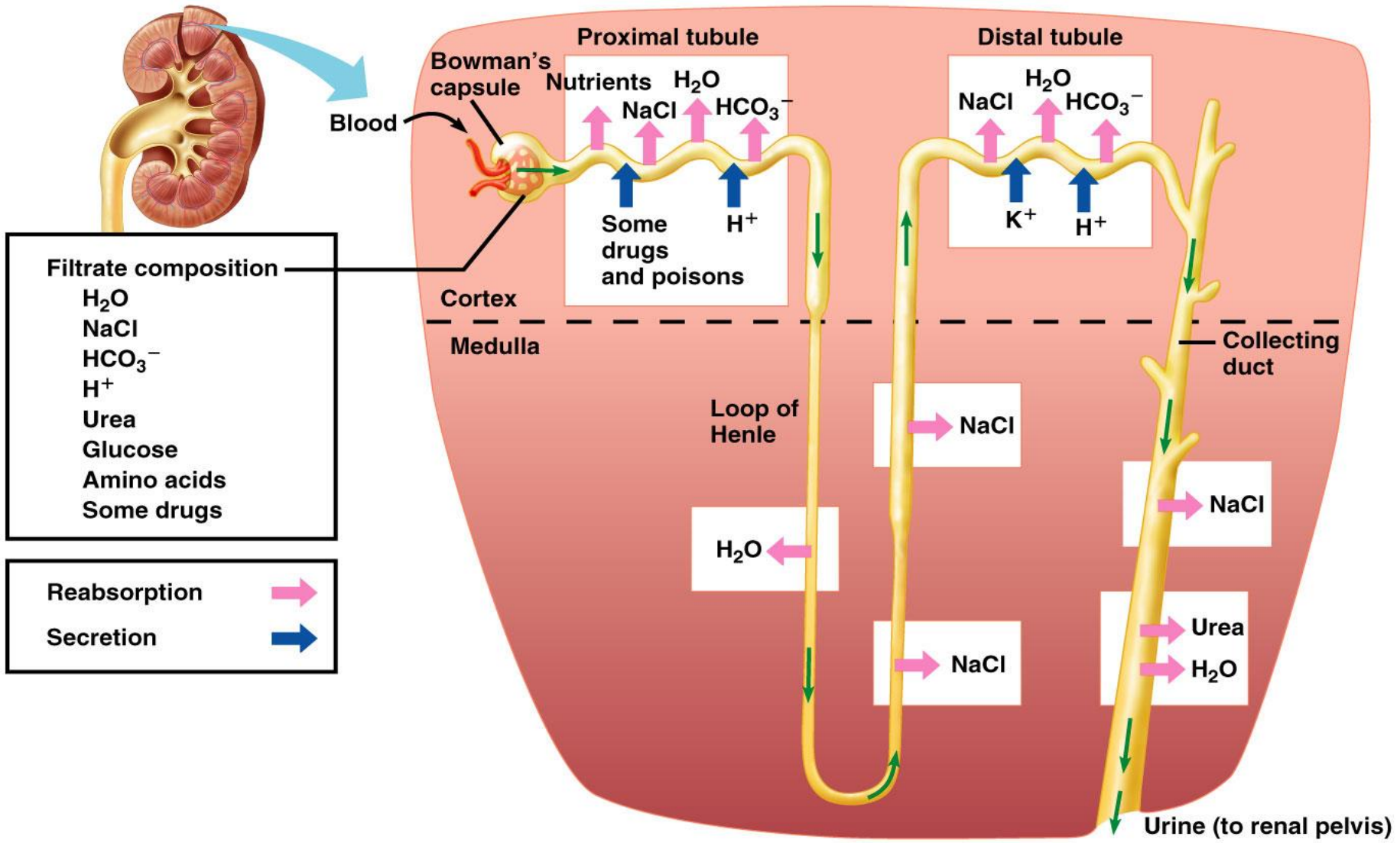
2] Back diffusion of urea to interstitium maintaining hyperosmolarity of medullary interstitium.

3]Na+ reabsorption

4]H+ secretion by primary active transport.

5]Synthesis of ammonia from glutamine.

Renal tubular transport



Na^+ reabsorption

Na^+ accounts for over 90% of osmotically active particles in extracellular fluid "ECF" so, determine extracellular fluid volume.

Mechanism:

1)At basal border: primary active, against electrochemical gradients. by Na^+-K^+ ATPase from inside cells of P.C.T across basal border to intercellular space

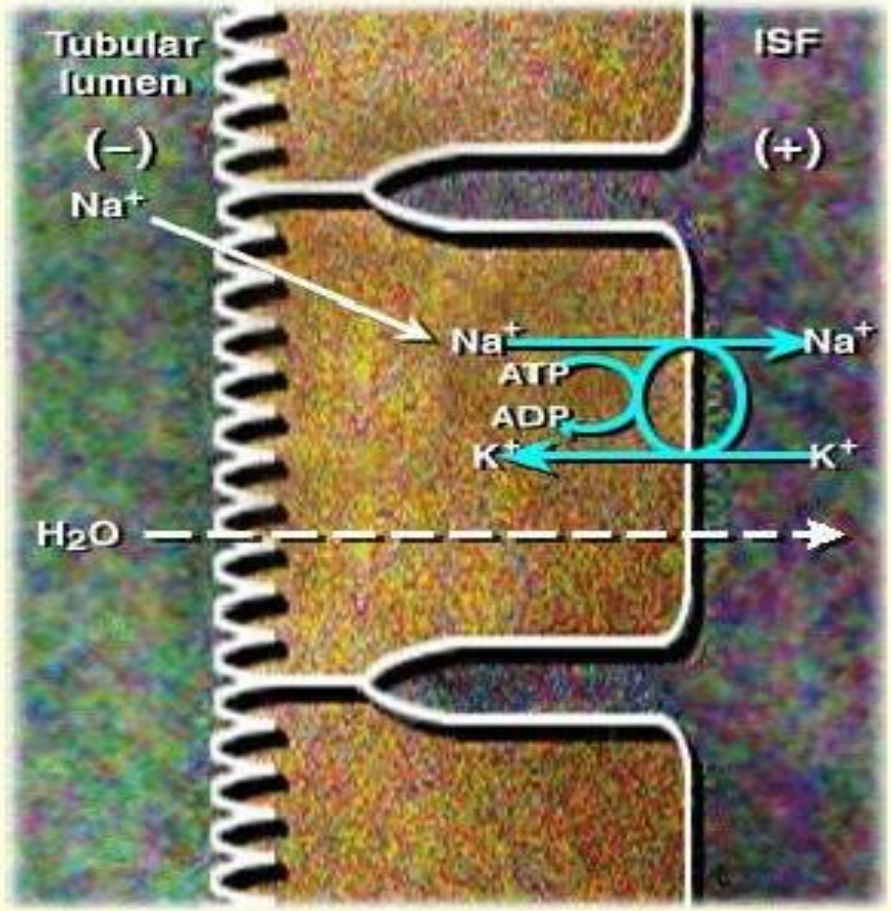
- 3 Na^+ are pumped out
- 2 K^+ are pumped inside the cell.

2)At luminal border : passive

The pump creates passive diffusion of Na^+ from tubular lumen into tubular cells down an electrochemical gradient.

PRIMARY ROLE OF SODIUM TRANSPORT

- Under some circumstances a portion of the reabsorbed sodium may diffuse back into the tubule but the net transport is always from the tubular lumen to the renal ISF.
- In the renal tubule this process is responsible for sodium reabsorption from the filtrate which establishes an osmotic gradient for water reabsorption and also indirectly provides the energy for the secondary active transport of other substances.



Sites of Na^+ reabsorption

96-99% of Na^+ is reabsorbed

1] At proximal tubules(65%) Primary active reabsorption

In upper half : coupled by active transport of glucose & a.a & organic acids & HCO_3

