URINE FORMATION BY THE KIDNEYS

1. Urine represents the sum of three basic renal processes

- Urine excretion = Glomerular filtration
- Tubular reabsorption + tubular secretion

2. Filtration = Glomerular filtration rate x plasma concentration.

3. Example = plasma glucose concentration is 1g/L, the amount of glucose filtered each day in about 180L/day x 1g/L or 180g/day.

- None of the filtered glucose is normally excreted, the rate of glucose reabsorption 180g/day.

4. Tubular reabsorption is selective and quantitatively large.

5. Many wanted substances like glucose, amino acids, water and electrolytes are reabsorbed from the tubules. This process is called tubular reabsorption

URINE FORMATION BY THE KIDNEYS (CONTINUED)

- Urinary excretion = Glomerular filtration – tubular reabsorption + tubular secretion
- Small change in Glomerular filteration or tubular reabsorption can cause a relatively large change in urinary excretion.
- 10% decrease in tubular reabsorption from 178.5 to 160.7L/day would increase urine volume from 1.5 to 19.3L/day (almost a 13 fold increase) if GFR remains containt.
- The reasborptive capacity of the tubular system is tremendous over 99% of the filtered plasma is returned to the blood through reabsorption on average 124ml out of 125ml filtered per minute are reabsorbed.
- Tubular reabsorption involves transepithelial transport from the tubular lumen into the peritubular capillary plasma. This process may be active (energy requiring) or passive (using no energy).

GLOMERULAR FILTERATION

- Glomerular filtrate is produced as a portion of a plasma flowing through each glomerulus is passively forced under pressure through the glomerular membrane into the lumen of the underlying Bowmans capsule.
- A high glomerular capillary blood pressure favouring filteration are the combined opposing forces of plasma colloid osmotic pressure and Bowmans capsule hydrostatic pressure
- Plasma flowing through the kidneys normally 20 % is filtered through the glomeruli,producing an average glomerular filtrate (rate)of 125 ml per minute
- The filterate is identical in composition to plasma except for plasma protein held back by the glomerular membrane.
- Afferent arteriolar vasoconstriction decreases flow of blood into the glomerulus,lowering glomerular blood pressure and GFR.
- Afferent arteriolar vasodilation leads to increased glomerular blood flow and a rise in GFR.

GLOMERULAR REABSORBTION

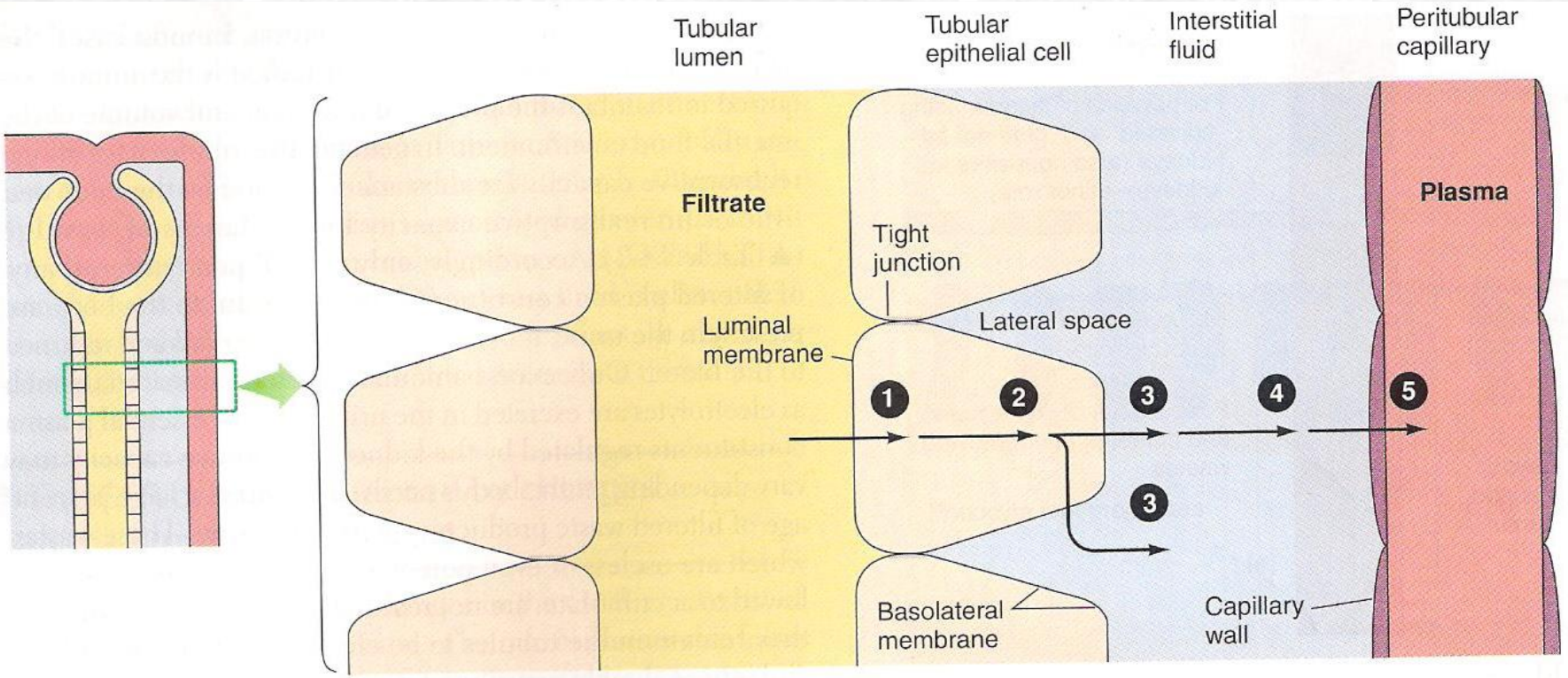
- Is highly selective
- Over 99% of the protein free filtered plasma is returned to the blood through re absorption
- On the average ,124ml out of 125ml filtered per min are reabsorbed so the final quantity of urine formed averages1ml / min.
- Thus of the 180L filtered per day,1.5L of the urine are excreted.

TUBULAR REABSORBTION

- Involves transepithelial transport from the tubular lumen into peritubular capillary plasma.This process may be active(energy requiring) or passive(using no energy).

STEPS INVOLVED IN TRANSEPITHELIAL TRANSPORT(ACROSS THE EPITHELIUM)

- **STEP 1:** Substances leave the tubular fluid by crossing the luminal membrane of the tubular cell.
- **STEP 2:** It must pass through the cytosol from one side of the tubular cell to the other.
- **STEP 3:** Traverses the basolateral membrane of the tubular cell to enter the interstitial fluid.
- **STEP 4:** It must diffuse through the interstitial fluid.
- **STEP 5:** It must penetrate the capillary wall to enter the blood plasma.



To be reabsorbed (move from the filtrate to the plasma), a substance must traverse five distinct barriers:

1. the luminal cell membrane
2. the cytosol
3. the basolateral cell membrane
4. the interstital fluid
5. the capillary wall

STEPS INVOLVED IN TRANSEPITHELIAL TRANSPORT(ACROSS THE EPITHELIUM)

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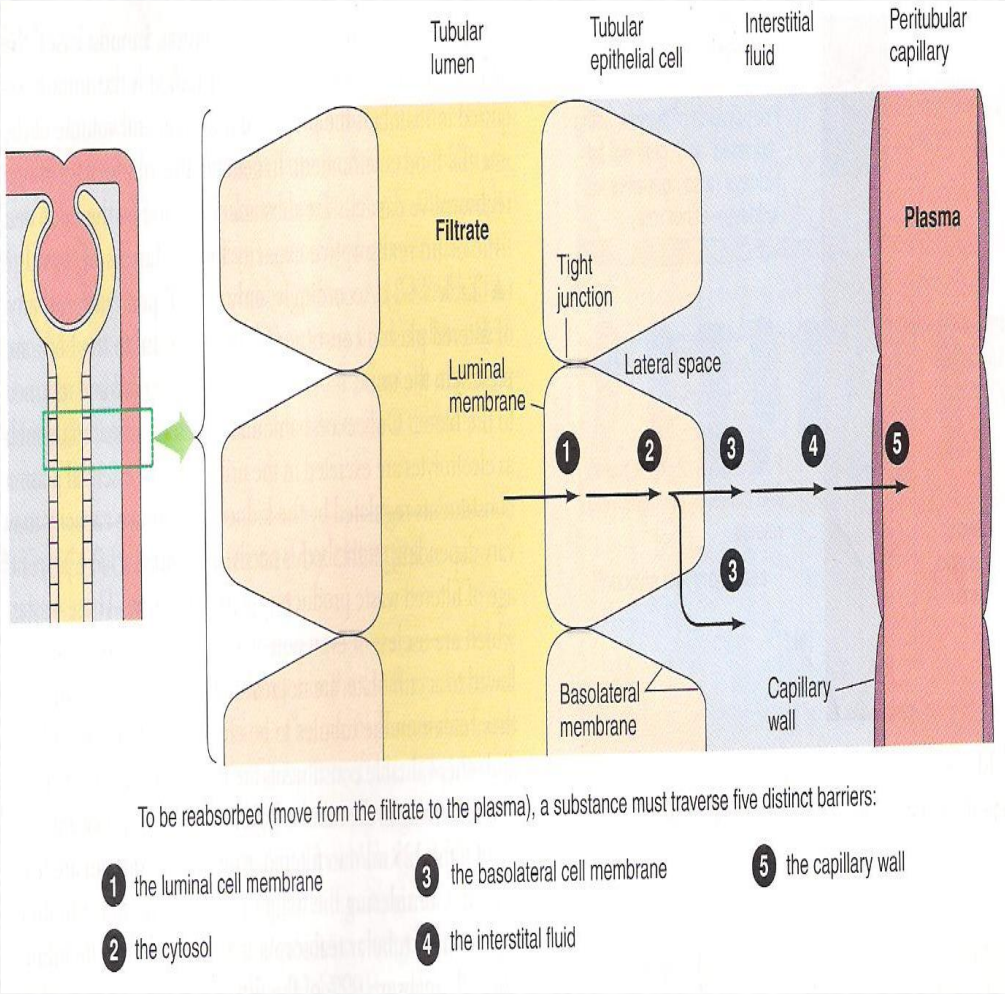


