Lec:

Renal system *(Urinary System)*

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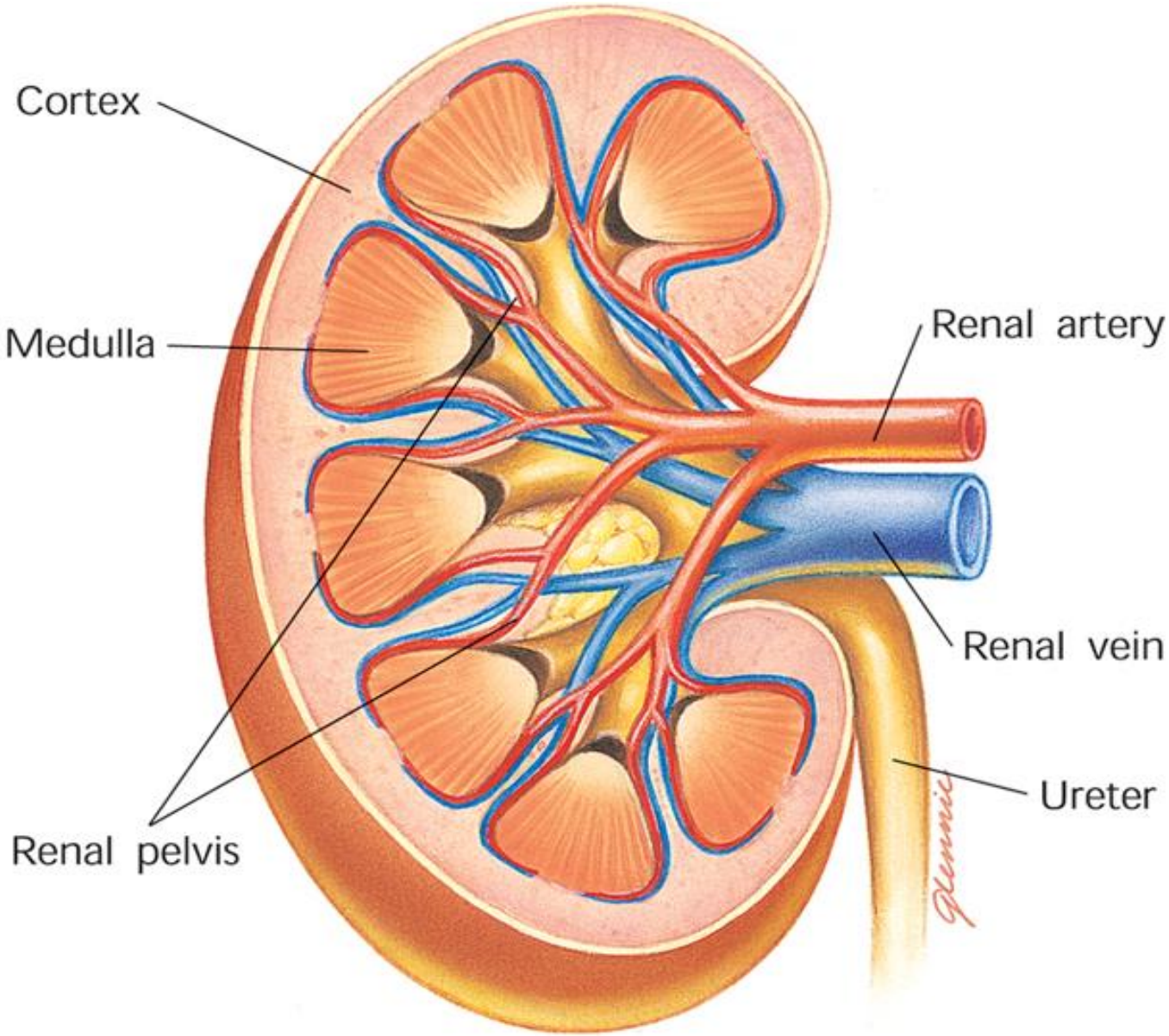
- ***Renal System:- (Urinary System)***
- - The urinary system is composed of:
- 1. Two kidneys. 2. Two ureters.
- 3. Urinary Bladder. 4. Urethra.
- - The kidney plays a major role in controlling the volume of blood(water) and also controlling ion concentration and PH.
- - The kidney is a major excretory organ, responsible for the removal of metabolic waste products from the blood.