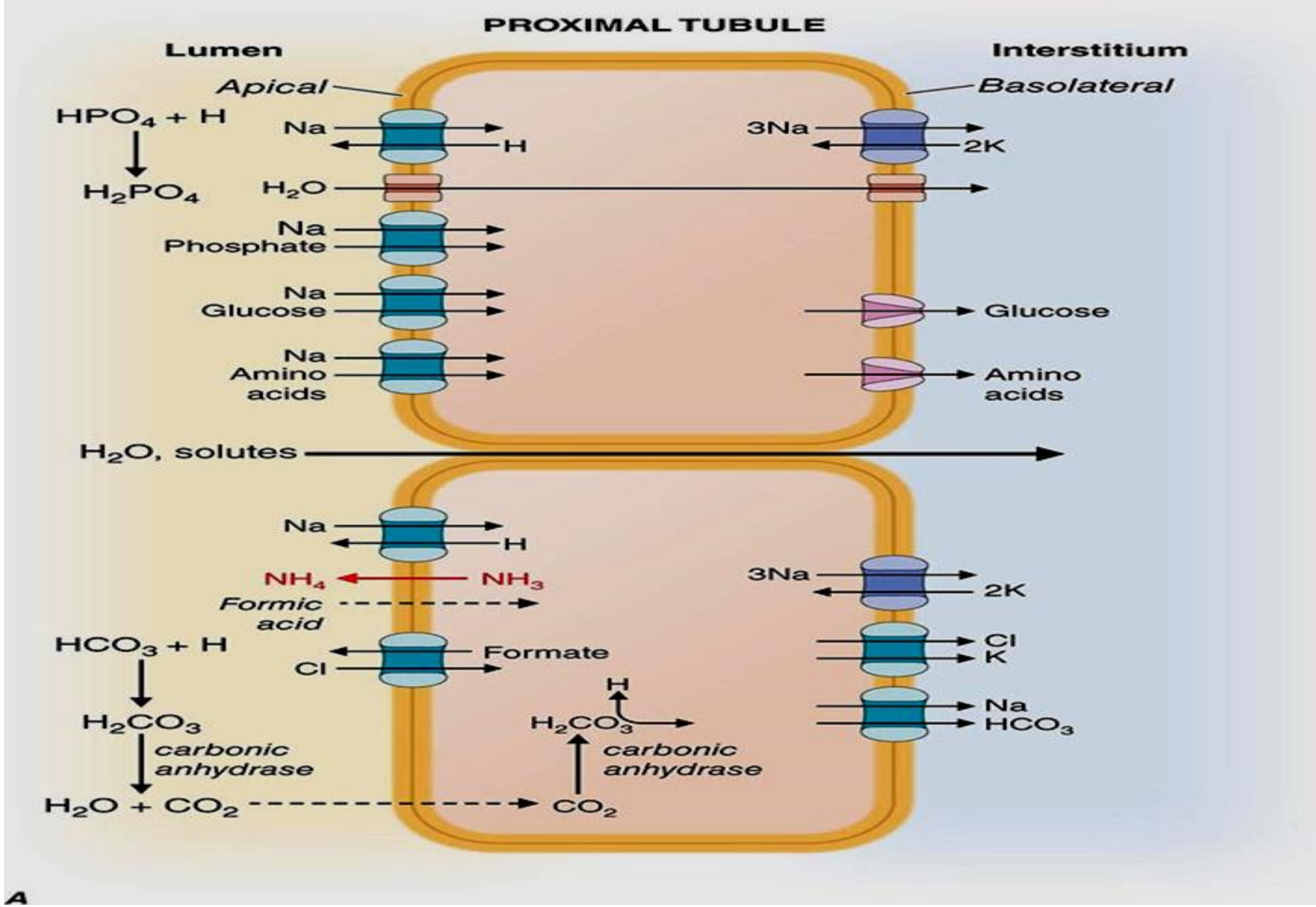
in lower half : accompanied with cl^-

-67% of filtered Na^+ is reabsorbed, accompanied with:

→Cl-, HCO_3 reabsorption , passive by electrical gradient.

→ H_2O reabsorption, passive by osmotic gradient

→ H^+ secretion, Counter transport.


PROXIMAL TUBULE
Lumen
Interstitium
Apical
Basolateral
HPO4 + H
H2PO4
Na
H
3Na
2K
H2O
Na
Phosphate
Na
Glucose
Glucose
Na
Amino acids
Amino acids
H2O, solutes
Na
H
NH4
NH3
Formic acid
3Na
2K
HCO3 + H
H2CO3
carbonic anhydrase
H2O + CO2
Cl
Formate
H
H2CO3
carbonic anhydrase
CO2
Cl
K
Na
HCO3
A

2]At loop of Henle: (25%)

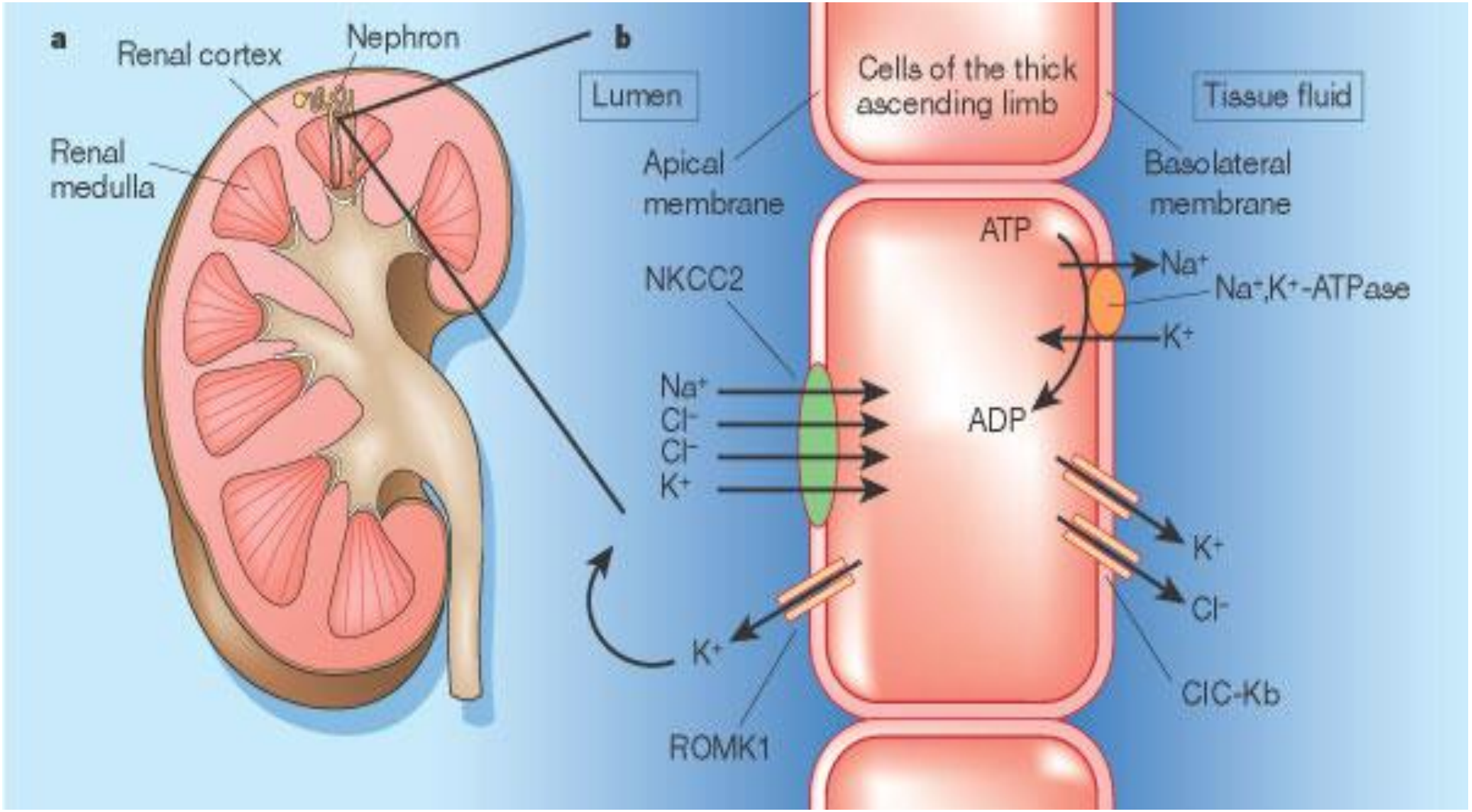
Only in ascending limb, (No Na^+ channels in descending limb)

30% of filtered Na^+ is reabsorbed

In the thin part, Na^+ reabsorption is limited(Passive)

In the thick part, by [1 Na^+, 2Cl^-, 1K^+ (co-transport)].

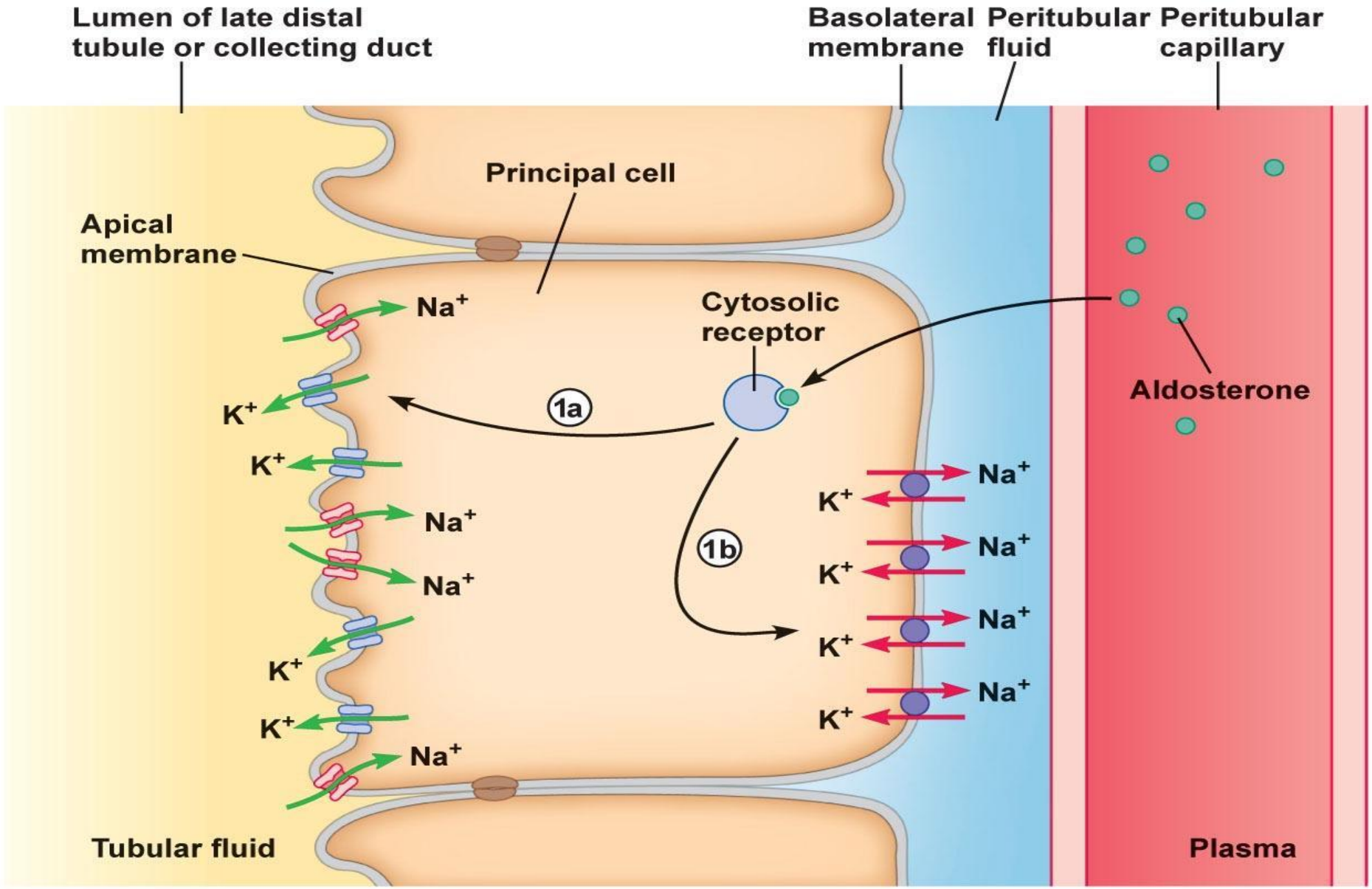
Loop of Henle



3] At DCT &collecting tubules : 3%

- Under the control of aldosterone, variable amounts of Na^+ are reabsorbed & associated with →Cl^-, HCO_3 reabsorption passively