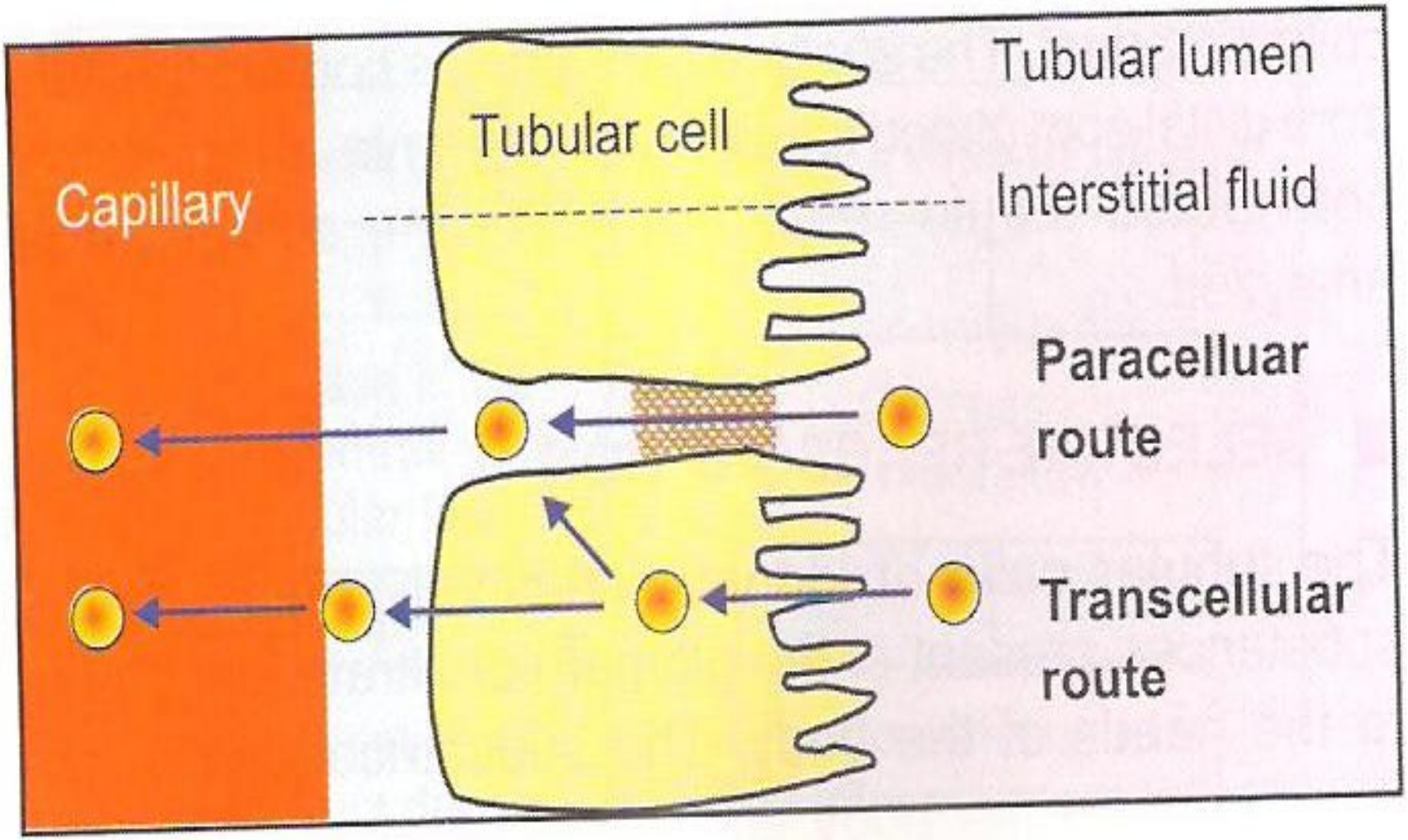
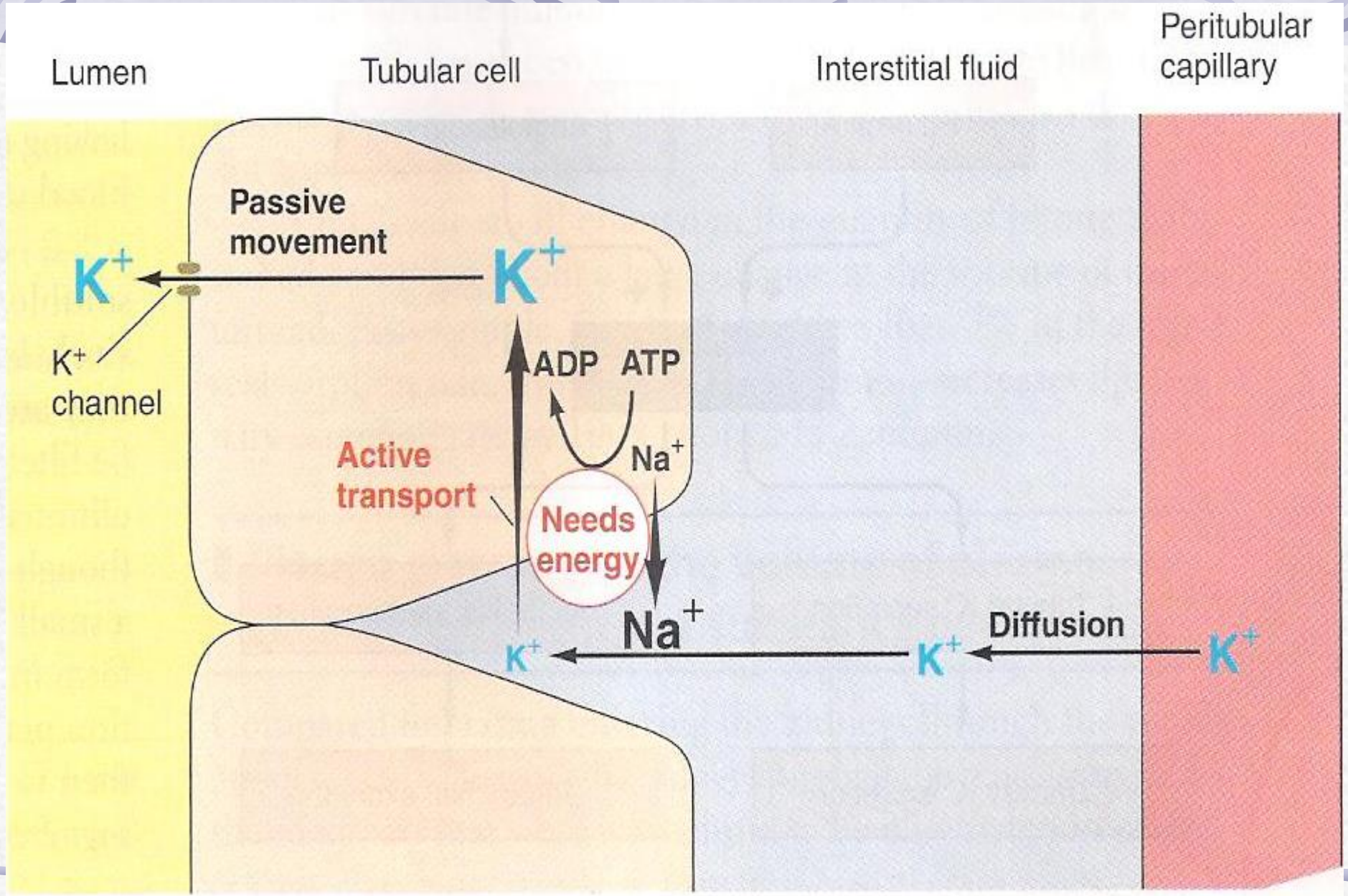


FIGURE 52-3: Routes of reabsorption


Lumen
Tubular cell
Interstitial fluid
Peritubular capillary
Passive movement
K+
K+
K+ channel
ADP ATP
Na+
Active transport
Needs energy
Na+
K+
K+
Diffusion
K+

TRANSEPITHELIAL TRANSPORT

- PASSIVE REABSORBTION
- All the steps in the transepithelial transport are passive(no energy expenditure)
- Net movement of substances occurs through osmotic gradient
- Example are Chloride,water,urea are passively absorbed.

- ACTIVE REABSORBTION
- If any one of the steps in the transepithelial transport of the substances require energy even if the four steps are passive.
- The net movement of the substances occurs against an electrochemical gradient.
- Example are glucose,aminoacids,sodium and electrolytes such as phosphates.