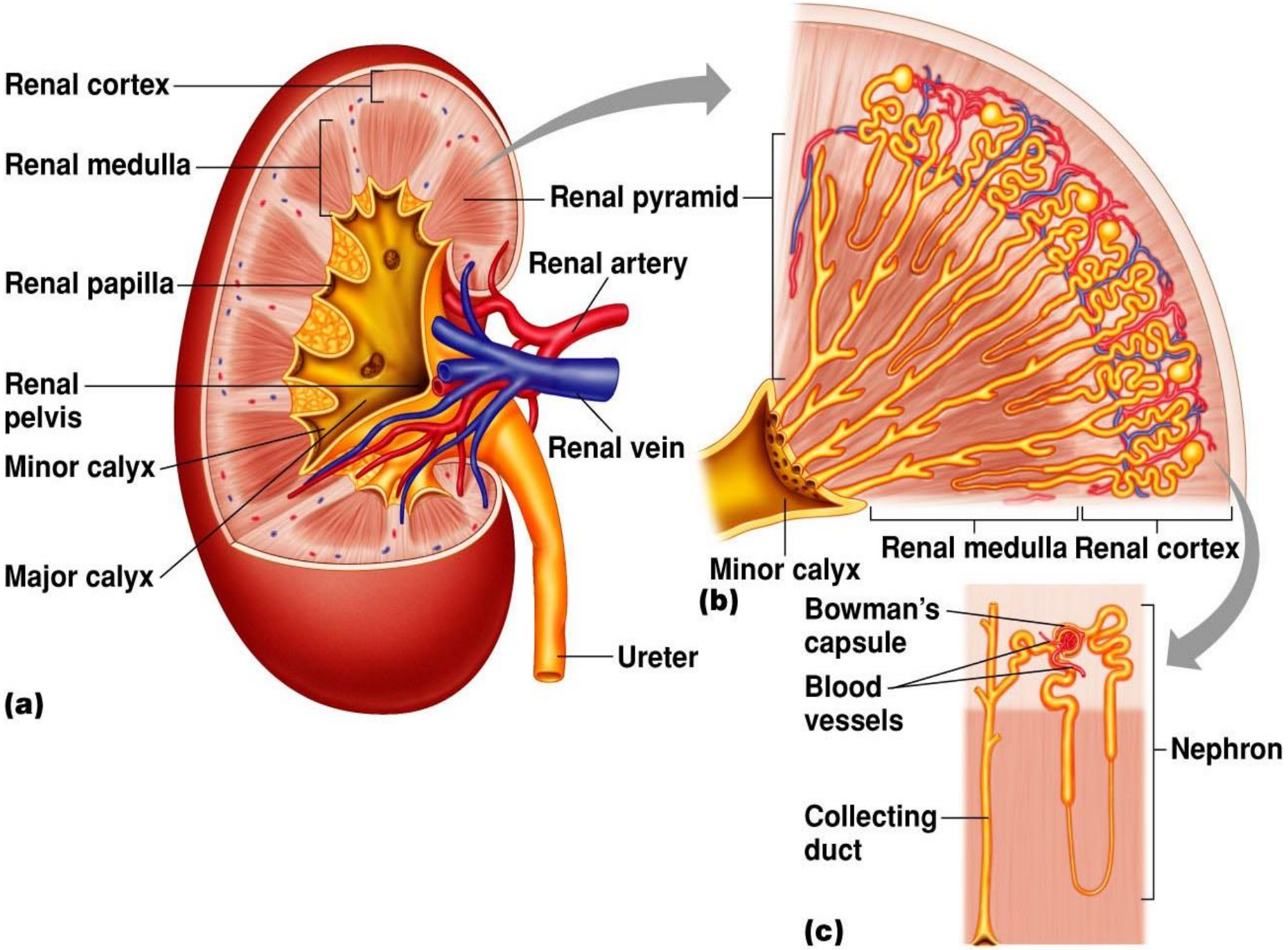
- - The kidney acts on the plasma first converting it to ultrafiltrate to which it later adds and removes substances so that the final product is urine.
- *Renal Functions:*
- regulation of body water and electrolytes.
- excretion of waste products.
- regulation of blood pressure (long and short term).
- regulation of acid-base balance.
- regulation of vitamin D3 production.