→ K^+, H^+ secretion (counter transport)



Regulation of Na^+ excretion

(1) Rate of tubular flow :

Slow rate of flow → increase tubular reabsorption of Na^+

As in decrease GFR which initiates tubuloglomerular feedback

(2) Glomerulotubular balance

Increase GFR →increase Na^+ filtered-→increase Na^+ reabsorbed--→slight increase in Na^+ excretion i.e. proximal tubule reabsorb constant %

(3)Physical forces: low hydrostatic pressure & high osmotic pressure in peritubular capillary--→increase fluid reabsorption & vice versa

(4) Pressure Naturesis (Effect of increased "ABP" on Na^+ excretion) :

Increase ABP → increase Na^+ , H_2O excretion to regulate ABP & return it to normal.

(5)Gradient-time transport : reabsorption is determined by 2 factors

(6) Sympathetic stimulation: increase Na+ reabsorption

(7) **Hormones:**

7) Hormones affecting Na reabsorption

1-Aldosterone: Acts on distal tubules & cortical collecting tubules

Increases Na^+ reabsorption, Cl^- reabsorption

Increases K^+ & H^+ secretion.

2-Angiotensin II: leads to Na^+ retention (increase Na reabsorption)

1)++ aldosterone

2)Direct effect on PCT (++ Na-K pump & H^+ pump)

3)Constrict efferent arterioles

3-Glucocorticoids: ↑ Na^+ reabsorption.

4- Sex hormones especially Estrogen: ↑ Na^+ reabsorption

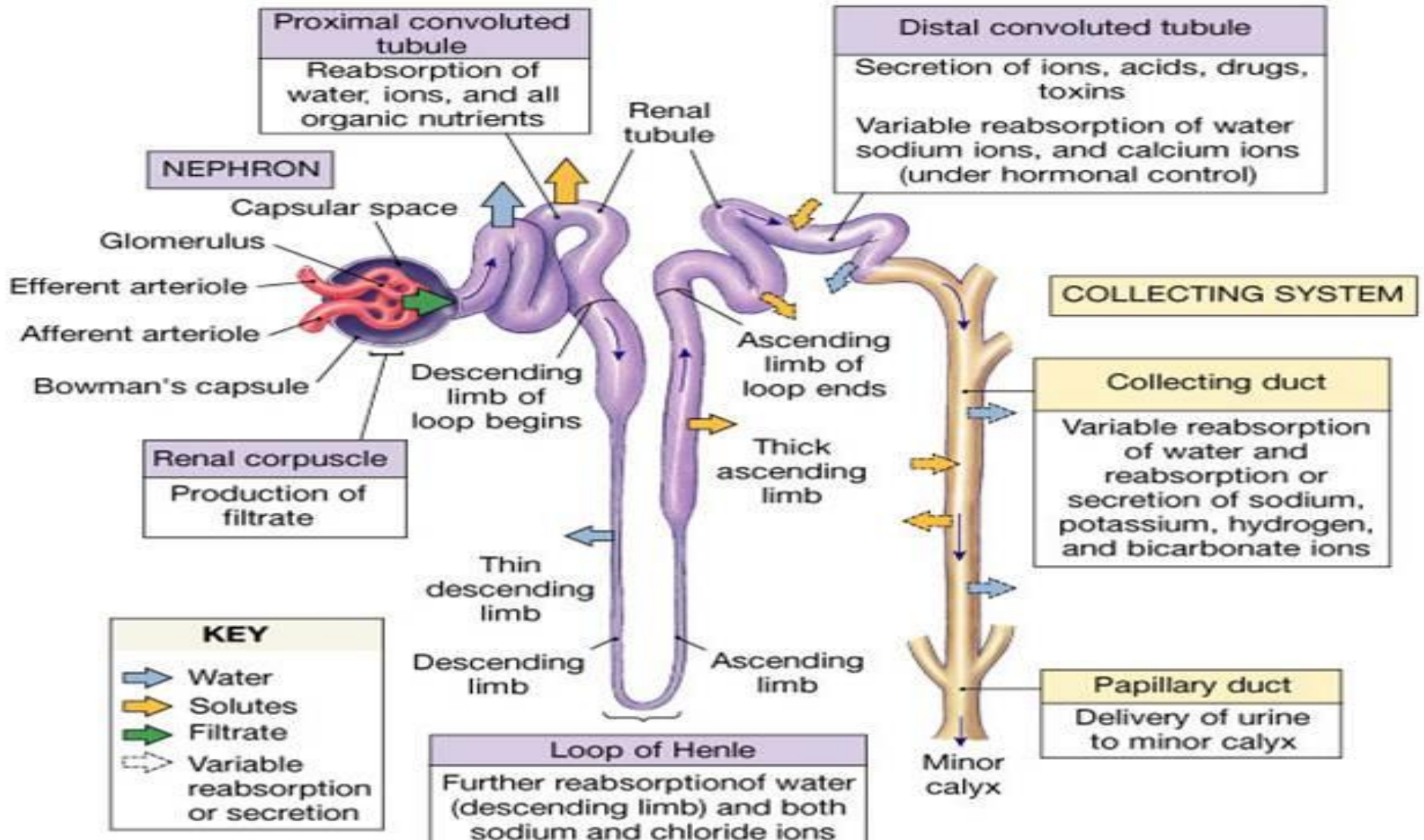
5-Endothelins: cause Na^+ excretion by increasing PGE_2

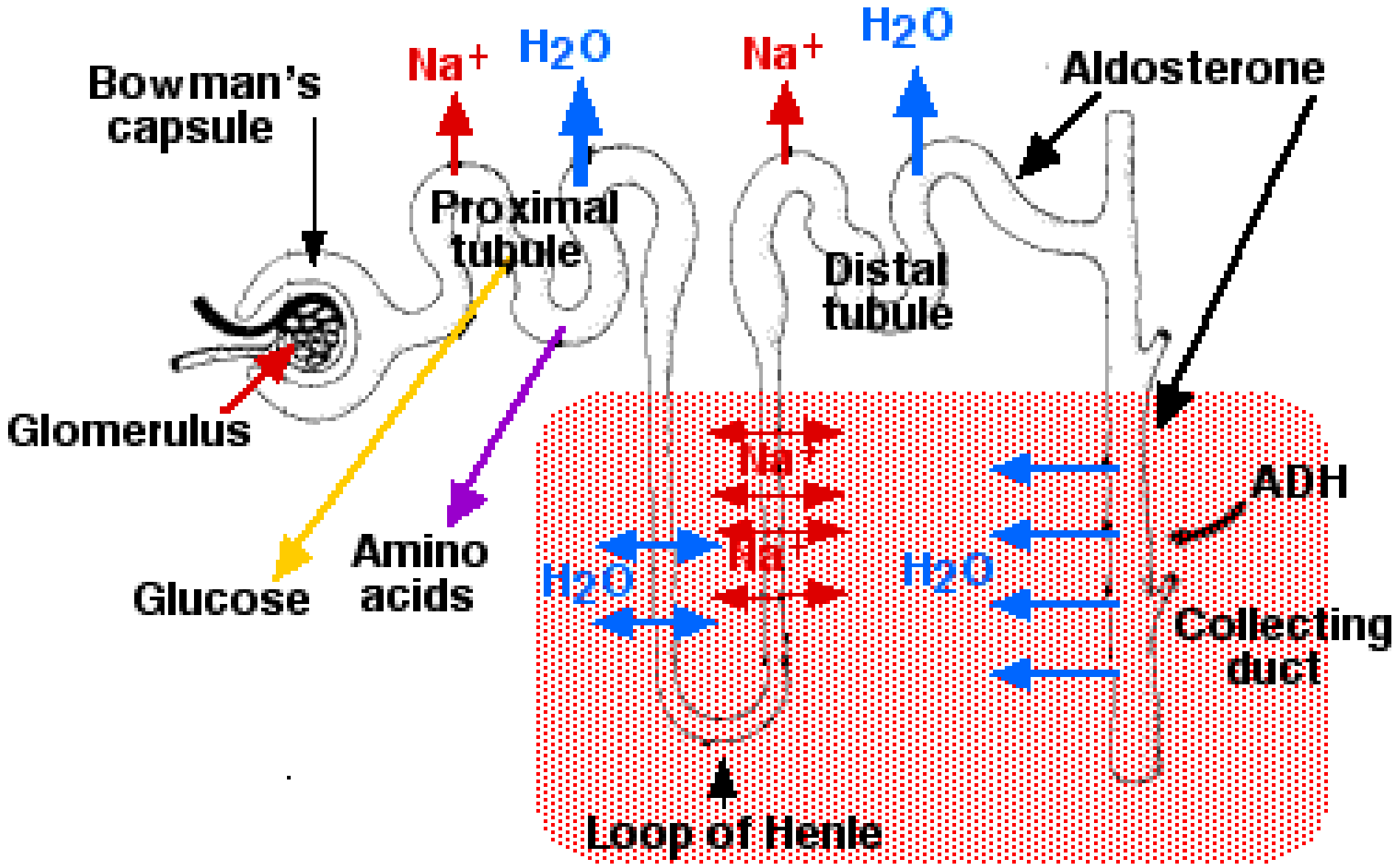
6-PGE_2: ↑ Na^+ excretion by inhibiting Na^+-K^+ ATPase & Na^+ channels