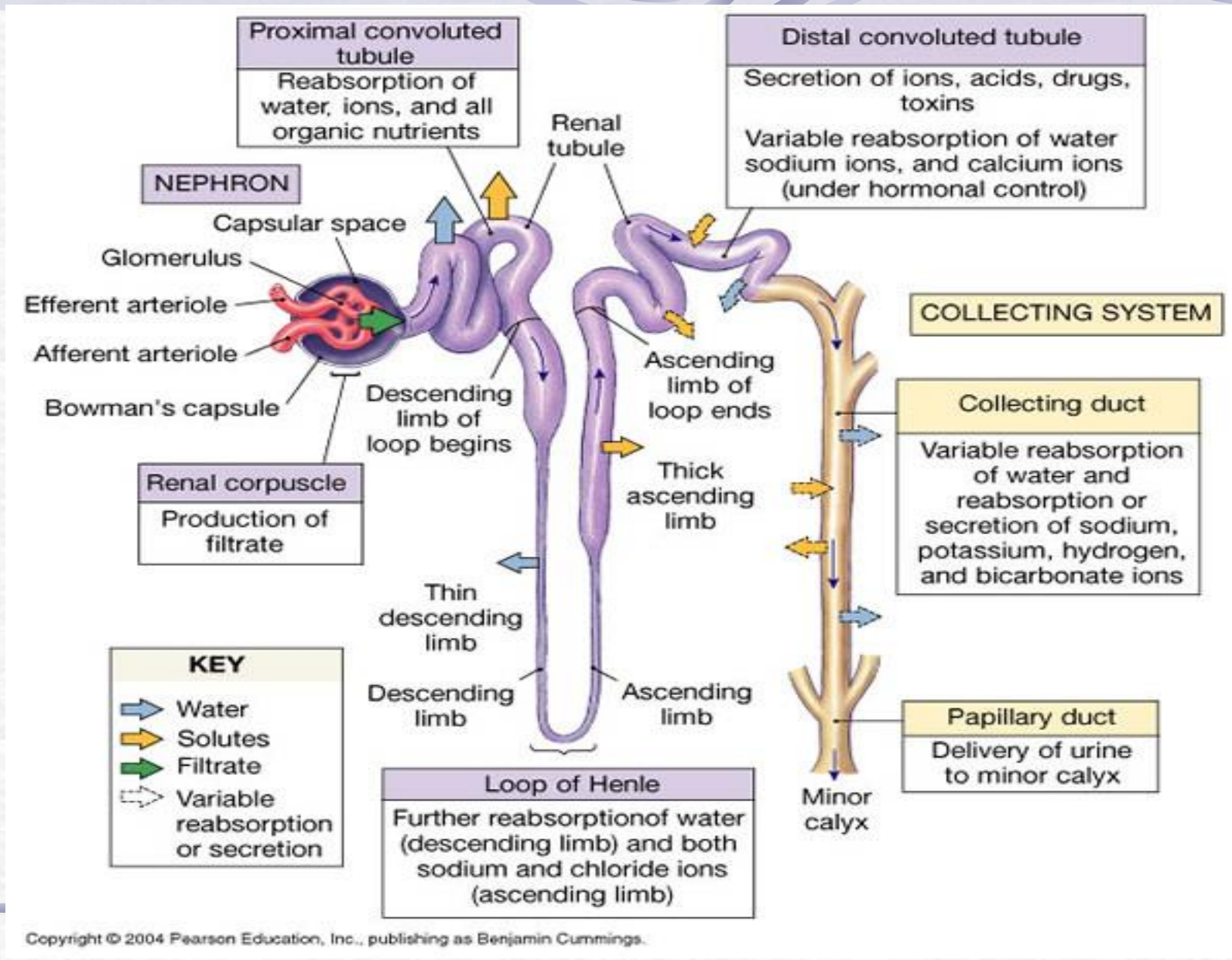


TABLE 20.4 Functions of Nephron Components

Part	Function
Renal Corpuscle	
Glomerulus	Filtration of water and dissolved substances from the plasma
Glomerular capsule	Receives the glomerular filtrate
Renal Tubule	
Proximal convoluted tubule	Reabsorption of glucose; amino acids; creatine; lactic, citric, uric, and ascorbic acids; phosphate, sulfate, calcium, potassium, and sodium ions by active transport
	Reabsorption of proteins by pinocytosis
	Reabsorption of water by osmosis
	Reabsorption of chloride ions and other negatively charged ions by electrochemical attraction
	Active secretion of substances such as penicillin, histamine, creatinine, and hydrogen ions
Descending limb of nephron loop	Reabsorption of water by osmosis
Ascending limb of nephron loop	Reabsorption of sodium, potassium, and chloride ions by active transport
Distal convoluted tubule	Reabsorption of sodium ions by active transport
	Reabsorption of water by osmosis
	Active secretion of hydrogen ions
	Secretion of potassium ions both actively and by electrochemical attraction
Collecting Duct	Reabsorption of water by osmosis

▲ TABLE 14-2

Fate of Various Substances Filtered by the Kidneys

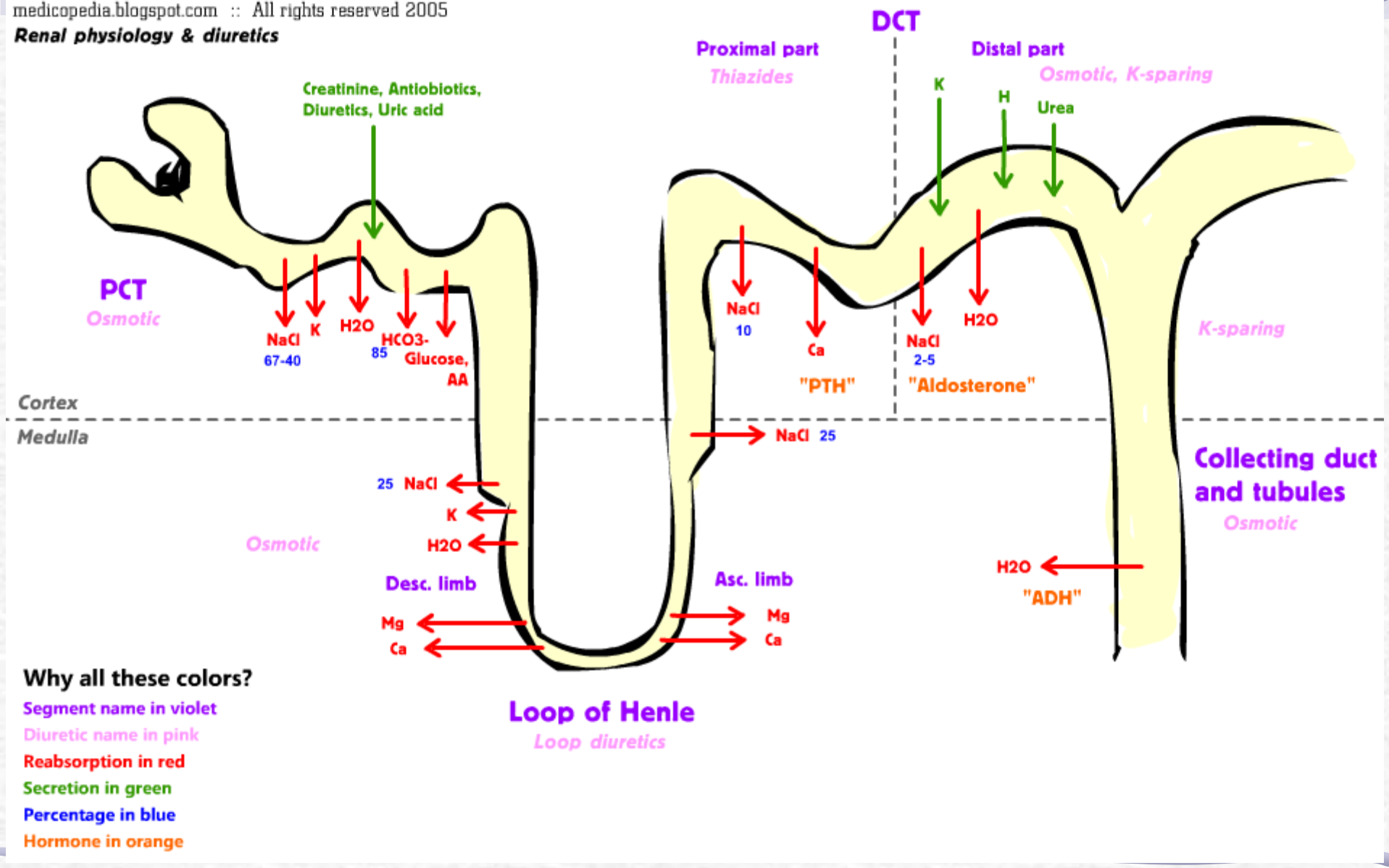
Substance	Average Percentage of Filtered Substance Reabsorbed	Average Percentage of Filtered Substance Excreted
Water	99	1
Sodium	99.5	0.5
Glucose	100	0
Urea (a waste product)	50	50
Phenol (a waste product)	0	100

SODIUM REABSORPTION IN THE PROXIMAL TUBULES

1. In the first half of the tubule sodium ions are transported from LUMEN OF RENAL TUBULES INTO THE TUBULAR EPITHELIAL CELLS by two ways

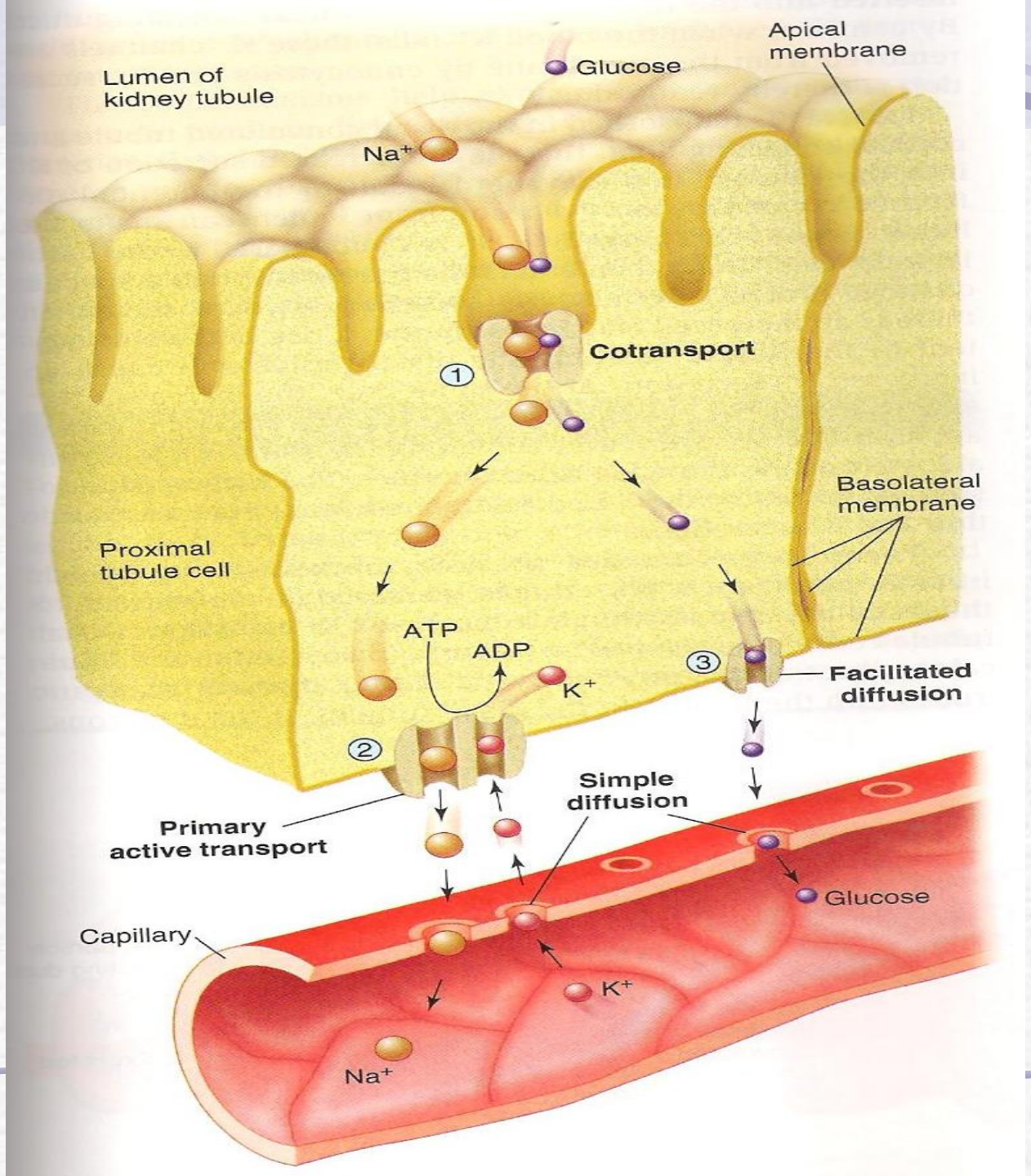
- In exchange for hydrogen ion by antiport(sodium counter port protein)
- Na+ is reabsorbed by symport(sodium co transport protein) with bicarbonate,glucose,aminoacids,phosphate and lactate
- Water follows the Na+ and since little Chloride is reabsorbed here, its concentration rises.