- ***Physiologic anatomy of the kidney:- (Cortex & Medulla)***
- **Medulla:-** this tissue appears as pyramids their apex are towards the renal pelvis it appears striated because of the collecting ducts and loops of Henle.
- **Cortex:-** this tissue appears granulated because of the large number of glomeruli, the cortex is surrounded by a connective tissue called Renal Capsule.
- *Outside the renal capsule there is a thick layer of fat called Renal Fat Pad which protects the kidney from mechanical shocks


Cortex
Medulla
Renal pelvis
Renal artery
Renal vein
Ureter

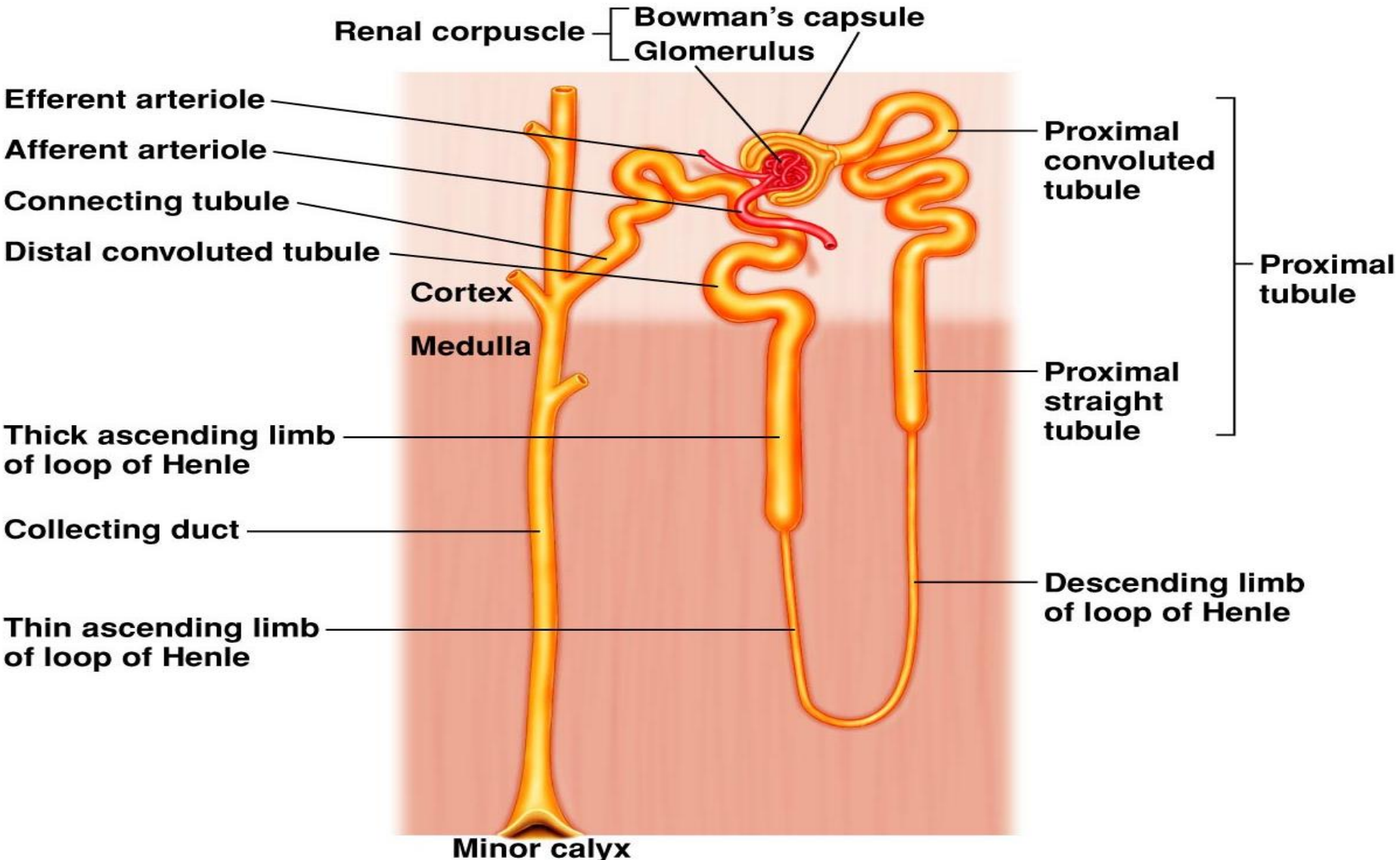
- ***Functional Anatomy:-***
- The kidney is a complex structure consisting of one million or more, structural and functional unites called Nephrons, separated by connective tissue(interstitial tissue).
- The Nephron is the functional unit because it accomplishes the entire complex of processes that result in the formation of urine.
- Each individual renal tubule and its glomerulus is a nephron. And the size of the kidney in various species is determined largely by the number of nephrons they contain.

