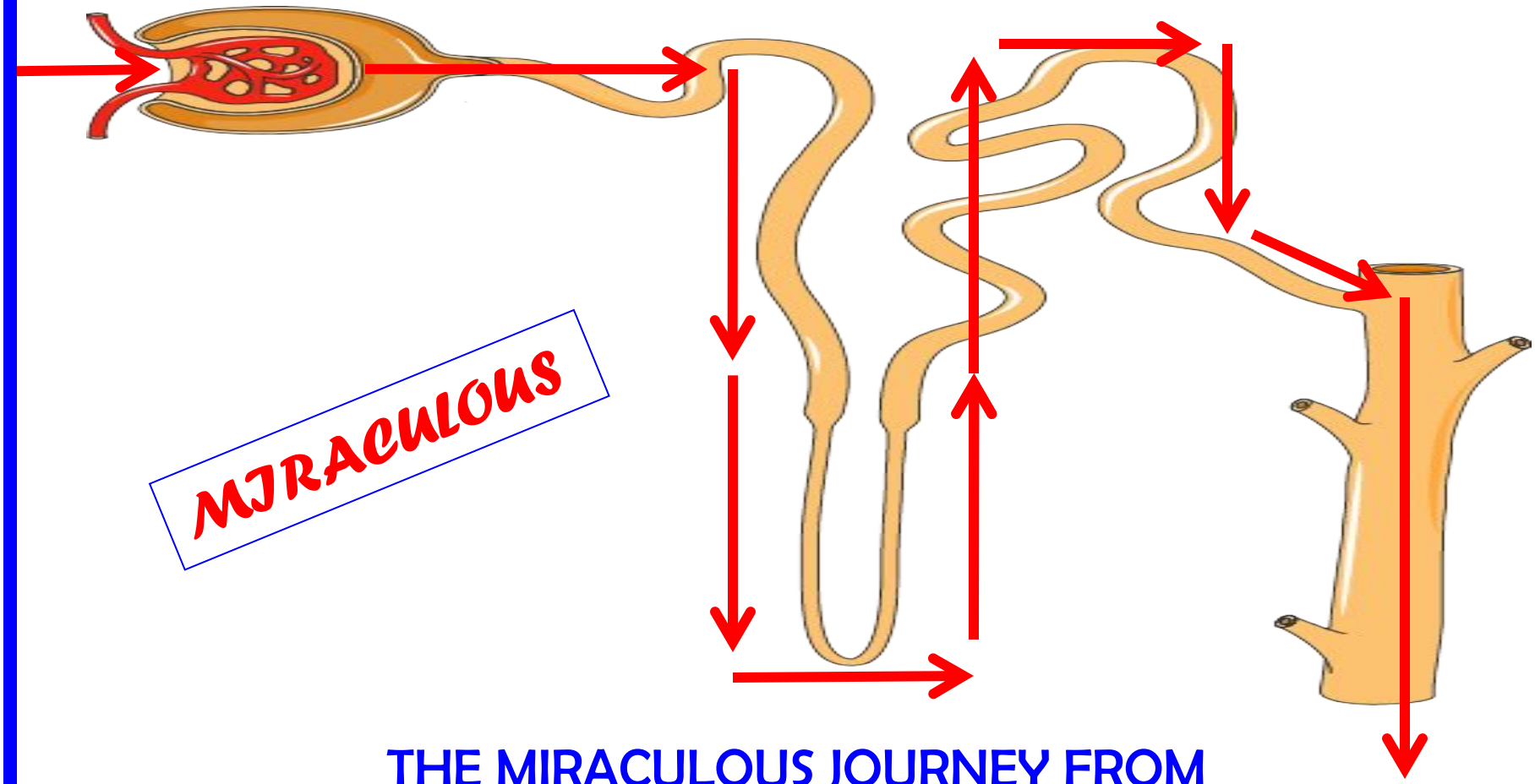


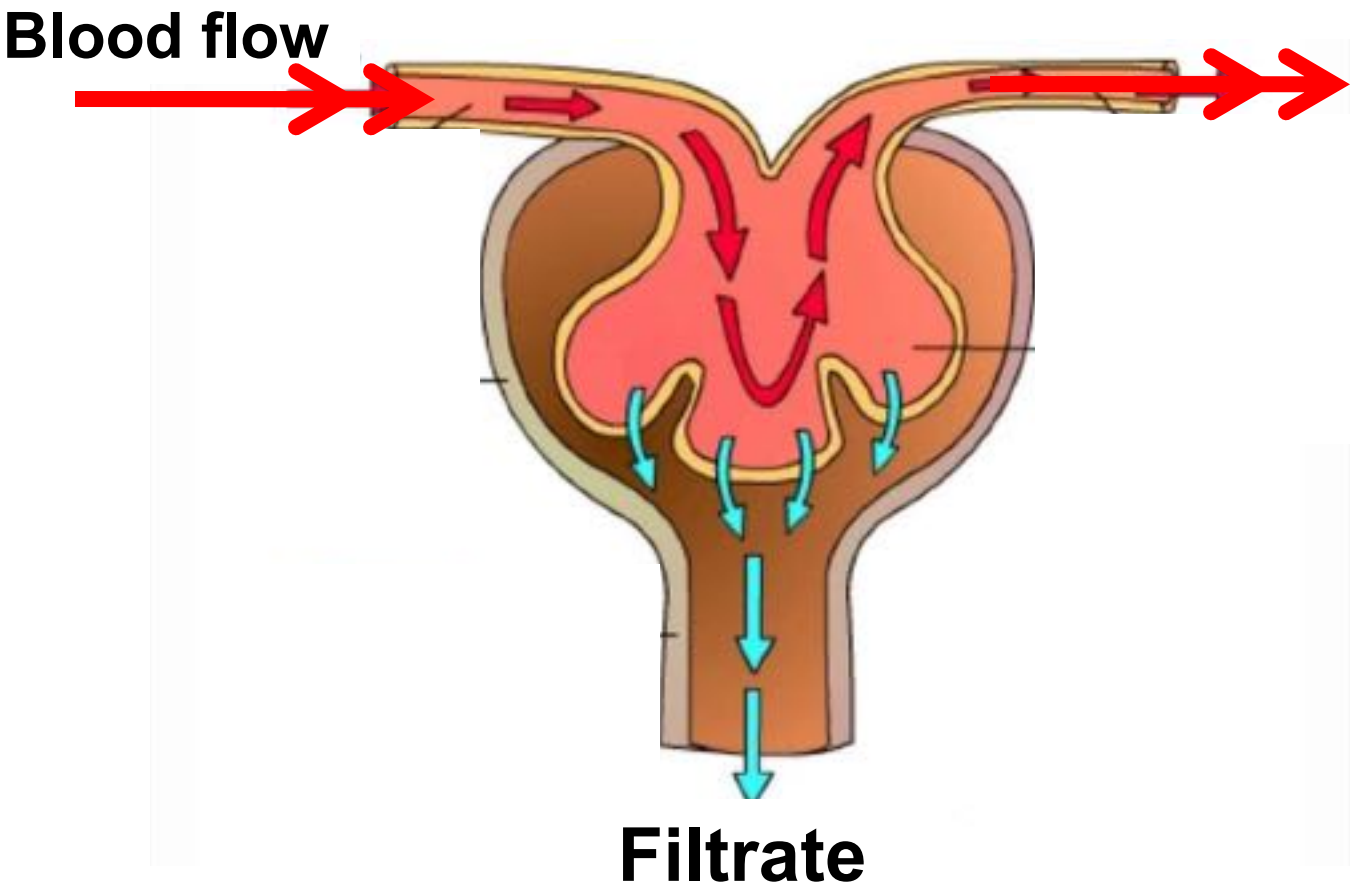
THE MIRACULOUS JOURNEY FROM "BLOOD TO BLADDER"

By

RAMZI EL-BAROUDY
PRESIDENT OF ESPNT

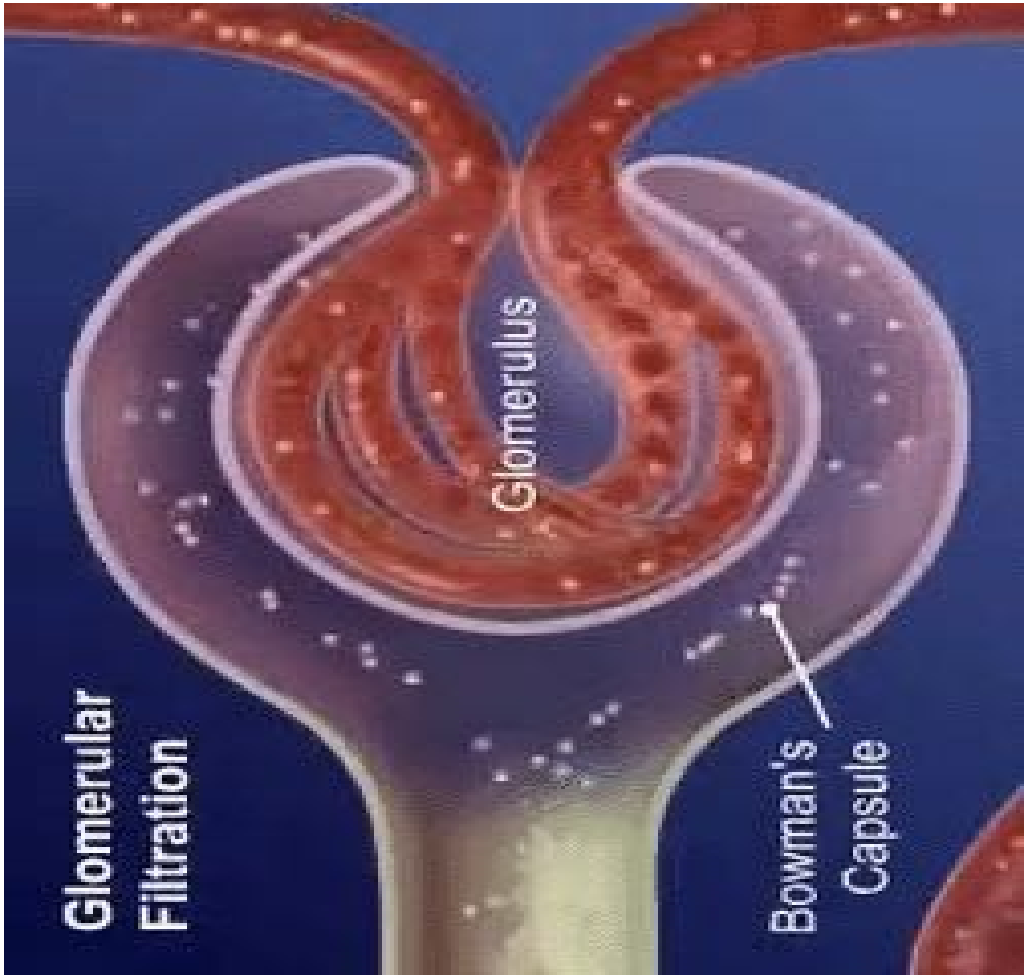
Key Words

Filtration



The glomerulus **acts as a filtering unit, retaining proteins and cells in the bloodstream, with *mass passage* of extra fluid and wastes.**

Filtrate = Plasma – cells and proteins



About **180 liters** of fluid are **filtered** by the **kidneys** every day.

If this filtrate flowed straight to your bladder and then out of your body, you would lose more than 10-times the entire volume of your body fluids every day.

THEN

Reabsorption

Should come into play

picture 1
180 L/day

And through this

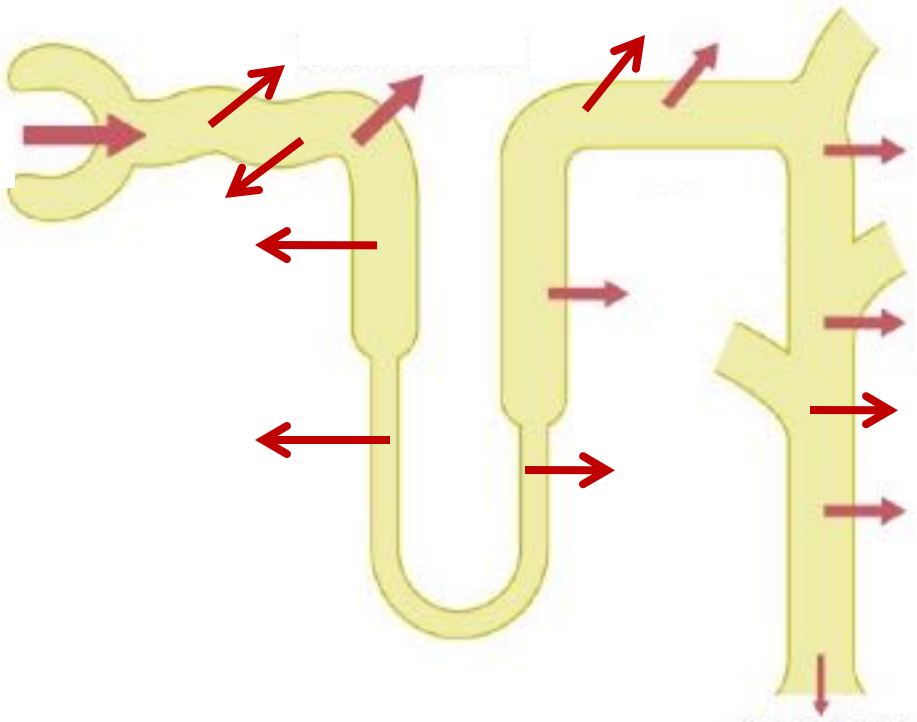
Tubular Reabsorption

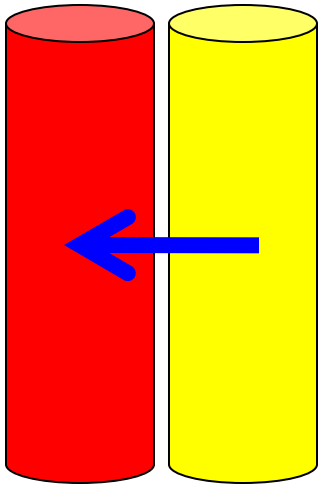
picture 2
1 L/day

out of the 180 L of glomerular filtrate, just 1 L is voided every day.

Reabsorption = picture 1 – picture 2

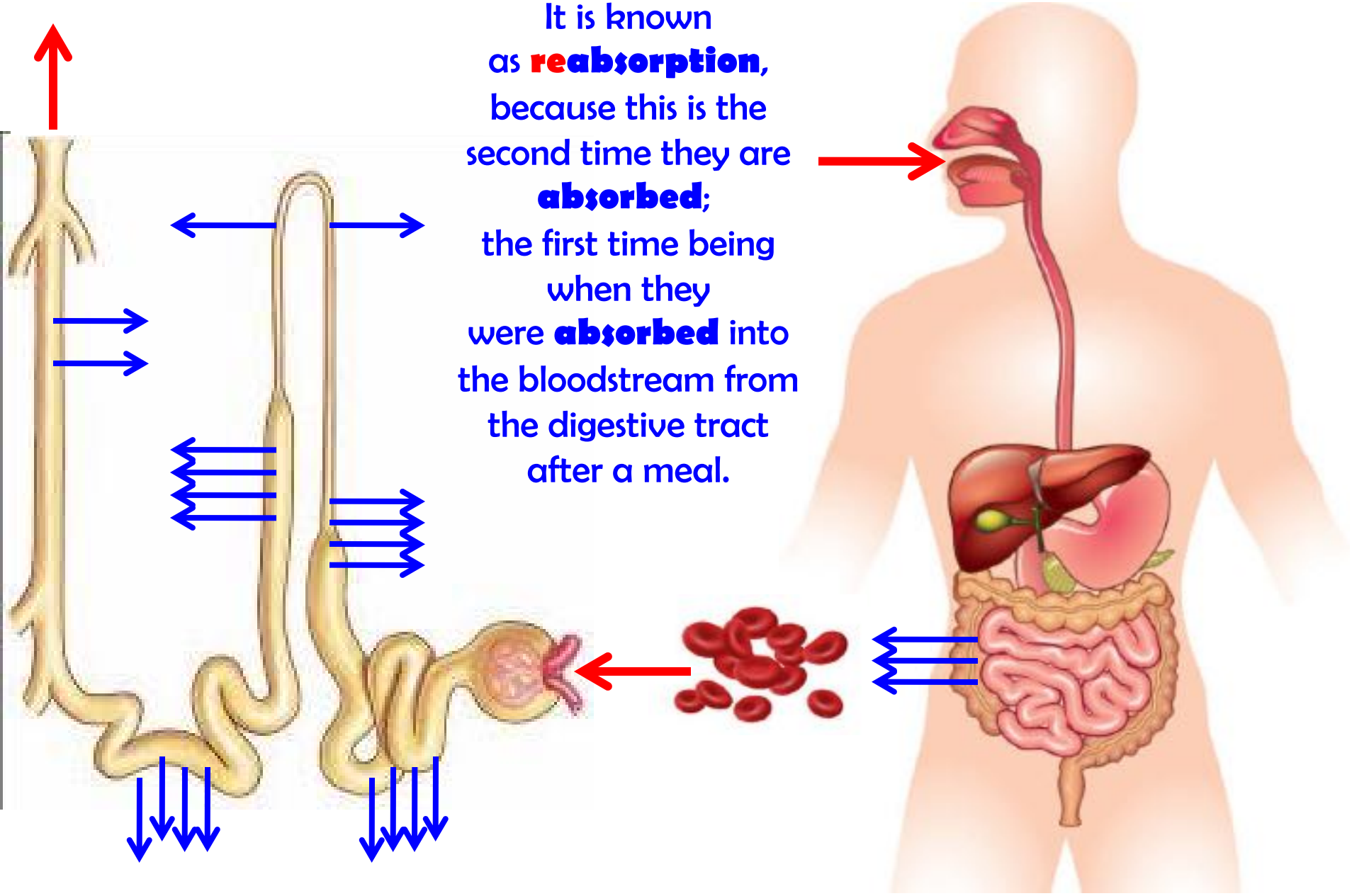
Reabsorption





Reabsorption is **thus** the process by which the **tubule removes** water and solutes from the tubular fluid (*pre-urine*) and ***returns them back*** to the circulating blood.

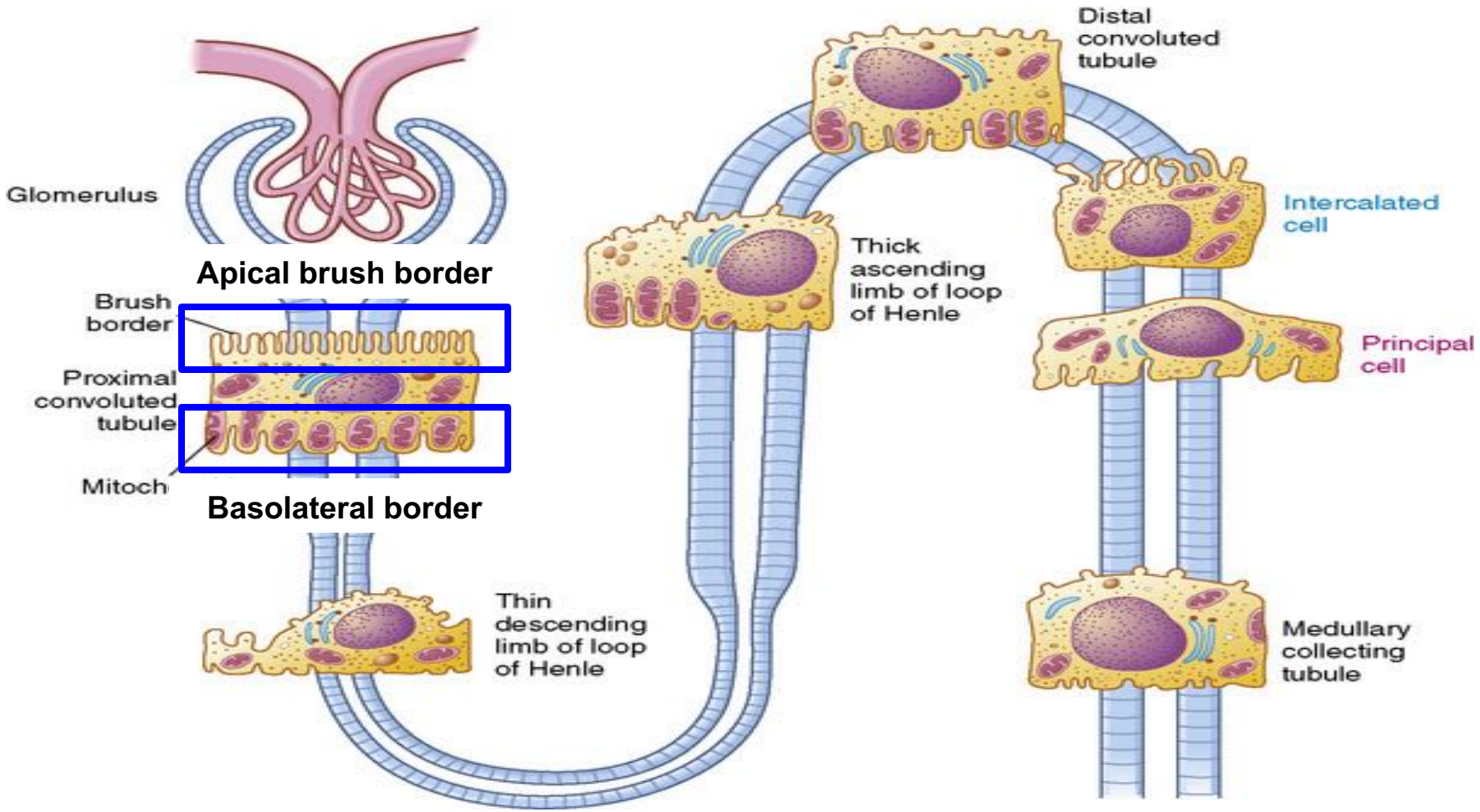
It is known as **reabsorption**, because this is the second time they are **absorbed**; the first time being when they were **absorbed** into the bloodstream from the digestive tract after a meal.



The

KEY PLAYER

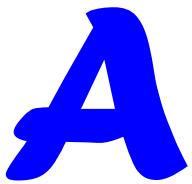
is the tubular cell of nephron



Reabsorption **claims back** what has been filtered

According to the needs of the body.

How can the tubular system judge and adjust its function according to the needs of the body ?



Renal tubules can sense and monitor a wide range of physiological challenges by several <u>sensory proteins on the brush border</u>, and adapt their function accordingly.

How can these sensory proteins on the brush border, which is on the other side of the blood, sense and monitor these blood physiological challenges ?

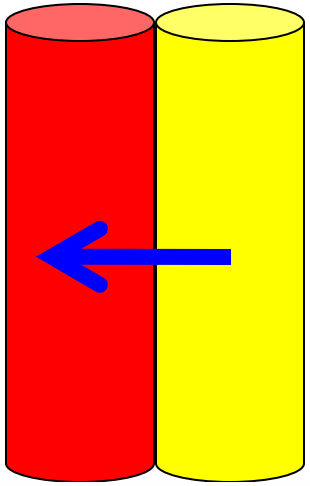
A

As the blood circulates, it's accumulating, gathering, and heaping different stuff and waste. When the glomerulus is sending an ultrafiltrate of the blood to the tubule, it is actually sending a copy of the blood, with all the details of its chemical composition, to the tubule to SENSE, MONITOR, AND MANAGE ACCORDINGLY.

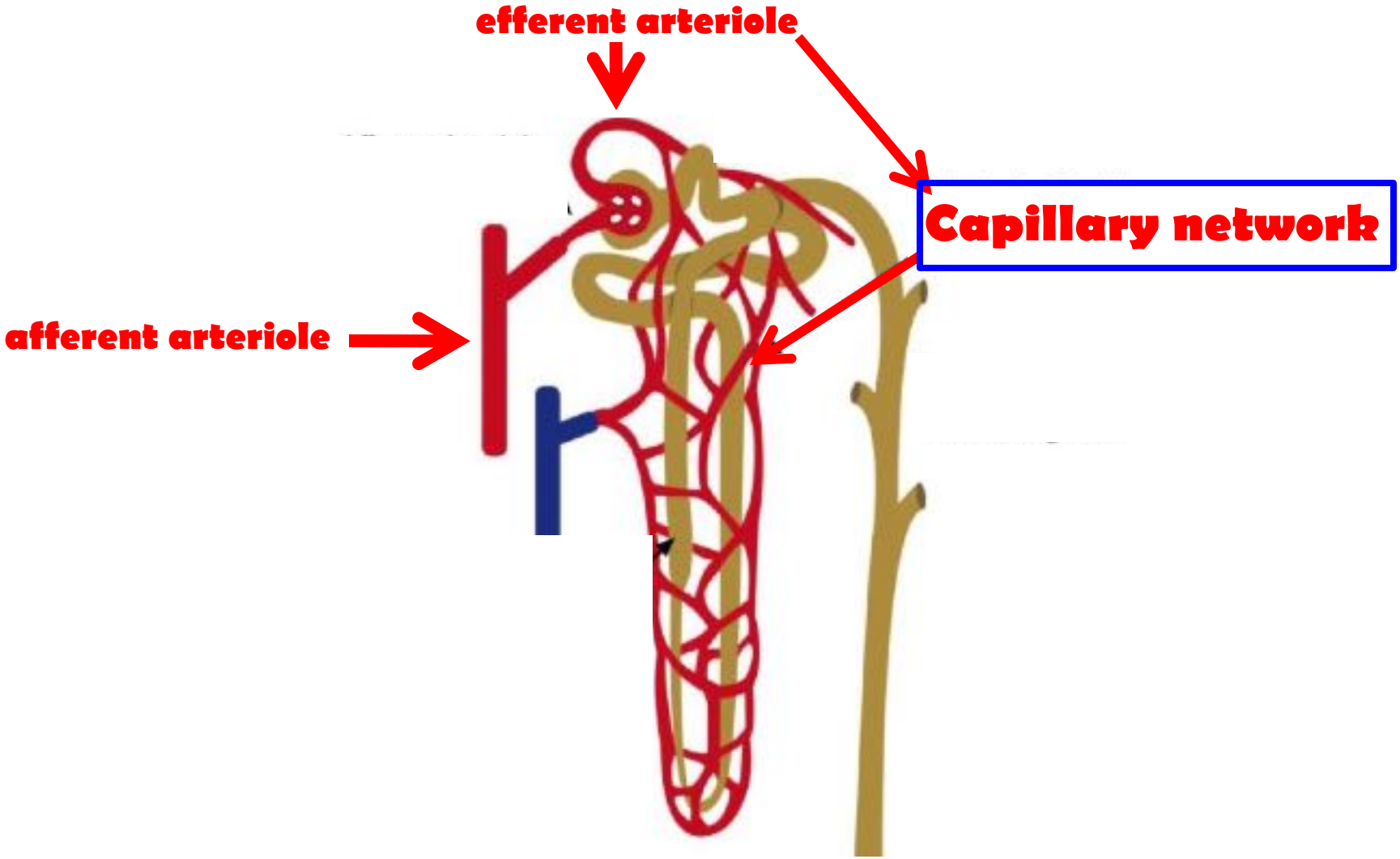
This is the big idea behind FILTERING everything, and then GETTING IT BACK. Getting it back will be ACCORDING to the needs of the body.

if

COMEBACK



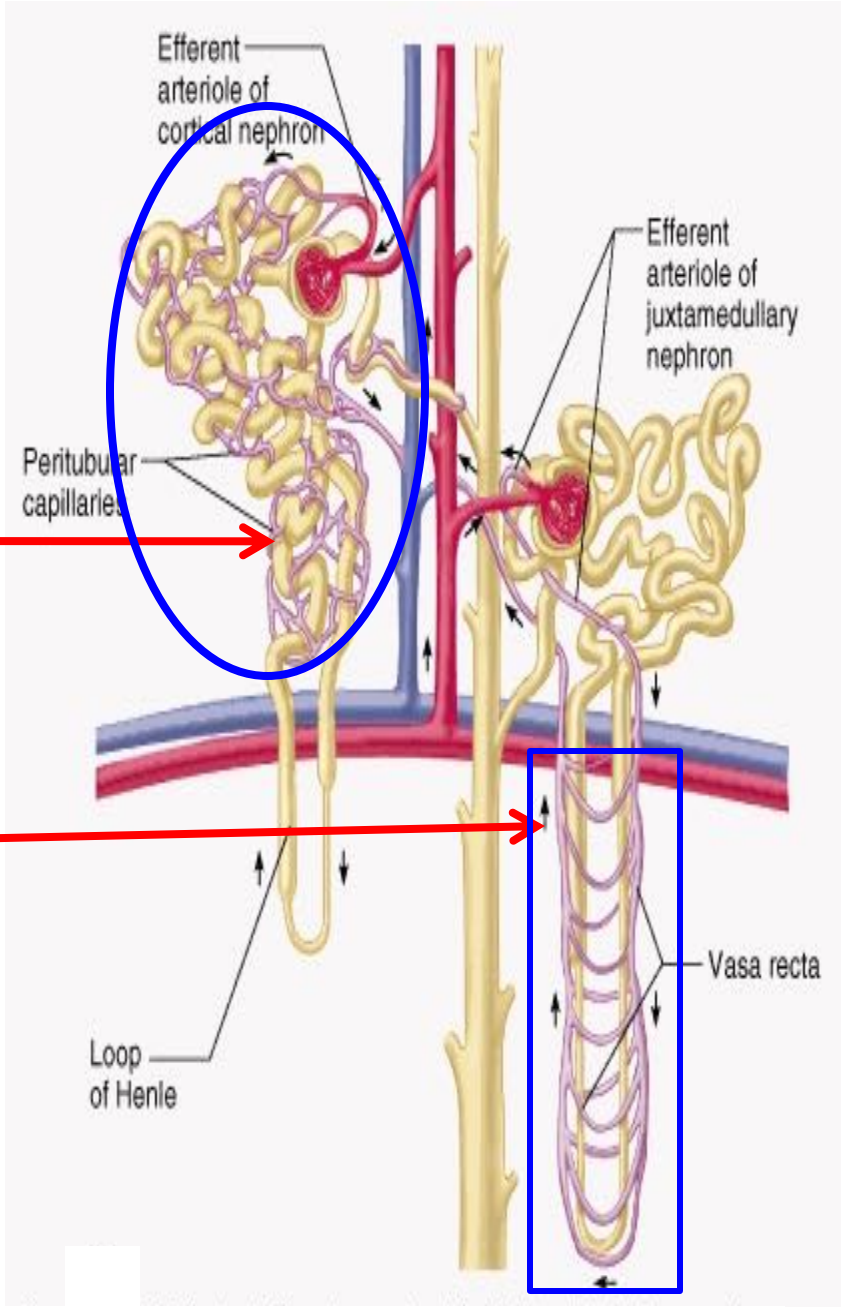
if



Reabsorption is achieved through a network of **capillaries** supplied by the **efferent arteriole.**

Whereas the **Peritubular capillaries** surround the *cortical* parts of the tubules.

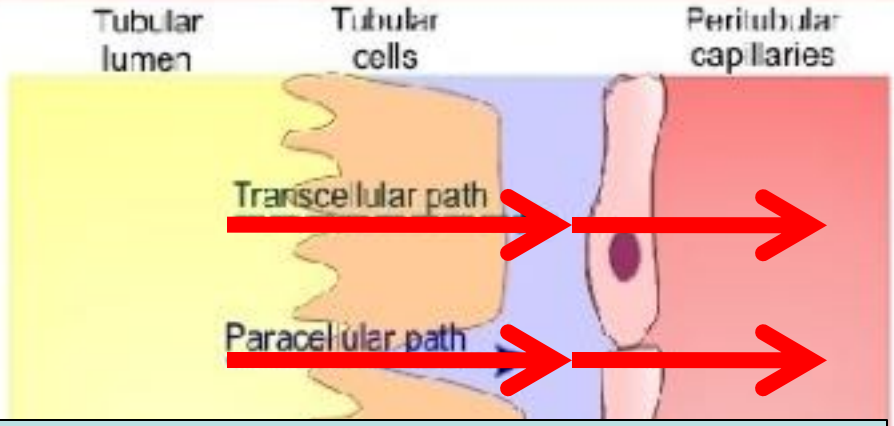
The **Vasa recta** surround the loop of Henle of *juxtamedullary* nephrons.



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.