7-Atrial Natriuretic peptide "ANP": Na^+ excretion

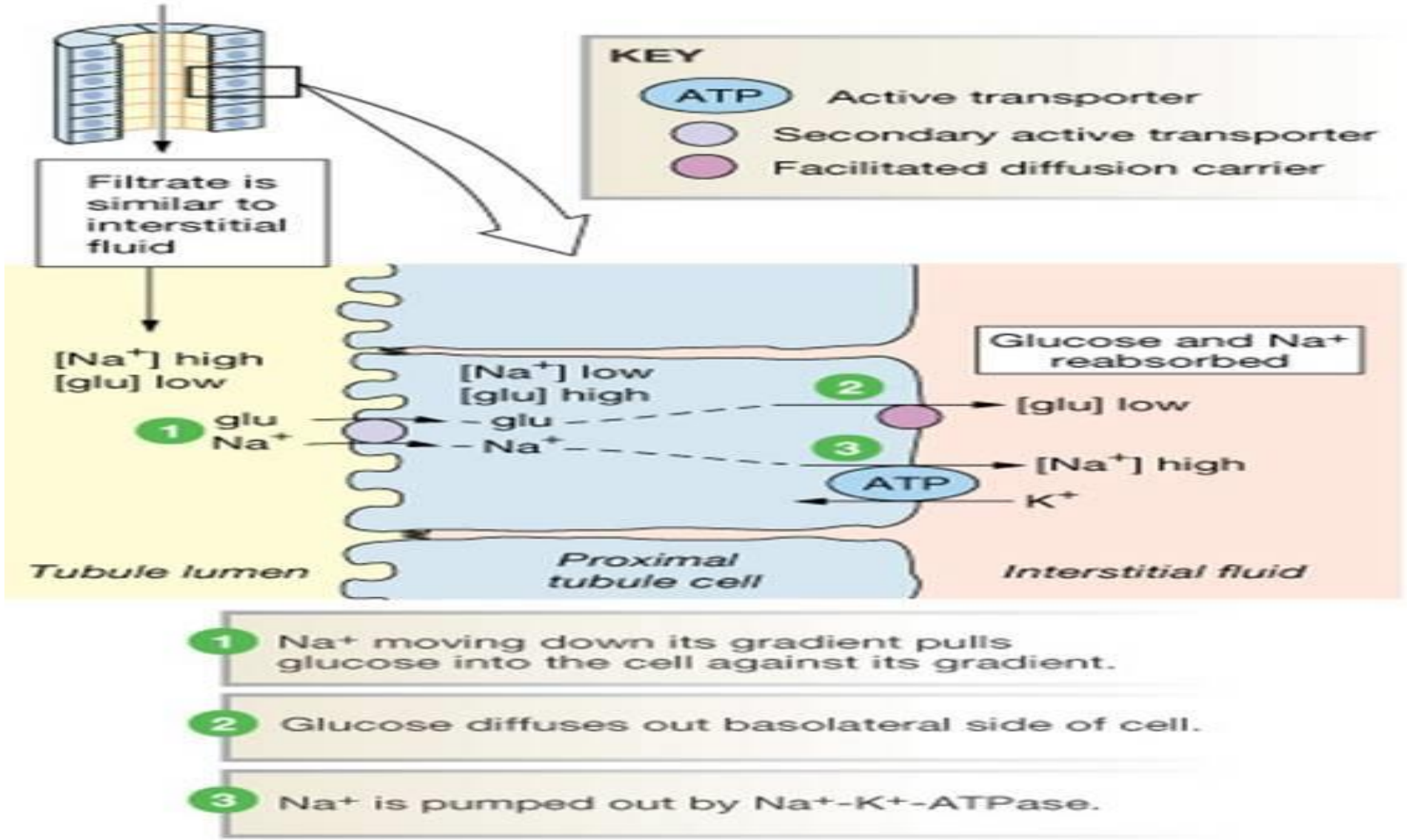
-increase GFR, inhibits renin secretion.&(inhibits Na-K^+ pump & Na^+ channels)

Functions of different parts of kidney




Bowman's capsule
Na+
H2O
Na+
H2O
Aldosterone
Proximal tubule
Distal tubule
Glomerulus
Glucose
Amino acids
Na+
Na+
H2O
H2O
ADH
Collecting duct
Loop of Henle

Glucose transport



Glucose transport

Glucose is: 1-Completely reabsorbed.

2- In proximal convoluted tubule (upper half)

3-By an active process (secondary active)

Glucose to be reabsorbed via tubular cells, it has to cross its luminal and basal borders.

Mechanism of Glucose transport

- **At luminal border**:
- By secondary active mechanism.
- It enters the cell against concentration gradient.
- A carrier (termed SGLT-2 = sodium dependant glucose transporter) **At basal border**:
- By facilitated diffusion, passive, the glucose passes to the extra cellular fluid & blood.
- The carrier needed here is not Na^+ dependent. It is termed (GLUT-2) glucose transporter.

Tubular maximum ™

- **TM** is The maximum amount of substance in mg, that can absorper or secreted by renal tubules in one minute.
- **Tubular load** is the amount of the substance, which is filtered to renal tubules per minutes

Tubular load = plasma level of the substance × GFR

Study of glucose reabsorption:-

- **Tubular load "TL"of glucose**, is the total amount of glucose that is filtered in glomerular filtrate/min = (**125** mg/min)

"TL" = GFR X concentration of glucose/ml plasma

125 ml/min X 1 mg glucose/ml plasma [100 mg/100 ml]

- **Glucose Renal Threshold**:
- This is the maximal concentration of glucose in plasma above which glucose appears in urine.
- **Normal glucose plasma level = 70-110 mg%**; Up to 180 mg%, all glucose filtered is reabsorbed. The glucose appears in urine at a plasma concentration above **180 mg%** .

Tubular Maximum of Glucose "TMG" :

Is the maximal amount of glucose which can be reabsorbed/min = **300** mg/min in female & **375** mg/min in male.

Above the renal threshold, glucose excretion rises. Finally, glucose reabsorption reaches a maximum rate called Transport Maximum for glucose (TMG) when the carrier for glucose is completely saturated. TMG depends on reabsorbed power of different nephrons which depends on amount of carrier protein.

Glucose starts to appear in urine before the TMG is reached, at 180 mg% . The tubular load is 225, away from TMG, why? Not all nephron has the same length & nimber of carriers, at 180 mg% some nephrons reach their TMG.

Glucosuria : is appearance of glucose in urine

Causes:

1. **Diabetes Mellitus**: decrease insulin→increase blood glucose above 180 mg%→increase tubular load of glucose above TMG.

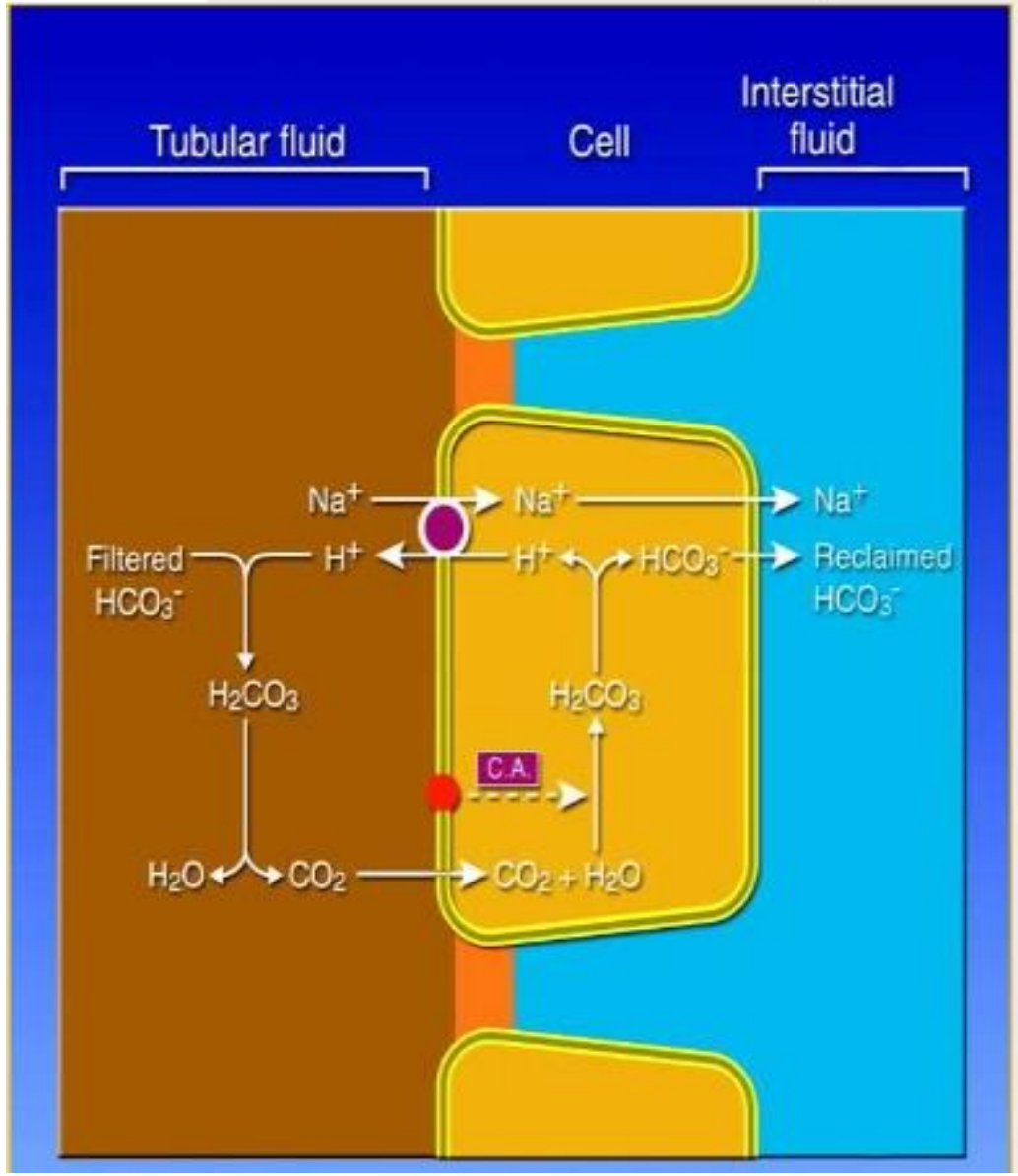
2- **Renal Glucosuria** : This is a hereditary disease in which the number of glucose carrier decreases or the affinity of the carrier towards glucose is reduced. This lower renal threshold &TM to about 100 mg%. Thus glucosuria occurs at normal fasting glucose level