Renal physiology & diuretics

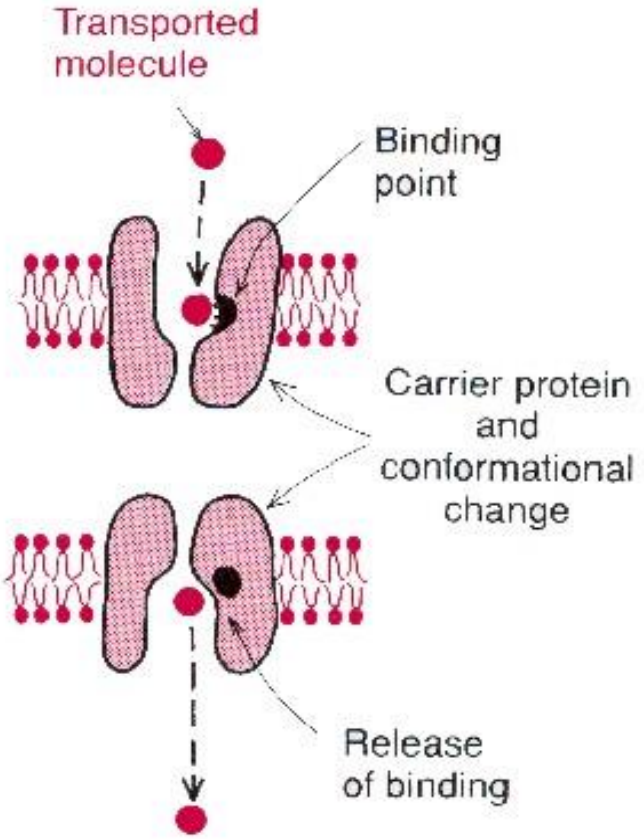


Why all these colors?

- Segment name in violet
- Diuretic name in pink
- Reabsorption in red
- Secretion in green
- Percentage in blue
- Hormone in orange

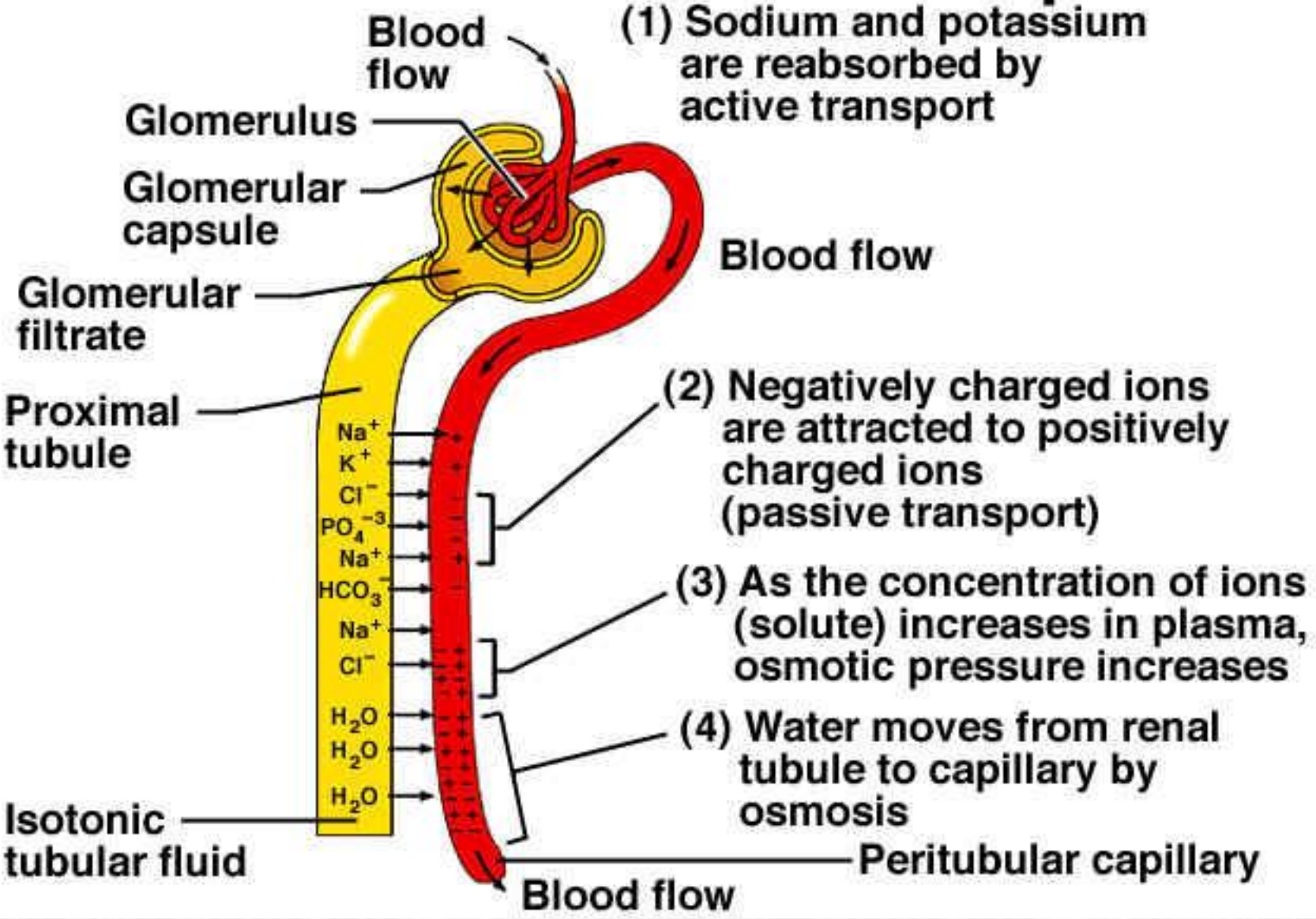

Lumen of kidney tubule
Glucose
Apical membrane
Na+
Cotransport
1
Basolateral membrane
Proximal tubule cell
ATP
ADP
K+
3
Facilitated diffusion
2
Simple diffusion
Primary active transport
Glucose
Capillary
K+
Na+

Postulated Mechanism for Facilitated Diffusion

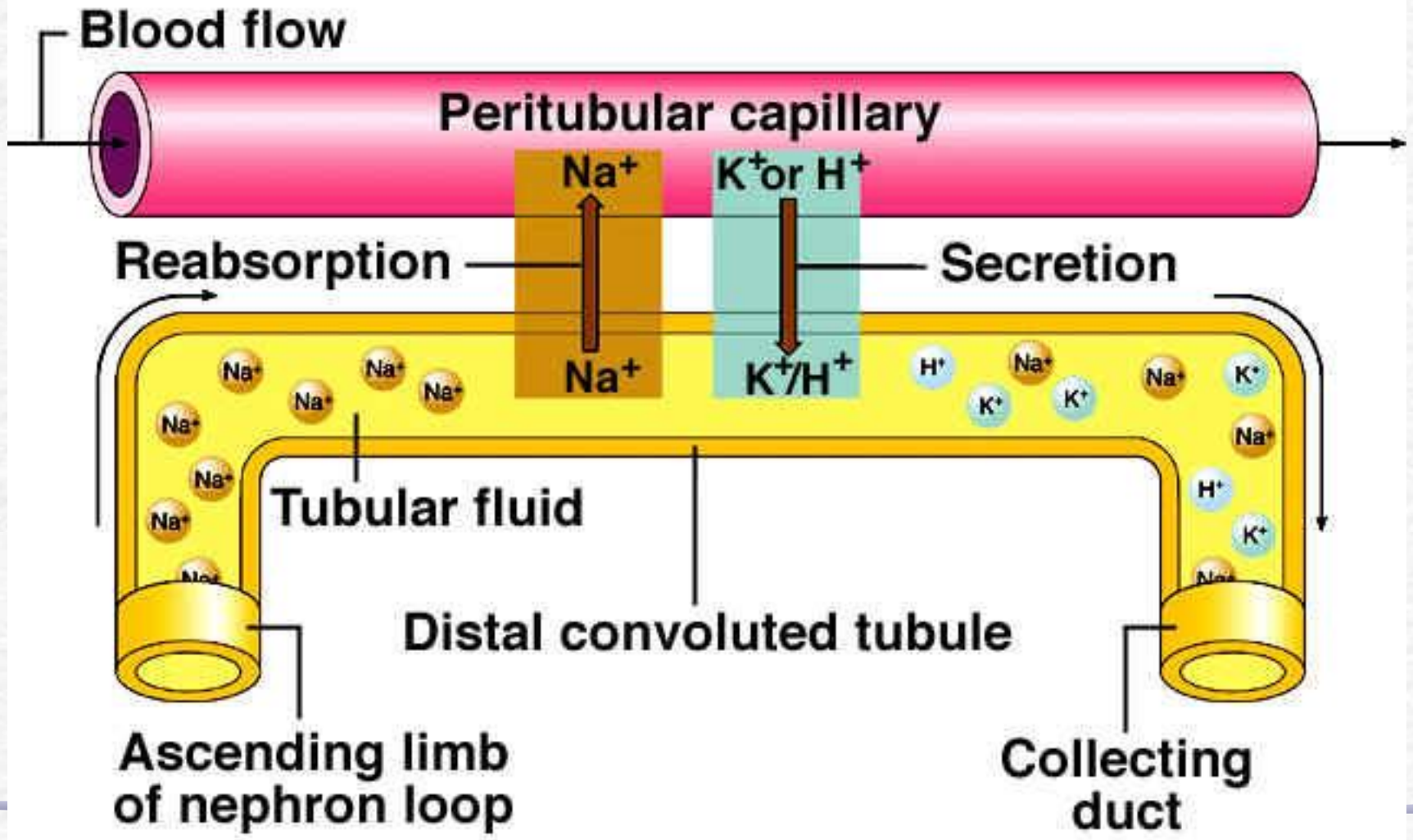


Molecule to be transported, e.g.-glucose, enters channel and binds to a receptor on the protein carrier. This causes a conformational change in the carrier which releases glucose to the opposite side of the membrane.