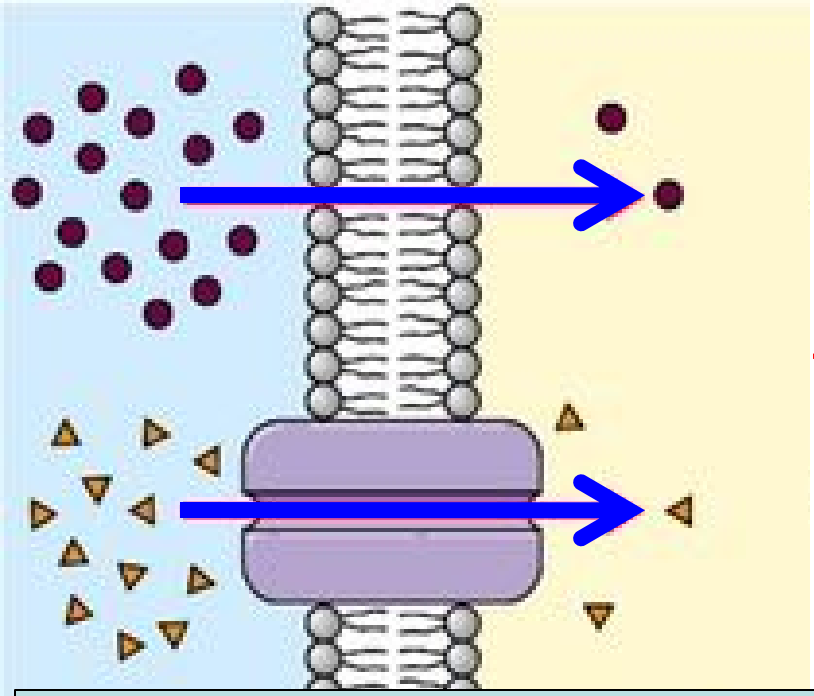


Step 1 Step 2

Reabsorption
"Transport"
may be carried out in
one of 2 ways;

either

Passive transport or Active transport



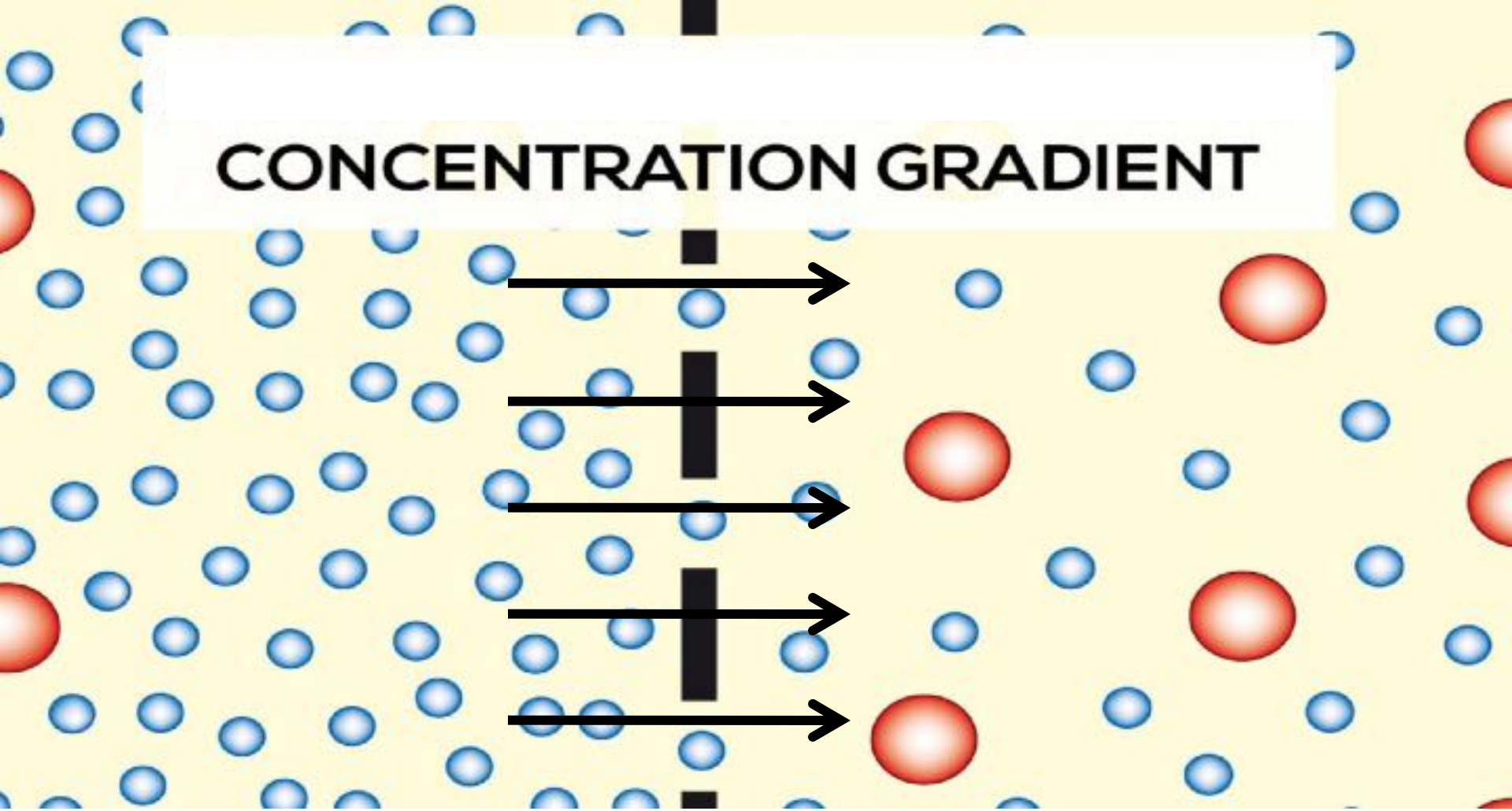
Passive transport

Passive transport

is when substances ***move down***

their ***concentration gradient*** *or* ***electrical gradient***

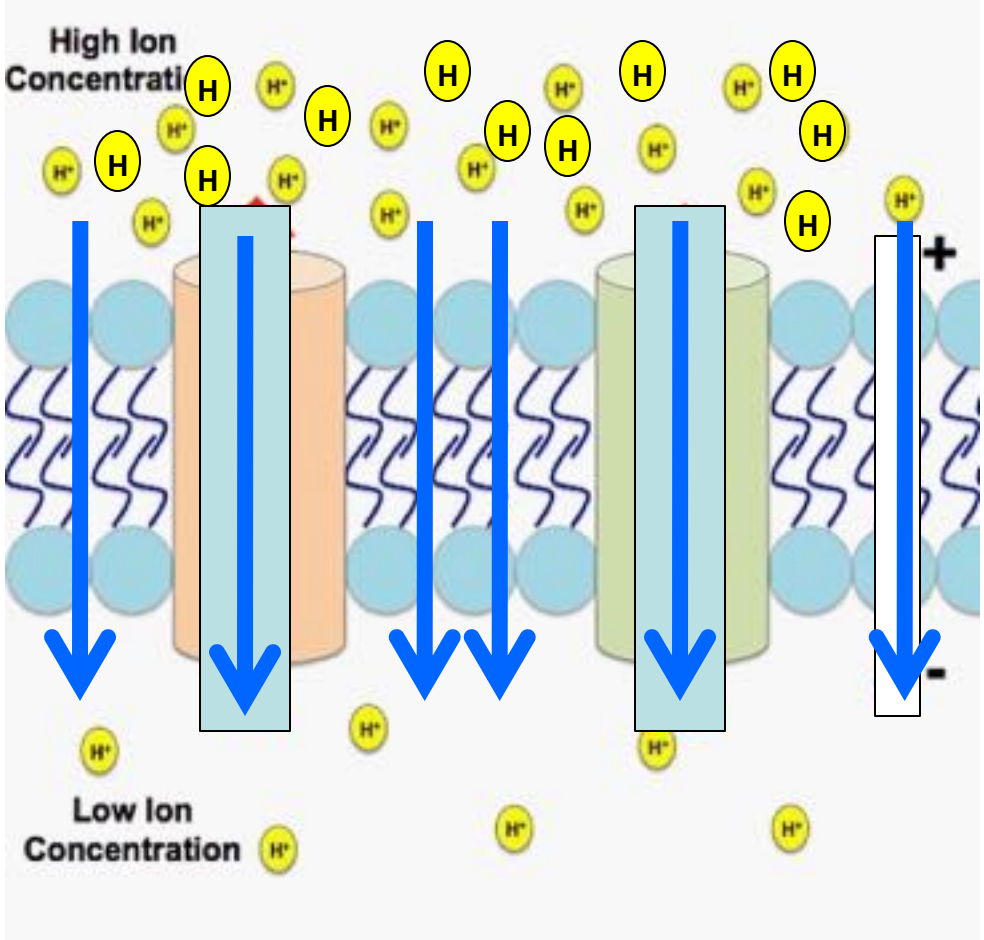
(***from high to low***)



Concentration gradient* is the** *difference in the* ***concentration *of a substance between two areas.*

Bigger *difference* → ***Faster*** *diffusion.*

ELECTRICAL GRADIENT



Electrical (ionic) gradient *is the* ***difference in charge*** *across a membrane.*

Bigger *difference* → ***Faster*** *diffusion*

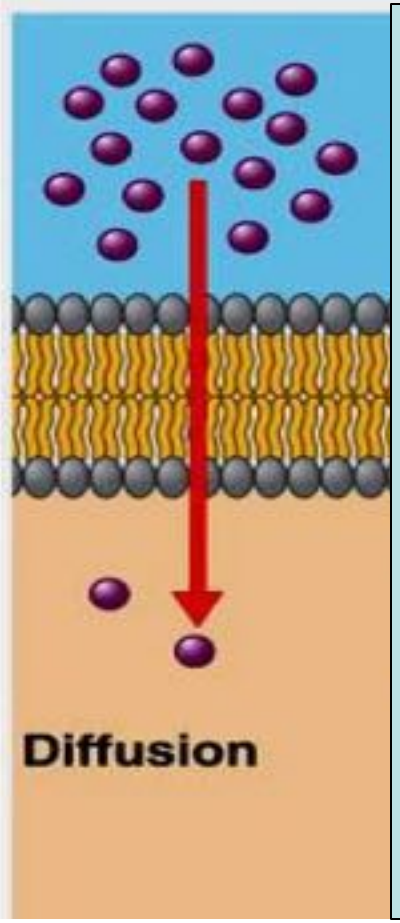
Once sliding from high to low


I don't need energy

Passive transport

is known in 2 forms

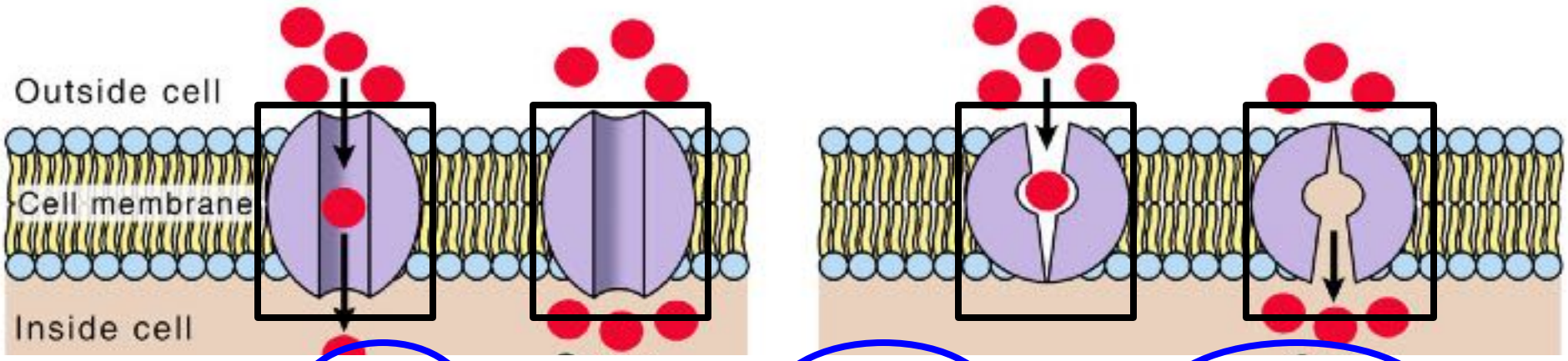
Simple Diffusion



When the substance flows easy along a gradient ***from high to low***

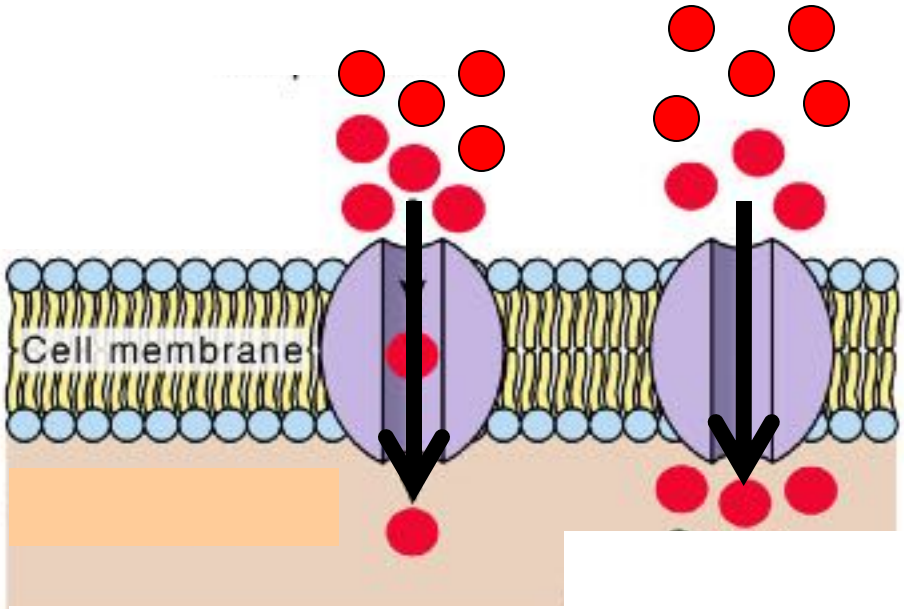
Facilitated diffusion

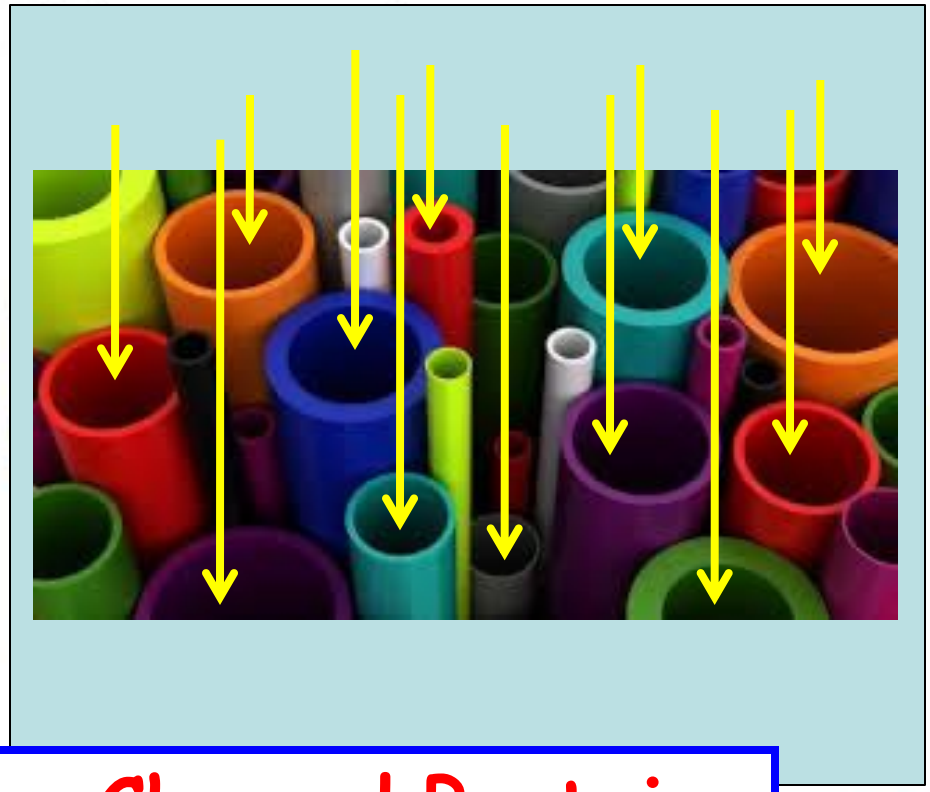
from high to low



Is the **same** as diffusion, **except** that it **requires** ***specific membrane receptors*** for movement.

Facilitated diffusion

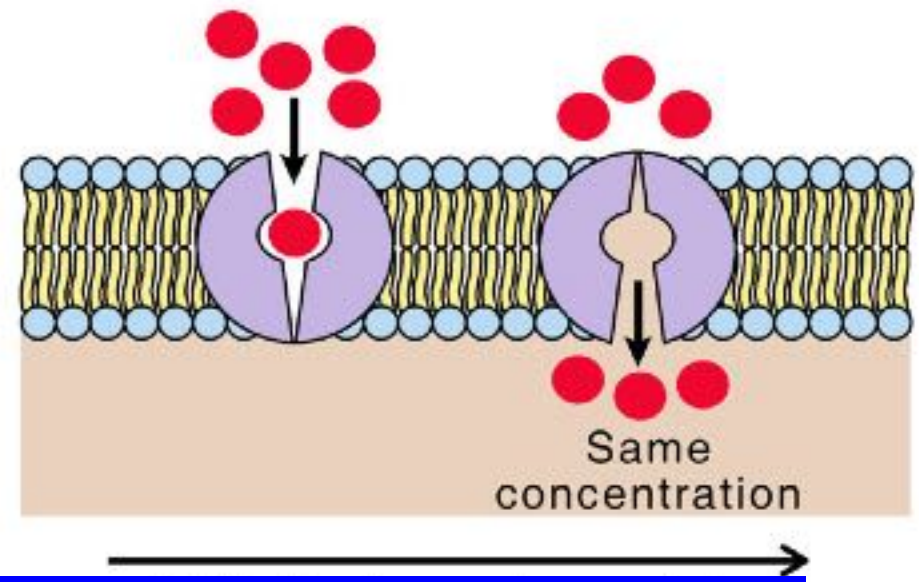




It may be through a Channel Protein

i.e. just like the fast track in an airport

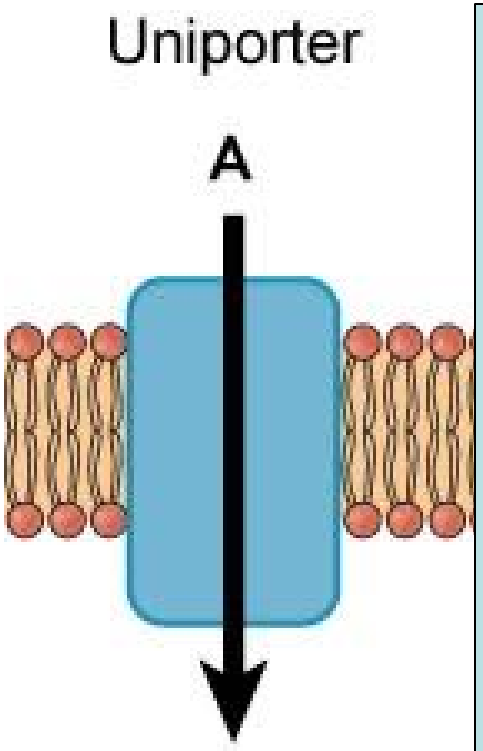
Facilitated diffusion



Or it may need a Carrier Protein

where

The substance being transported combines with a carrier, which then releases it, ***chemically unchanged ,*** inside the cell.



Both

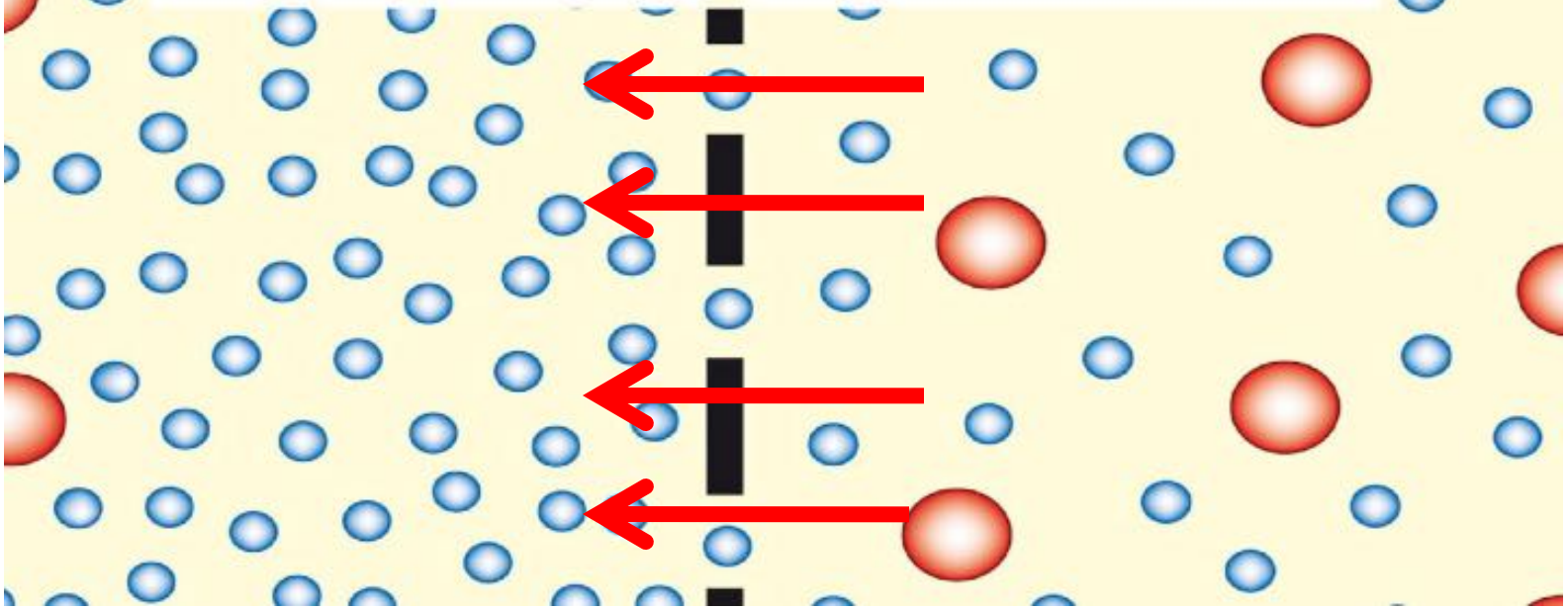
carriers and channels,

are referred to as **Uniporters**

or facilitated transporters.

Osmosis

(Water diffusion)



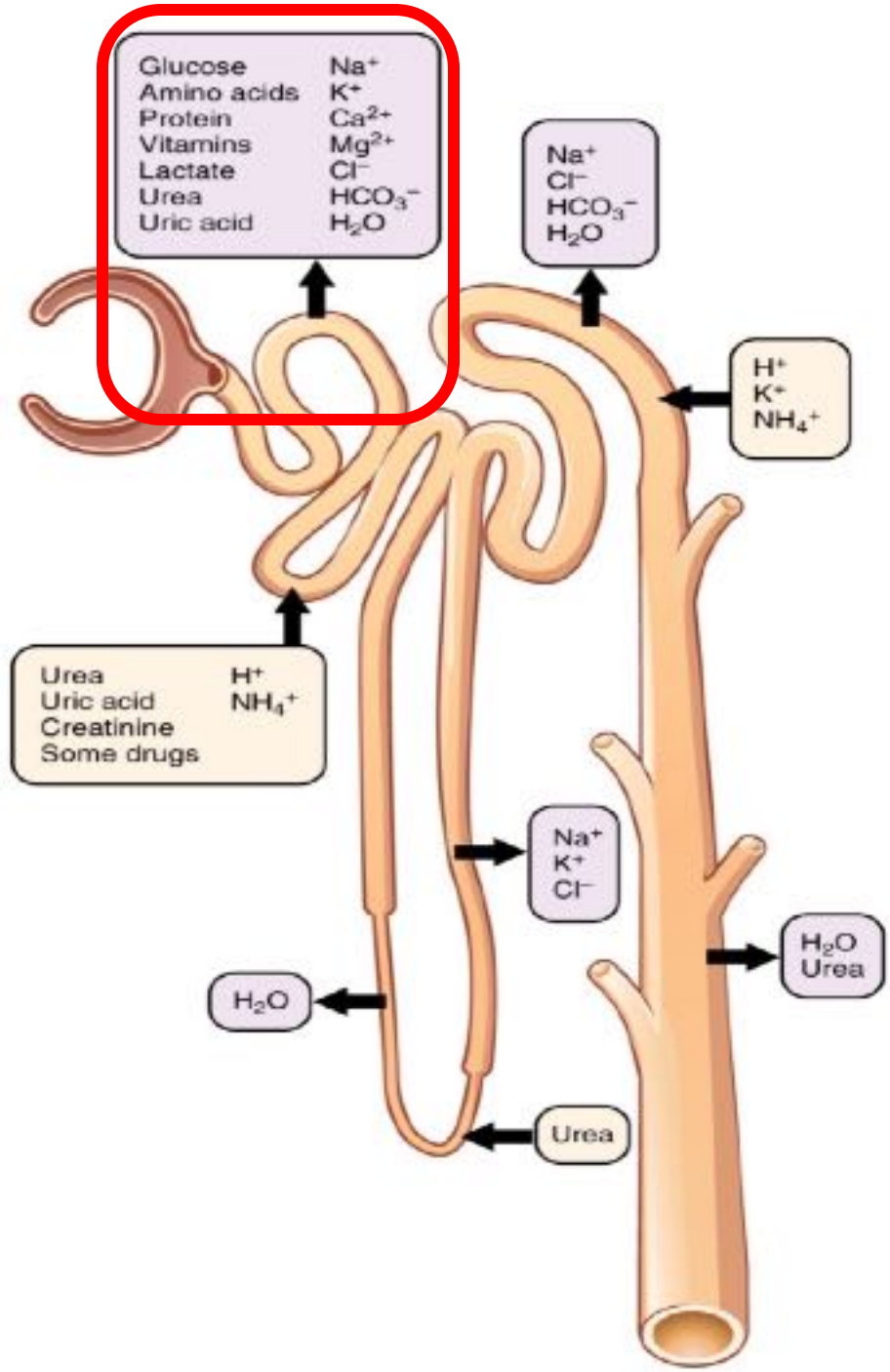
Osmosis (water diffusion)
is the movement of water from an area of
Dilute solution to an area of Concentrated solution,
across a semipermeable membrane.

Selective reabsorption

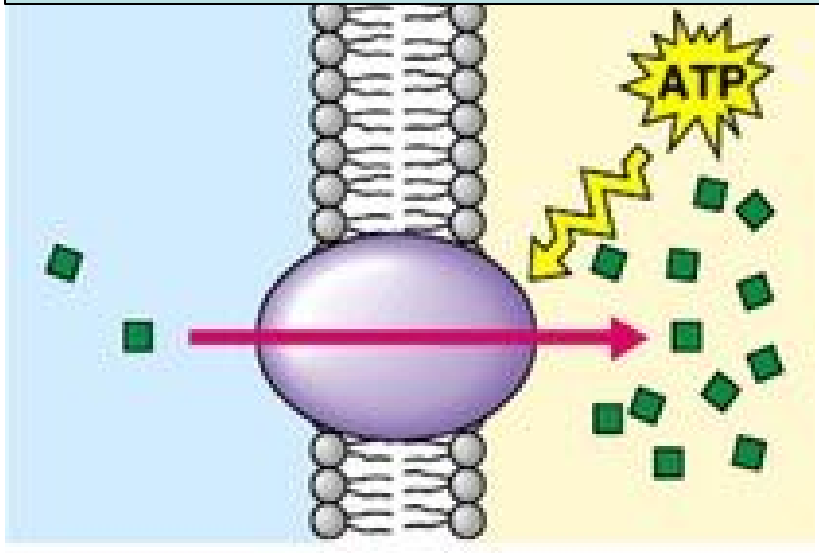
is the process whereby certain molecules are **reabsorbed** from the filtrate as they pass through the **PCT**.

ions, glucose, amino acids, vitamins, and water

And by the time the filtrate has reached the mid part of the proximal tubule, 100% of the filtered glucose, amino acids, and vitamins have been **reabsorbed,** with large amounts of *sodium, bicarbonate, phosphate, lactate, and citrate ions, along with urea & uric acid.*



Active transport



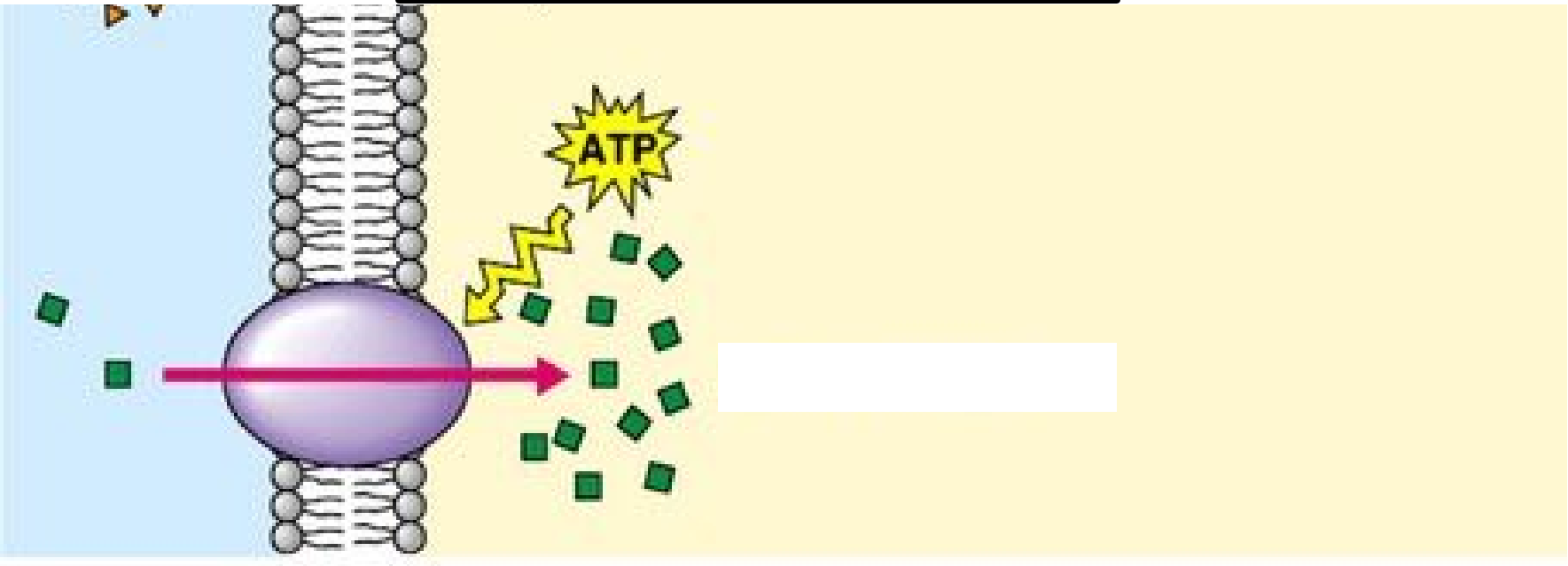
Active transport

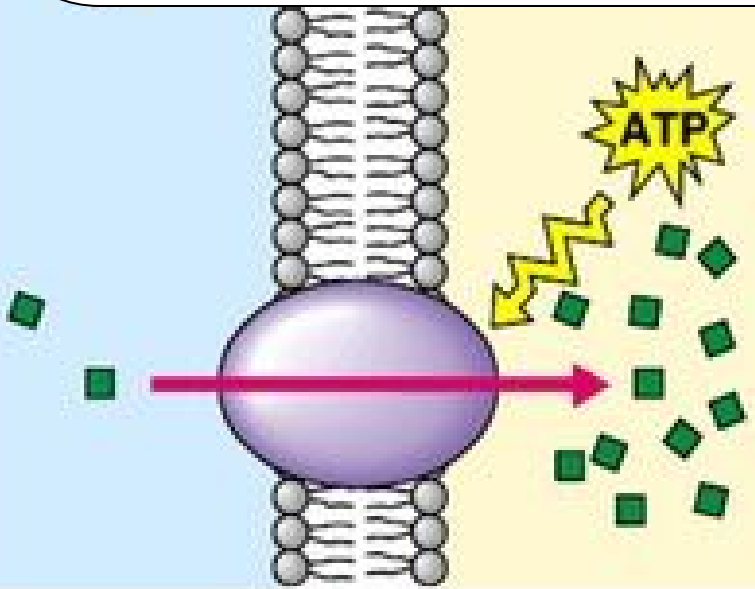
is when substances are transported back into the blood stream

against

their concentration or electrical gradients

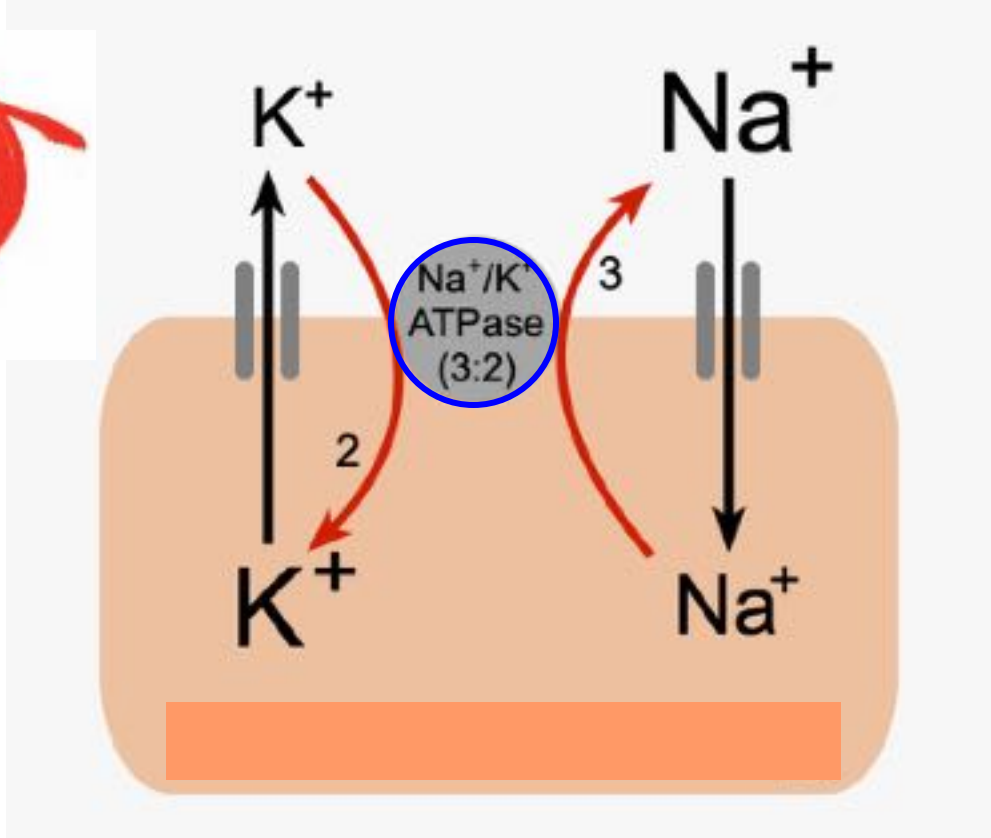
(**from low to high**).





energy-dependent process .