3- Other monosacchrides as galactose , xylose & fructose, when present simultaneously with glucose they depress its transport. This is called "competition for transport"

4- **Oubain** which block Na^+ -K^+ ATPase

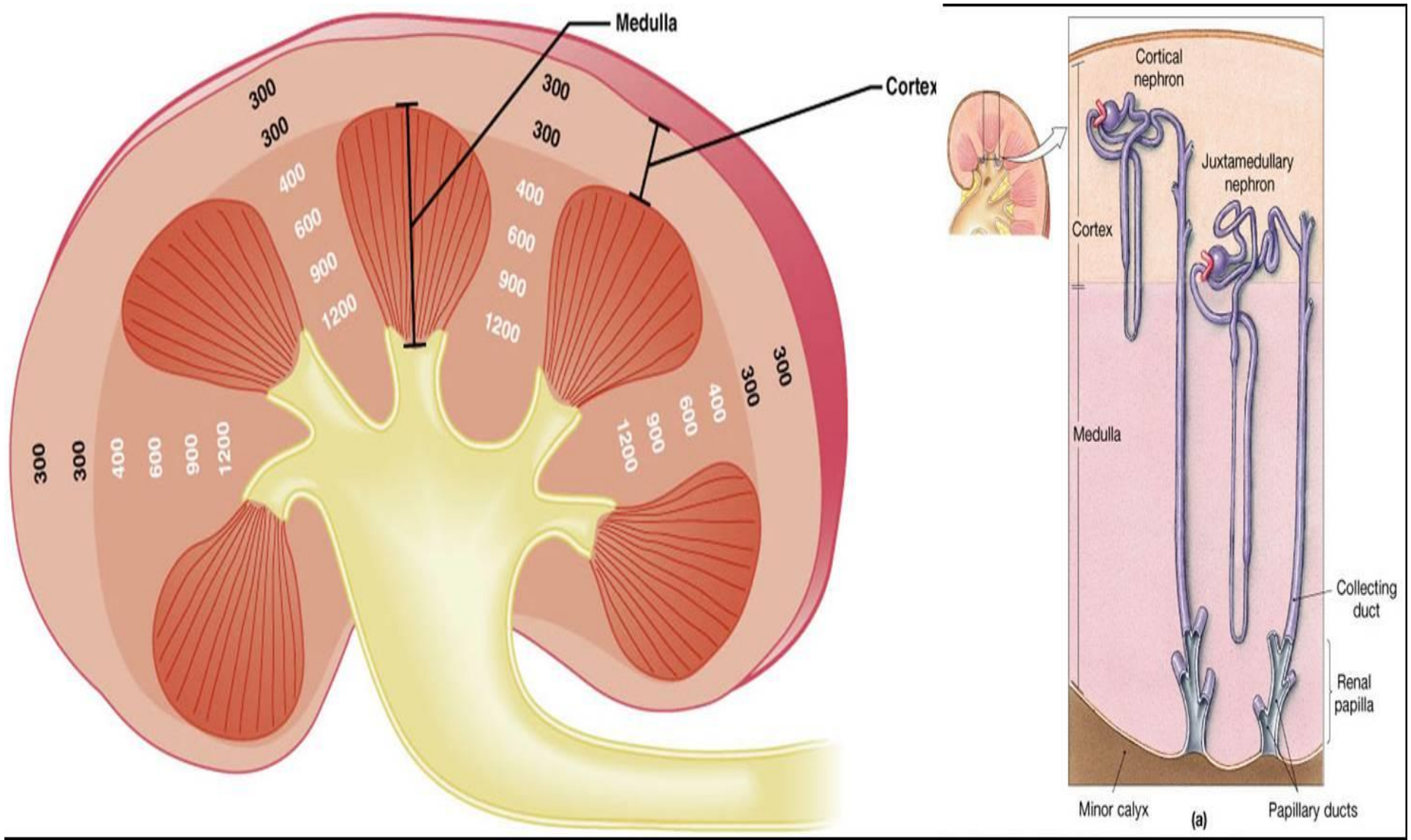
5- **Phlorizin** which blocks sugar access to the carrier protein.

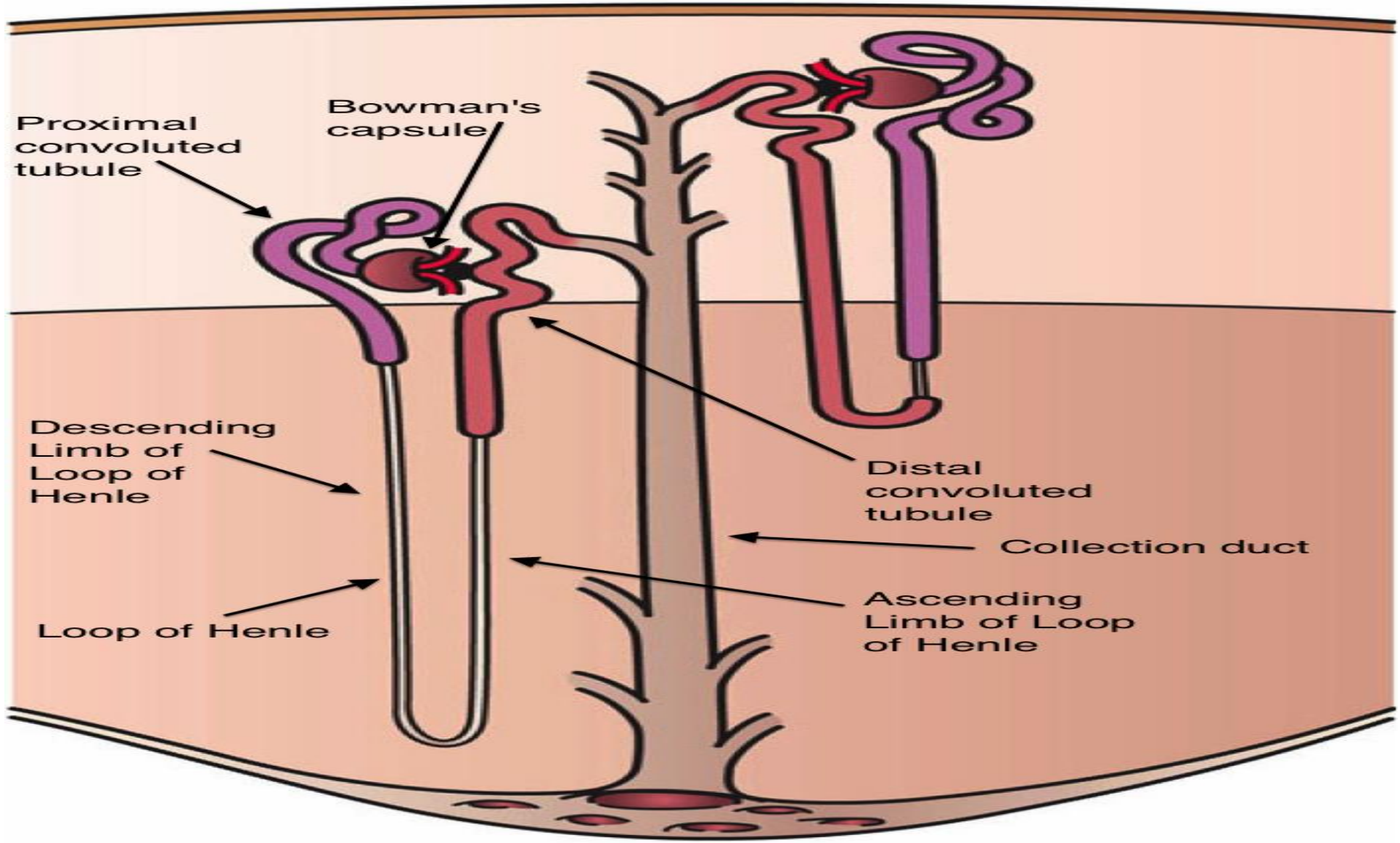
Renal reabsorption of bicarbonate



- Proximal tubule: 70-90%
- Loop of Henle: 10-20%
- Distal tubule and collecting ducts: 4-7%