Sodium and Water Reabsorption



Tubular Reabsorption and Secretion



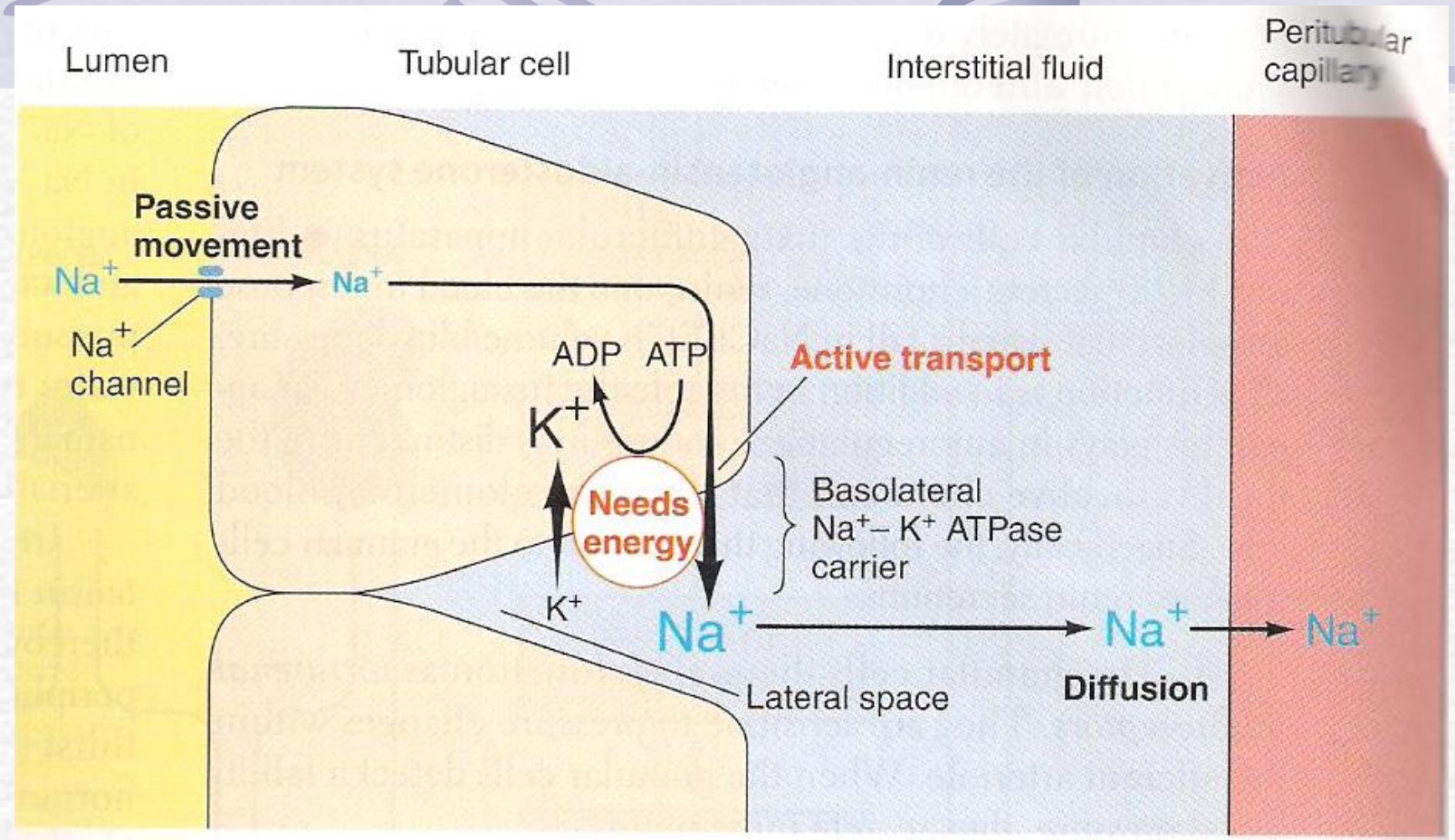


FIGURE 14-18

Sodium reabsorption

The basolateral Na^+–K^+ ATPase carrier actively transports Na^+ from the tubular cell into the interstitial fluid within the lateral space. This process establishes a concentration gradient for passive movement of Na^+ from the lumen into the tubular cell and from the lateral space into the peritubular capillary, accomplishing net transport of Na^+ from the tubular lumen into the blood at the expense of energy.

SODIUM REABSORPTION IN PROXIMAL TUBULES(CONTINUED)

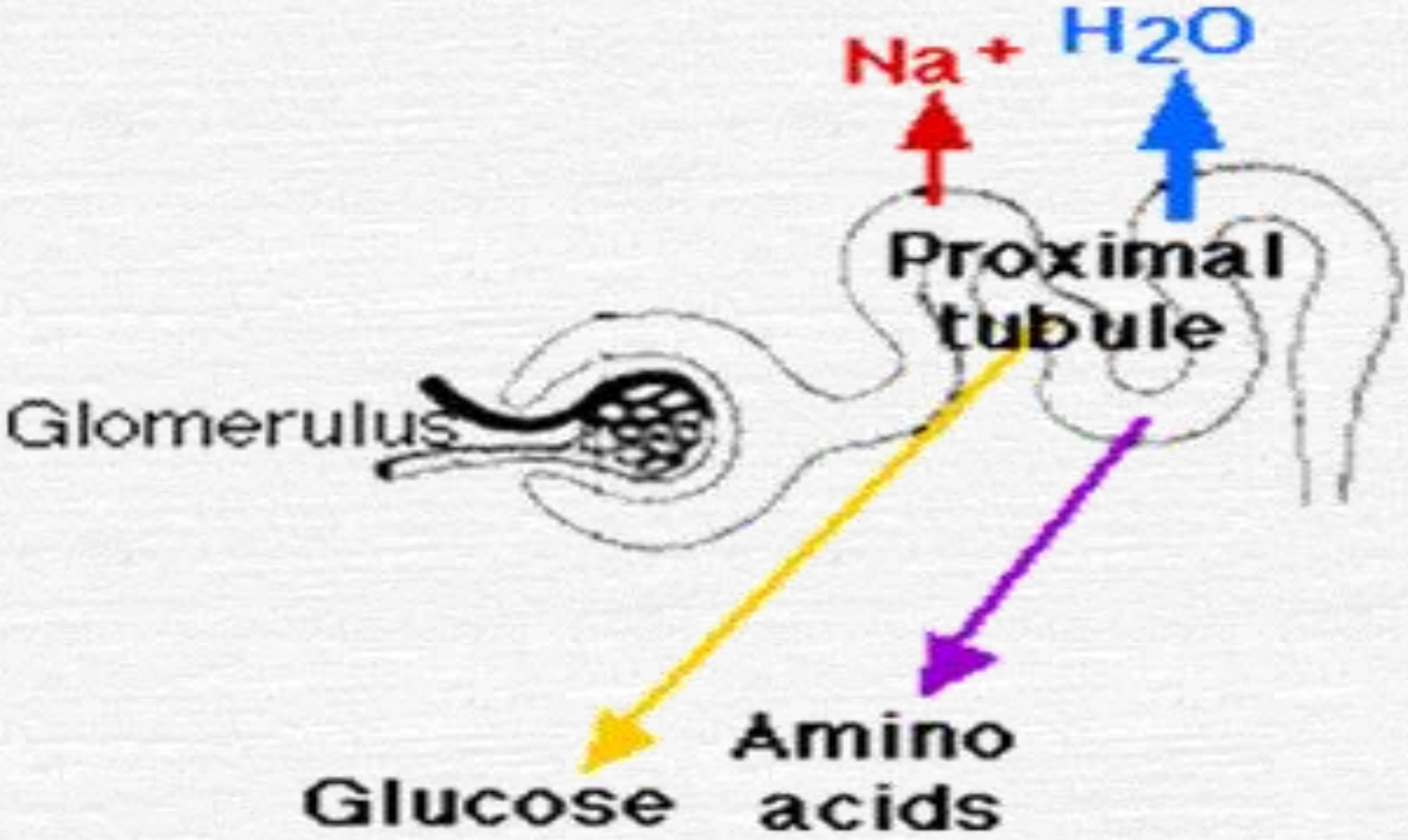
2. TRANSPORT FROM TUBULAR CELLS INTO THE INTERSTITIAL FLUID

- Sodium is pumped outside the cells by sodium potassium pump(Na+,k+ ATPase system) in the basal and lateral surfaces of the tubular epithelium cells of proximal tubules transport 3 Na+ ions out of the cell and 2K+ ions into the cell(2K+ diffuse back out of the cell into the interstitium due to increase permeability) creating _70mv inside epithelial cells.
- Transport of sodium out of the tubular cell by sodium potassium pump,decreases the sodium concentration within the cell.
- This develops an electrochemical gradient between the lumen(for example,_70mv inside the cell and_3mv in tubular lumen) resulting in diffusion of the sodium into the cell.