There are two main types of active transport



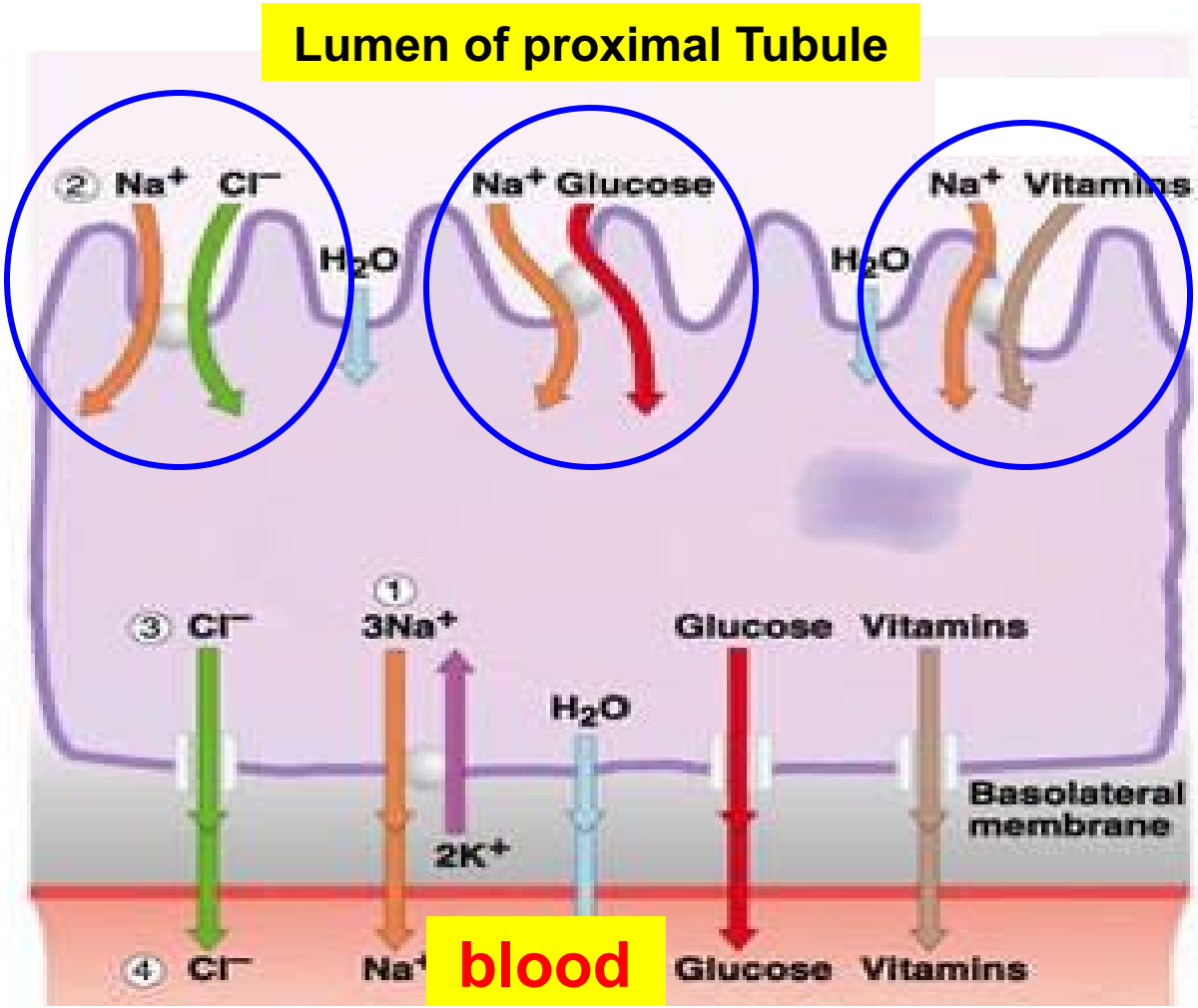
Primary active transport

(active **pump** mechanism)

Involves the direct use of metabolic energy.

Na-K-ATPase
may be the best known example.

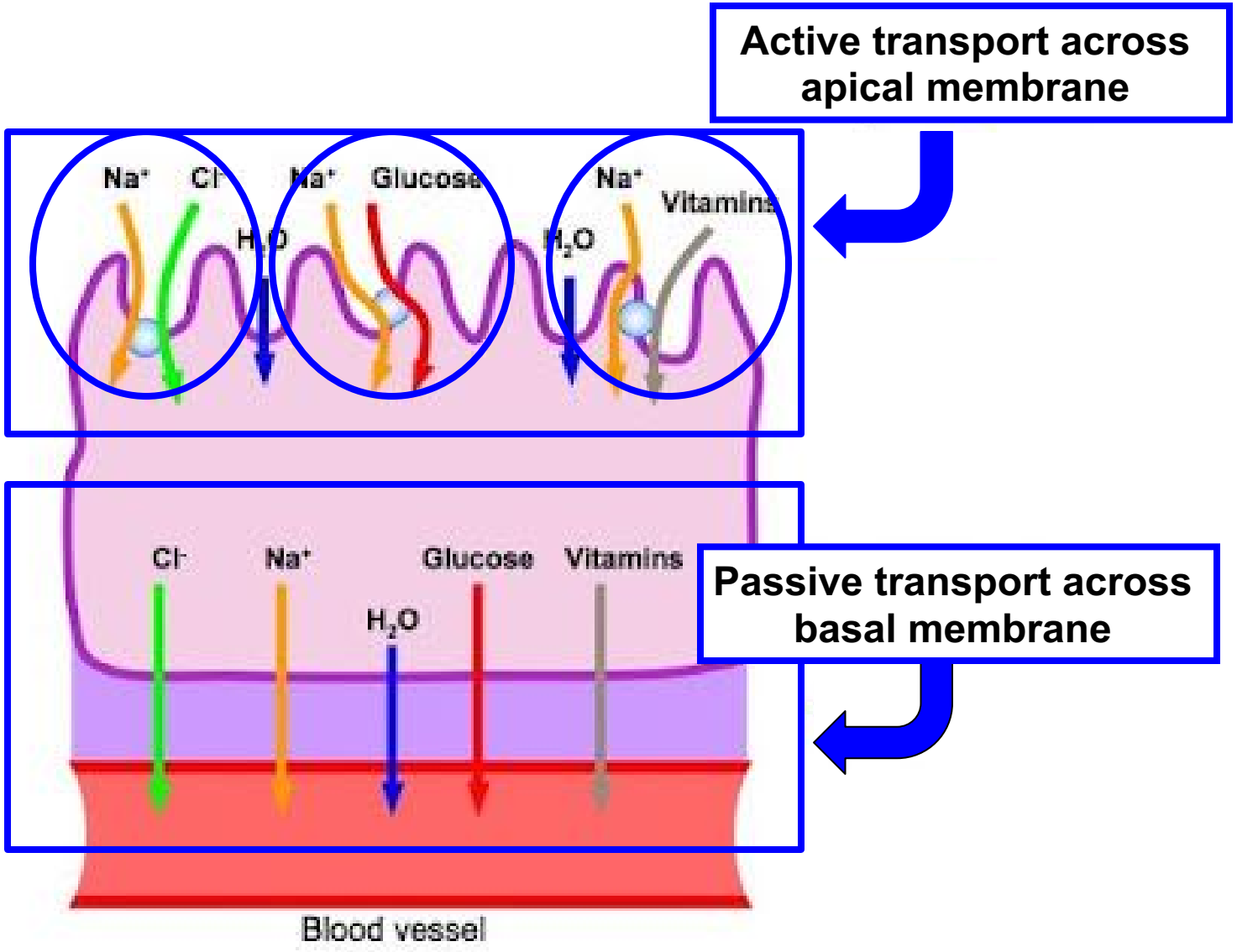
Substances that are transported across the cell membrane by **primary** active transport include ***metal ions*, *such as* Na^+, K^+, Mg^{2+}, *and* Ca^{2+}.**



Secondary active transport

(coupling or *co-transport*)

Involves the use by a molecule of the same door opened for another moving molecule (Na+).

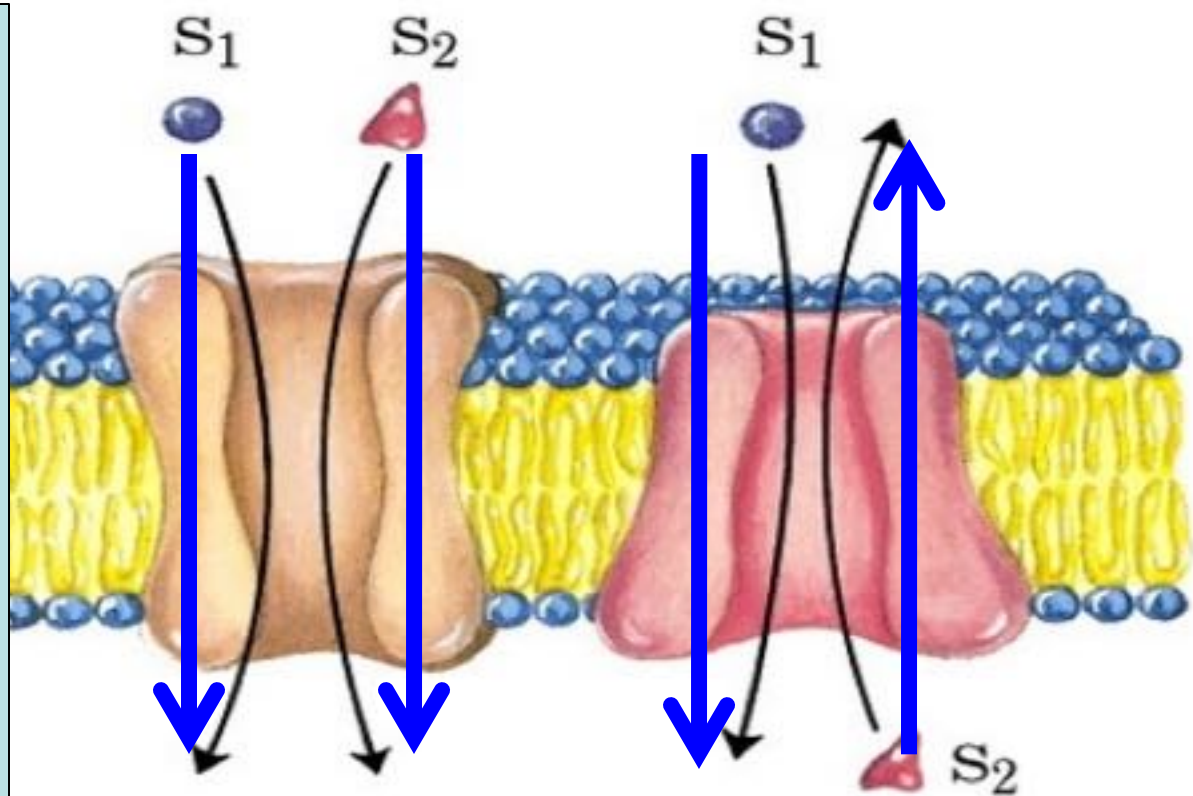

Active transport across apical membrane
Na+
Cl-
Na+
Glucose
Na+
Vitamins
H2O
H2O
Cl-
Na+
Glucose
Vitamins
H2O
Passive transport across basal membrane
Blood vessel

Substances transported by **secondary** active transport are

sugars, most amino acids, organic acids, and a number of inorganic ions, such as sulfate, phosphate, and potassium.

transport of two molecules across a membrane in the **same** direction	transport of two different molecules or ions in **opposite** directions

co-transport

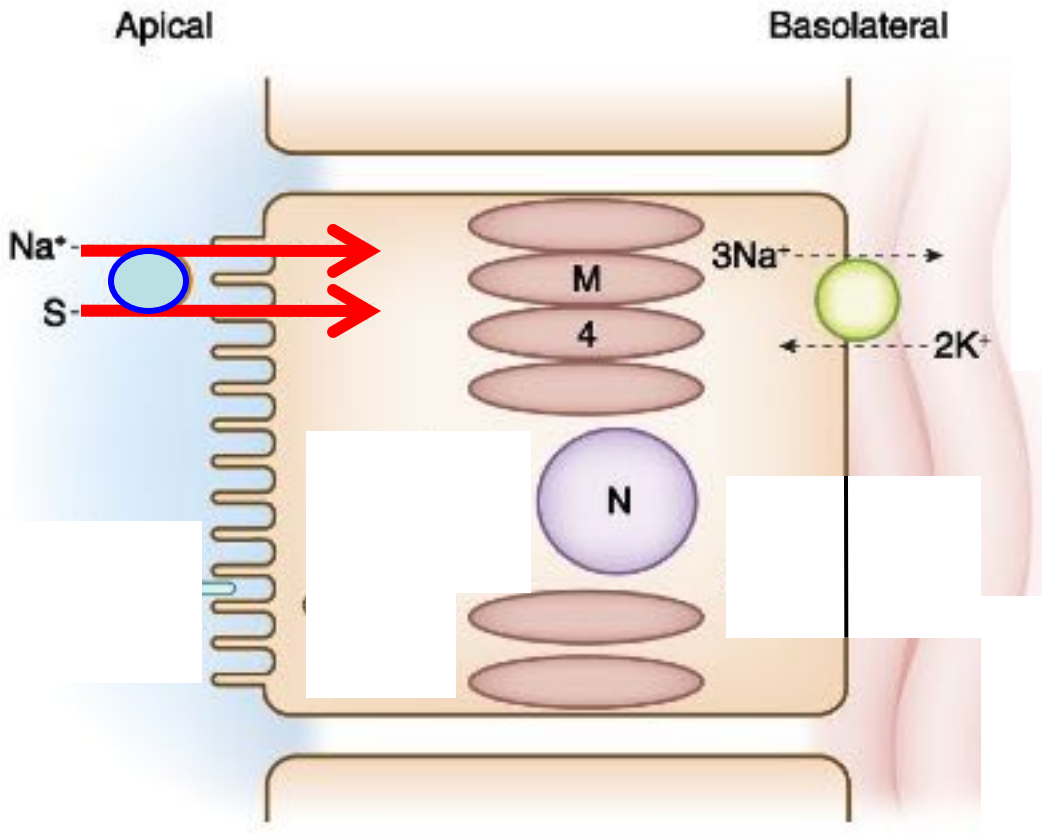


Symporter

Antiporter

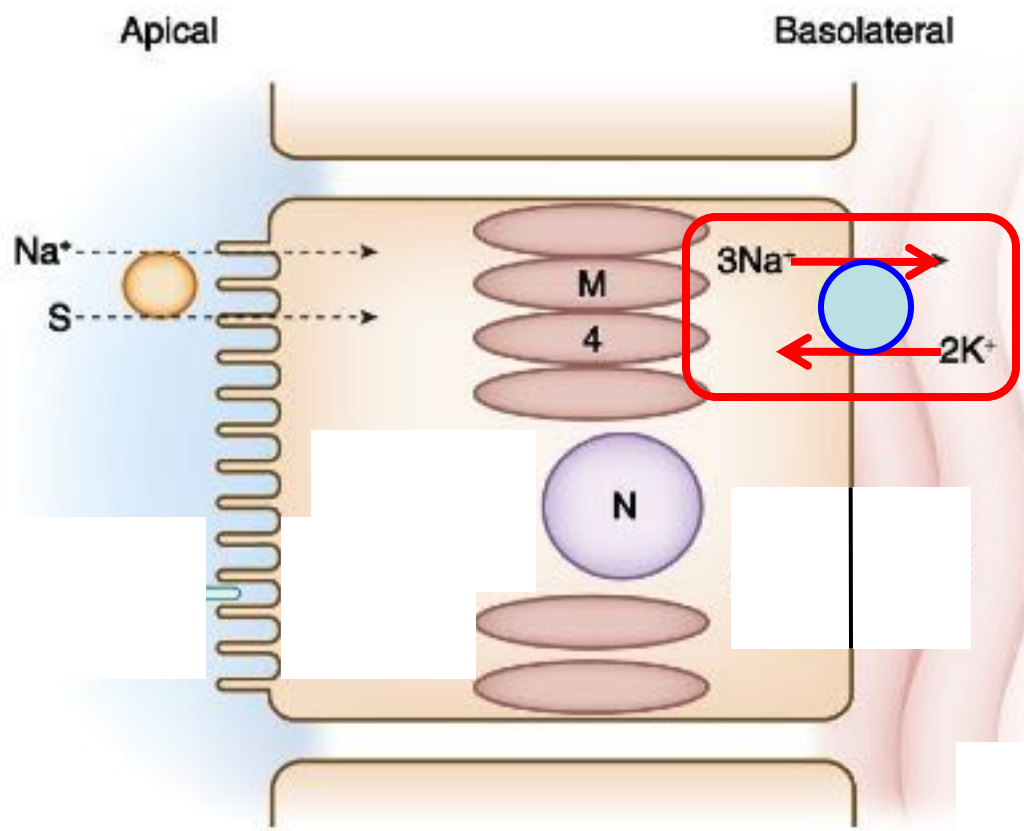
Co-transport

Secondary active transport



Reabsorption in the PCT
depend mainly on
coupling *with sodium*
*(**co**-transporting)*

So, Sodium entering the tubular cell drags with it the substance(S) to be recovered



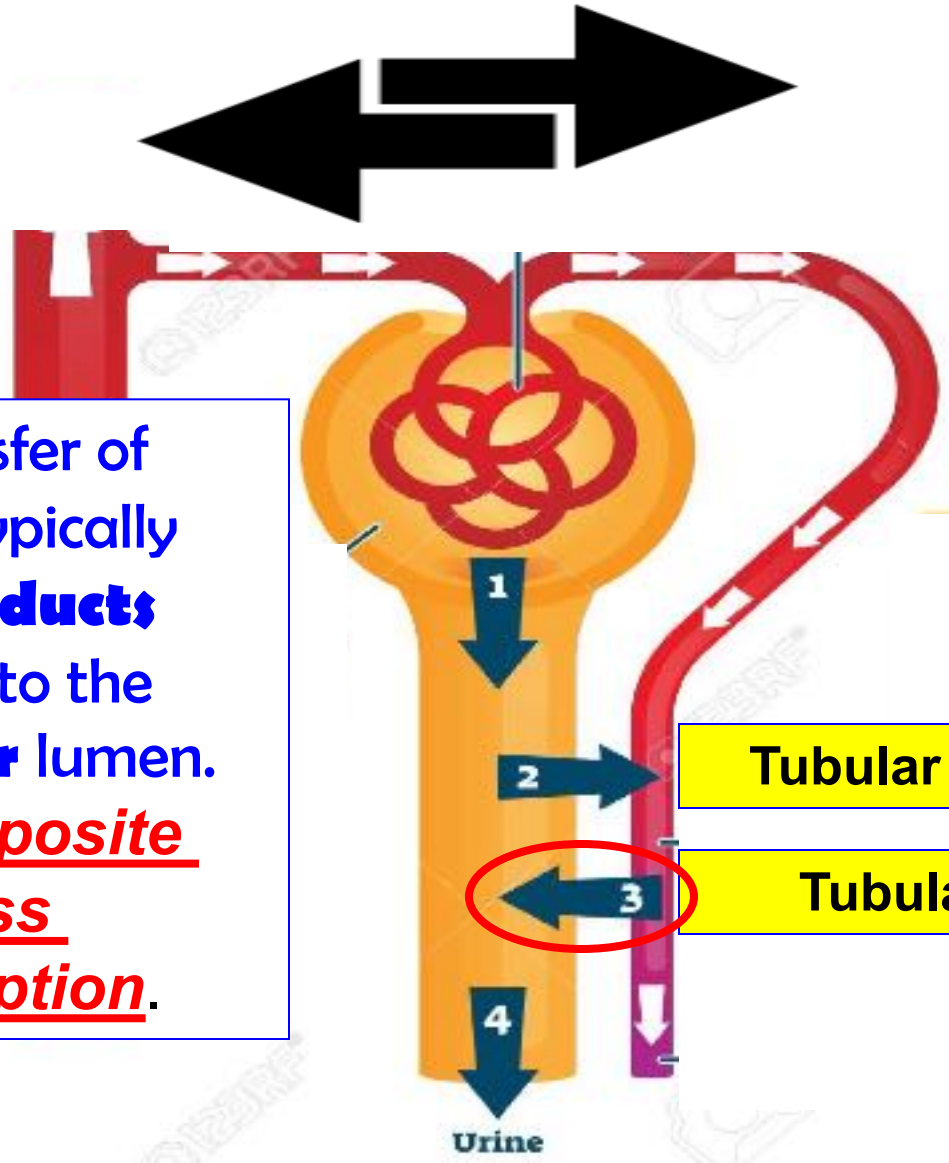
<u>For this to continue</u>, sodium **cannot** be left to build up inside the epithelial cells of the proximal tubule wall.

Tubular secretion

Tubular secretion

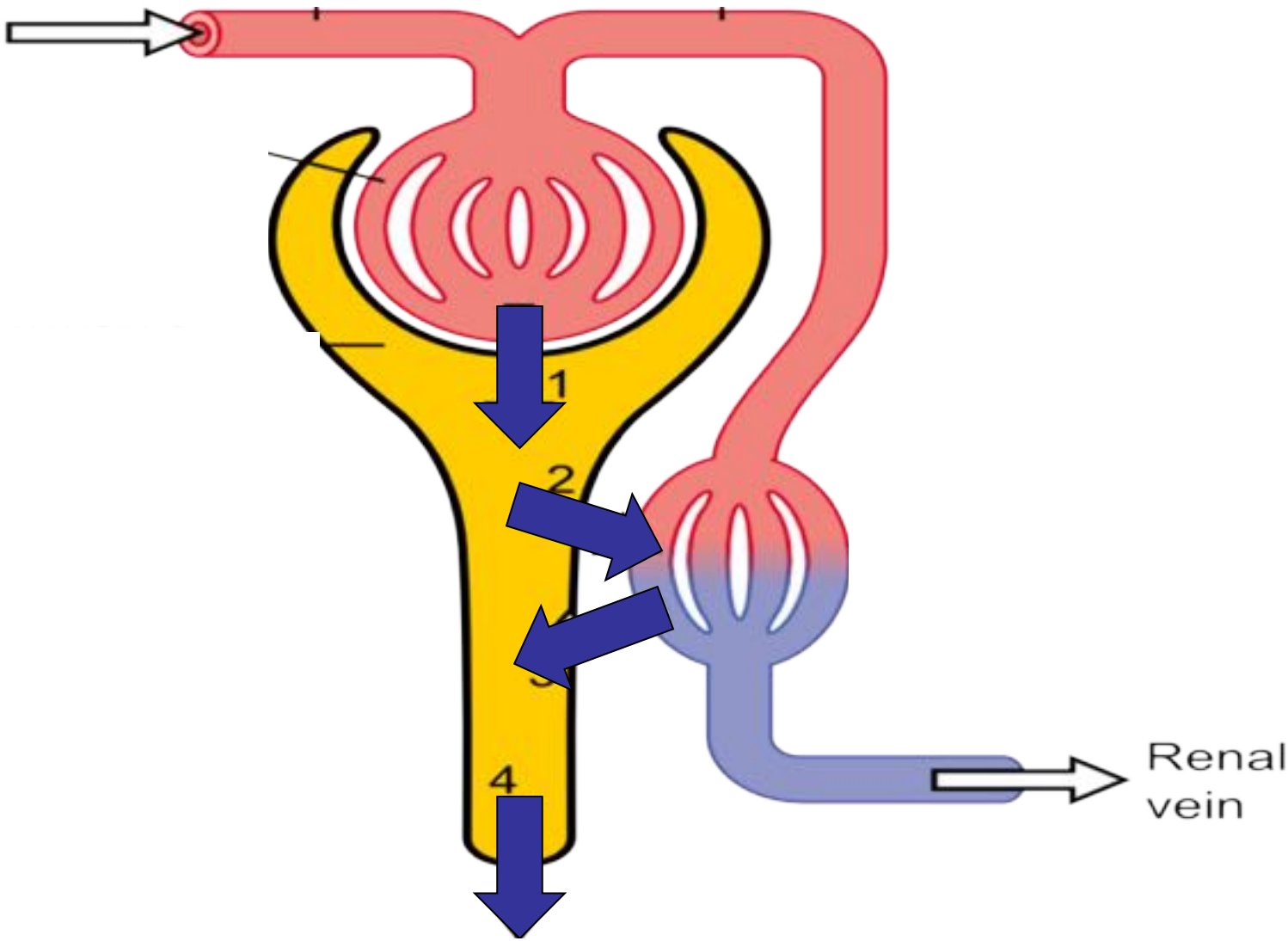
is the transfer of materials, typically **waste products** from blood to the **renal tubular** lumen.

it is the opposite process of reabsorption.



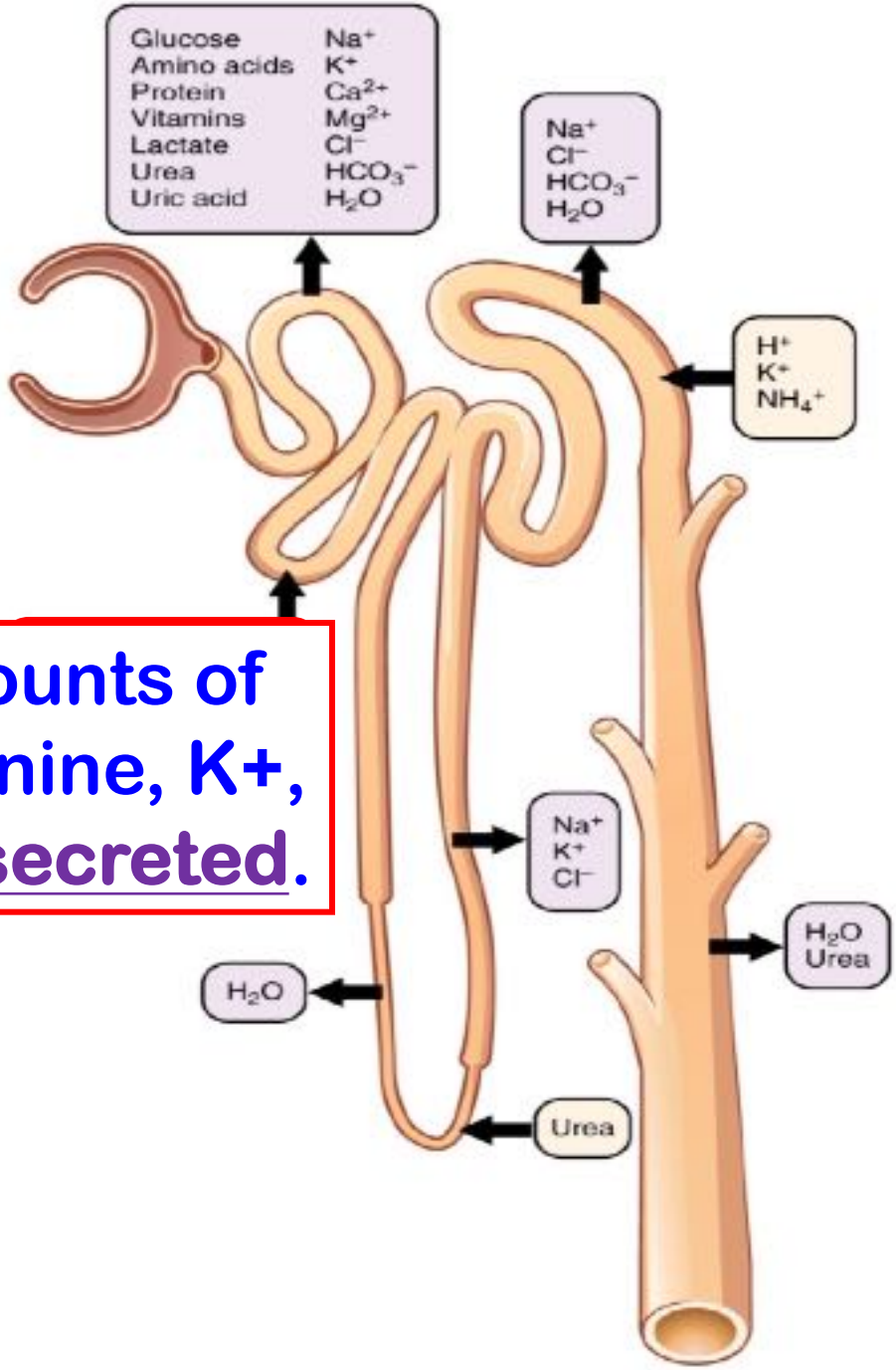
Tubular Reabsorption

Tubular Secretion



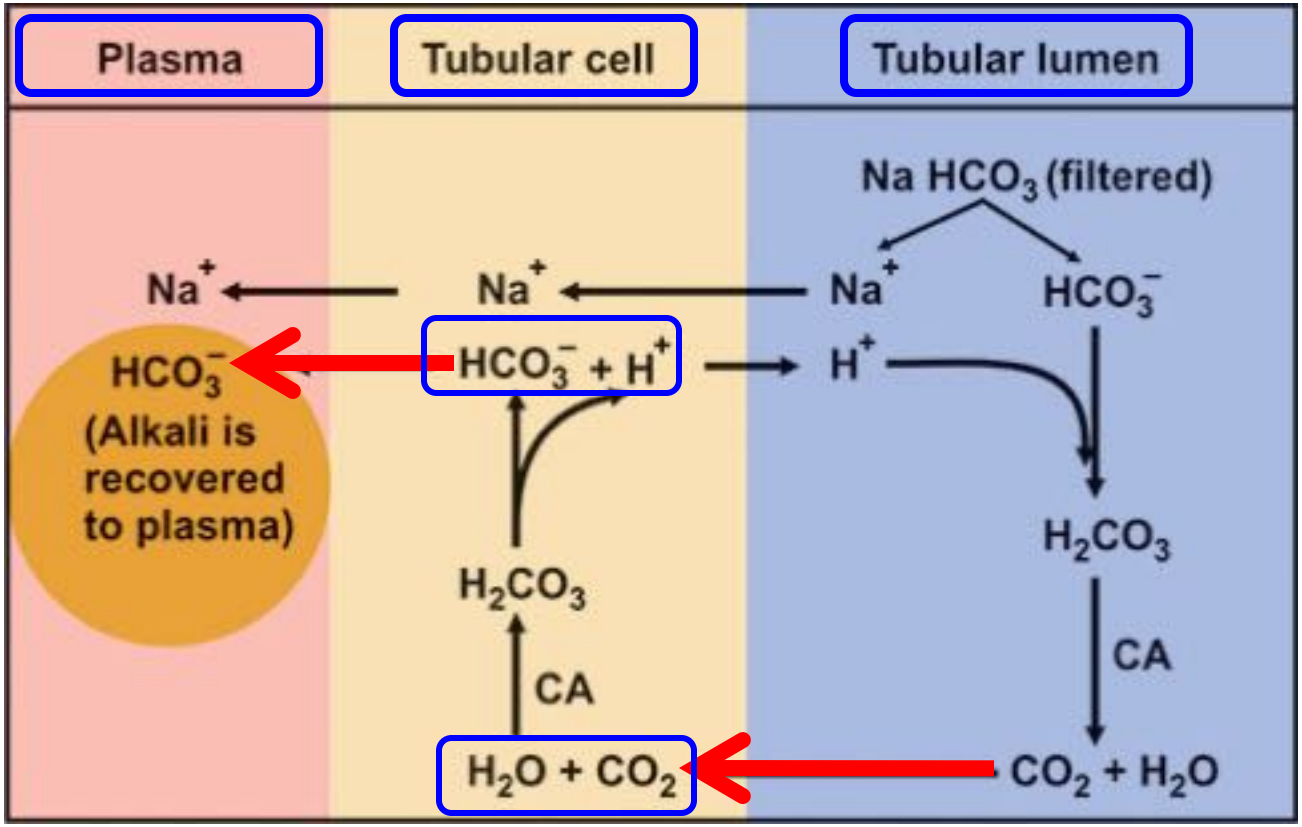
Excretion = **Filtration** - **Reabsorption + Secretion**

In the PCT, large amounts of urea, uric acid, creatinine, K+, and some drugs, are <u>secreted</u>.