Countercurrent mechanism




Proximal convoluted tubule
Bowman's capsule
Descending Limb of Loop of Henle
Loop of Henle
Distal convoluted tubule
Collection duct
Ascending Limb of Loop of Henle

Formation of a Concentrated Urine

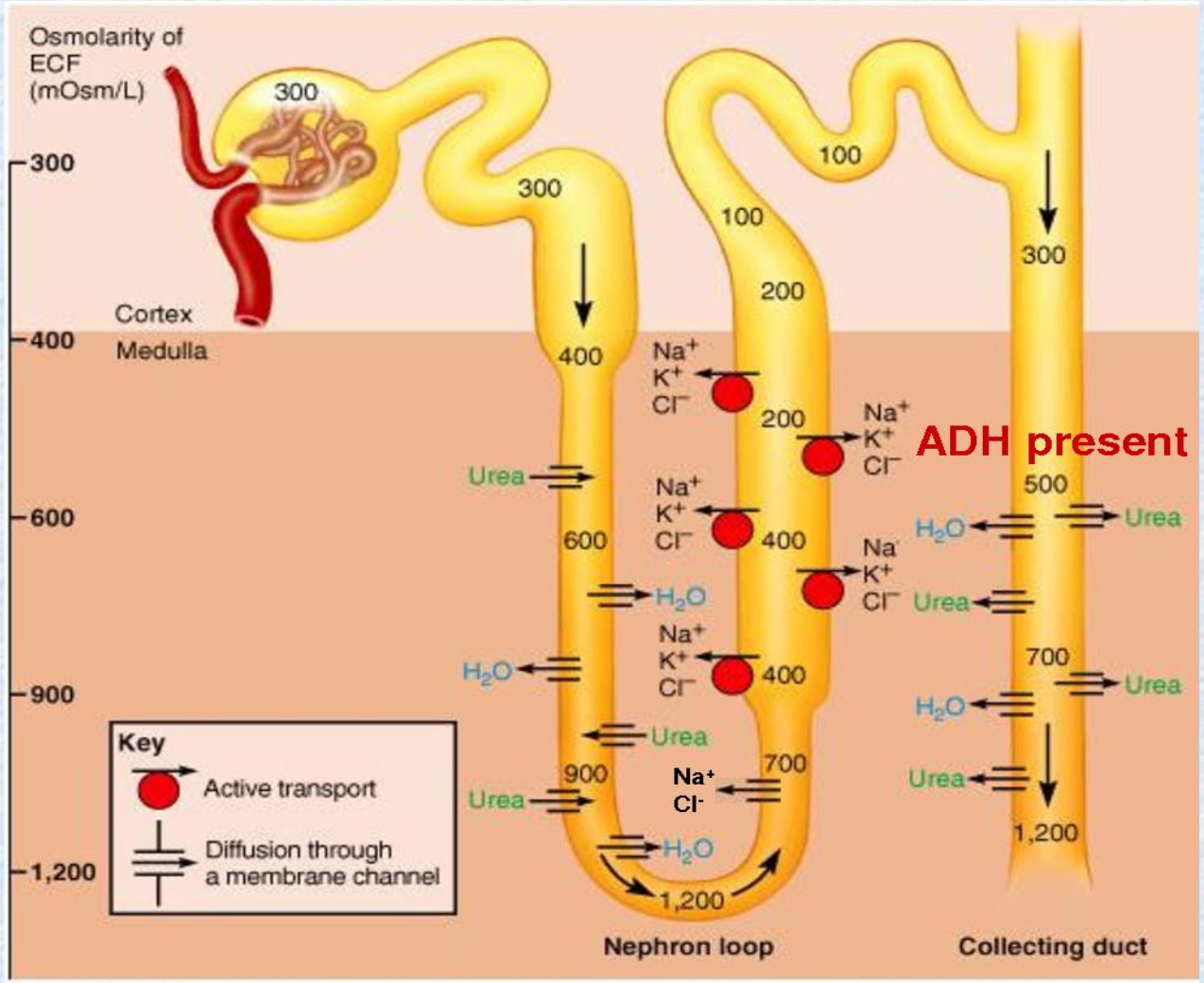
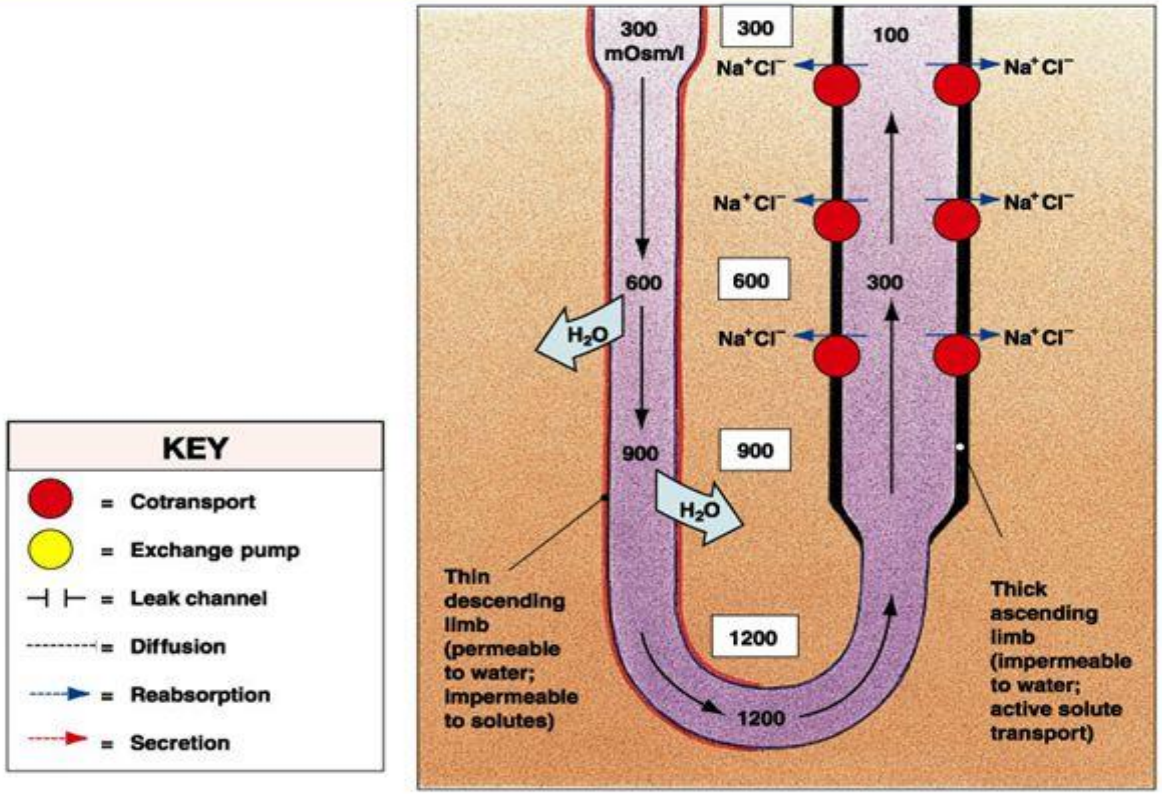