- Each human kidney has approximately 1.3 million nephrons.(the human needs 1/3 of the 1.3 million nephrons in order to survive.
- ¤ the glomerulus 200µm in diameter is formed by the imagination of a tuft of capillaries into the dilated blind end of the nephron(Bowman's Capsule).
- The capillaries are supplied by an afferent arteriole and drained by an efferent arteriole.

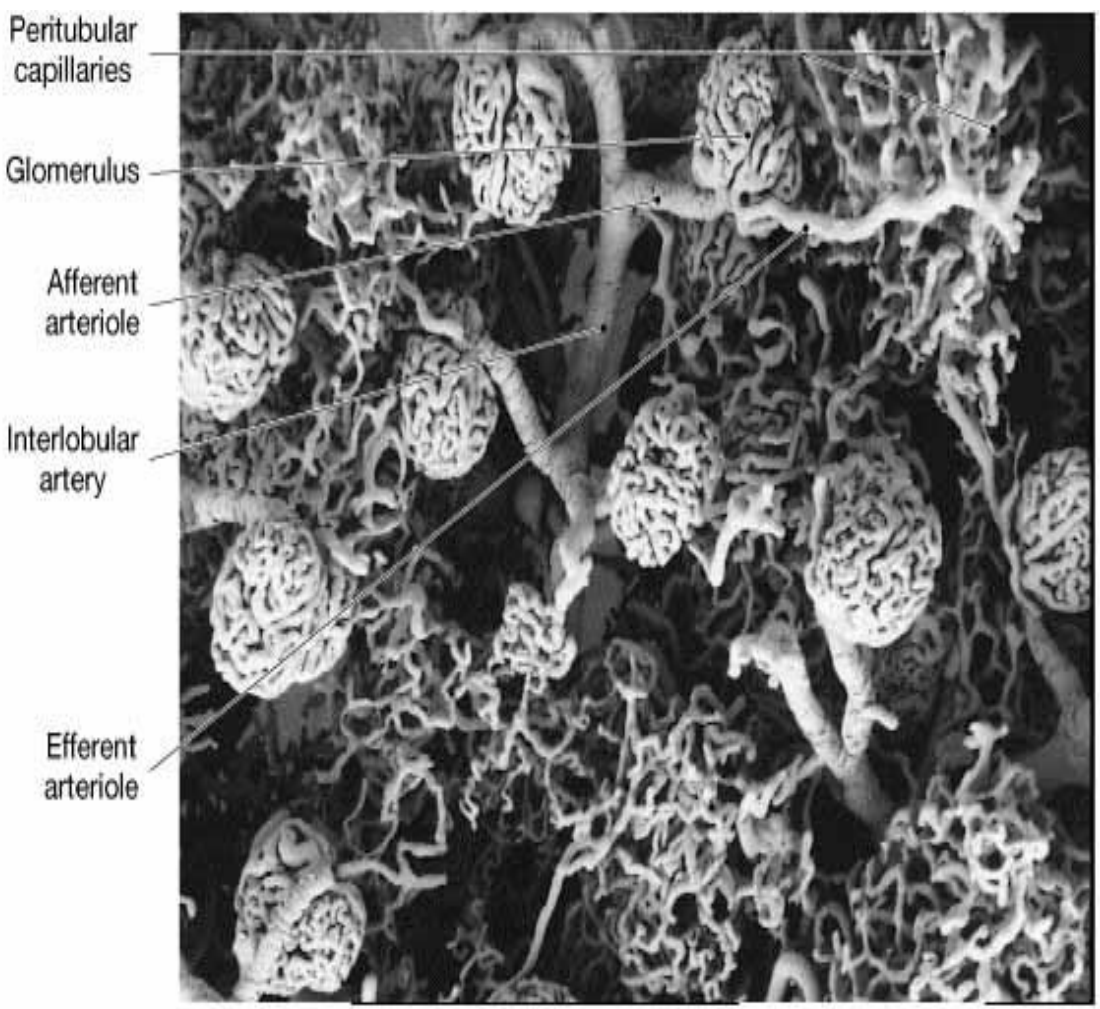

Renal cortex
Renal medulla
Renal pyramid
Renal artery
Renal papilla
Renal pelvis
Renal vein
Minor calyx
Major calyx
Ureter
(a)
Minor calyx
Renal medulla
Renal cortex
(b)
Bowman's capsule
Blood vessels
Nephron
Collecting duct
(c)

- ¤ The tubule starts with:-
- **1- Bowman's capsule:** the invaginated end of the tubule surrounding the glomerular tuft. {two cellular layers separate the blood from the glomerular filtrate in Bowman's capsule, the capillary endothelium, and specialized epithelium of the capsule made up of podocytes.
- The layers are separated by a basal lamina (basement membrane)}, in addition to the Mesangial cells located between the basal lamina and endothelium (they are contractile and play a role in the regulation of glomerular filtration).