SODIUM REABSORPTION(DISTAL TUBULES AND COLLECTING DUCTS)

3. TRANSPORT FROM INTERSTITIAL FLUID INTO THE BLOOD

- From the interstitial fluid, sodium ions enter the Peritubular capillaries by concentration gradient
- In the distal convoluted tubule, the sodium reabsorption is stimulated by the hormone aldosterone secreted by adrenal cortex.
- Distal tubules and collecting ducts reabsorb about 10% of the filtered Na+.
- Loop of Henle(thick ascending limb) reabsorbs about 25% of the filtered Na+

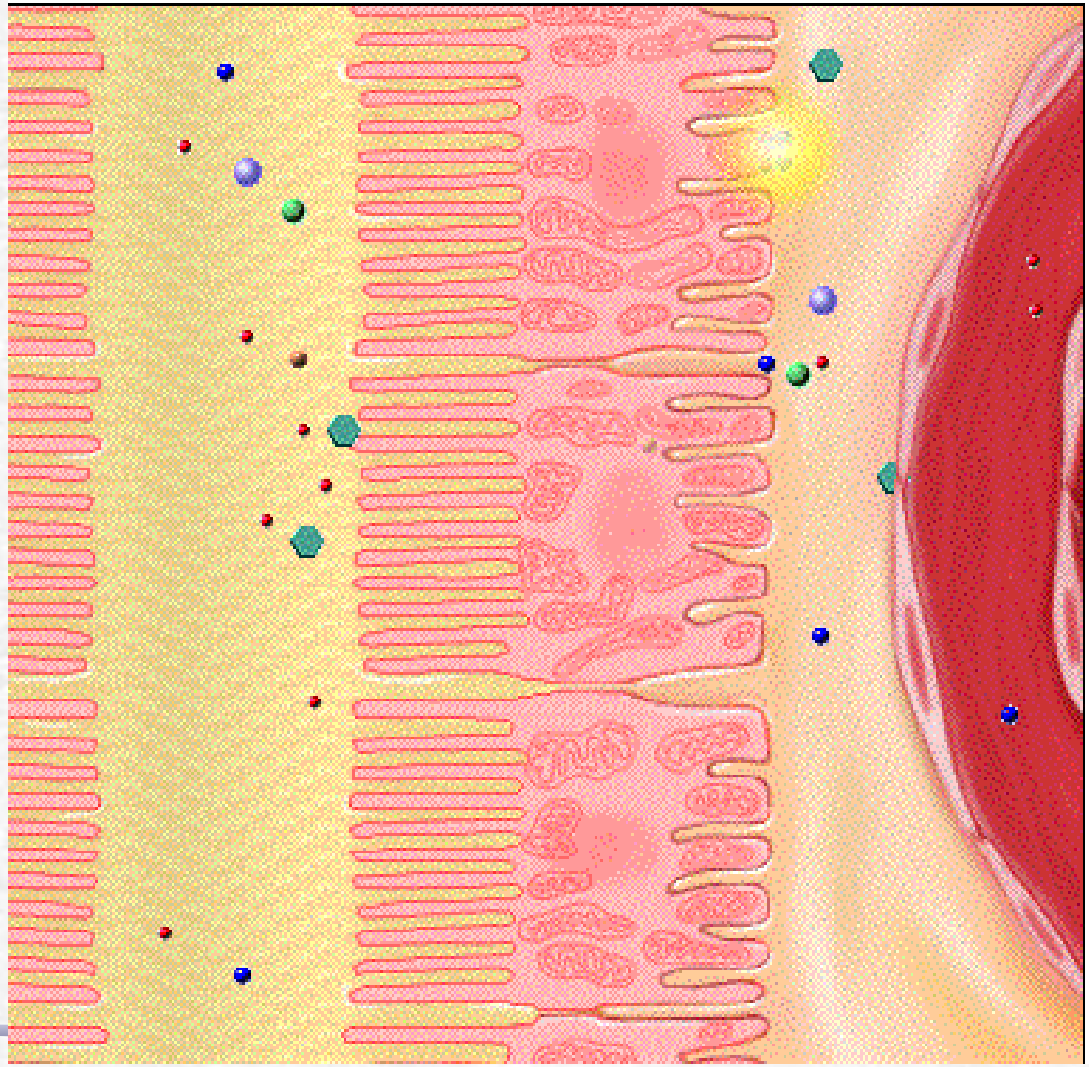

Na+
H2O
Proximal tubule
Glomerulus
Amino acids
Glucose

WATER REABSORPTION

- Occurs from the Proximal and Distal convoluted tubules and in collecting duct

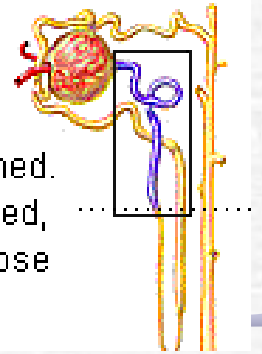
  REABSORPTION OF WATER FROM PROXIMAL CONVOLUTED TUBULE(OBLIGATORY WATER REABSORPTION)
- Proximal convoluted tubule is highly permeable to water,it is secondary(obligatory) to sodium reabsorption.When Na+ is reabsorbed from the tubule, the osmotic pressure decreases.It causes osmosis of water from tubule.

Summary of Reabsorption in the PCT



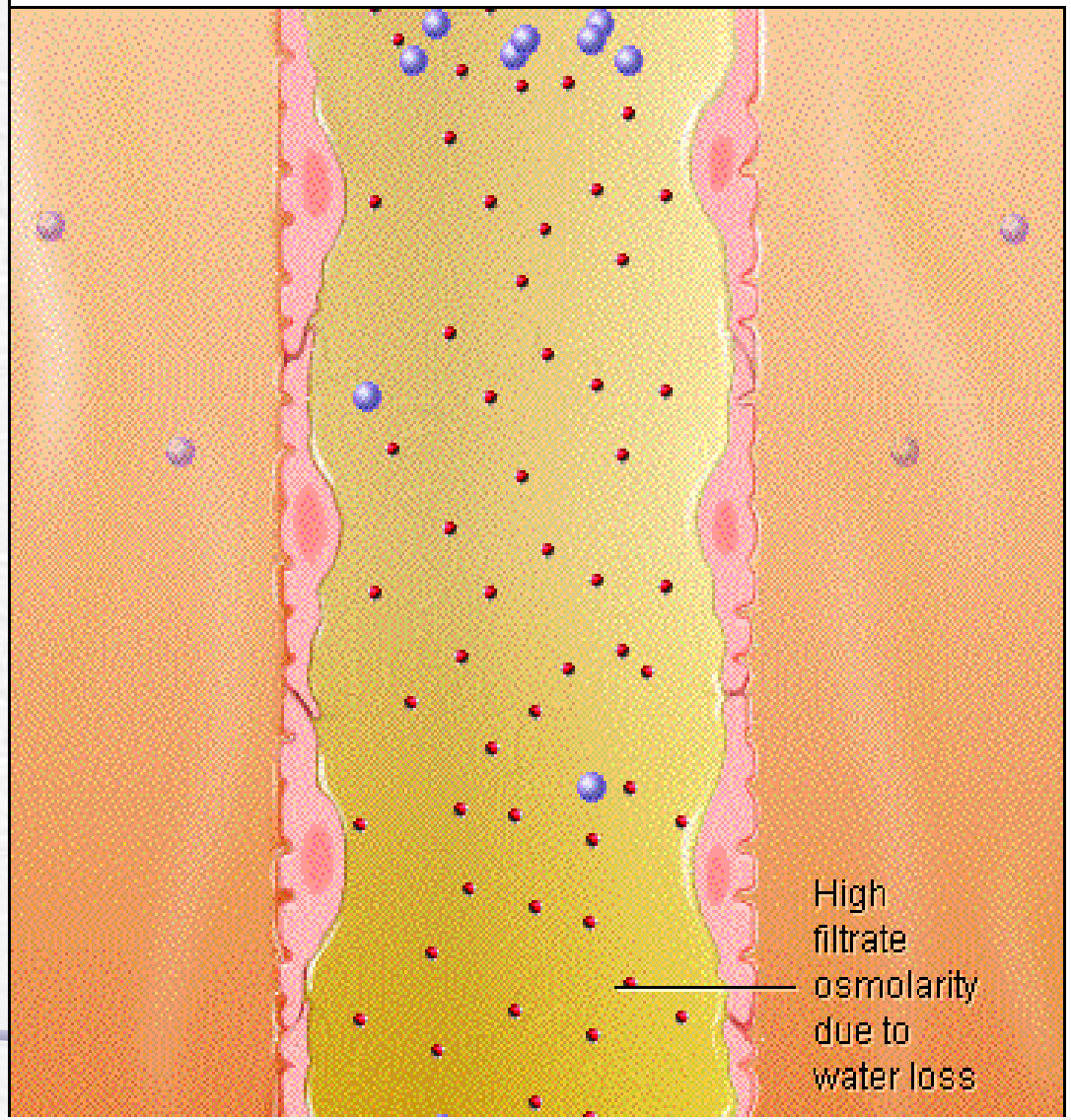
Summary of PCT activities:

- Na^+/K^+ ATPase ion pumps drive the reabsorption of water and solutes by increasing sodium ion concentration of interstitium
- Hydrogen ions are secreted into the filtrate to provide an acid/base balance
- Channels and transport molecules provide passage for solutes to diffuse between filtrate and cytosol
- Water and solutes move by **bulk flow** from interstitium into peritubular capillaries



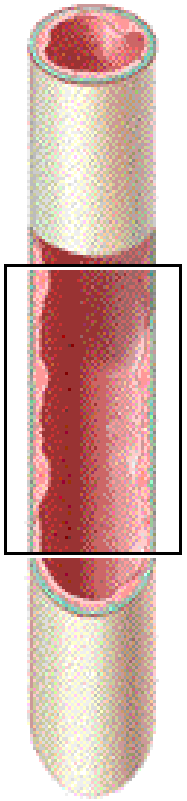
Net result: valued substances are reclaimed. 65% of filtrate reabsorbed, including 100% of glucose and amino acids.

Reabsorption in Thin Descending Loop of Henle



Epithelium transitions from **cuboidal epithelial cells** to **simple squamous epithelial cells**.

Membranes are permeable to water but not to NaCl.



Few membrane proteins serving as channels or transporter molecules.

Net result is increased osmolarity of filtrate.