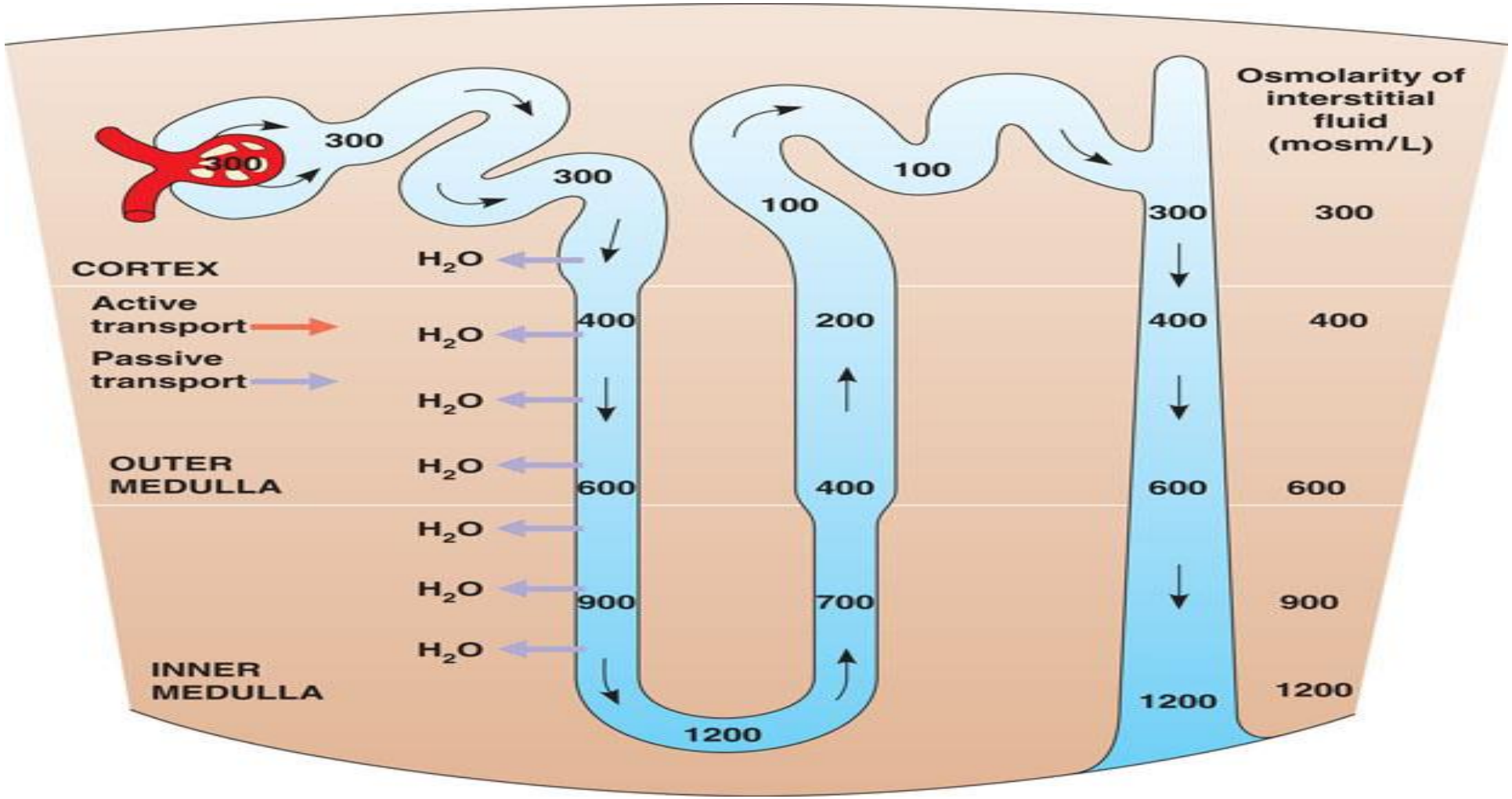
Fig. 23.19 modified

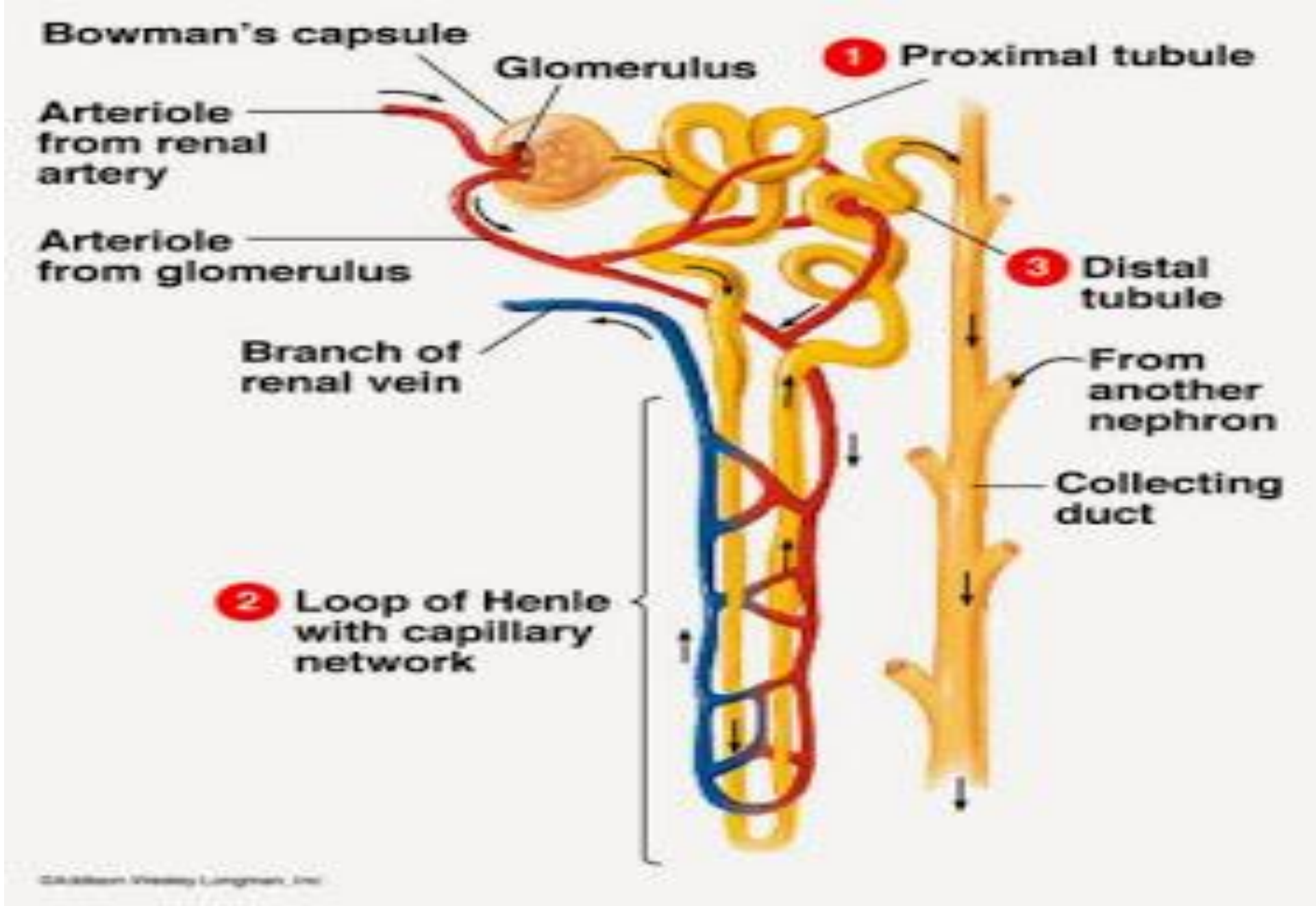
Urine Concentration via Countercurrent Multiplication

- Thin descending limb of Henle is permeable to water but not solutes
- Thick ascending limb of Henle is impermeable to water and solutes. Contains active transport mechanisms for sodium and chloride.



Counter current multiplier




Bowman's capsule
Glomerulus
1 Proximal tubule
Arteriole from renal artery
Arteriole from glomerulus
3 Distal tubule
Branch of renal vein
From another nephron
Collecting duct
2 Loop of Henle with capillary network

Counter current exchanger

A] Descending limb of Vasa Recta :

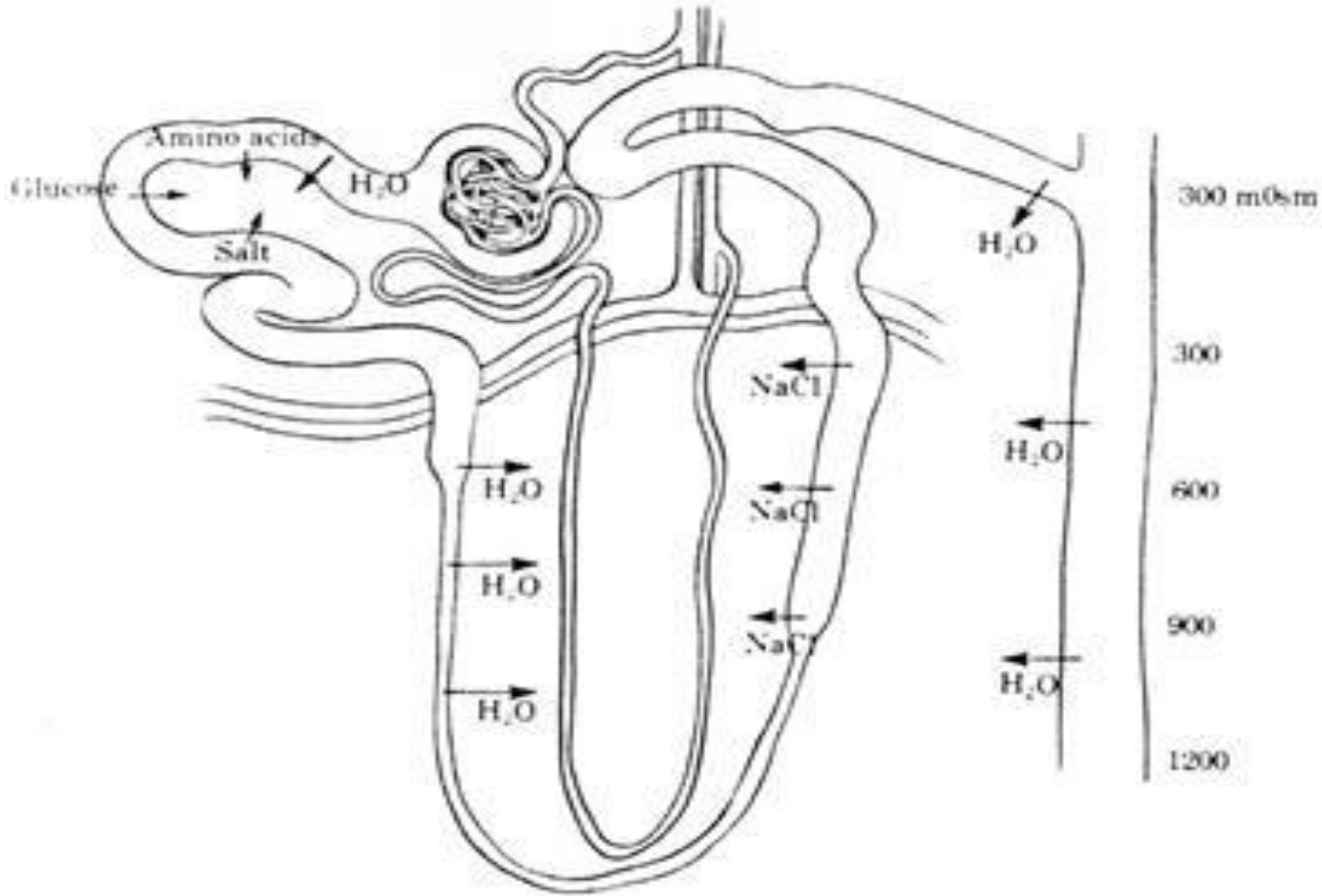
•Nacl and urea diffuses from the interstitial fluid to the blood along concentration gradient.