Tubular secretion occurs by both active transport and passive diffusion

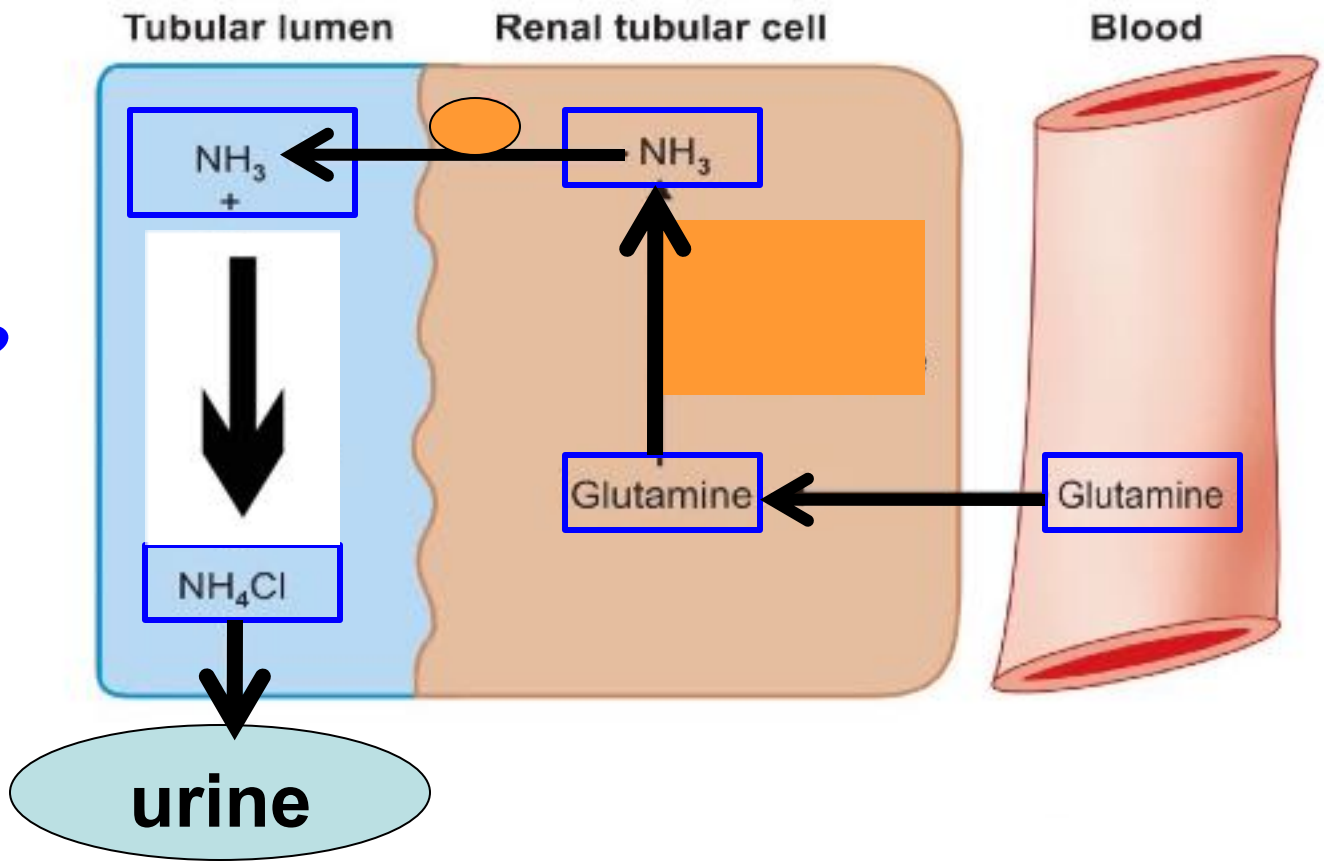
Tubular Synthesis



The kidneys have **two** major functions in acid-base homeostasis,

1. **reabsorption** of filtered bicarbonate and **synthesis** of new bicarbonate.

acid-base homeostasis



2. **synthesis** of ammonia (NH3)
in the **PCT** from glutamine,
to be excreted in urine as an acid load (NH4Cl)

In Summary

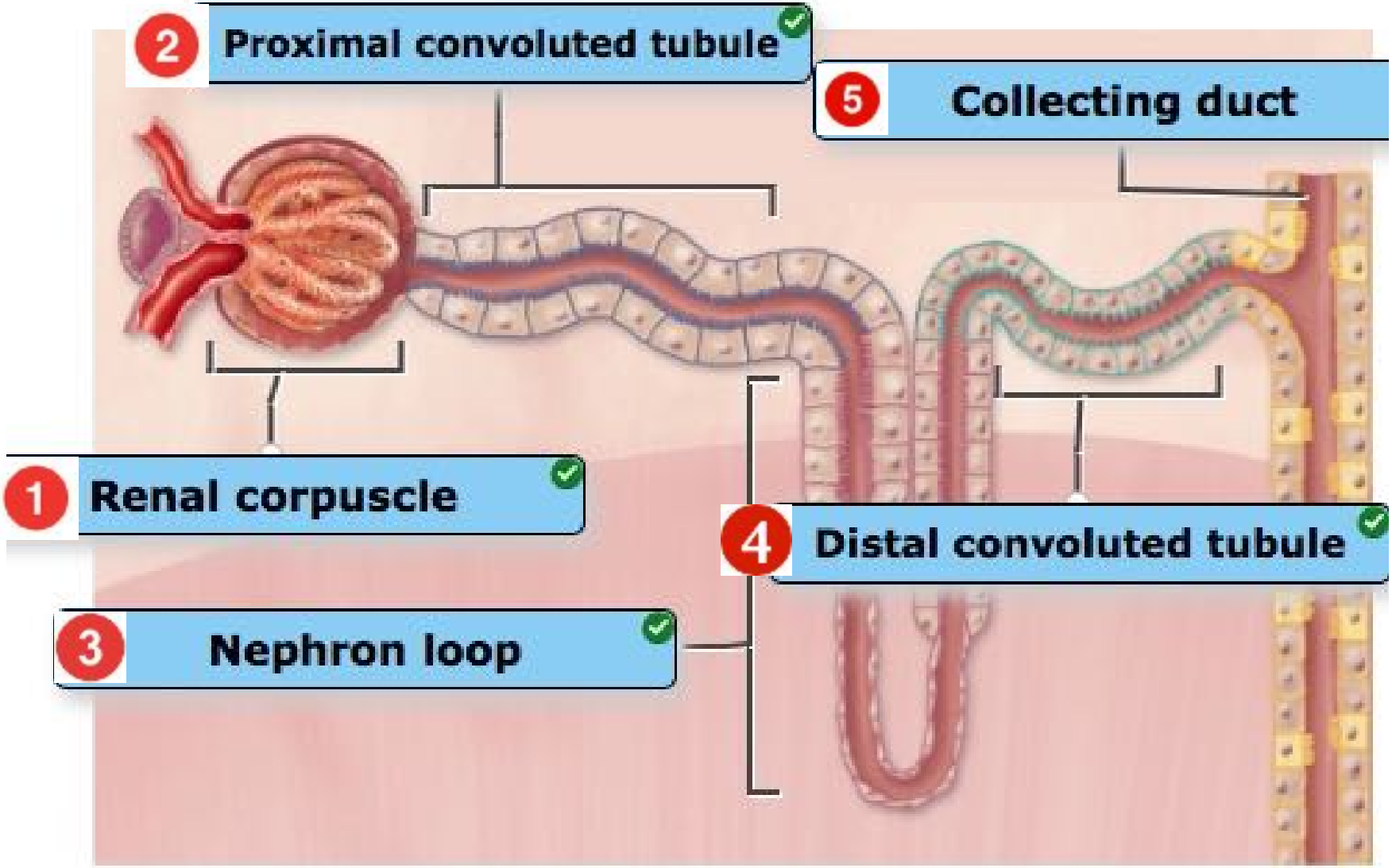
Tubular Functions

Reabsorption

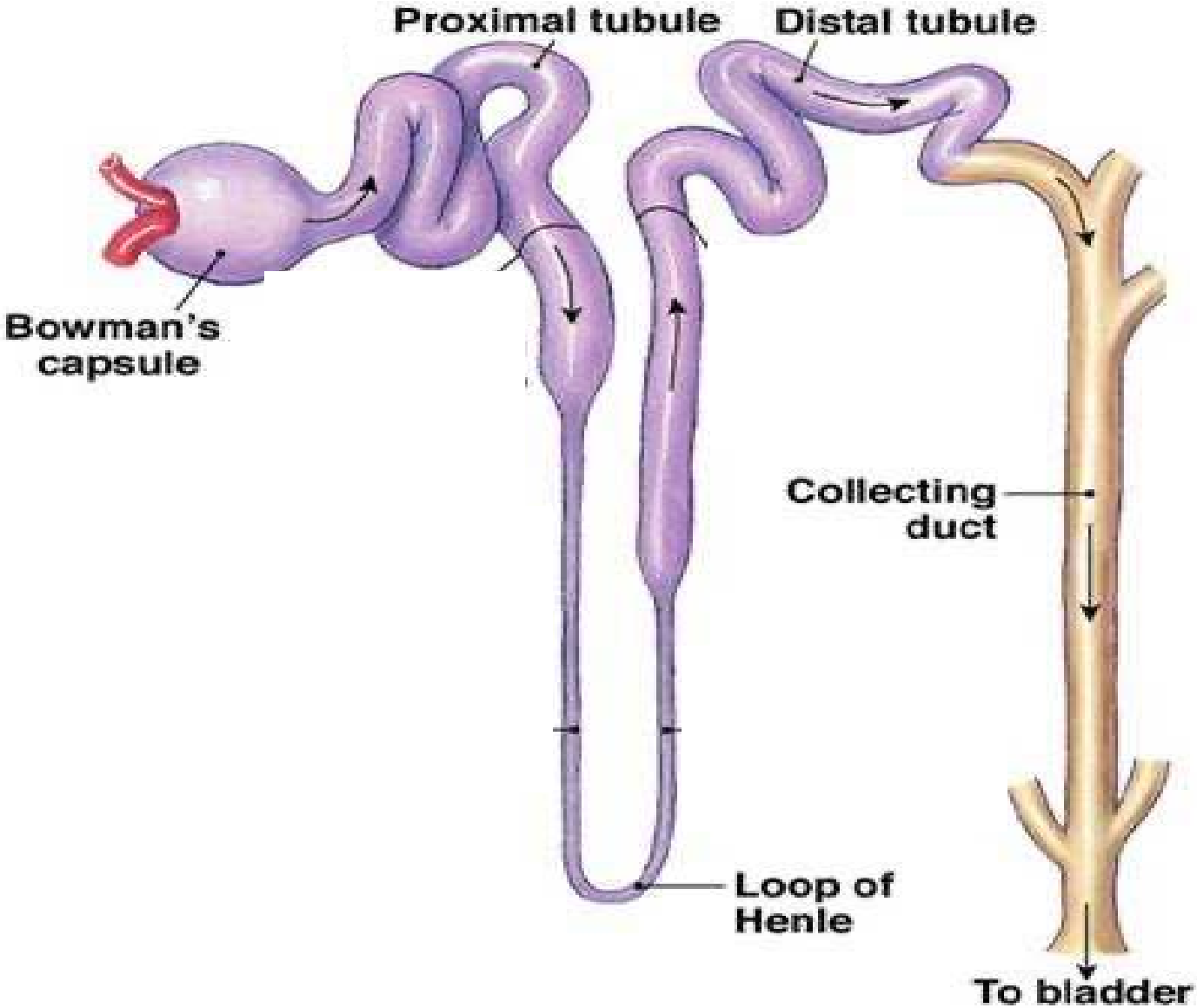
Secretion
(waste products)

Synthesis
(HCO_3 & NH_3)

NOW



Nephrons are divided into **five** segments.



Each of these segments has got a Certain job to perform.

to

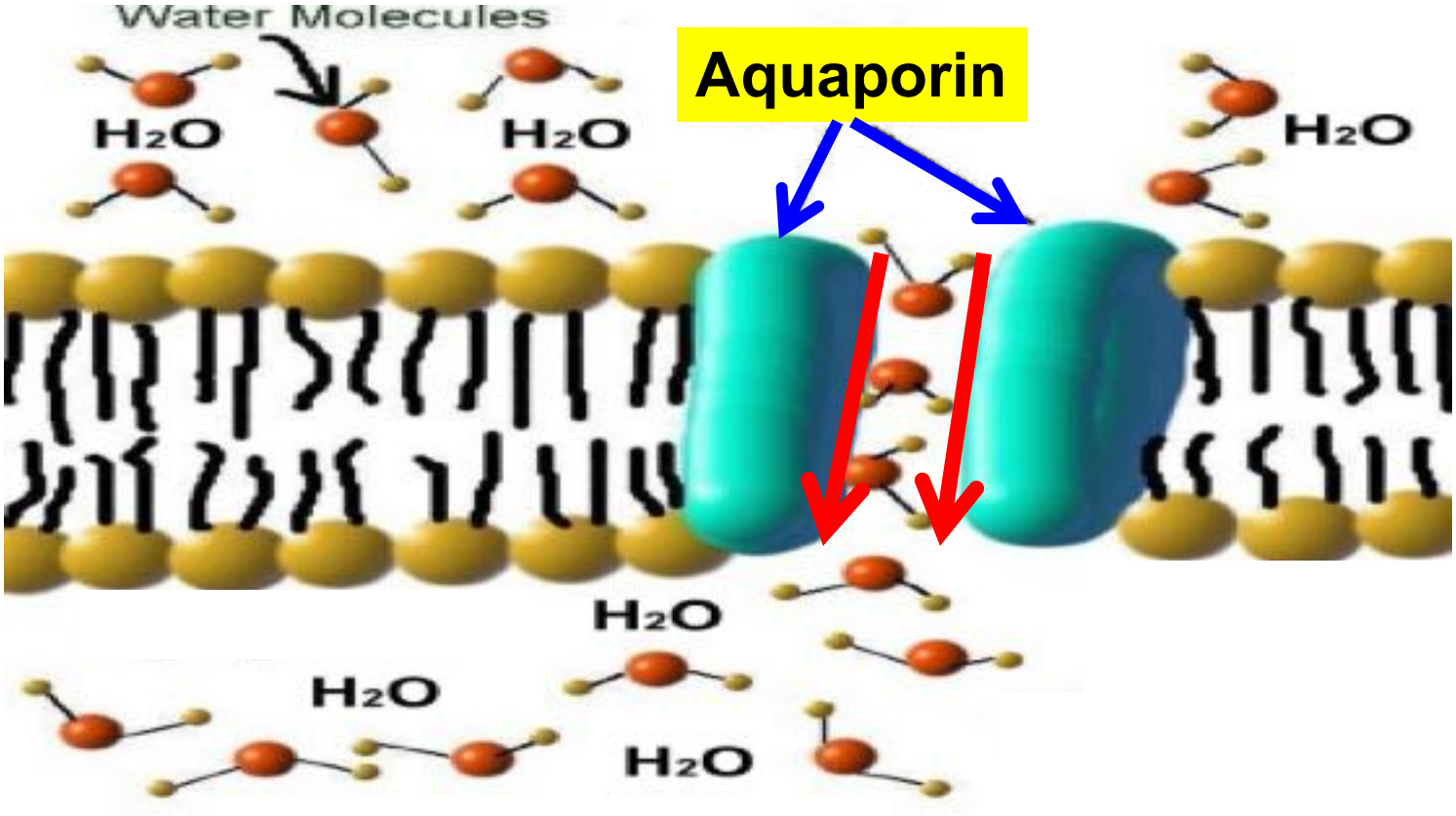
ACHIEVE

Water balance
Electrolyte balance
Acid-Base balance

&
Waste elimination

Water balance

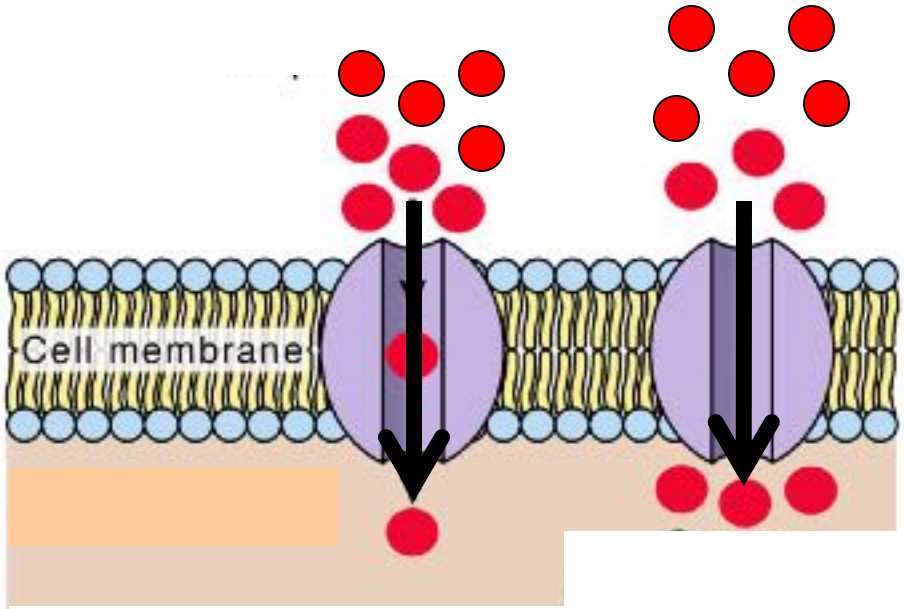
Introduction

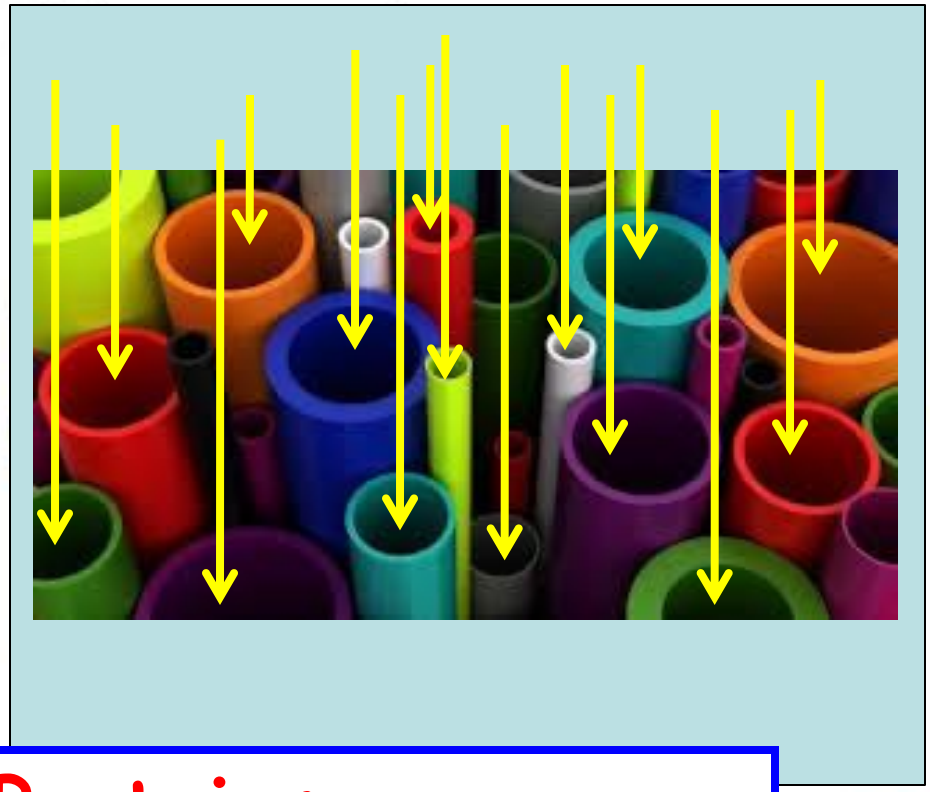


Water reabsorption by the kidney requires the presence in the nephron epithelium of *water channels* **(aquaporins)**

Facilitated diffusion

Do you remember the CHANNELS ?





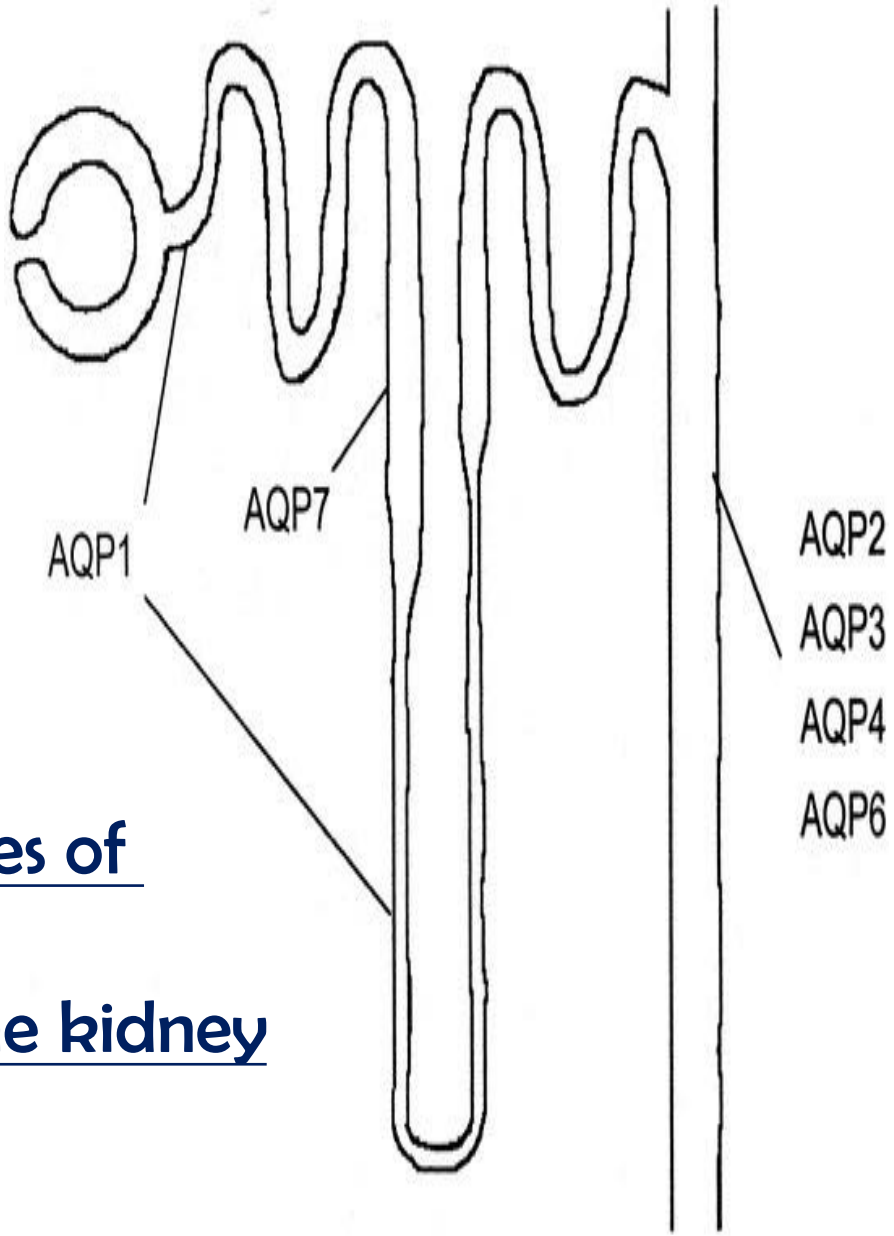
Channel Proteins

Passive

Water permeation through aquaporins is
a passive process
that follows the direction of
osmotic pressure across the membrane.

Wherever water is moving,
an aquaporin is there.


AQUAPORIN
The private passage for queen water



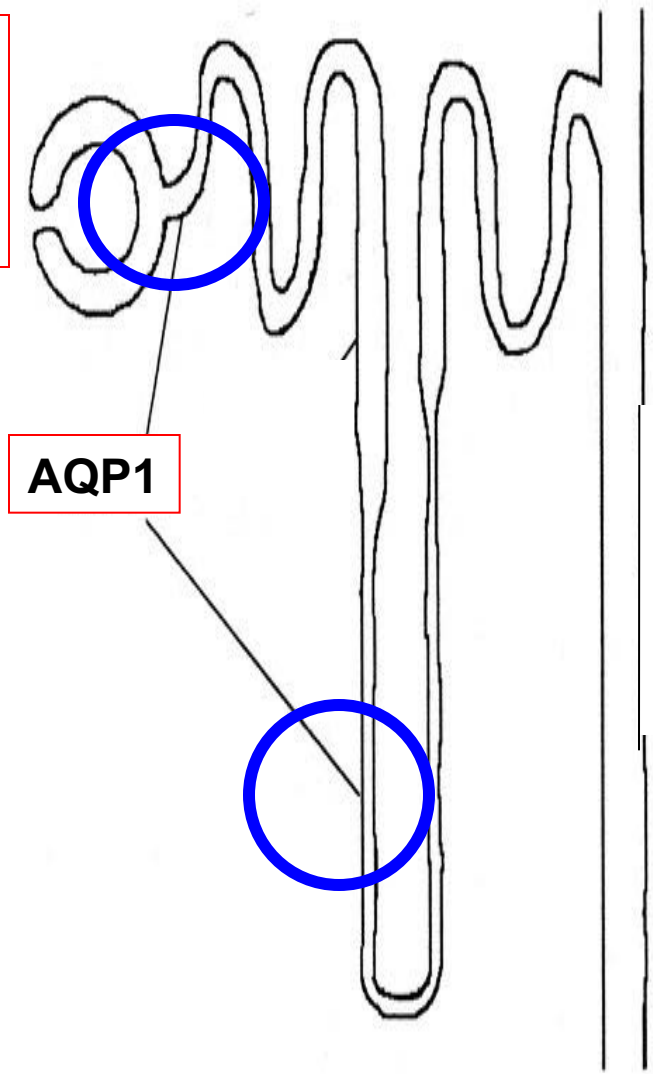
There are 13 known types of aquaporins,
six of them are located in the kidney

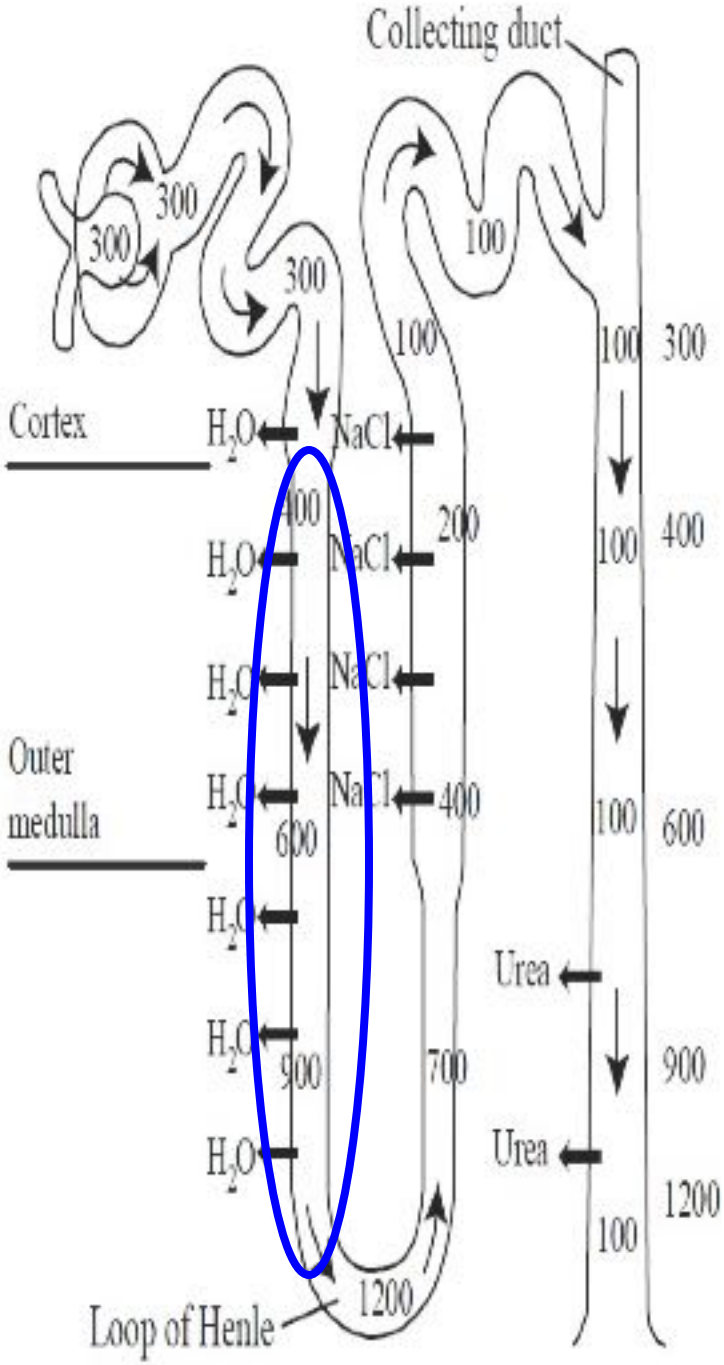
Aquaporins
(water channels)
Are responsible for **both** the
"obligatory"
water reabsorption in the
PCT, DCT, & LH,
and the
"facultative"
water reabsorption in the
CD
(under the control of **ADH**).

Obligatory water movement

Most of the water filtered at the glomerulus is reabsorbed in the PCT, and the descending limb of the loop of Henle,

Irrespective of the person's state of hydration.

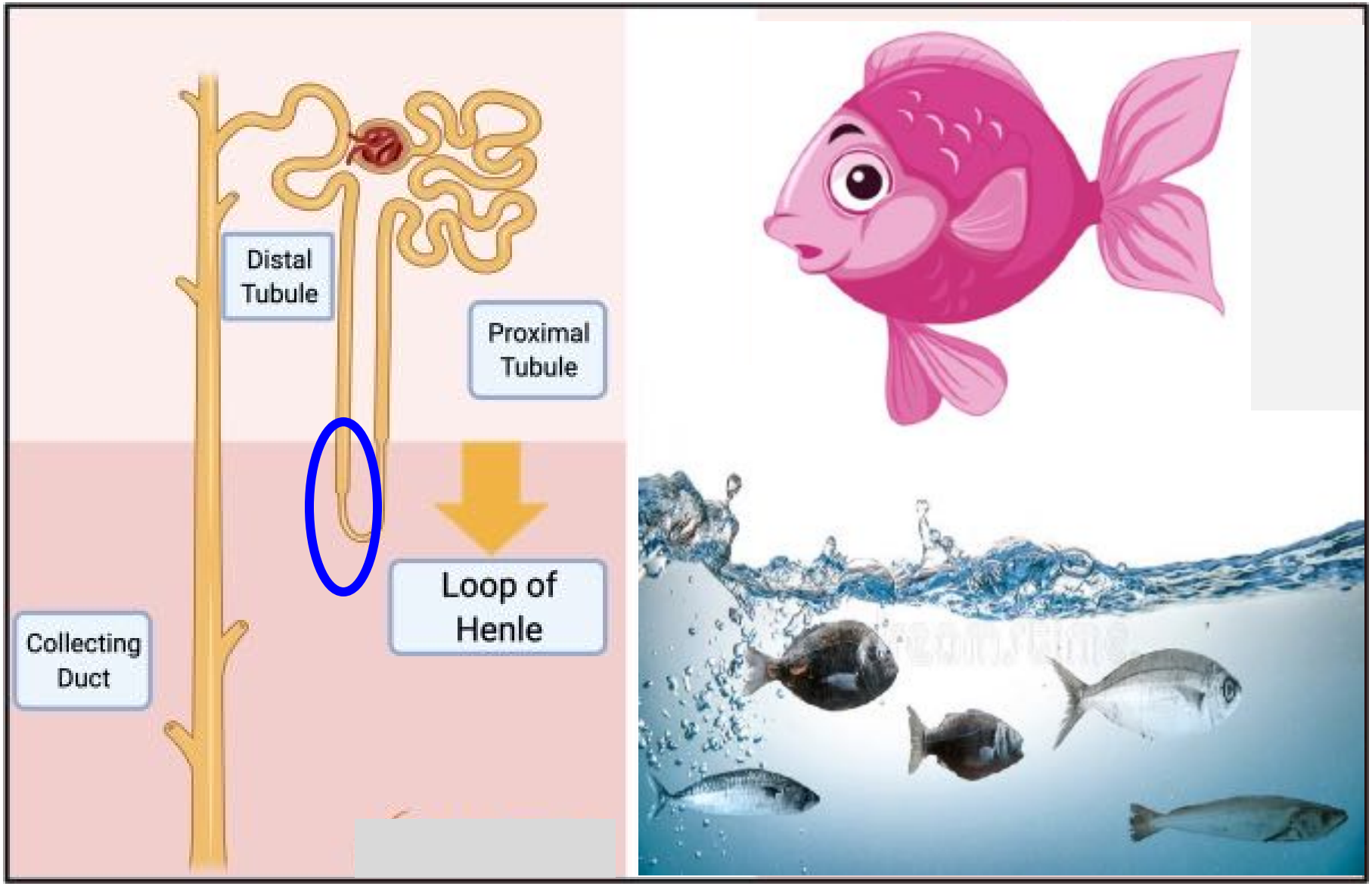




When water is scarce,

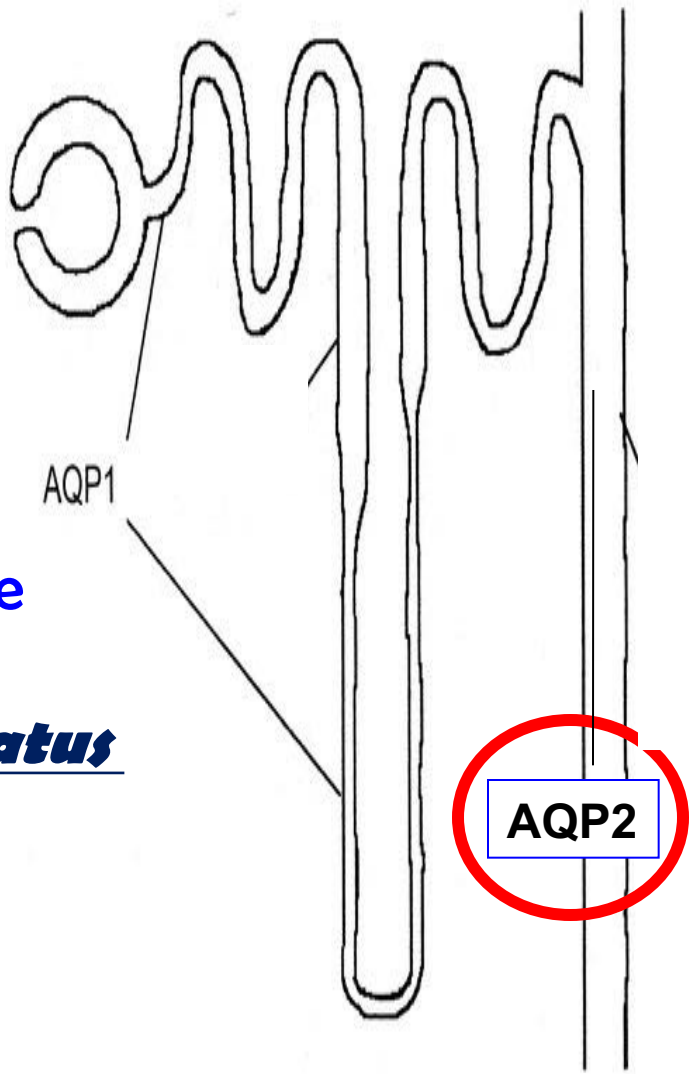
a longer descending limb is crucial for a more claim-back of water out of the filtrate.