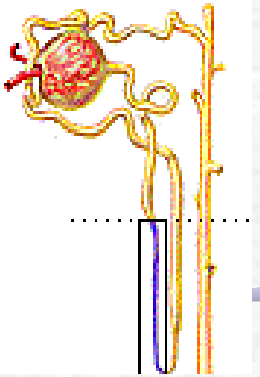
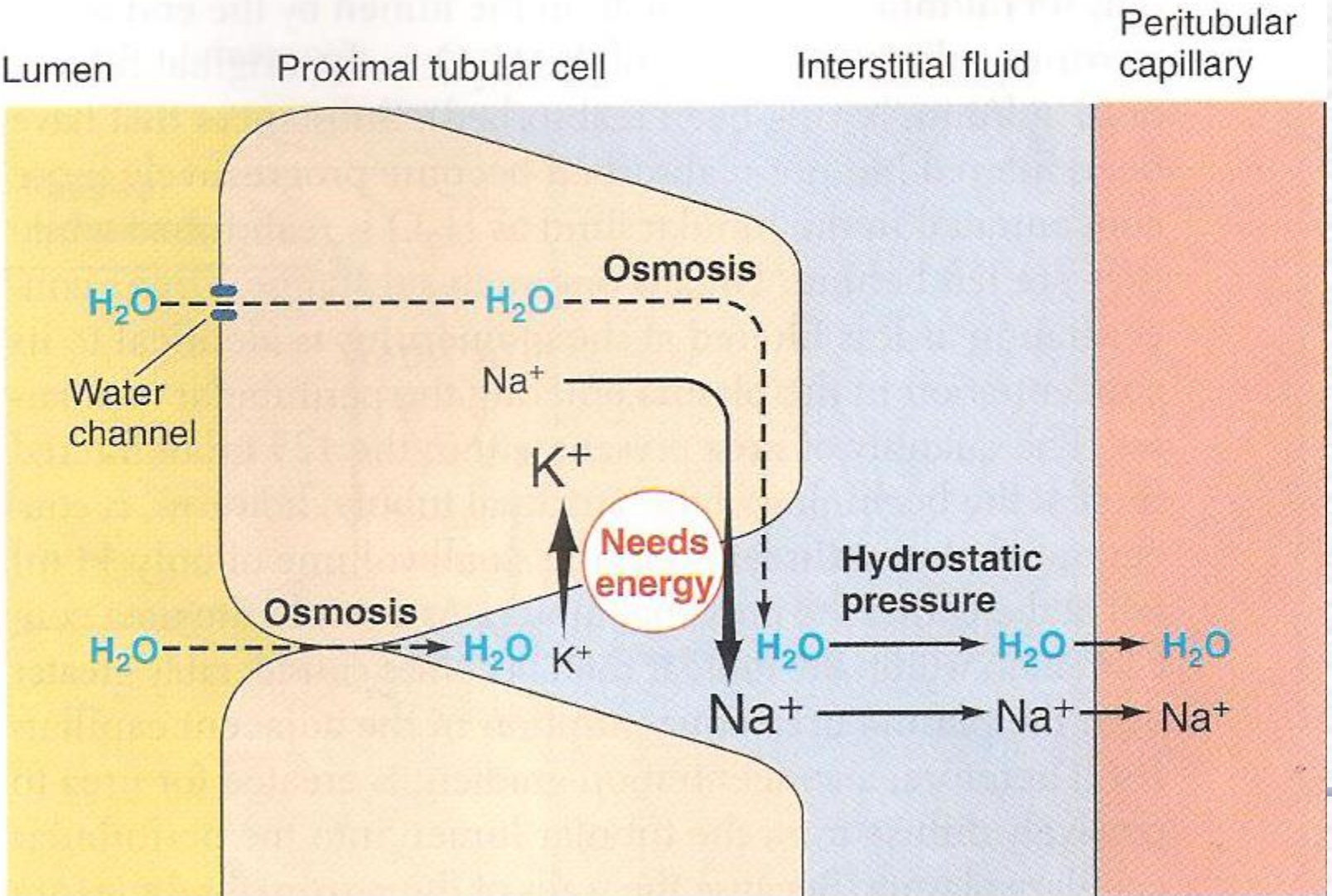


FIGURE 14-22

Water reabsorption in the proximal tubule

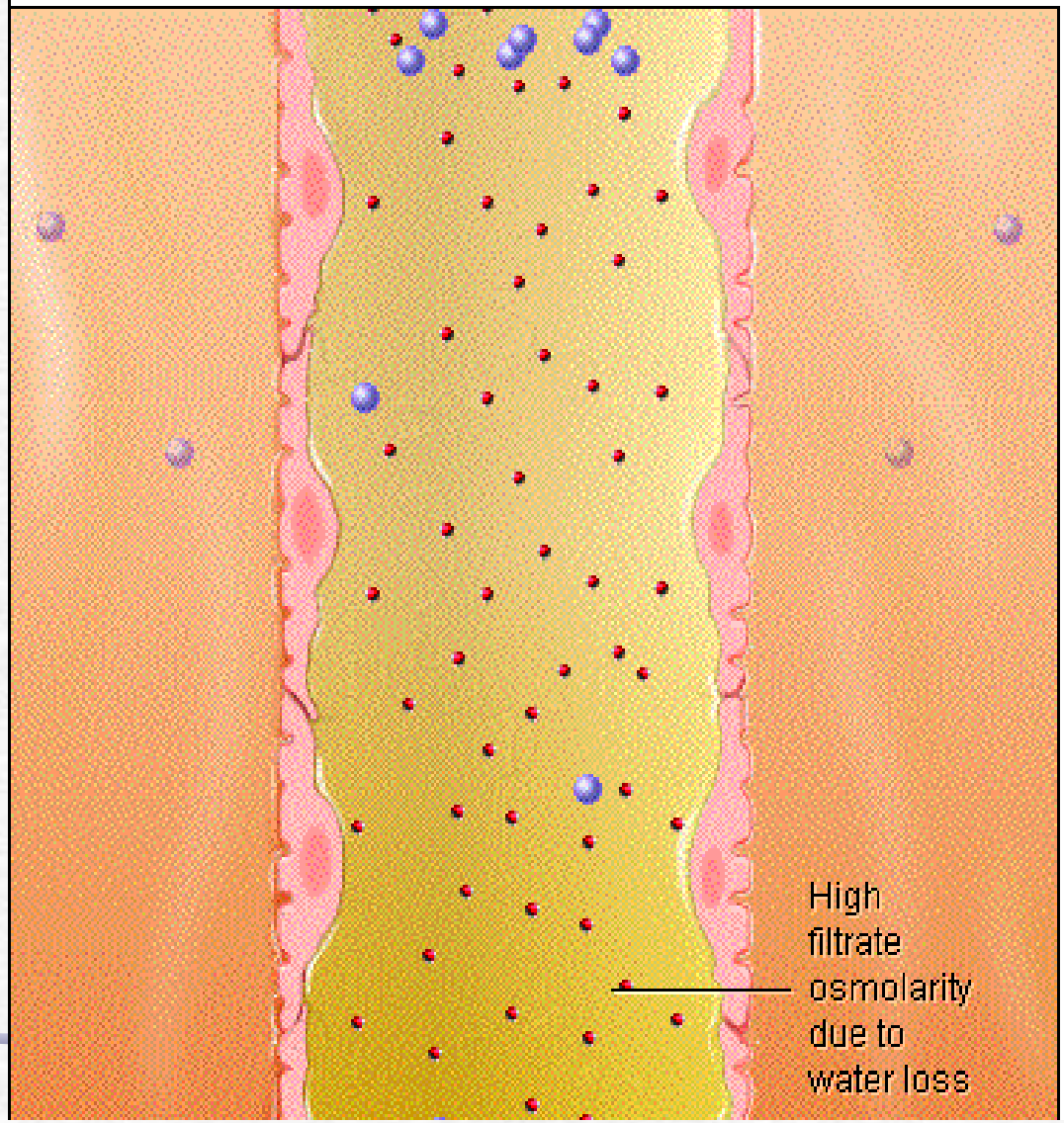
The force for H_2O reabsorption is the compartment of hypertonicity in the lateral spaces established by active extrusion of Na^+ by the basolateral pump. The dashed arrows show the direction of osmotic movement of H_2O.



WATER REABSORPTION

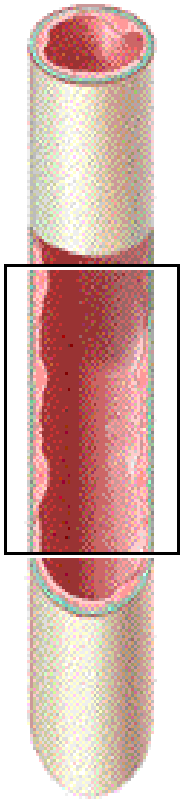
- REABSORPTION OF WATER FROM DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT(FACULTATIVE WATER REABSORPTION)
- Normally, the distal convoluted tubule and the collecting duct are not permeable to water.
- Presence of antidiuretic hormone(ADH),these segments become permeable to water.This type of water reabsorption in the presence of ADH is called facultative water reabsorption.

Reabsorption in Thin Descending Loop of Henle



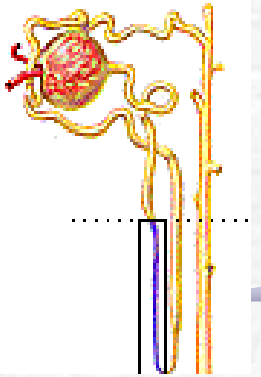
Epithelium transitions from **cuboidal epithelial cells** to **simple squamous epithelial cells**.

Membranes are permeable to water but not to NaCl.

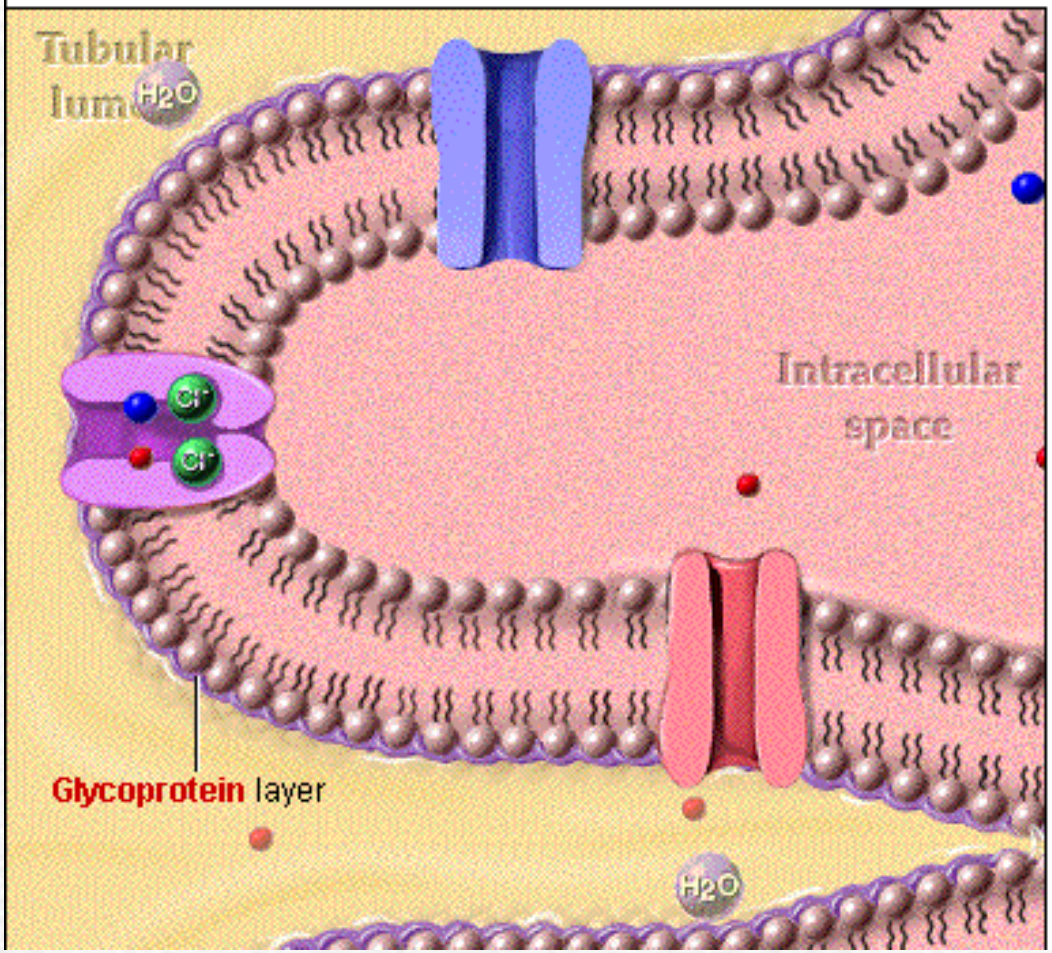


Few membrane proteins serving as channels or transporter molecules.