• H_2O diffuses from blood to the interstitium as :

(a) The interstitial fluid is hyperosmotic.

(b) The capillary blood pressure (35 mmHg) is higher than the osmotic pressure of plasma proteins (25 mmHg).

Net result: blood now is hypertonic at the tip of vasa recta.


Amino acids
Glucose
Salt
H_2O
H_2O
H_2O
H_2O
H_2O
NaCl
NaCl
NaCl
H_2O
H_2O
300 mOsm
300
600
900
1200

•B] Ascending limb of Vasa Recta :

•Nacl and urea diffuse from the blood to the interstitium

• However, water coming from **collecting tubules**, **descending limb of vasa** recta and **loop of Henle** diffuse from the interstitium to the blood of the general circulation as →

a) blood becomes more concentrated than interstitium

b) Plasma protein becomes more concentrated → higher osmotic pressure than capillary pressure.

•The net result: Solutes (Nacl and urea tend to recirculate in the medullary interstitium →(Nacl and urea cycle) while water tends to leave the interstitium and passes to the general circulation.

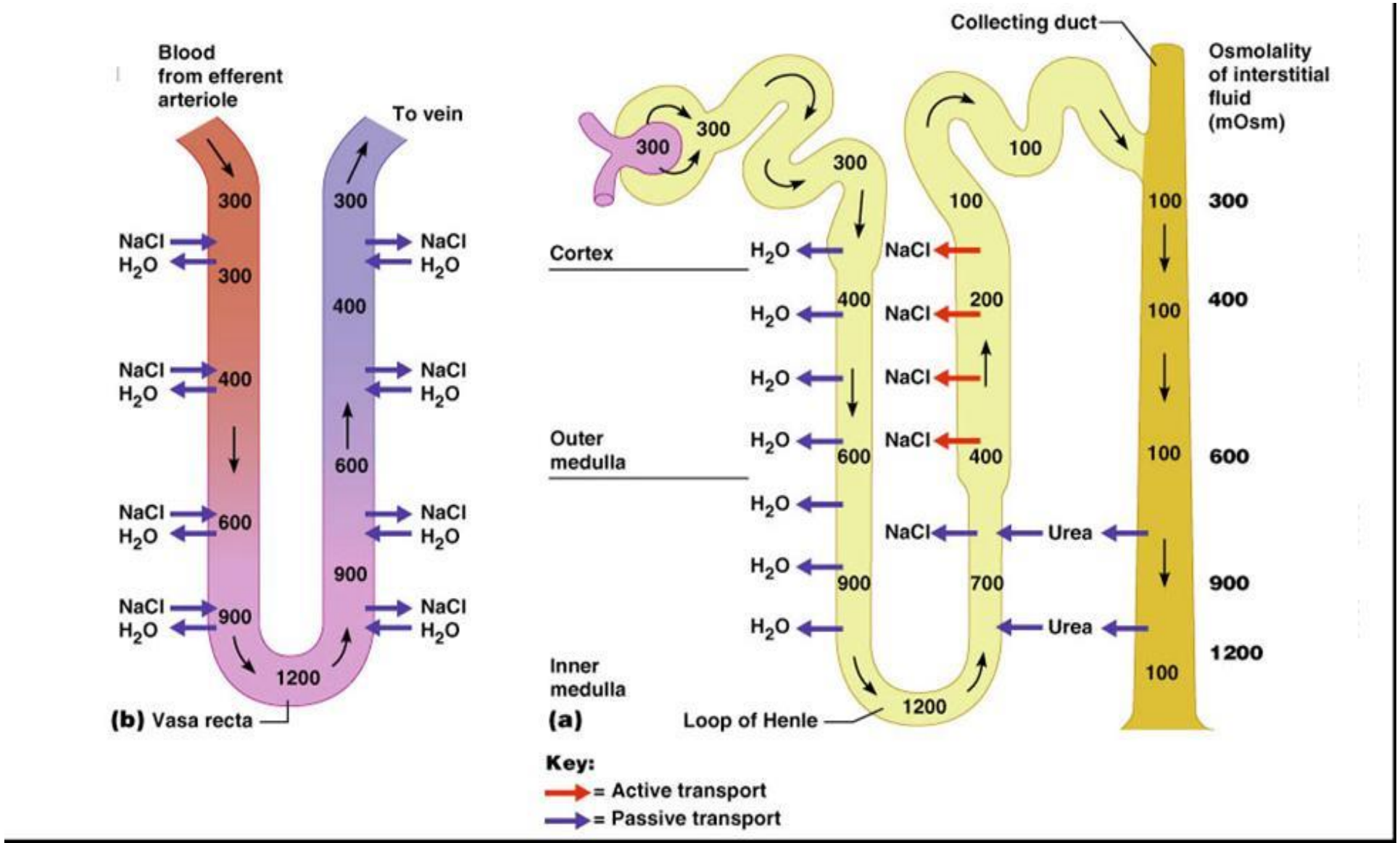
•This maintains the hyperosmolarity of the medullary interstitium.

Thus, the Vasa recta perform two important functions:

1] Trapping solutes (Nacl and urea) in the renal medulla.

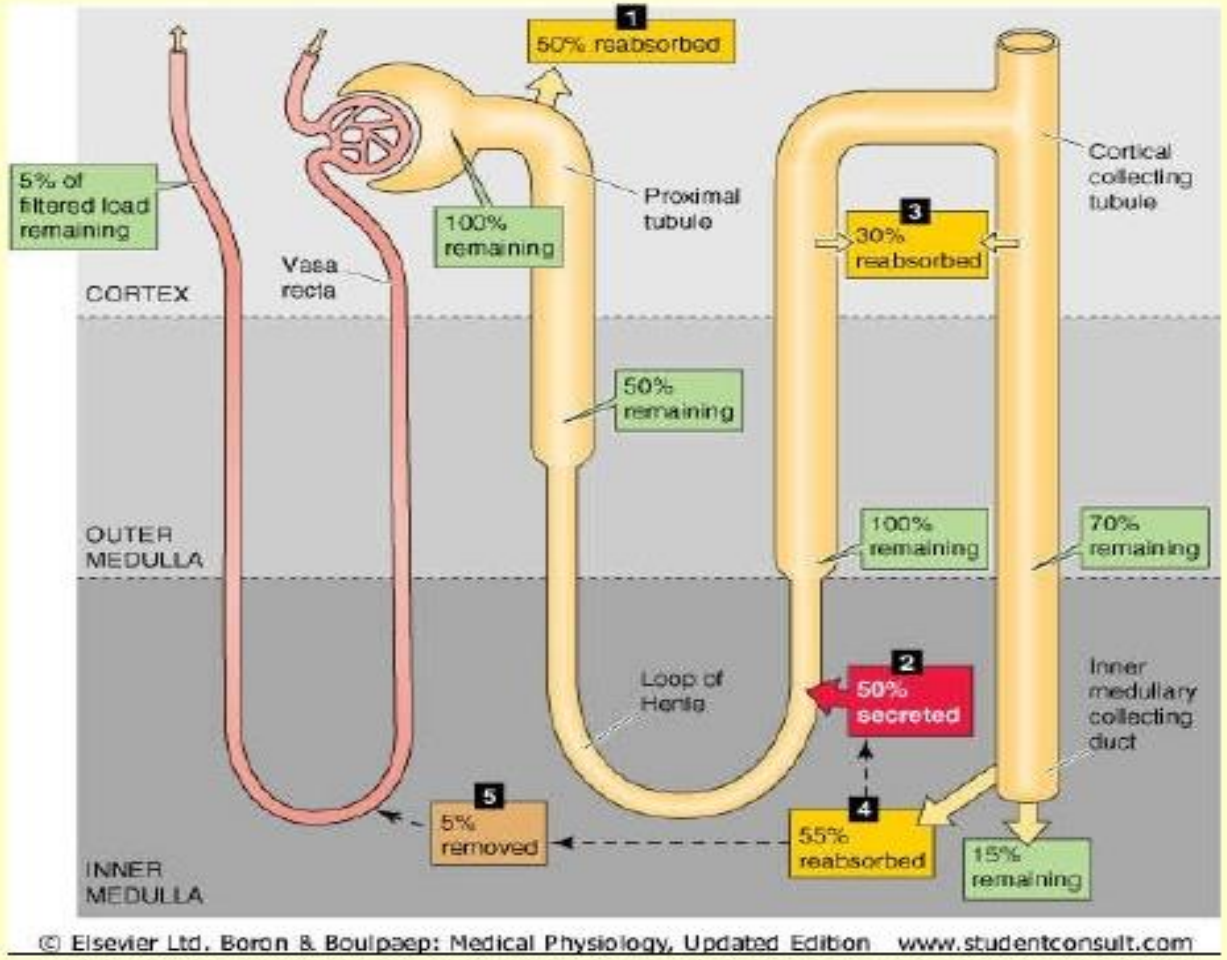
2] Removing the absorbed water from the medulla to the general circulation.

Countercurrent mechanism



Urea recycling

- Urea toxic at high levels, but can be useful in small amounts.
- Urea recycling causes buildup of high [urea] in inner medulla.
- This helps create the osmotic gradient at loop of Henle so H_2O can be reabsorbed.




Thank
You