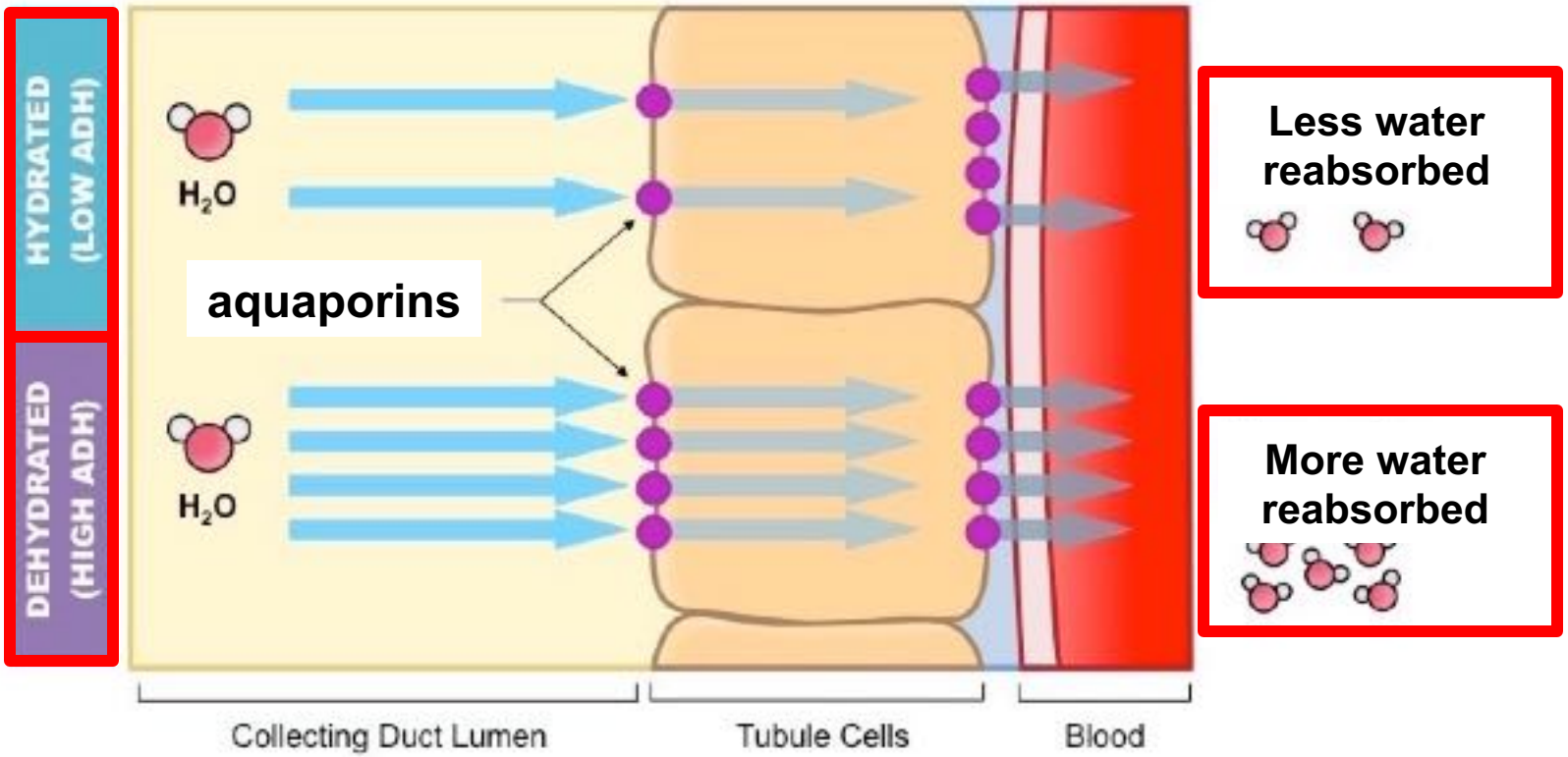
But when water is all around, a short loop is enough.



Facultative water reabsorption

Is the water withdrawn from the Tubular fluid (pre-urine)
according to the hydration status
under the influence of
ADH



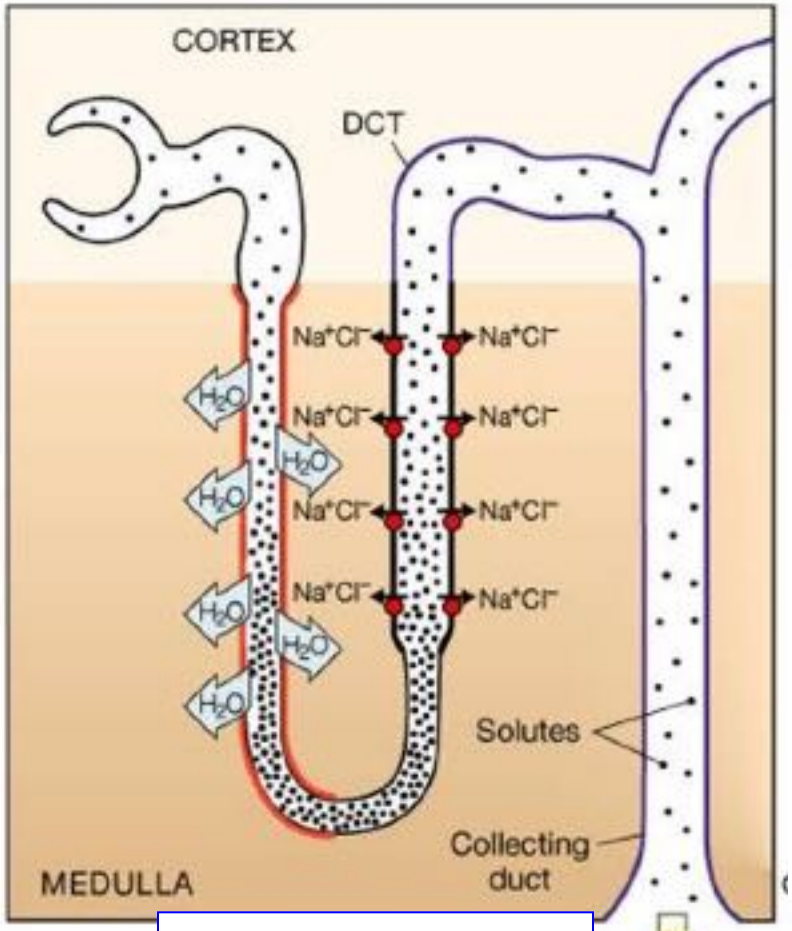


Under the control of antidiuretic hormone (ADH),

AQUAPORINS (WATER CHANNELS),

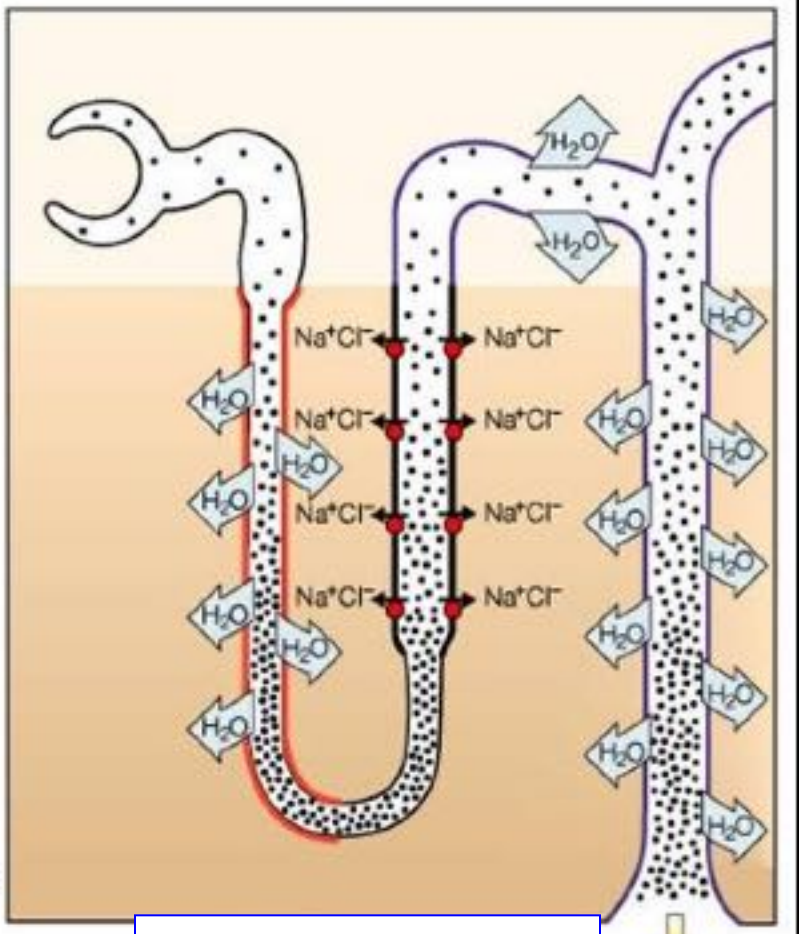
affect water reabsorption as

it passes further down in the **CD**.



Absence of ADH

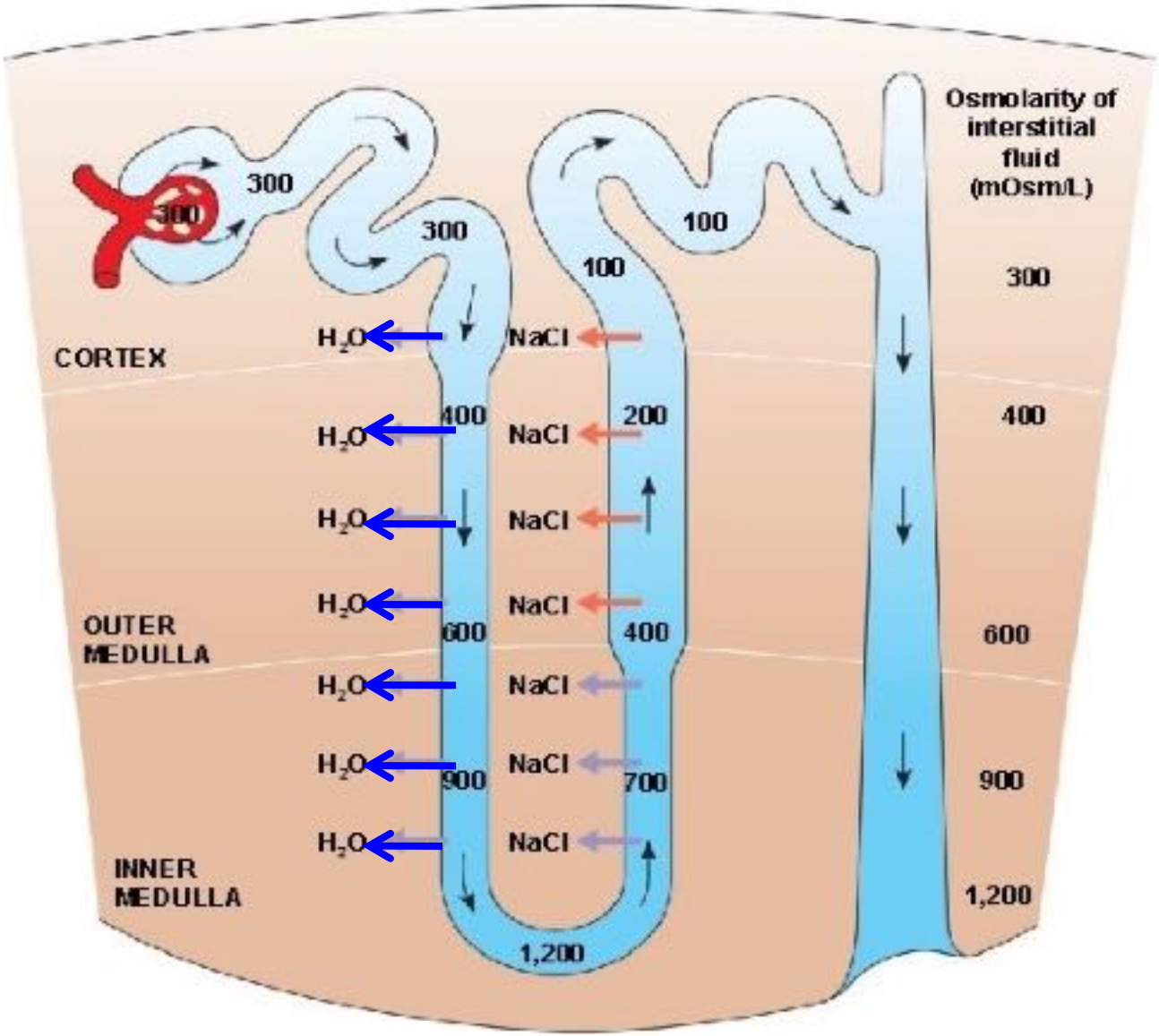
Less water absorbed, Large volume of dilute urine



Presence of ADH

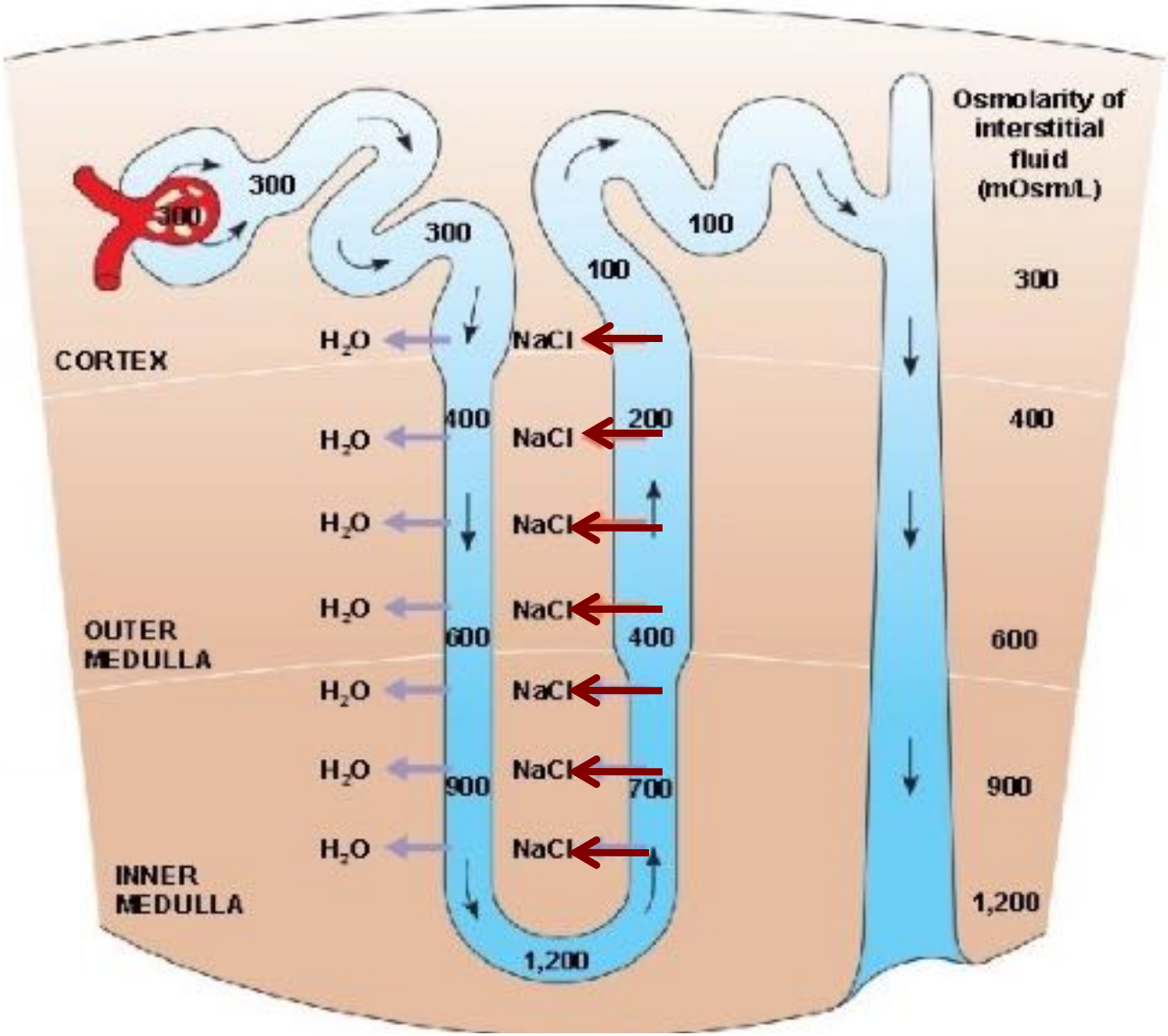
More water absorbed, Small volume of concentrated urine

The **CD** is normally **impermeable** to water, but it becomes **PERMEABLE** to it in the presence of **ADH**.



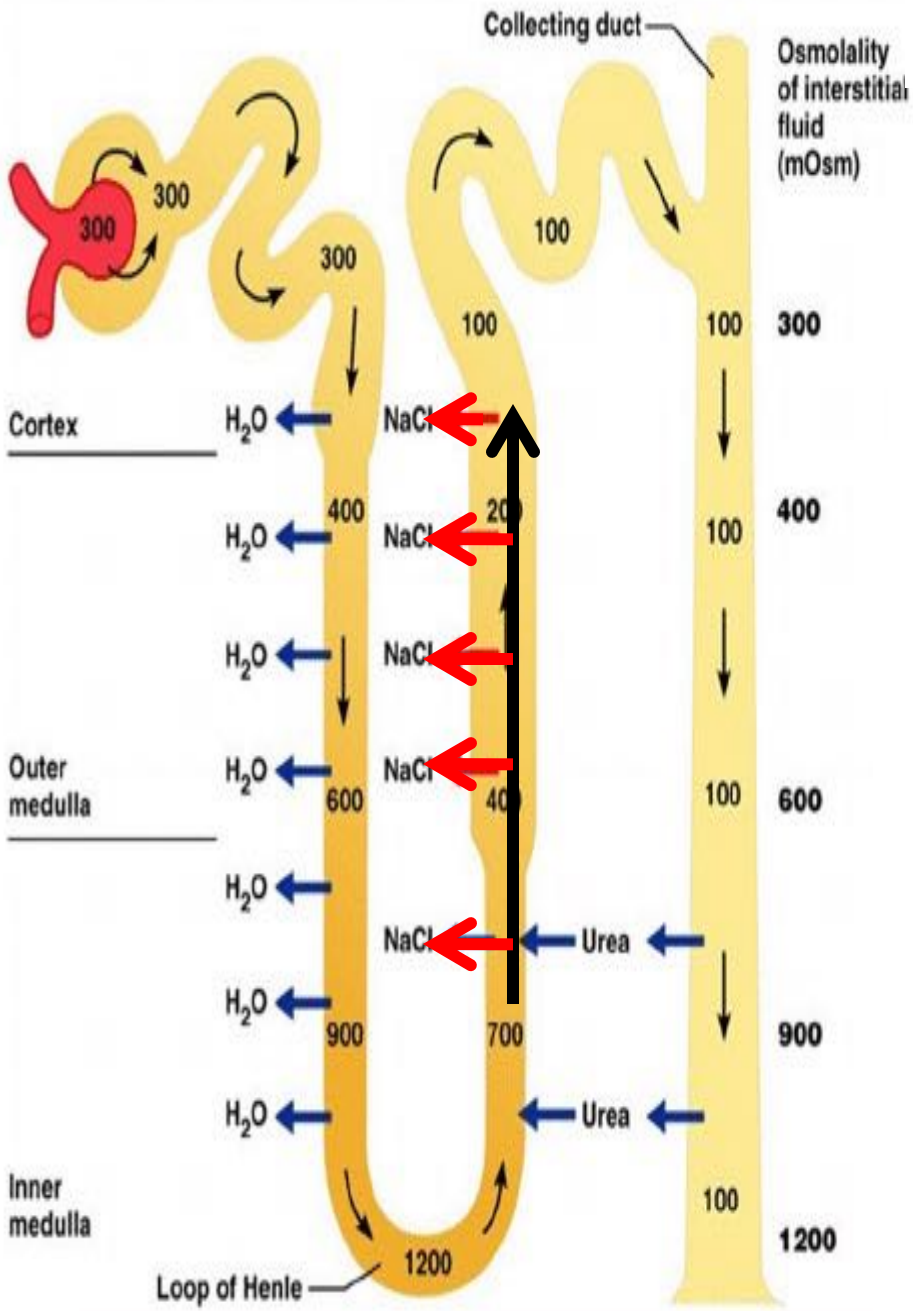
The Descending limb is

PERMEABLE to WATER, but **NOT** SALT.



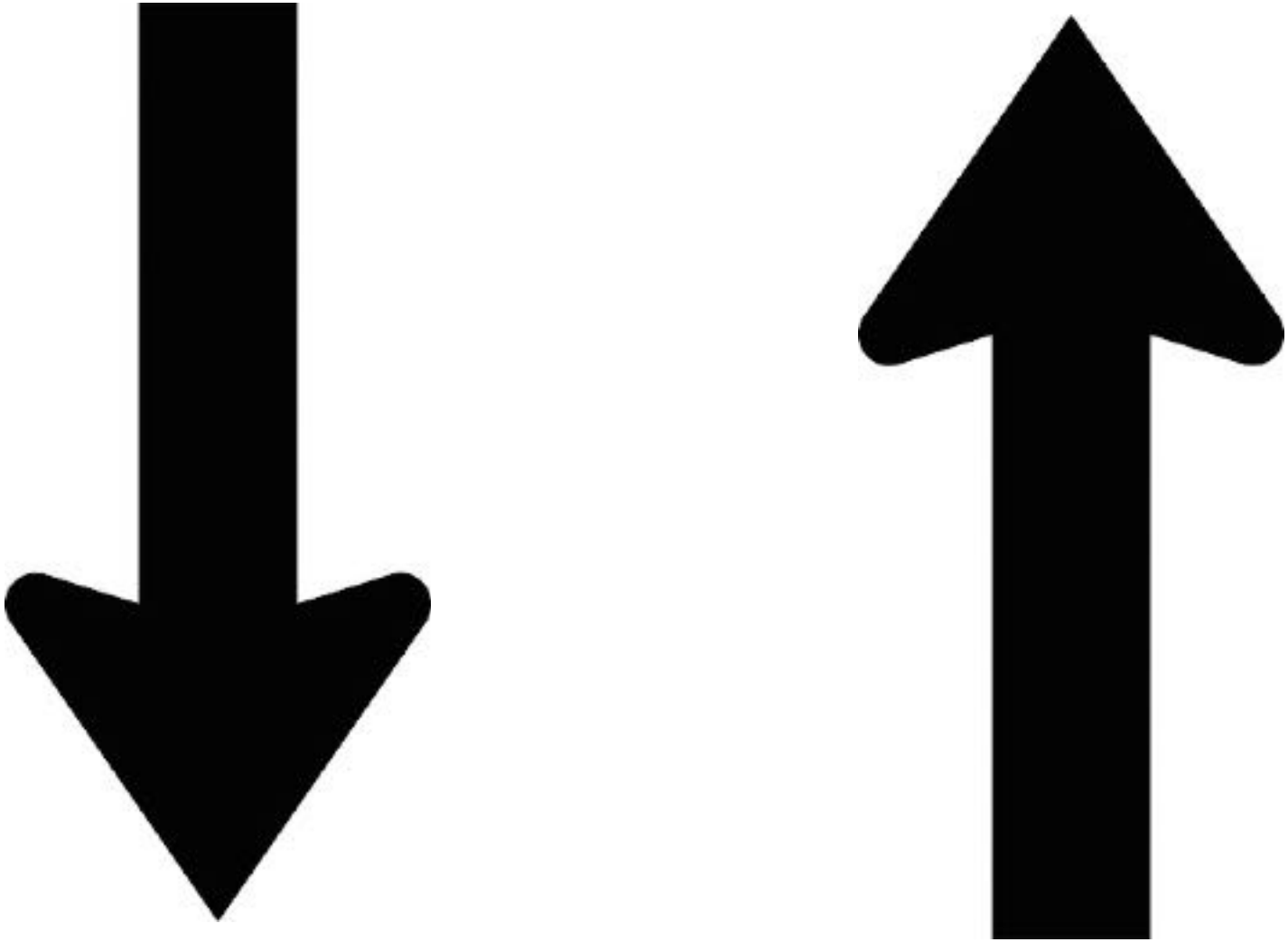
The Ascending Loop is

PERMEABLE to SALT but **NOT** WATER;



Consequently,

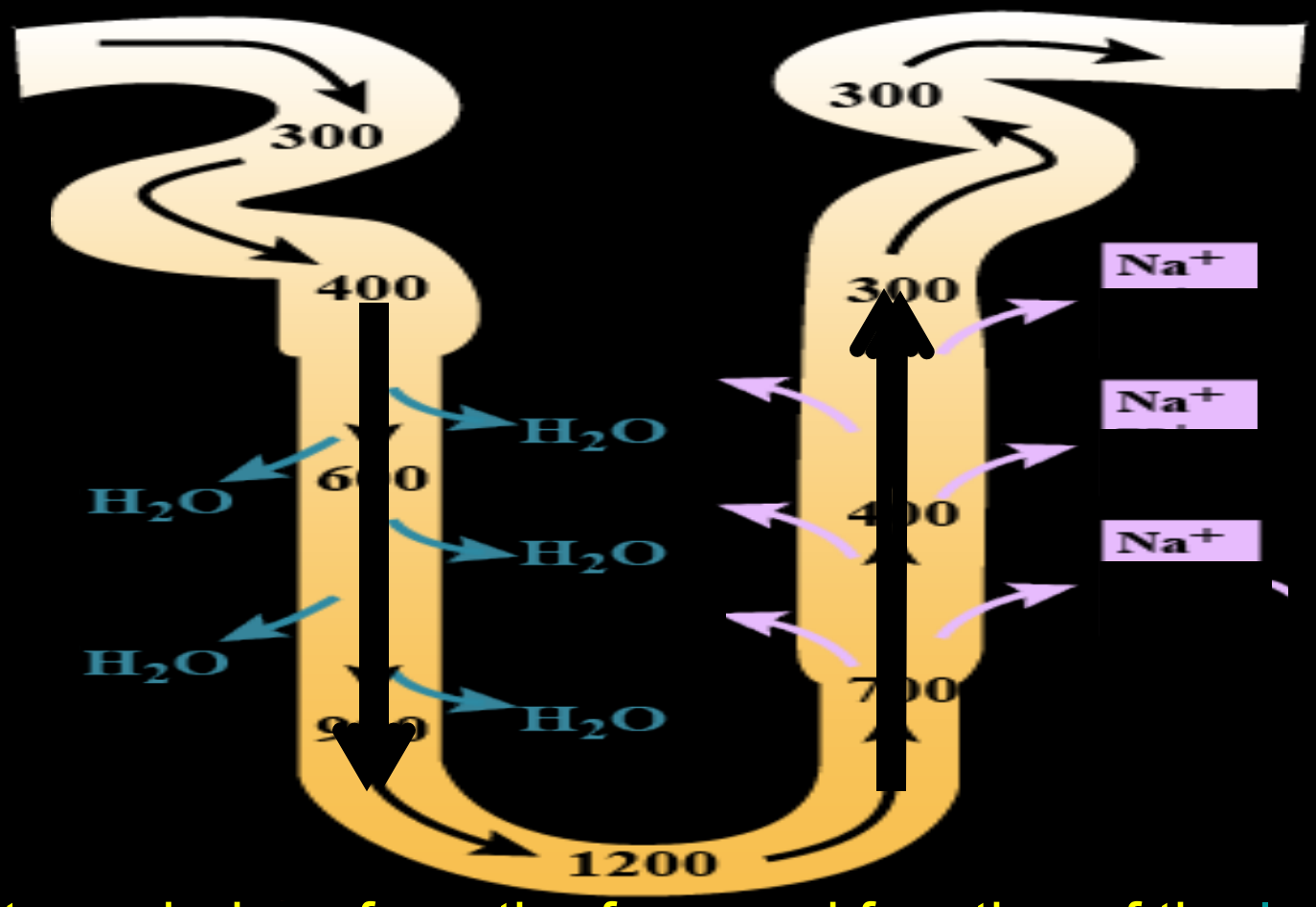
as the urine goes up, Na+ is actively pumped out, generating a hypertonic interstitium necessary for the **countercurrent multiplier system**.



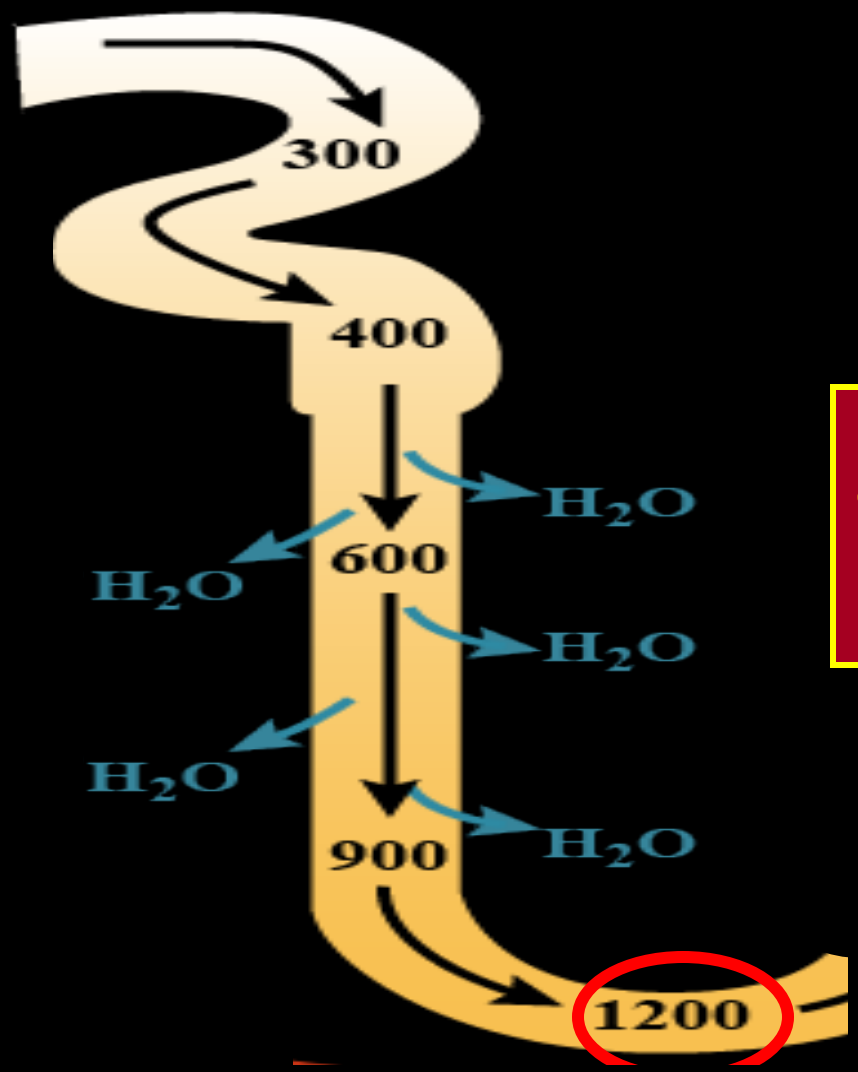
Countercurrent mechanism

Countercurrent

What does it mean ?



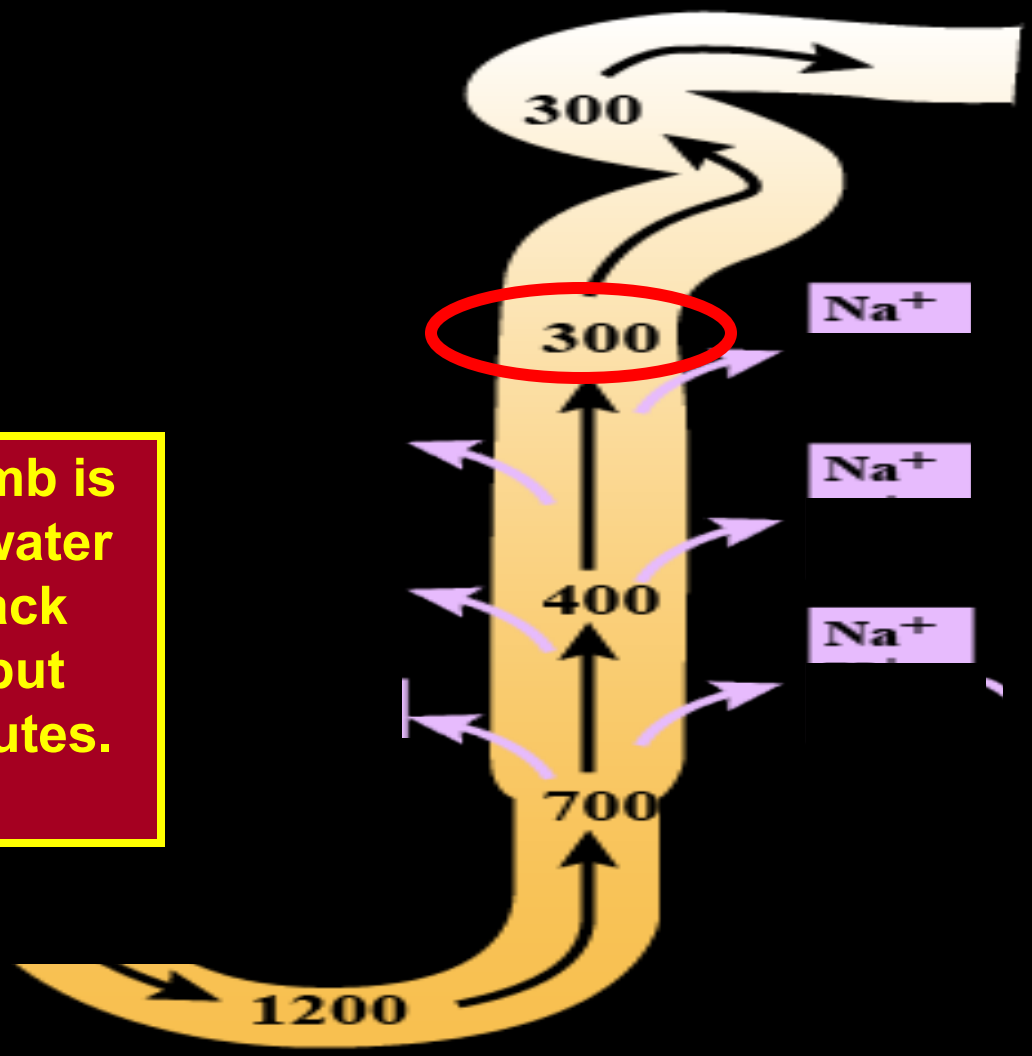
The term derives from the form and function of the loop of Henle, which consists of two parallel limbs of renal tubules, with **the current of tubular fluid in the DLH flowing against that in the ALH.**



due to the presence of aquaporin 1 , the DLH is permeable to water but impermeable to solutes.