Net result is increased osmolarity of filtrate.



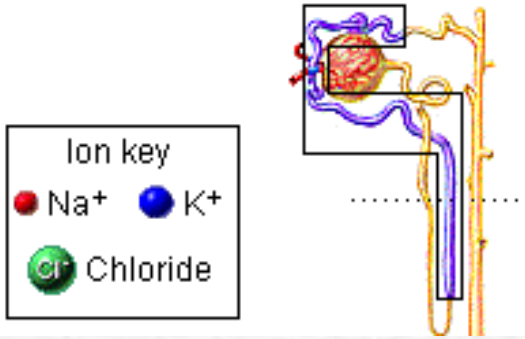
Reabsorption in Ascending Loop of Henle and Early DCT: Luminal Membrane



Carrier molecule cotransports a potassium ion, two chloride ions, and a sodium ion.

Intracellular potassium concentration changes little because potassium returns to the filtrate and interstitium through its channels.

Imported chloride ions follow sodium ions to the basolateral membrane and diffuse into interstitium.



DEFINITIONS

- REABSORPTION OF WATER FROM PROXIMAL CONVOLUTED TUBULE(OBLIGATORY WATER REABSORPTION)
- 80 percent

- REABSORPTION OF WATER FROM DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT(FACULTATIVE WATER REABSORPTION)
- 20 percent

REABSORPTION OF GLUCOSE

- Glucose is completely reabsorbed in the proximal convoluted tubule.
- It is transported by **sodium co transport mechanism**. Glucose and sodium bind to a common carrier protein in the luminal membrane of tubular epithelium and enter the cell.

REABSORBTION OF AMINO ACID

- Amino acids are also completely absorbed completely in proximal convoluted tubule.
- Amino acids reabsorbed actively by the secondary active transport mechanism along with sodium.

REABSRPTION OF BICARBONATE

- Bicarbonate is completely actively, mostly in proximal tubule. It is reabsorbed in the form of carbon dioxide.
- Bicarbonate is mostly present as sodium bicarbonate in the fitrate.Sodium bicarbonate dissociates into sodium and bicarbonate in the tubular lumen
- Sodium diffuses into tubular cell in exchange of hydrogen.
- Bicarbonate combines to with hydrogen form carbonic acid.

REABSORPTION OF BICARBONATE

- H + HCO3 combined to form H2CO3
- H2CO3 SPLITS UP TO FORM H2O +CO2(Lipid soluble)
- H2O+CO2 COMBINED TO FORM H2CO3
- H2CO3 splits to form H +HCO3(Bicrbonate)
- Bicarbonate from the tubular cell enter the interstitium.There it combine with sodium to form sodium bicarbonate

THRESHOLD SUBSTANCES

- Depending upon the degree of reabsorption,the various substances are classified into three substances

1. High threshold substances
2. Low threshold substances
3. Non threshold substances

HIGH THRESHOLD SUBSTANCES

- The food substances like **glucose,aminoacids,acetoacetate ions and vitamin** are completely reabsorbed from renal tubules and do not appear in the urine under normal conditions.
- These substances can appear in the urine, only if their concentration in plasma is abnormally high or in renal diseases when reabsorption is affected.

LOW THRESHOLD SUBSTANCES

- The substances such as **urea,uric acid and phosphate** are reabsorbed to little extend.
- These substances appear in the urine even under normal conditions. Such substances are known as the low threshold substances.

NON THRESHOLD SUBSTANCES

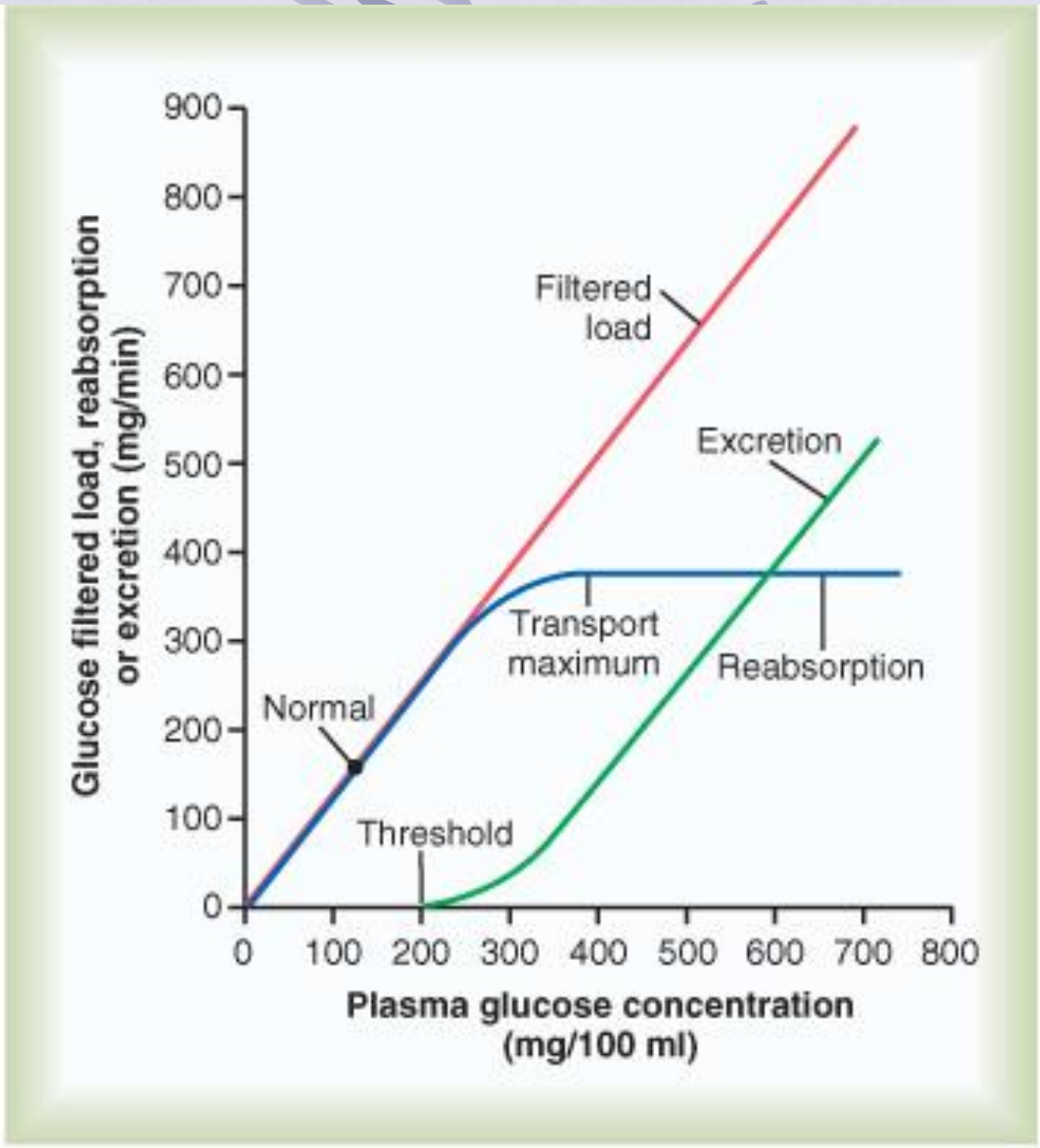
- The metabolic end products like **creatinine** are not at all reabsorbed and are excreted in urine irrespective of their plasma level.These substances are called non theshold substances.

DEFINITIONS

- **Saturation** refers to the maximum rate of transport that occurs when all available carriers are occupied with substrate. When concentration are below the saturation point, then the transport rate is dictated by solute concentration.
- The transport rate at saturation is called the **transport maximum.**
- The plasma concentration of substrate at which the transport maximum occurs is called the **renal threshold.**

TM VALUE

- The substances reabsorbed actively from the renal tubules require some specific transport system.
- The rate of reabsorption of any substance depends upon the rate at which this specific transport system operates.
- The transport system in turn depends upon the carrier substances or enzymes.
- So,for every actively reabsorbed substance, there is a maximum rate at which it could be reabsorbed.
- The max rate at which a substance is reabsorbed from the renal tubule is called tubular transport maximum or Tm.The Tm for glucose(TmG)Is 380mg/min.



THRESHOLD LEVEL IN PLASMA FOR SUBSTANCES HAVING Tm VALUE

- Every substance having Tm value has also a threshold level in plasma or blood.
- Below that threshold level, the substance is completely reabsorbed and does not appear in urine.
- When the concentration of that substance increases above that level, the excess amount is not reabsorbed and so it appear in urine.
- This level is called the renal threshold of that substance,(for glucose is 180mg%).
- Glucose is completely absorbed from tubular fluid, and does not appear in urine if the concentration in blood is below 180mg%.
- Blood glucose rises beyond 180mg% it is not reabsorbed completely hence it appear in urine.

TUBULAR SECRETION

- Some substances are secreted into the lumen from the peritubular capillaries through the tubular epithelial cells.It is known as tubular secretion or tubular excretion
- Substances found to be secreted are

1. Para aminohippuric acid(PAH)
2. Penicillin.