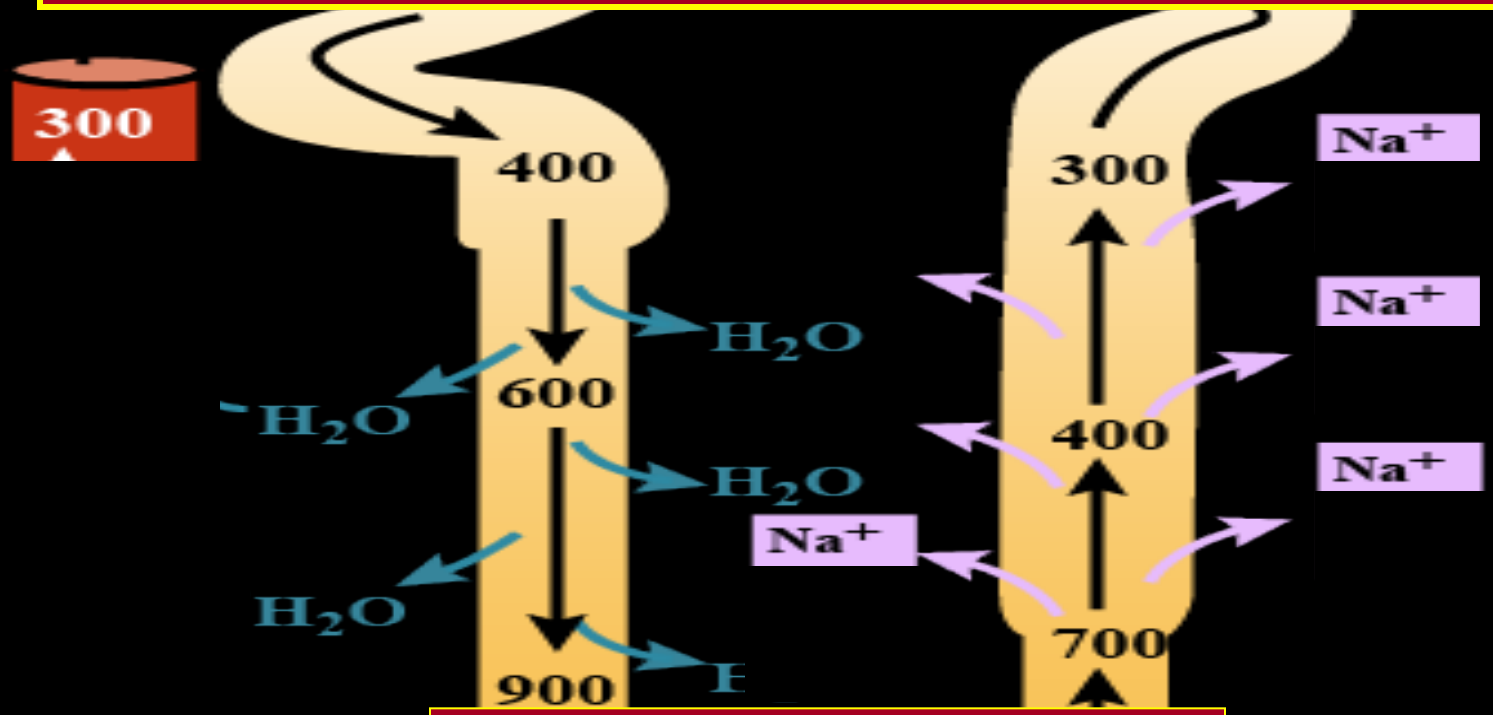
Thus, Water moves from DLH to Renal Medulla, making the filtrate hypertonic. This is the filtrate that continues to the ascending limb

The ascending limb is impermeable to water (because of a lack of aquaporin), but permeable to solutes.



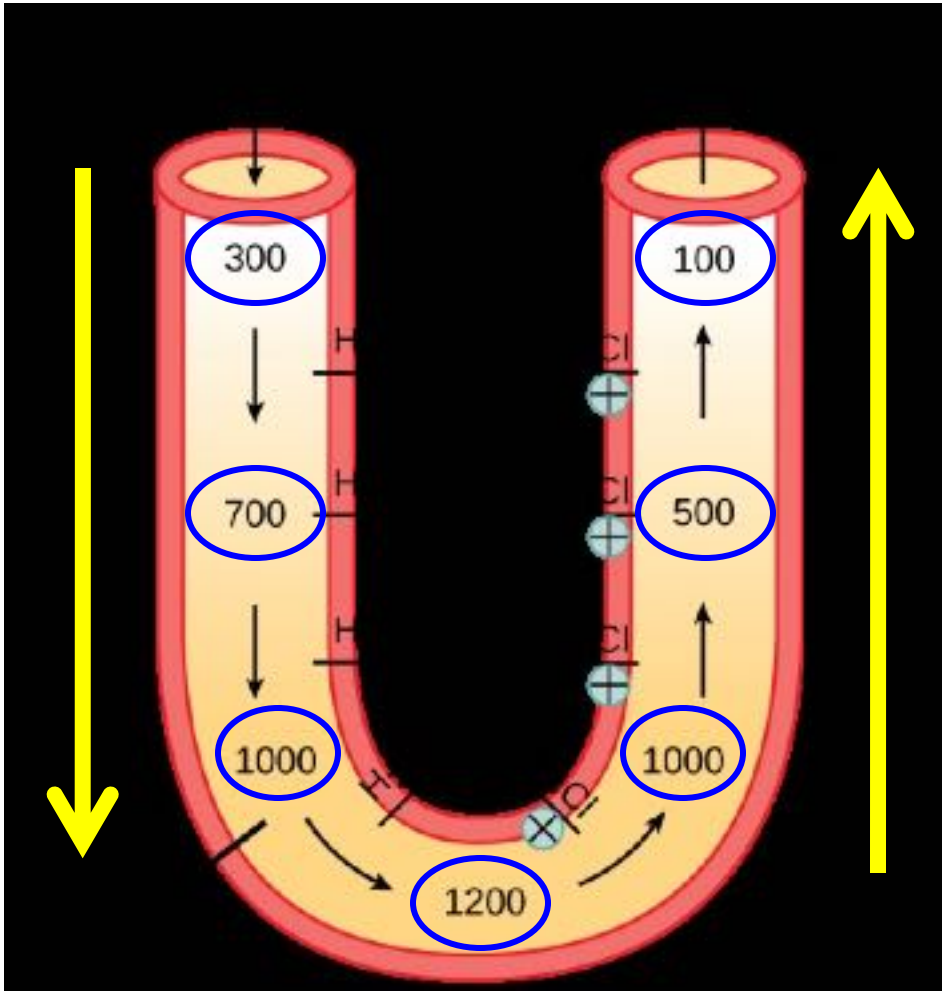
Thus, Na+ moves from ALH to Renal Medulla, making the filtrate hypotonic.

The interstitium is now "salty" or hypertonic, and will attract water.



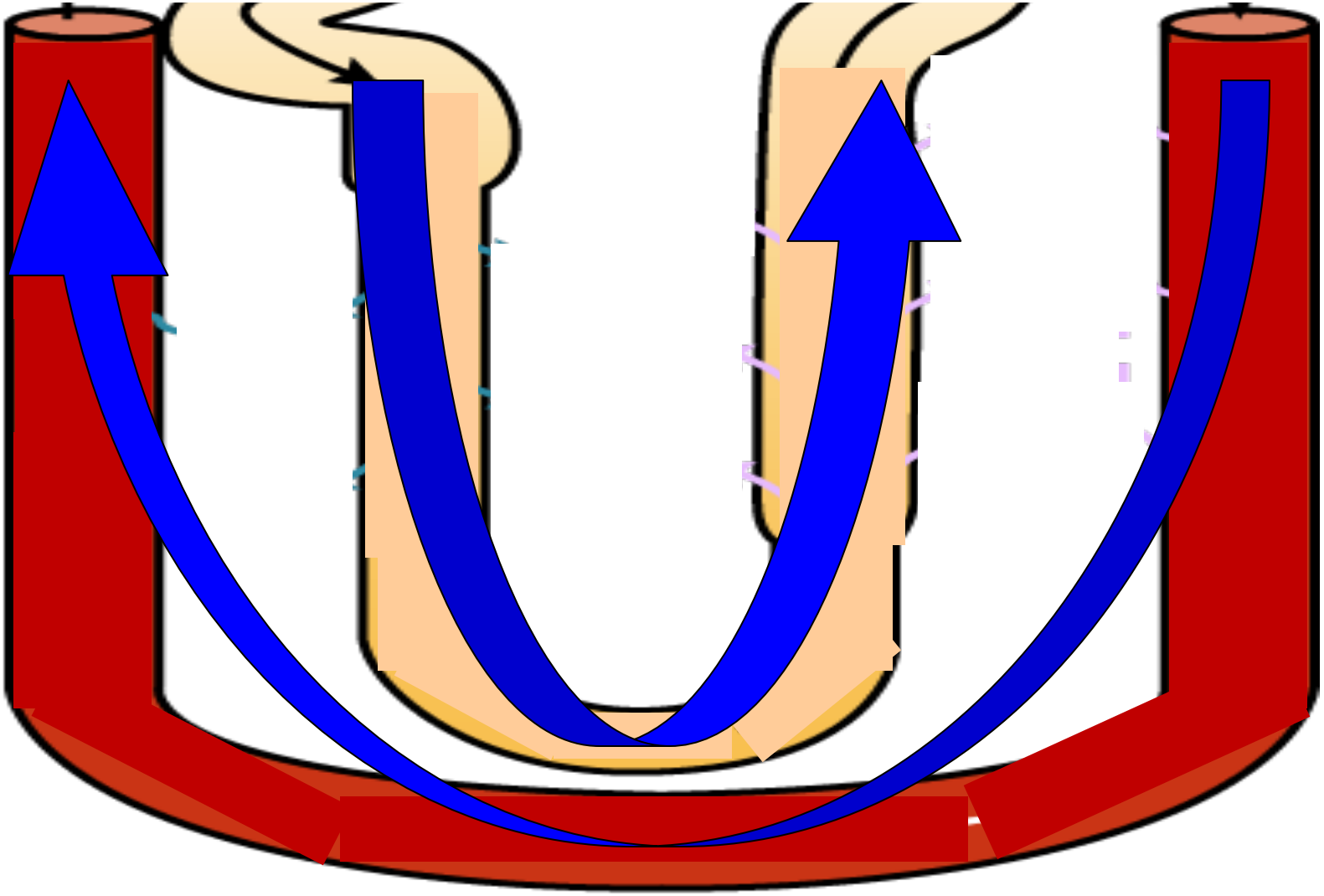
outcome

Restoration of water ← **hyperosmolar medulla**

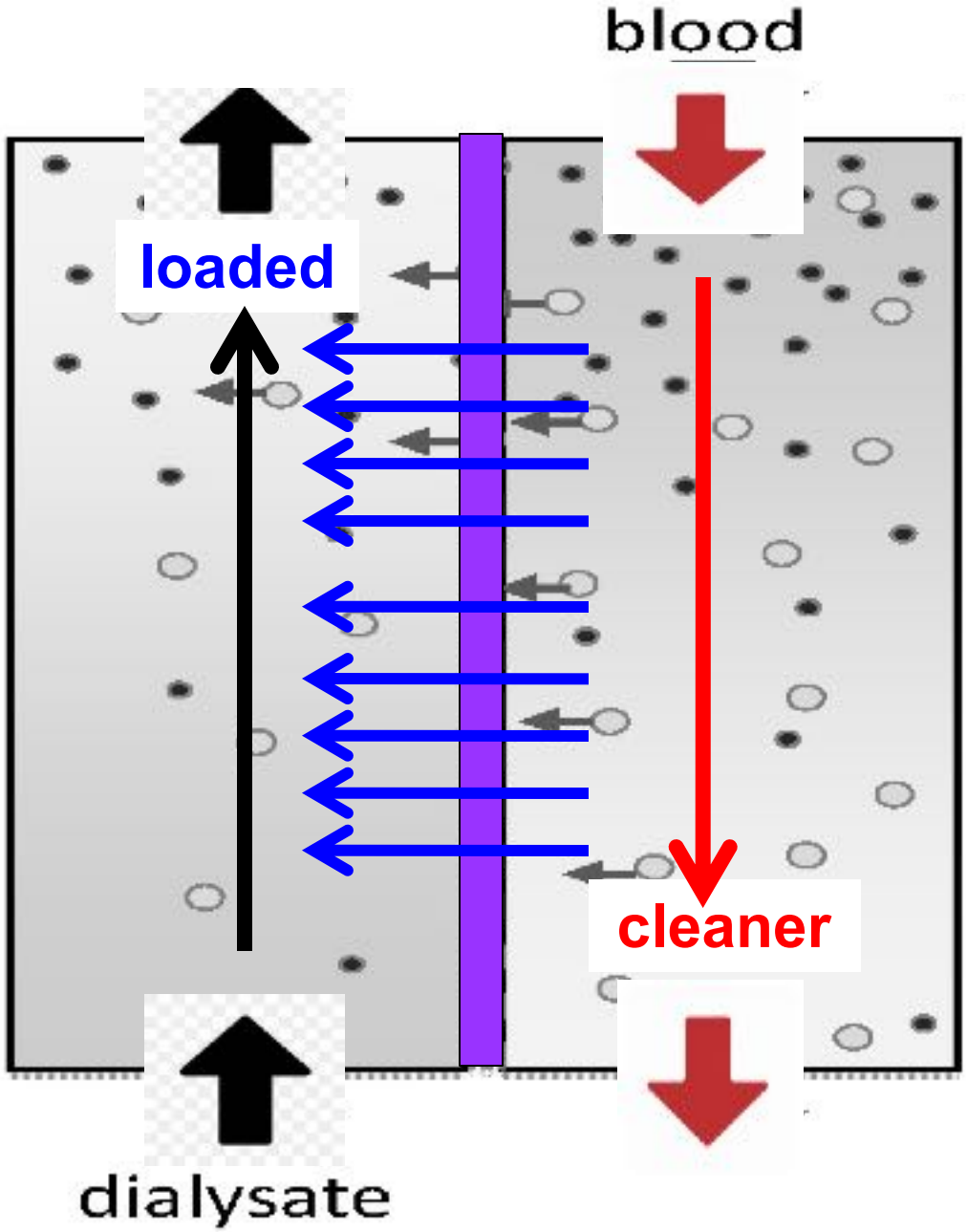


The countercurrent flow thus increases, or ***multiplies*** the osmotic gradient between tubular fluid and interstitial space.

In the extended meaning of the term, another countercurrent is working there; the urine flow in the **loop**, against the blood flow in the **vasa recta**.



Counter Current Mechanism



A dialysis machine uses a ***semipermeable membrane***, *which separates the opposing currents of blood and dialysate.* It works in a similar way to a nephron.

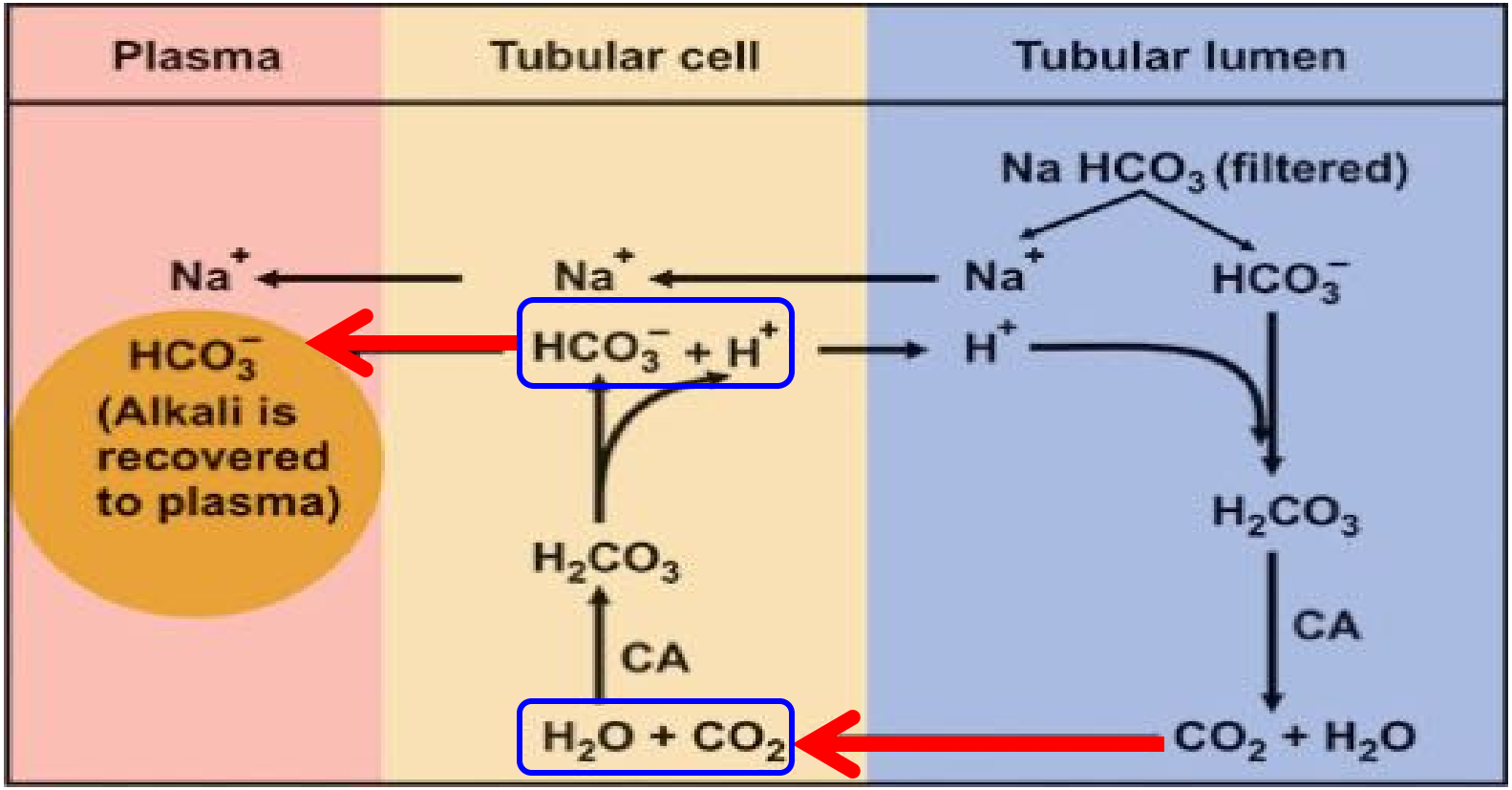
Because of **osmosis**, the **water** in the blood moves across the membrane into the dialysis fluid.

And through **diffusion**, very small **molecules of waste** go to the dialysis fluid.

Eventually the dialysis fluid will remove water, as well as all of the waste materials it can from the blood.

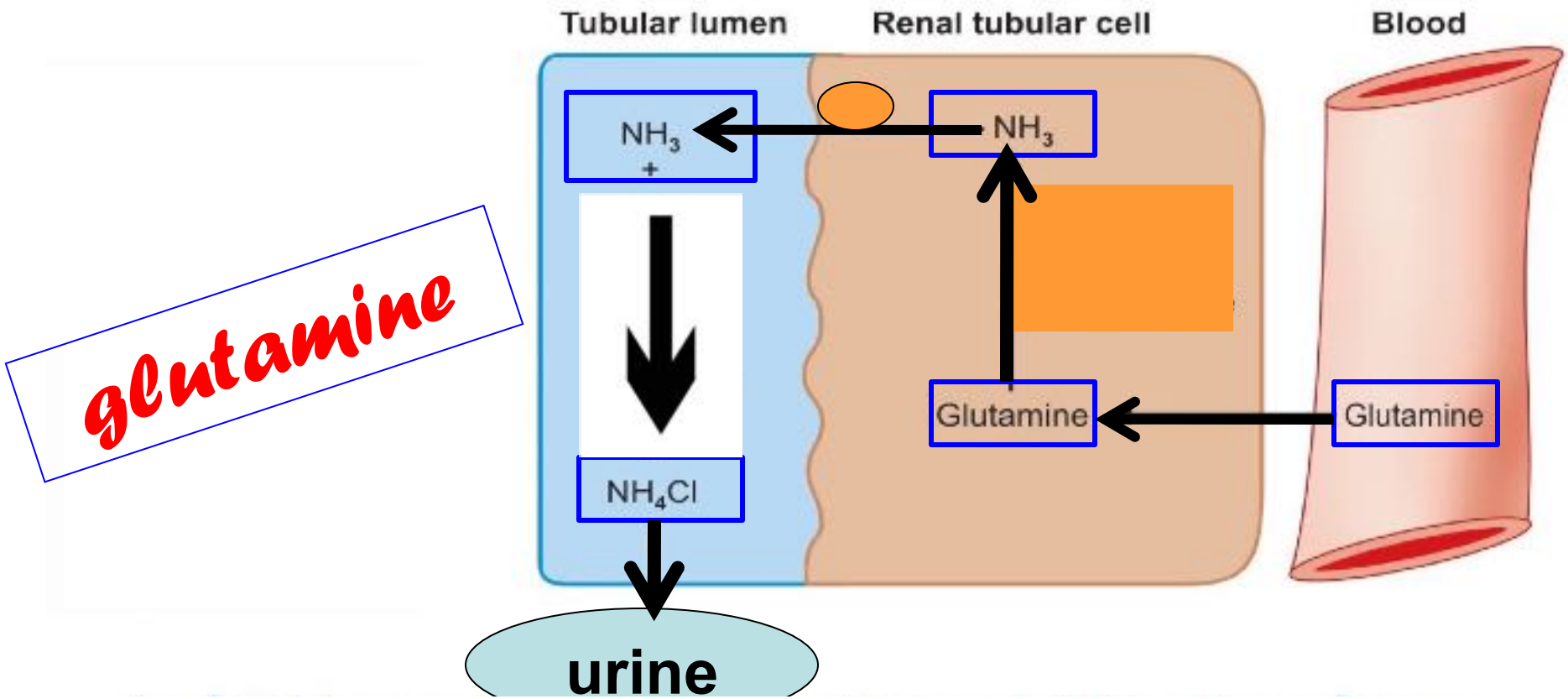
Acid-Base balance

The kidneys have <u>two</u> main ways to maintain
acid-base balance.

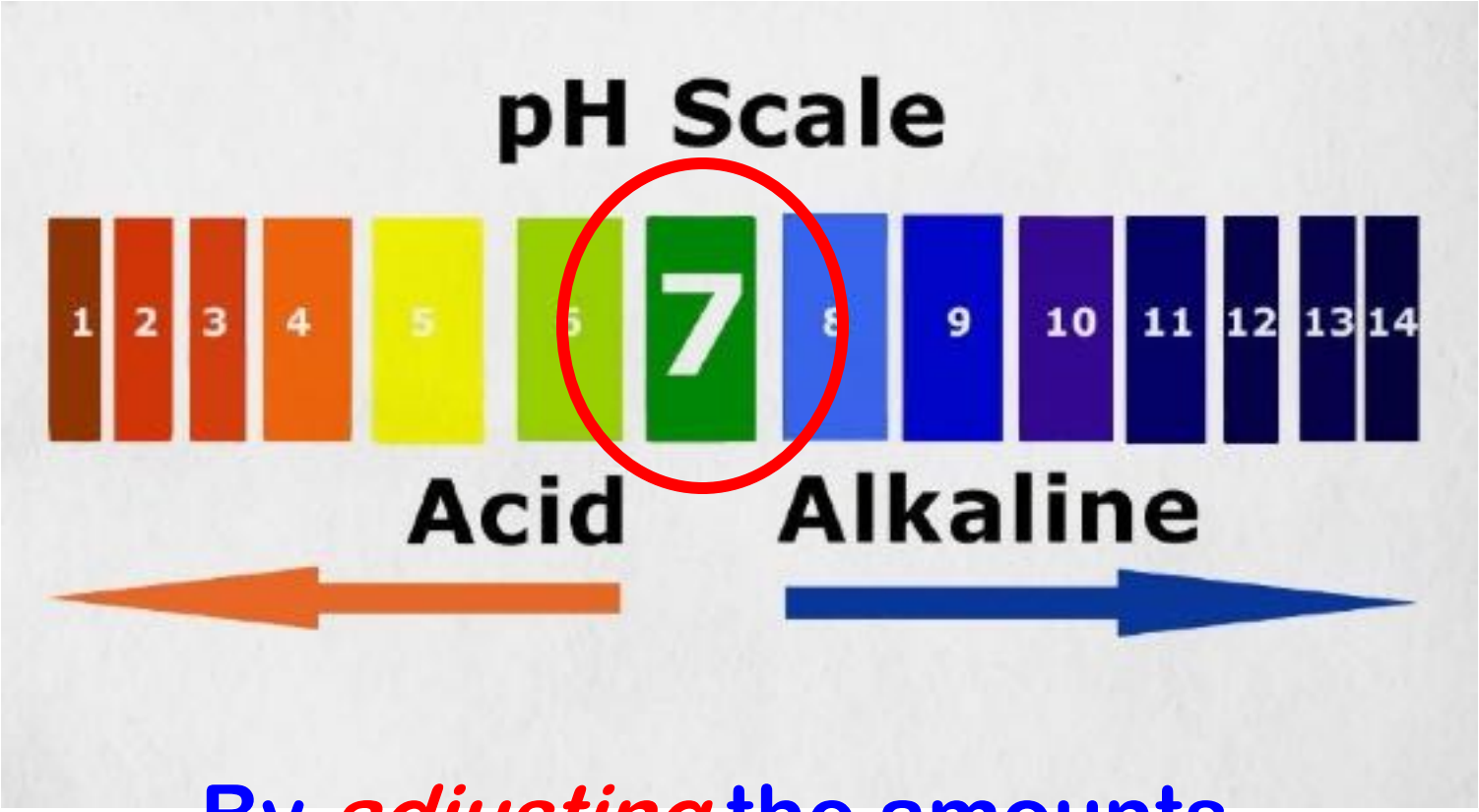


***1.Bicarbonate reabsorption*, and**

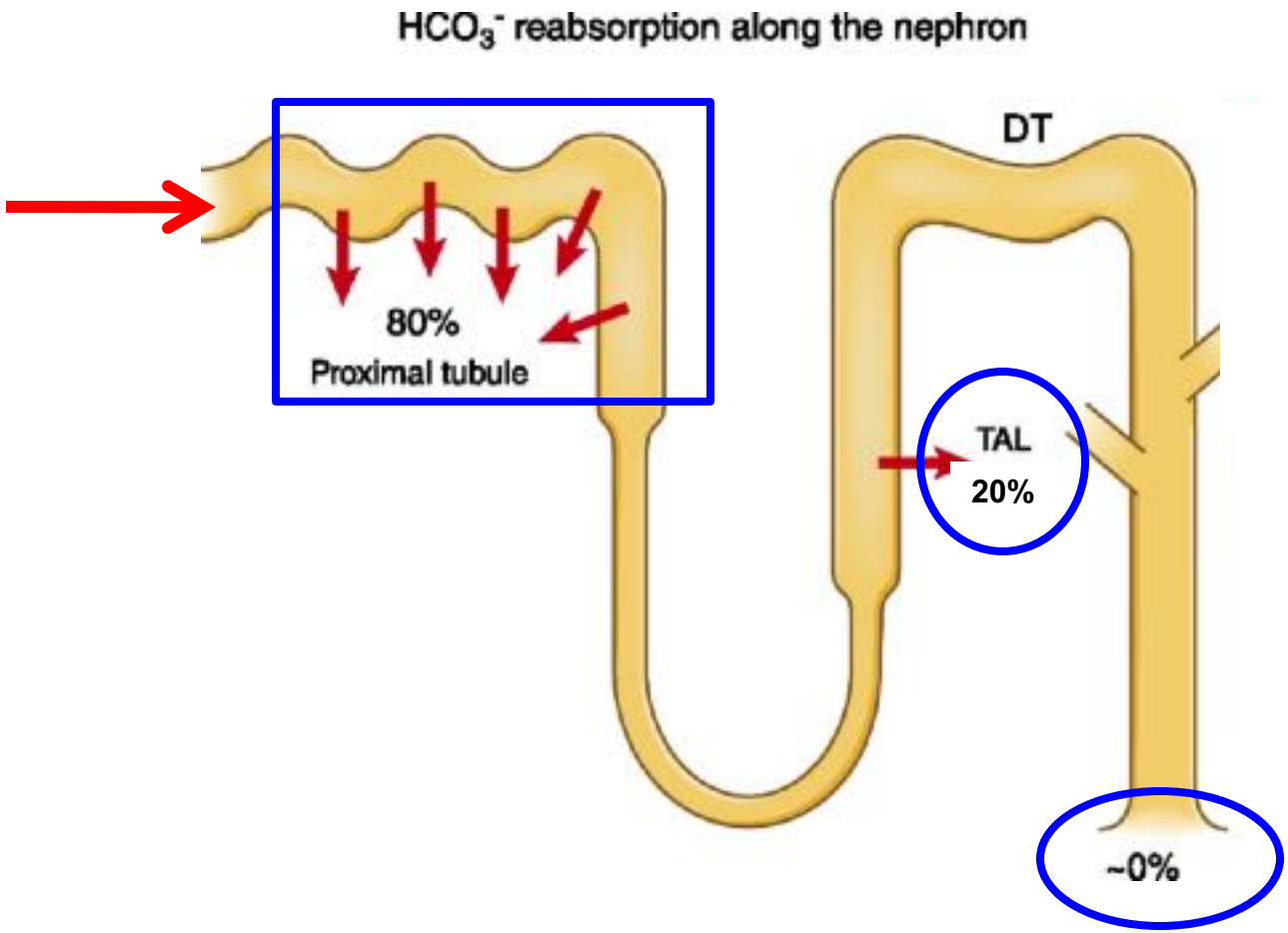
***Generation of new bicarbonate*.**



2.secretion of hydrogen into the urine through synthesis of ammonia.

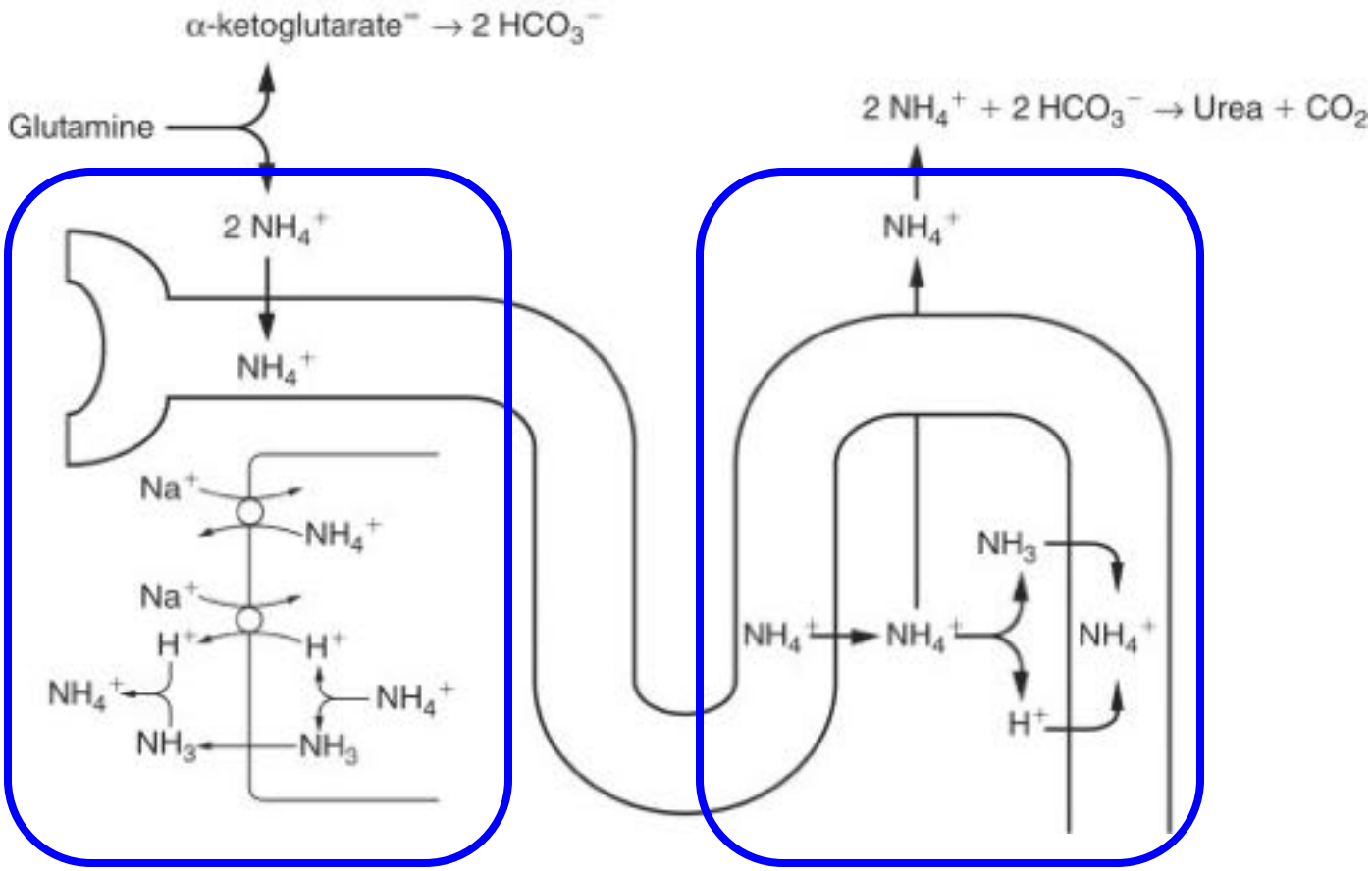


By *adjusting* the amounts reabsorbed and secreted, they *balance* the bloodstream's pH



Bicarbonate is freely filtered at the glomerulus. 80% of this is reabsorbed by the proximal tubule, and 20% is reabsorbed in the distal nephron.

The final urine, under normal conditions, is nearly free of bicarbonate.



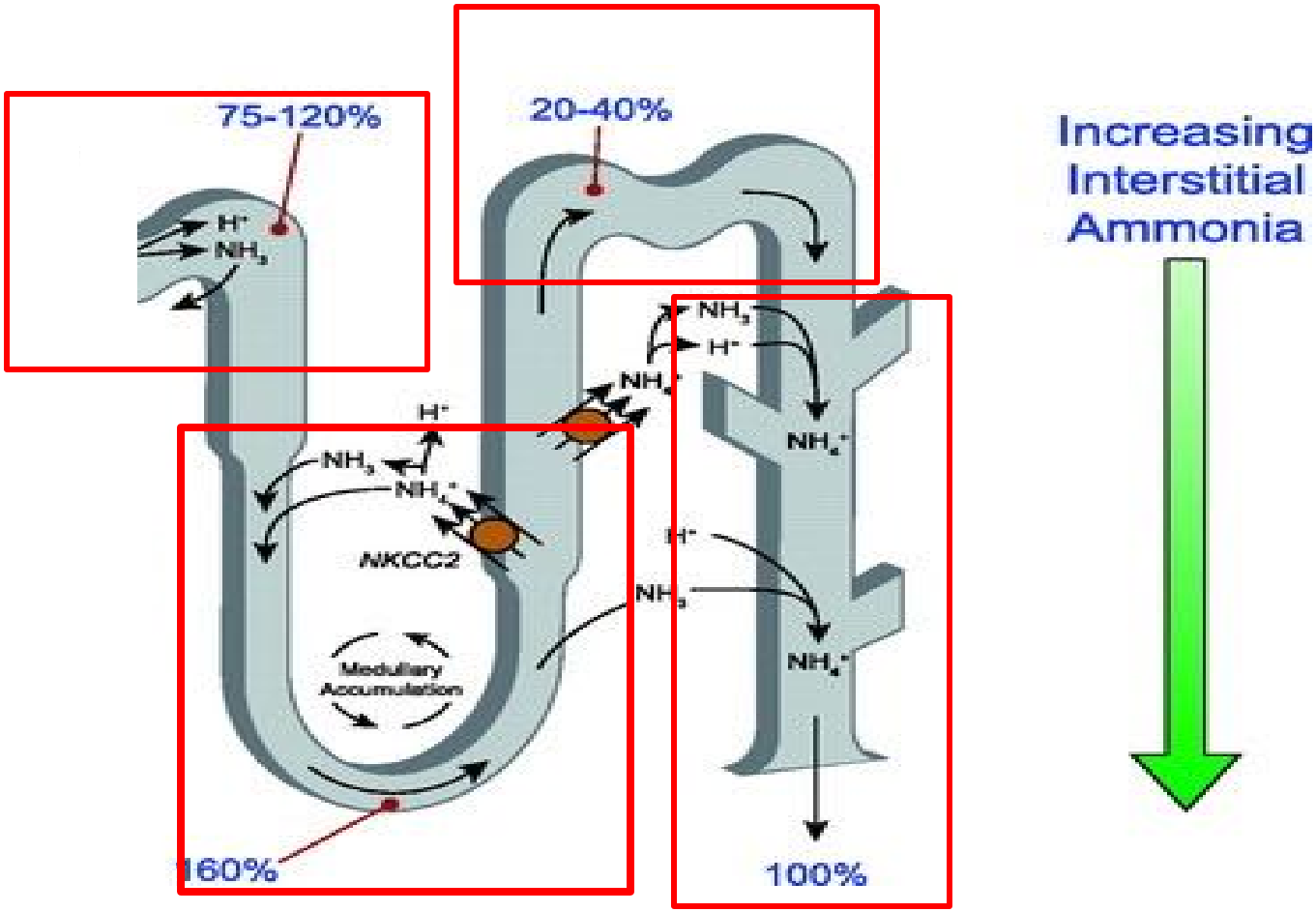
In addition, the kidney must excrete H^+ ions. Excreted H^+ ions are bound to ammonia (NH_3). The *proximal tubule* is the primary site of production of ammonia which accounts for 1/2 to 2/3 of net acid excretion.

This illustrates the uniquely important role of the proximal tubule in regulating acid-base transport, with regard to

both

bicarbonate reabsorption **and** ***ammoniagenesis***

NH3

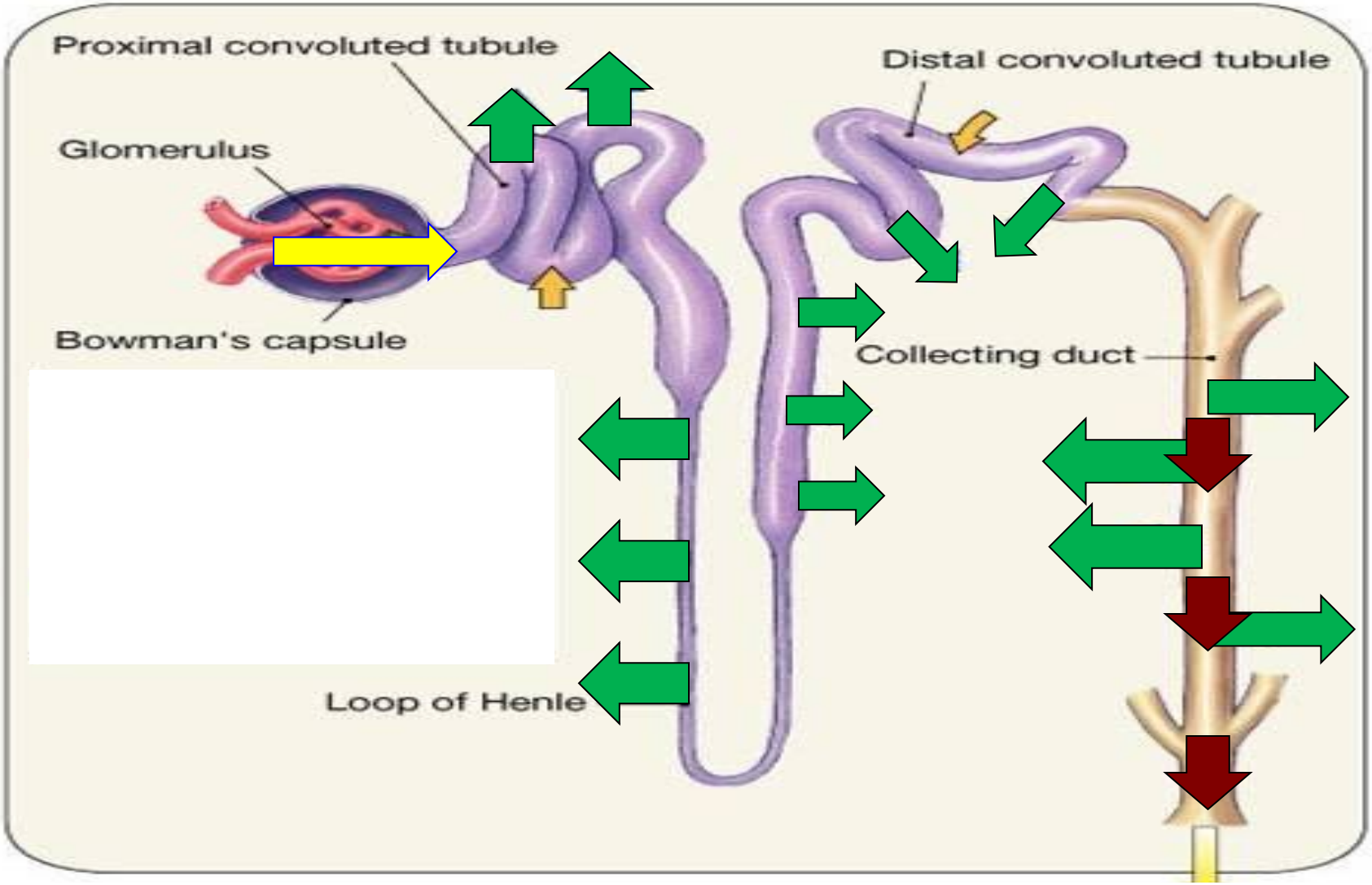


However, apart from the main synthesis in PCT, parts of the LH, DCT, and CD can synthesize ammonia.

Renal ammonia excretion is the predominant component of renal net acid excretion.

Ammonia exists in two molecular forms, NH_3 and NH_4^+.

Electrolyte balance

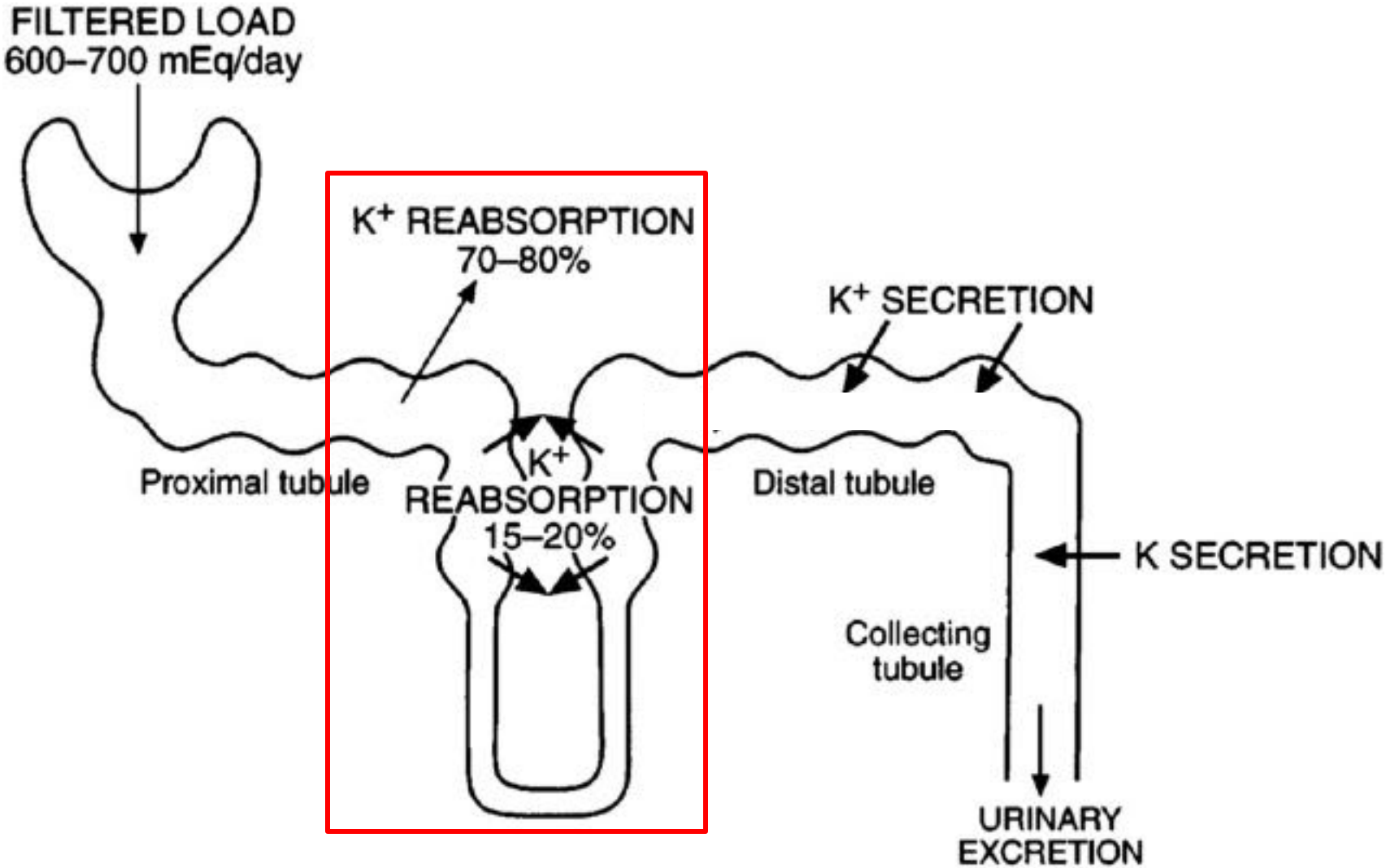


The kidneys help maintain electrolyte concentrations by

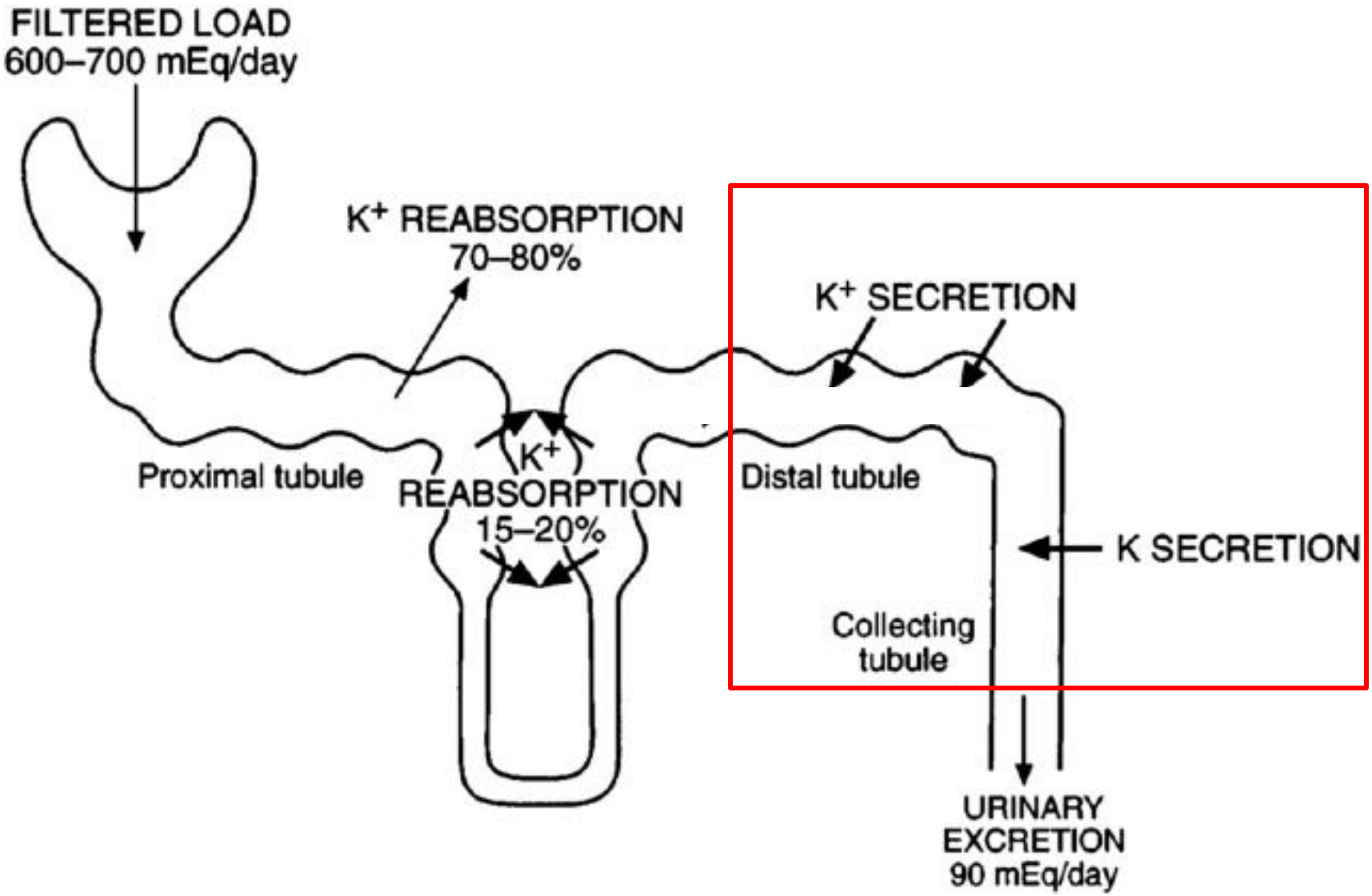
filtering electrolytes and water from blood,

returning some to the blood, and

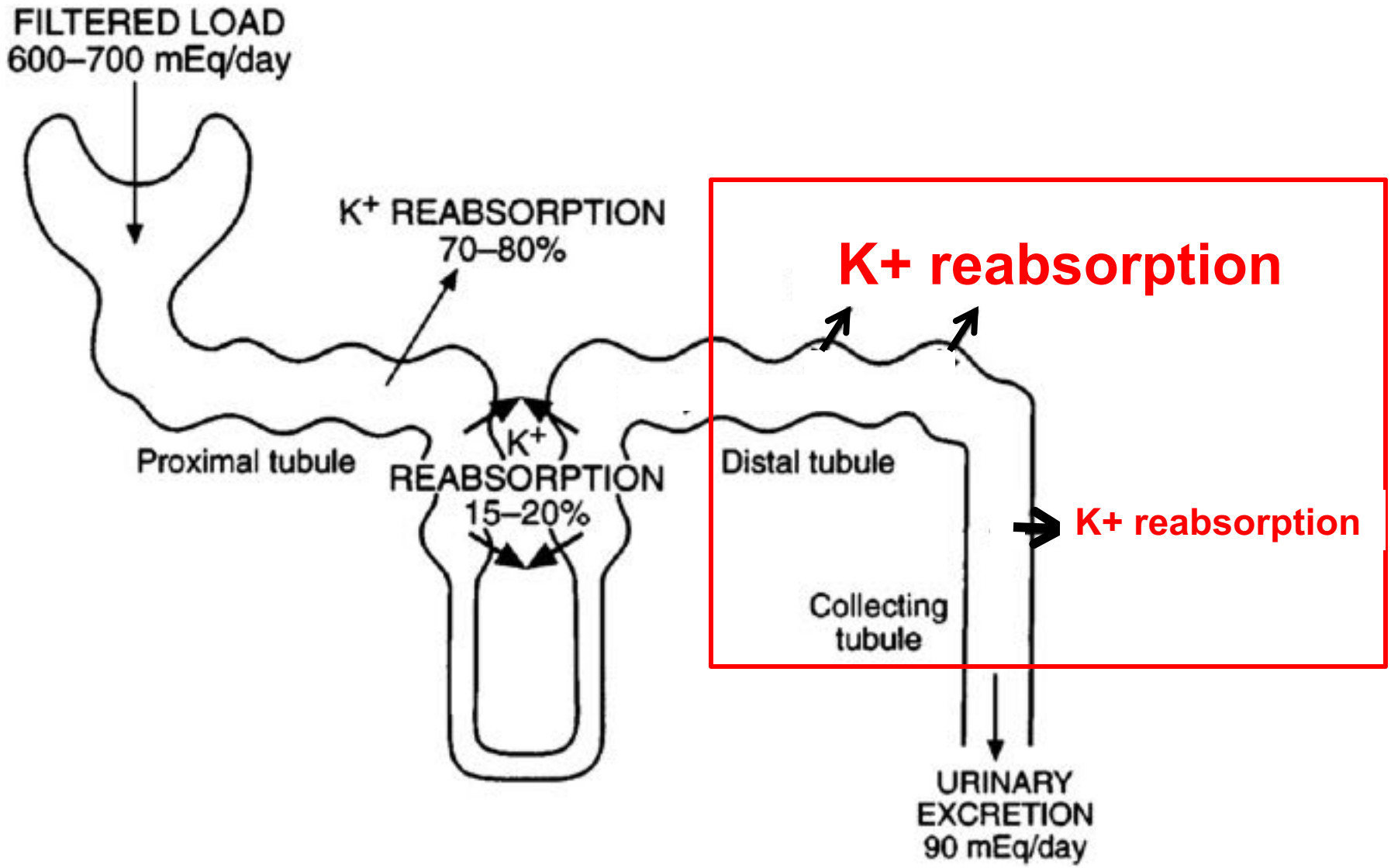
99% of the filtrated sodium and Chloride are reabsorbed in the renal tubules.



Potassium is freely filtered by the glomerulus.
The bulk of filtered K^+ is *reabsorbed*
in the PCT and LH.

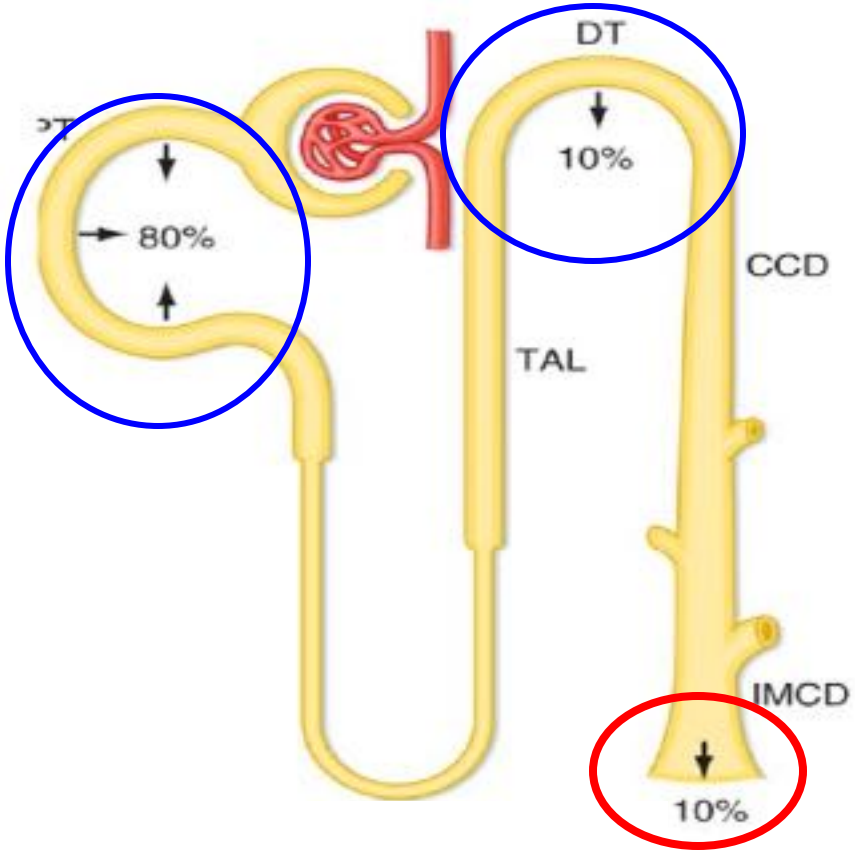


Along the DCT and CD, there is net *secretion* of K+ (stimulated by aldosterone) and when there is dietary *K excess*.



Secretion decreases and becomes net reabsorption in K+ deficiency.

Phosphate handling in the nephron

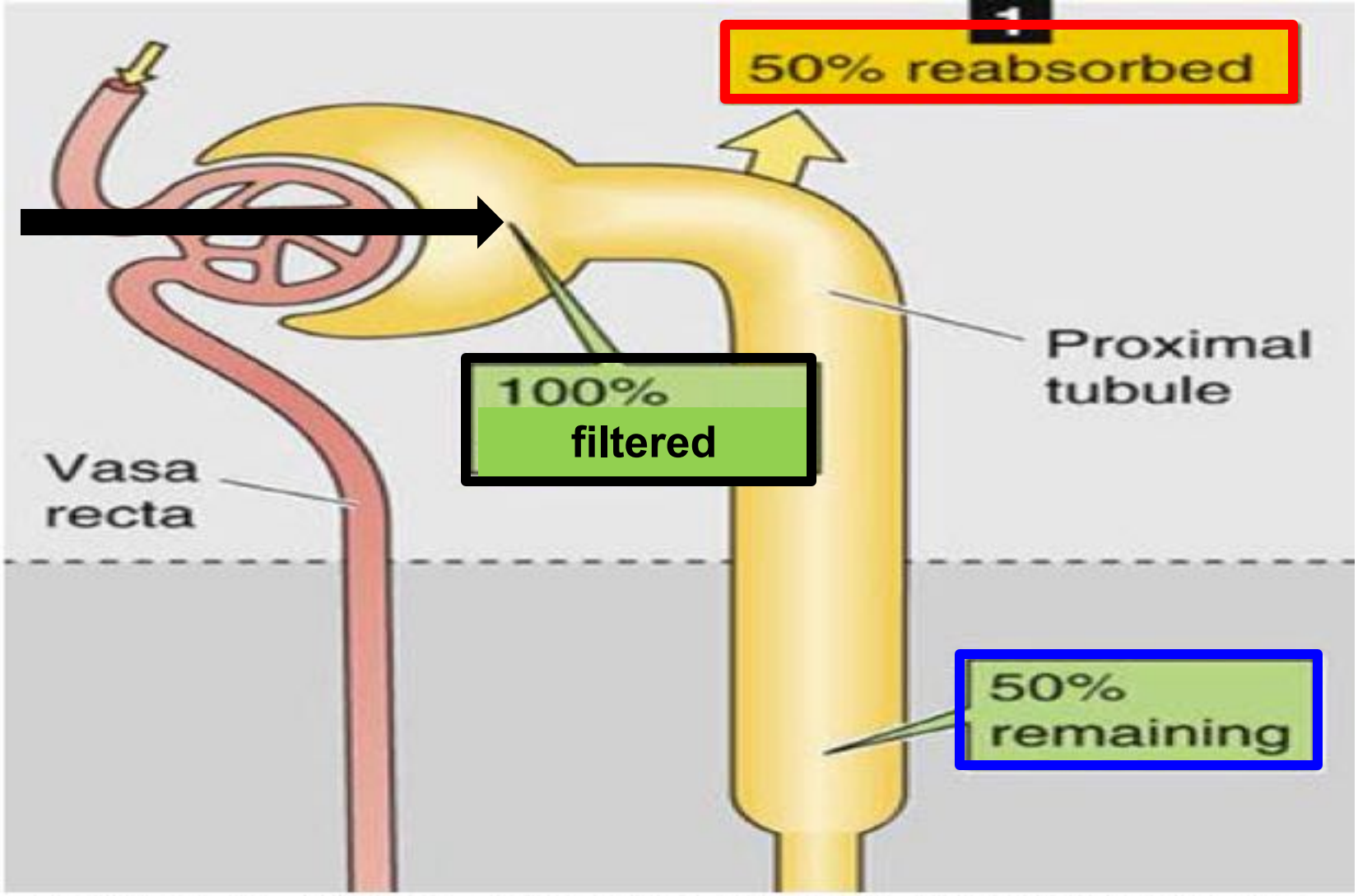


The PCT and the DCT are the major sites of excretion and removal of excess phosphate from the body.

A high level of phosphate in the blood is usually caused by a kidney problem.

Waste elimination

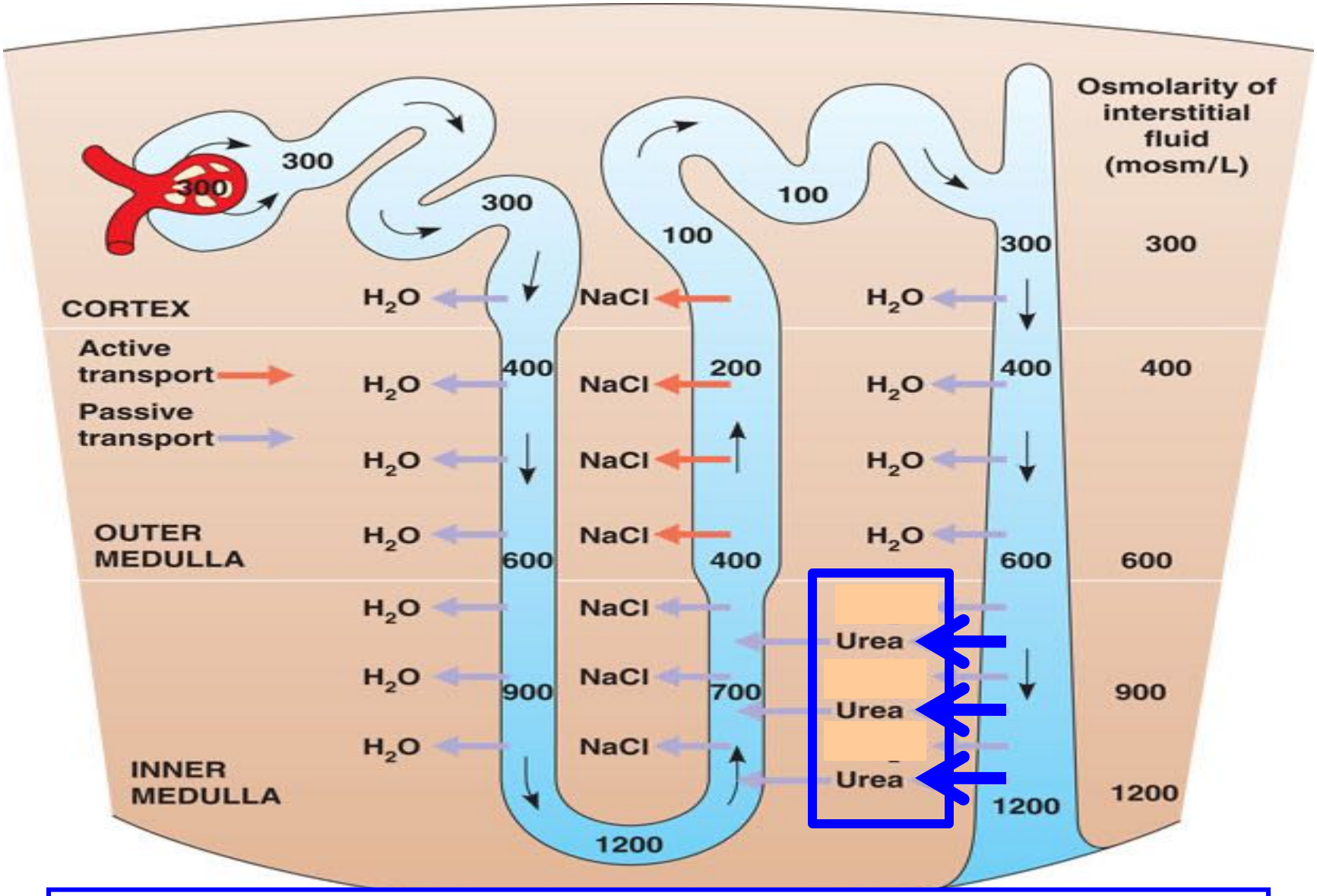
Urea



Urea is freely filtered, 50% are reabsorbed in the proximal tubule.

About 40% of which is normally found in the final urine.

Where is the remaining 10% ?

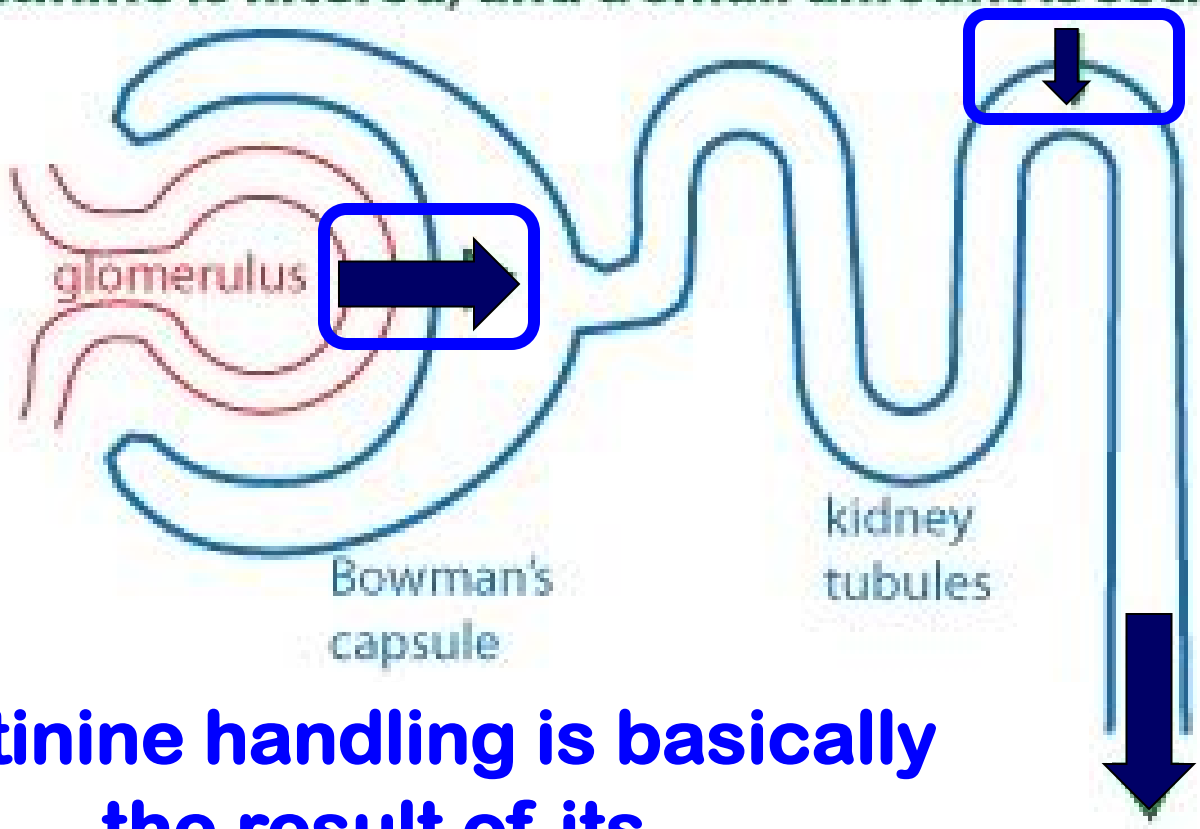


In the CD, urea is reabsorbed to create a high osmolarity in the renal medulla.

creatinine

creatinine:

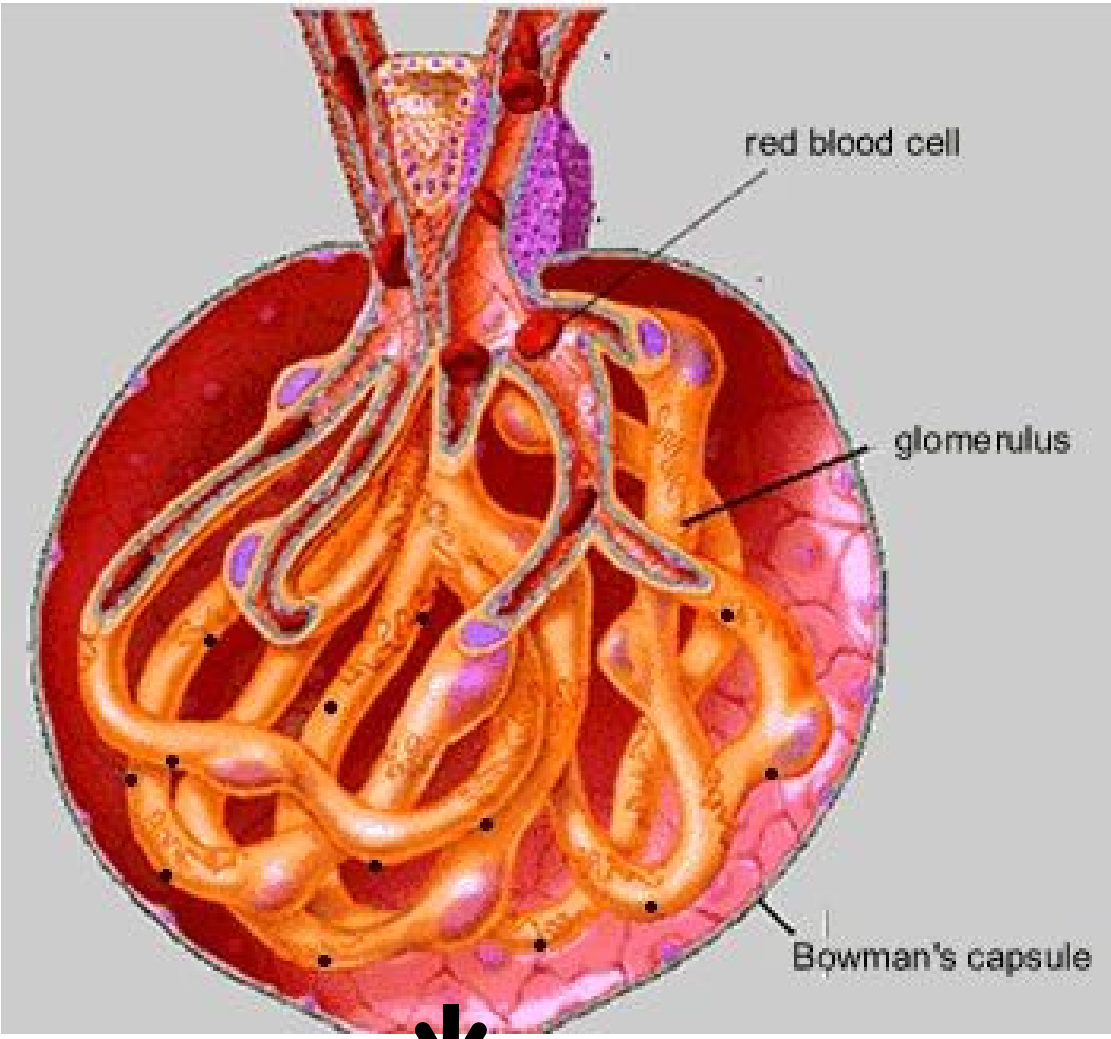
creatinine is filtered, and a small amount is secreted



Creatinine handling is basically the result of its <u>glomerular filtration</u> and to a lesser extent to its <u>proximal tubular secretion</u>.

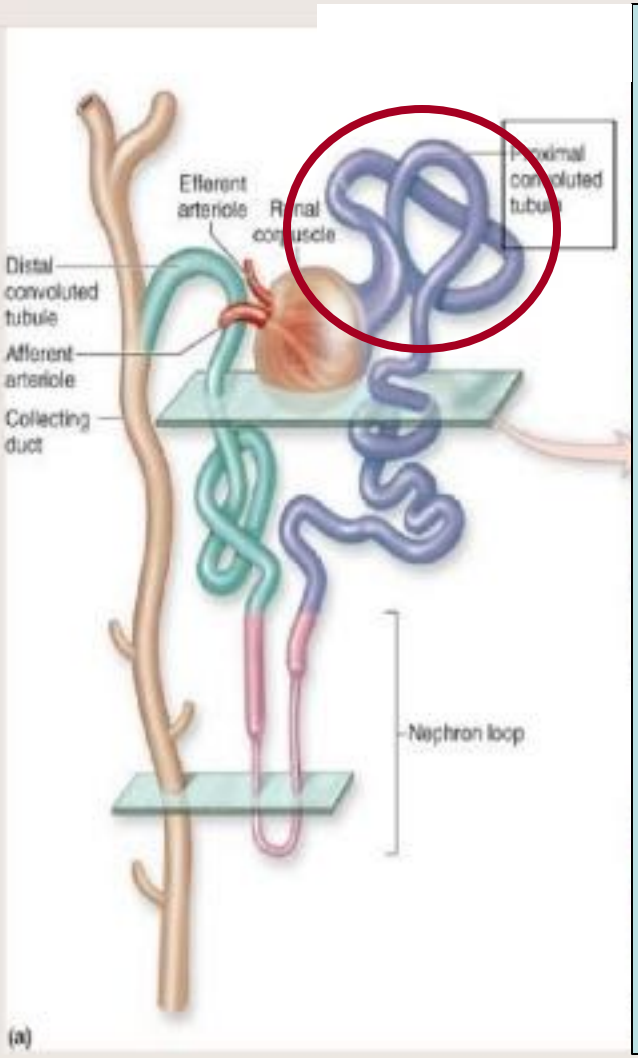
Consequently, an elevated serum creatinine is usually a sign of glomerular disease

LET'S SUM IT UP

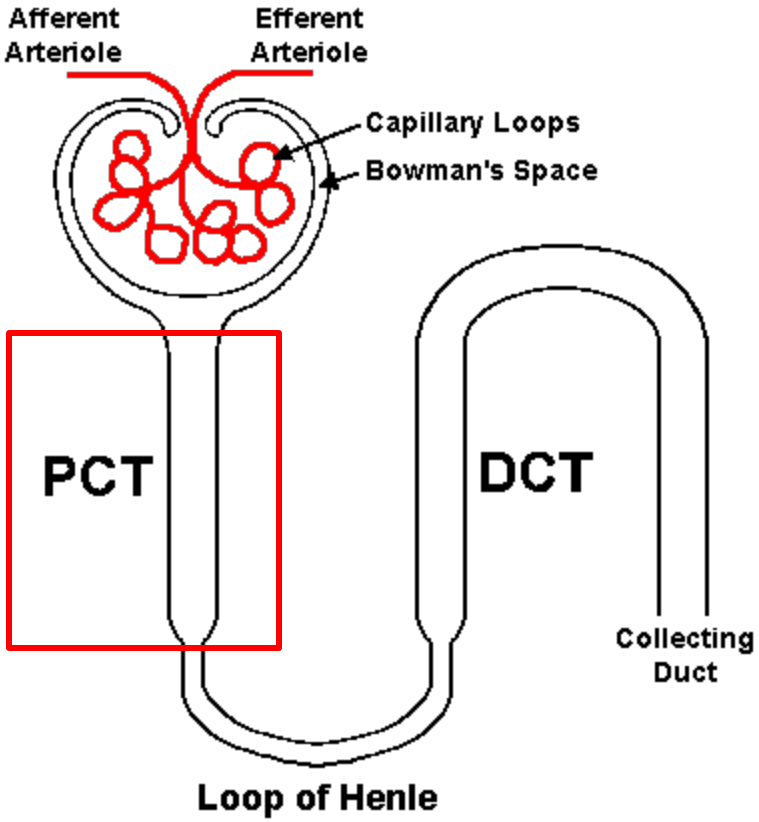


The glomerulus **acts as a filtering unit,**
Delivering extra fluid and wastes to the tubule.

Proximal Convoluted Tubule



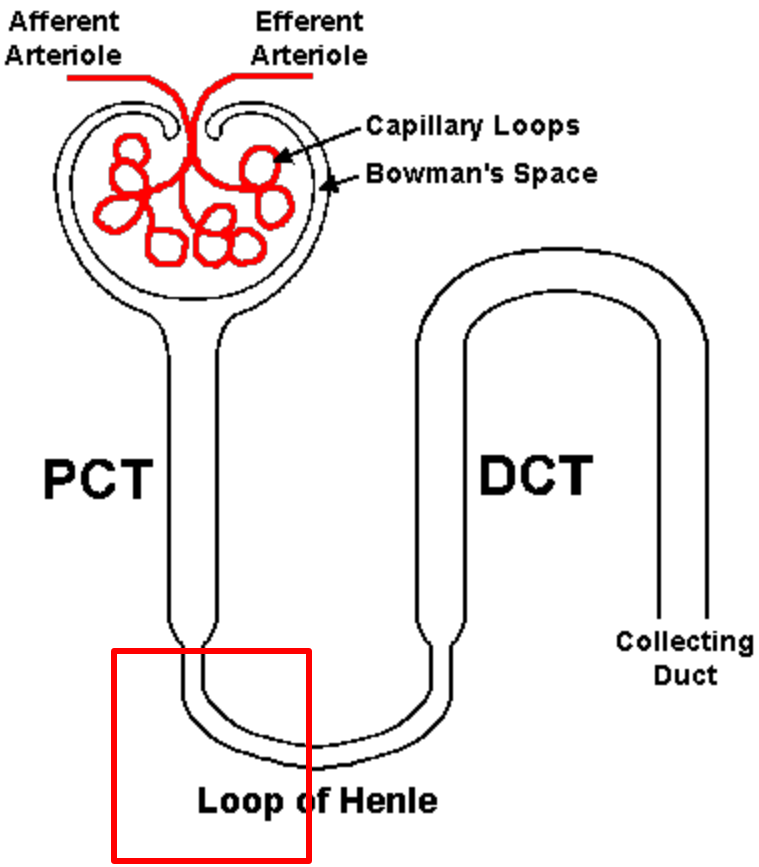
The PCT is the most metabolically active part of the nephron and uses a wide array of protein micromachines to maintain homeostasis; symporters, antiporters, and ATPase active transporters, in conjunction with diffusion, both simple and facilitated.



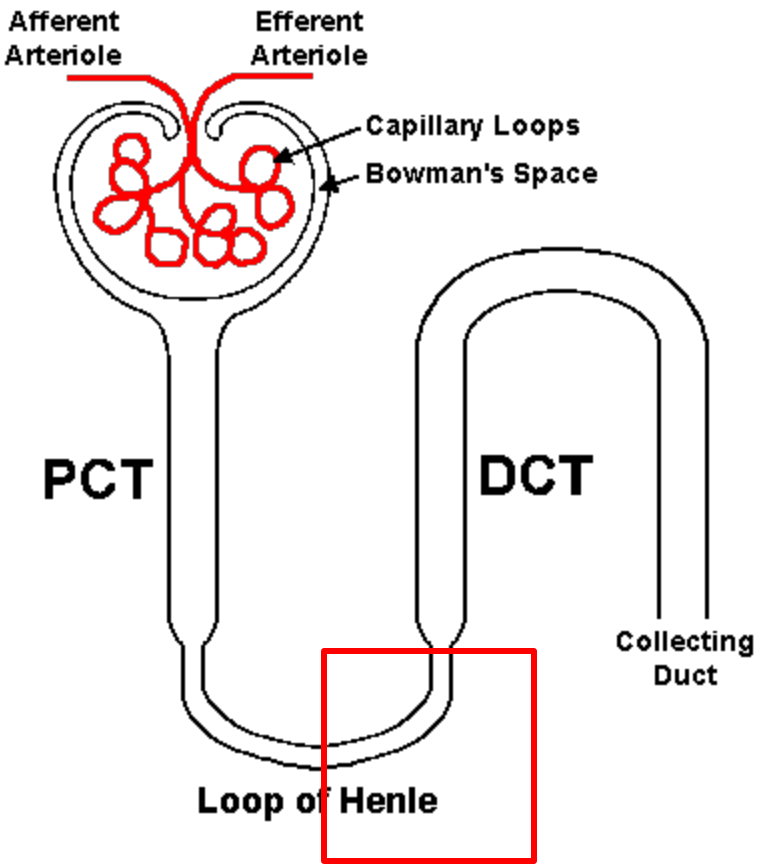
The function of the **proximal tubule** is essentially ***reabsorption*** of filtrate in accordance with the needs of homeostasis (***equilibrium***)

Secretes urea and creatinine.

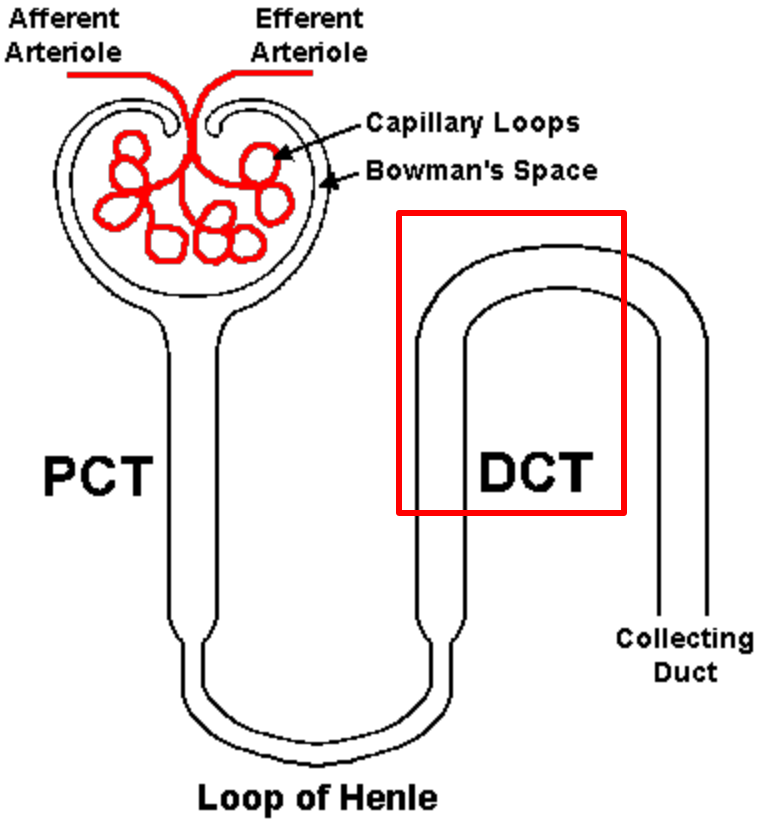
Synthesizes HCO3, NH3, and 1,25(OH)2-CC



The main role of the **descending loop** is to recover water.



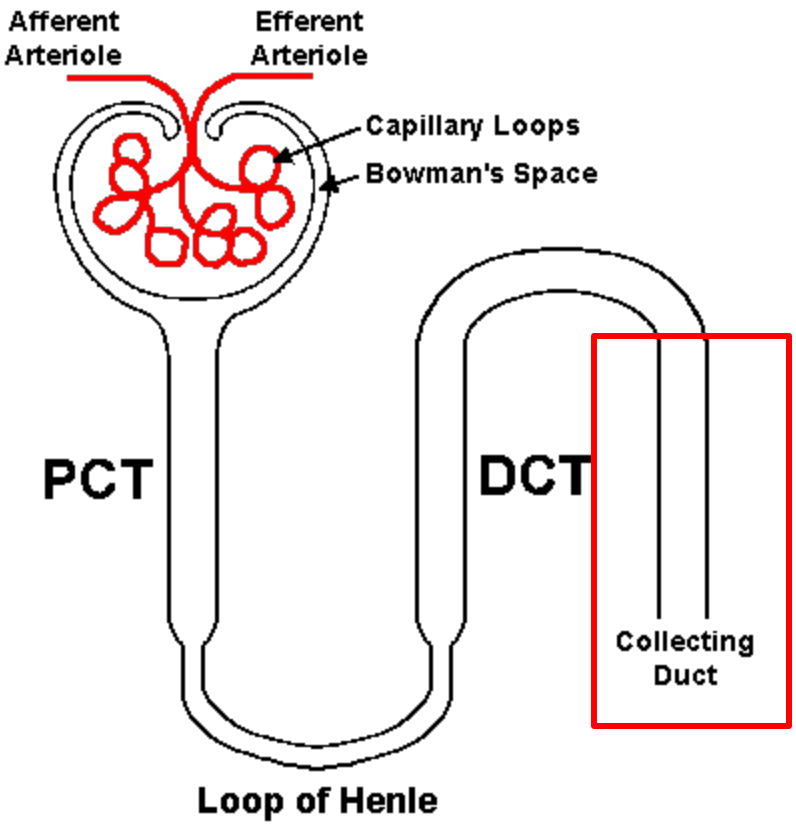
The main role of the **ascending loop** is to concentrate the salt in the medullary interstitium,



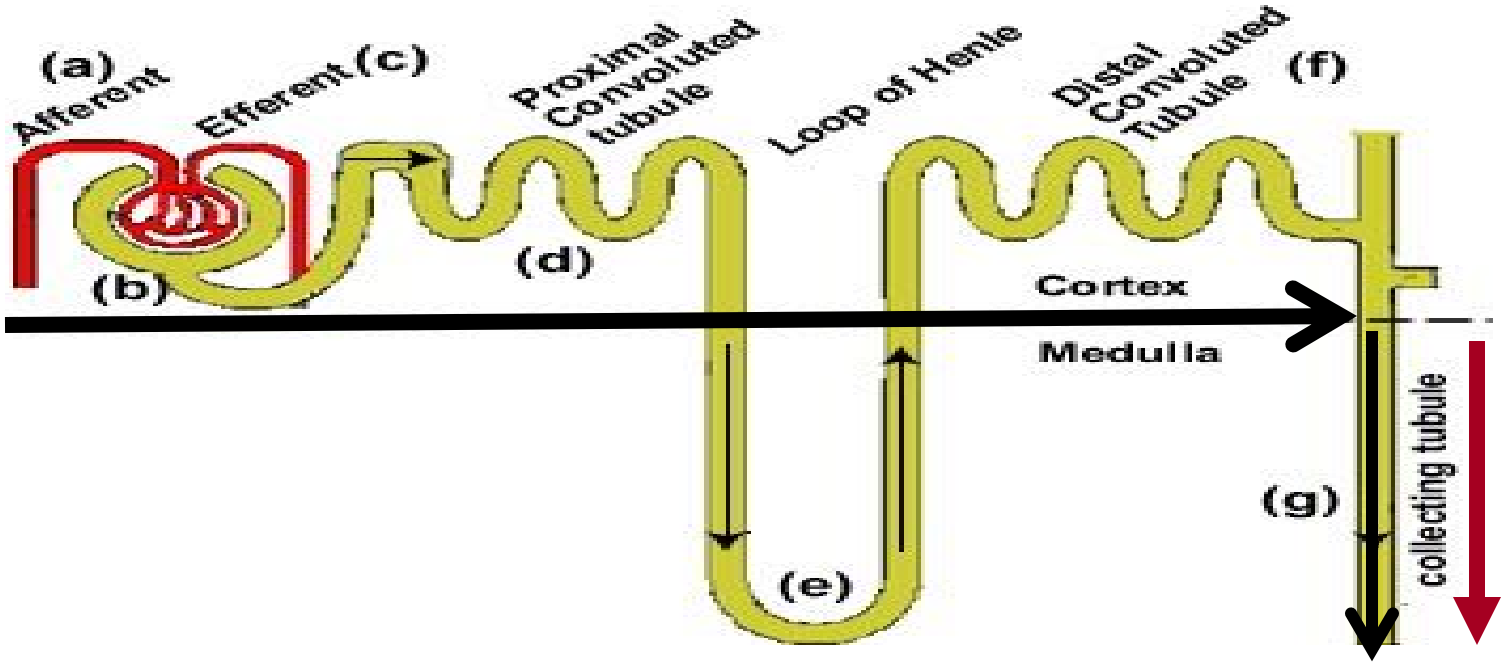
Distal Convoluted Tubule plays a critical role in **NaCl reabsorption, K+ secretion, and secretion of Extra salts.**

It **secretes H+**

as a way to get rid of acid loads. .



Collecting Duct is the final station for water regulation.



And after all this, the final product is *excreted* as urine.

In this way, the kidneys *regulate* the body's level of these substances, as well as, that of water and pH.

Achieving :

- Water balance
- Electrolyte balance
- Acid-Base balance

And as well,

CLEANING THE BODY OFF THE WASTE PRODUCTS OF METABOLISM

Ramzi El-Baroudy

MCQs

The PCT can perform :

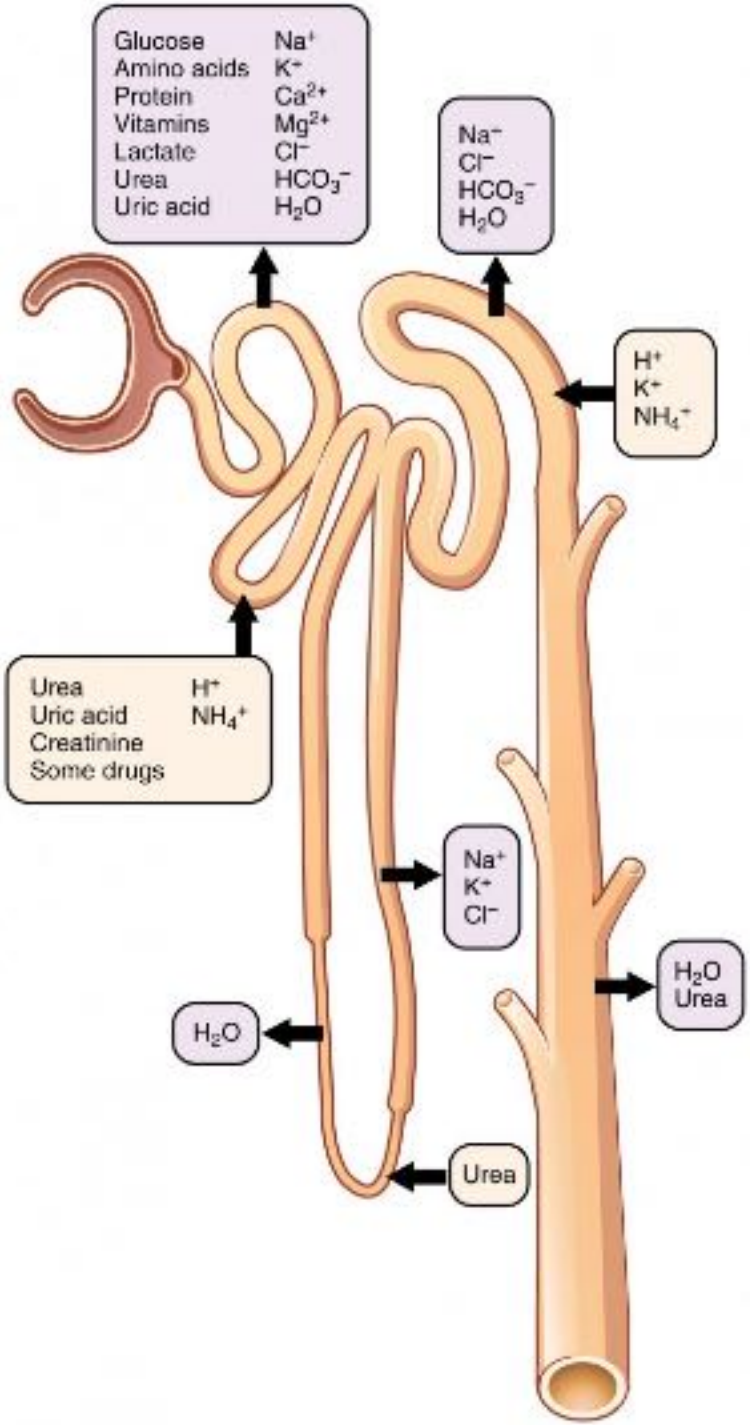
1. Reabsorption
2. Secretion
3. Synthesis
4. All of the above

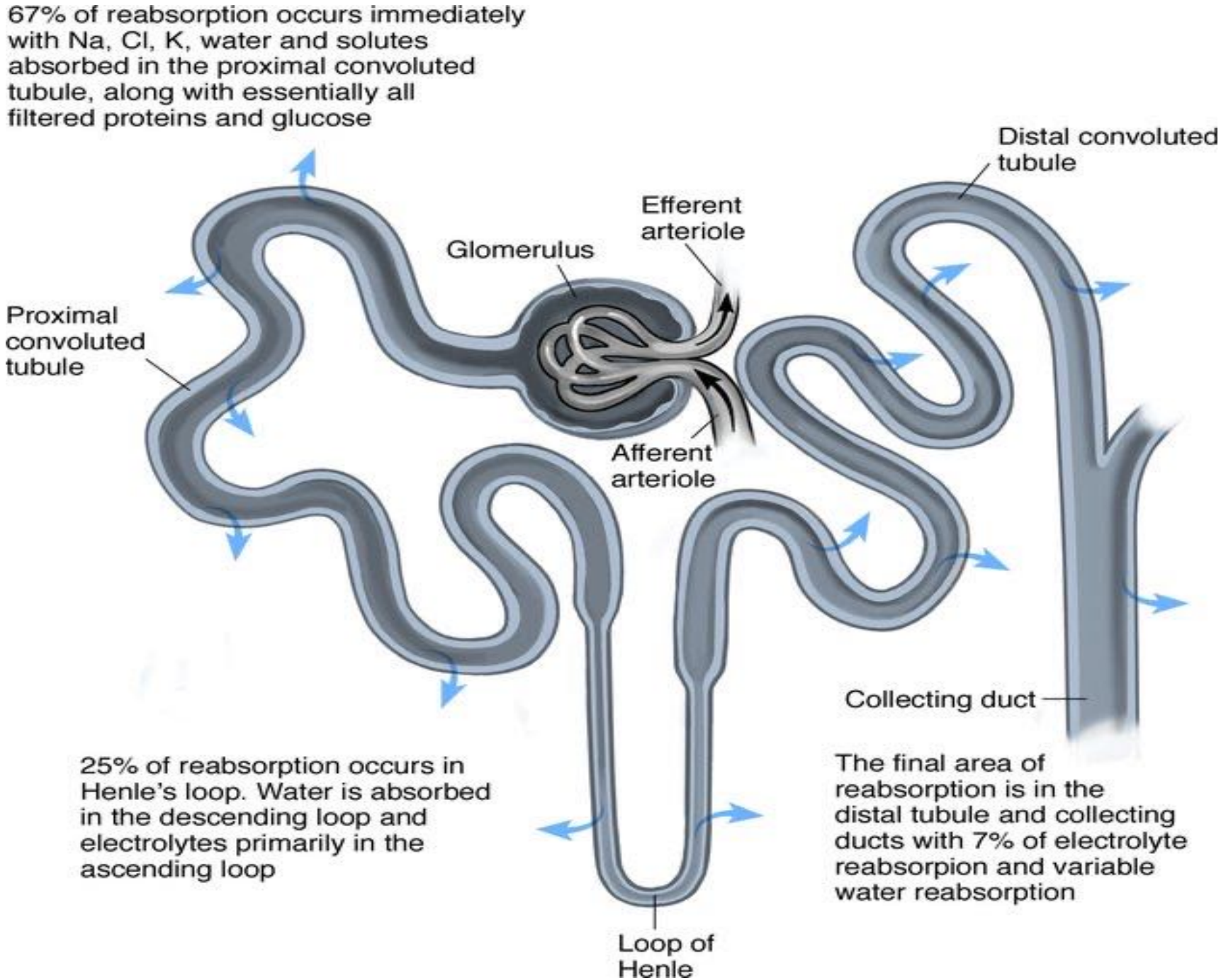
All the parts of the nephron are permeable to water <u>EXCEPT</u> :

1. **PCT**
2. **DLH**
3. **ALH**
4. **DCT**

The hypertonic renal medulla is created by :

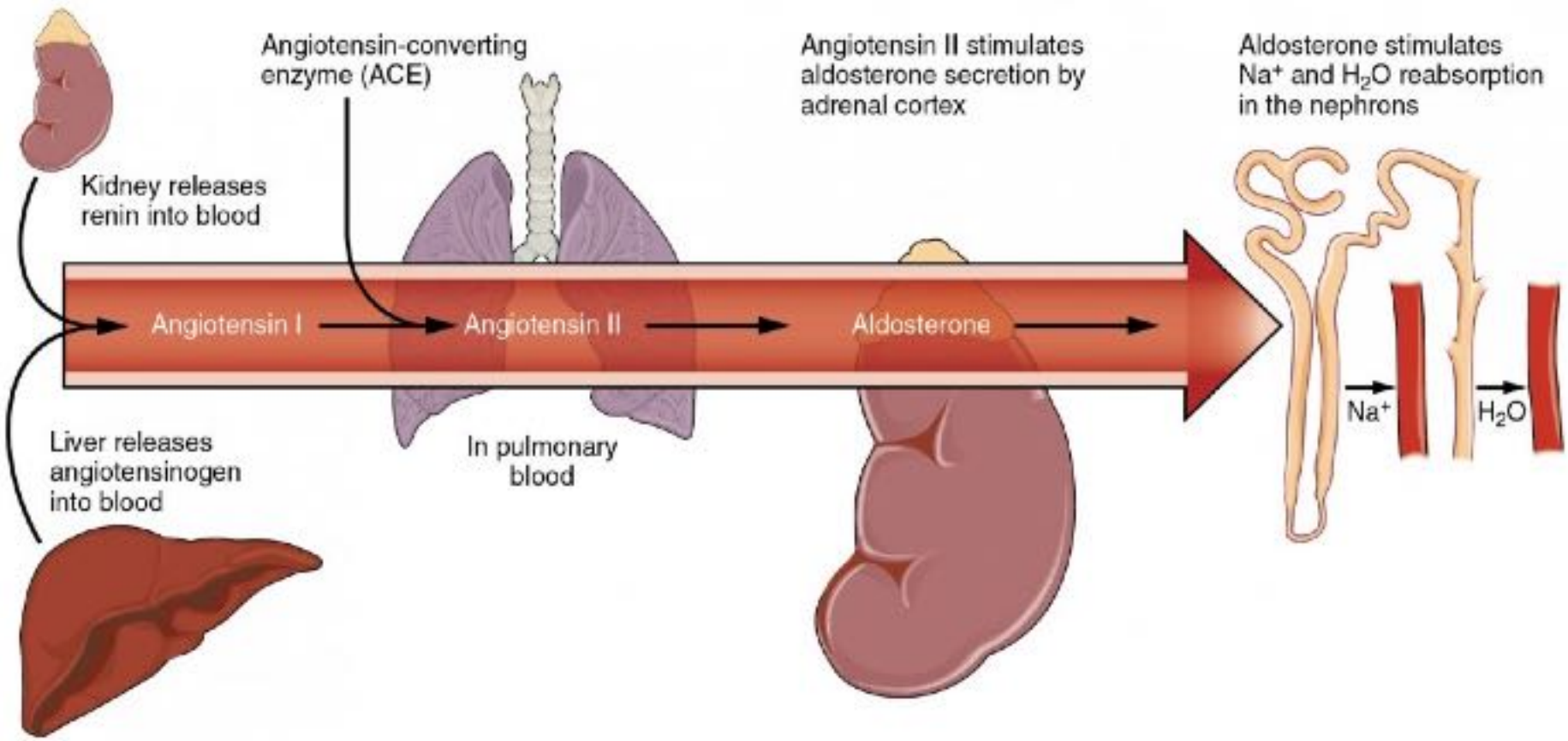
1. Na+ absorbed from the ALH
2. Water reabsorption by the VR
3. Urea transport from the CD
4. All of the above


Glucose
Amino acids
Protein
Vitamins
Lactate
Urea
Uric acid
Na^+
K^+
Ca^{2+}
Mg^{2+}
Cl^-
HCO_3^-
H_2O
Na^+
Cl^-
HCO_3^-
H_2O
H^+
K^+
NH_4^+
Urea
Uric acid
Creatinine
Some drugs
H^+
NH_4^+
Na^+
K^+
Cl^-
H_2O
Urea
H_2O
Urea

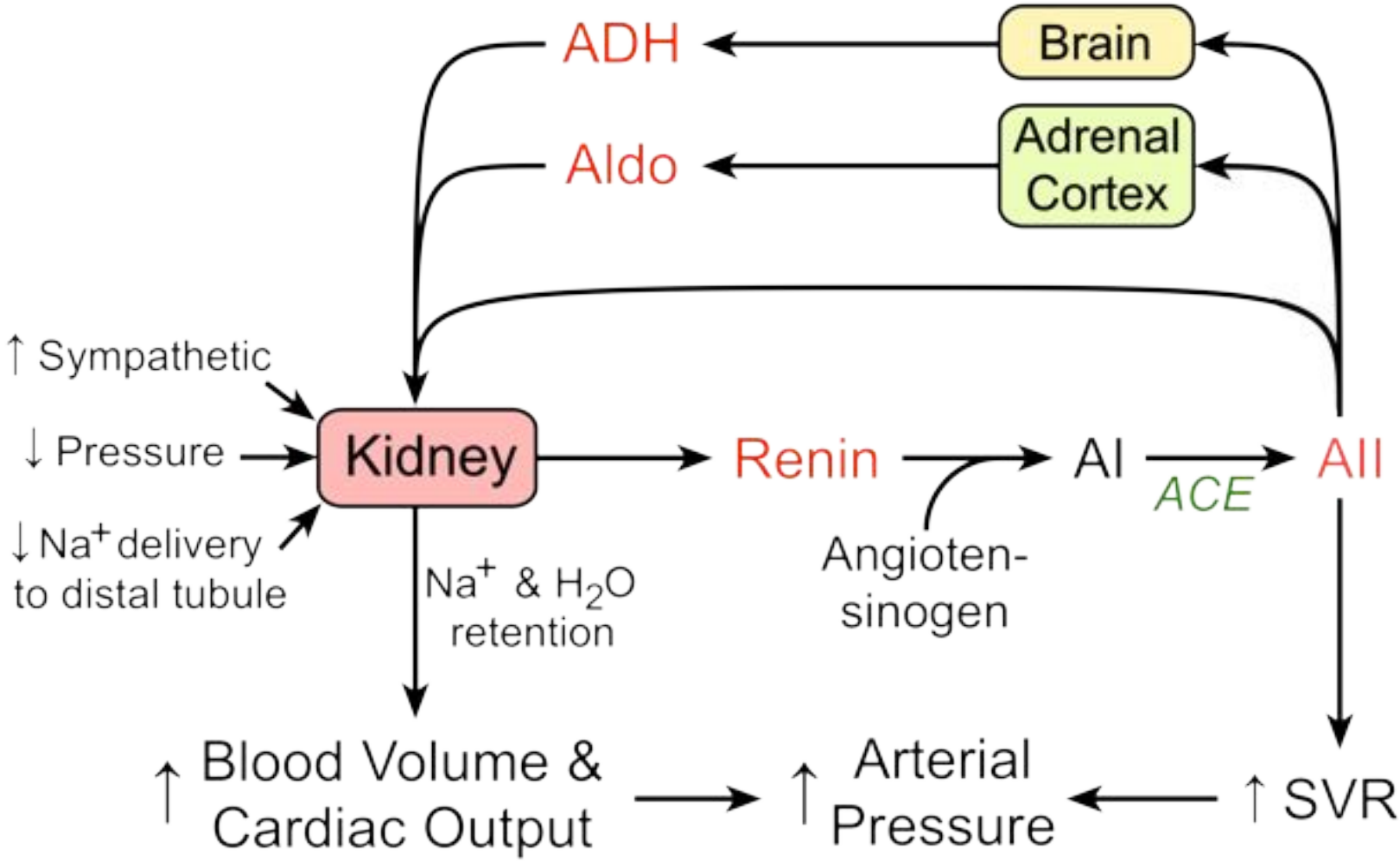

67% of reabsorption occurs immediately with Na, Cl, K, water and solutes absorbed in the proximal convoluted tubule, along with essentially all filtered proteins and glucose
Distal convoluted tubule
Efferent arteriole
Glomerulus
Proximal convoluted tubule
Afferent arteriole
Collecting duct
25% of reabsorption occurs in Henle's loop. Water is absorbed in the descending loop and electrolytes primarily in the ascending loop
The final area of reabsorption is in the distal tubule and collecting ducts with 7% of electrolyte reabsorpion and variable water reabsorption
Loop of Henle

NOW

Water balance



The **kidneys stimulate the adrenal glands to secrete the hormone aldosterone**. Aldosterone causes the kidneys to retain sodium and to excrete potassium. When sodium is retained, less urine is produced, eventually causing blood volume to increase.



Aldosterone release is stimulated by a **decrease in blood sodium levels, blood volume, or blood pressure**, or an increase in blood potassium levels.