Anatomy of the Nephron



Renal Corpuscles



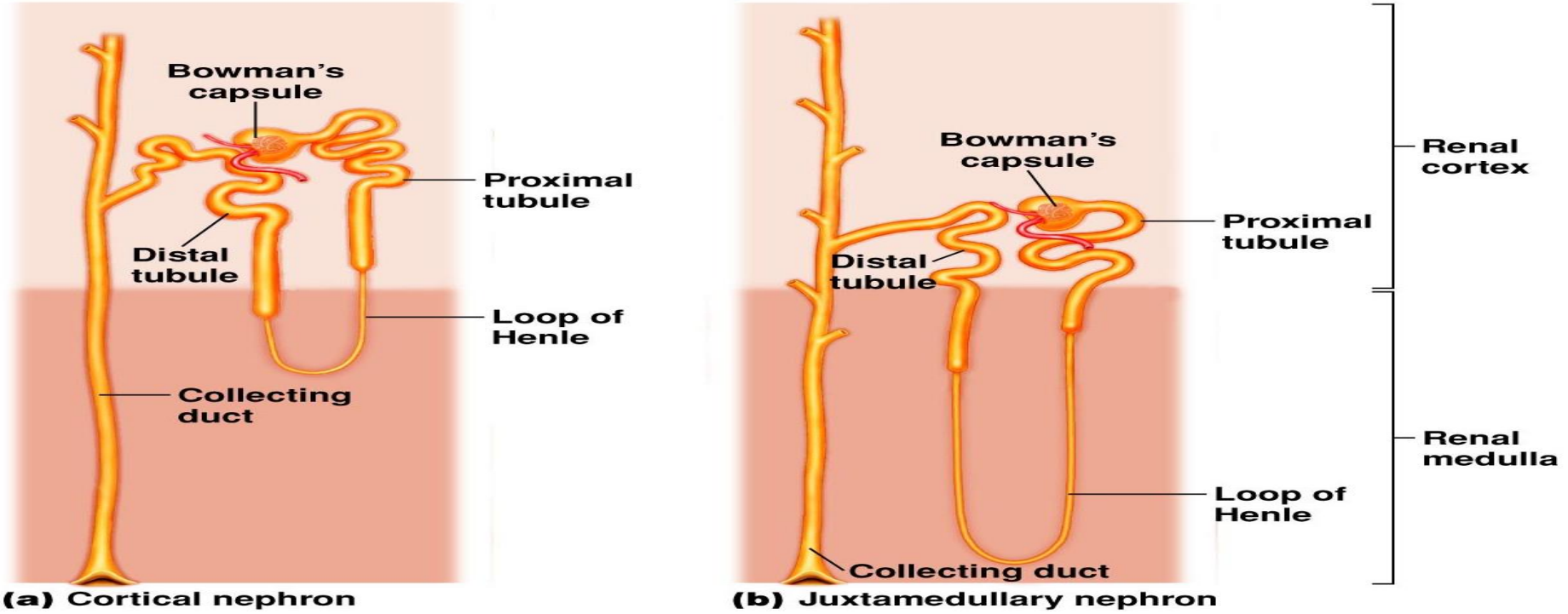
(b) Glomeruli and associated blood vessels (SEM x 94)

- * The endothelium of glomerular capillaries is fenestrated with pores that are 50-100 nm in diameter.
- * The epithelium(podocytes) form filtration slits approximately 5-9 nm in diameter.
- **2- Proximal Convoluted Tubule:** (PCT) it contains cuboidal cells that are linked tightly at the apex but contain large lateral intracellular space. Its rich with mitochondria & the surface is covered with micro-villi. Around 65% of filtrated fluid is reabsorbed in the PCT.

- **3- Loops of Henle:** thin descending loop with high permeability to water & thick ascending loop which is impermeable to water but permit Cl^- active reabsorption followed by Na movement.
- * Thick ascending loop passes between the afferent and efferent arterioles of the same nephron forming the juxta glomerular apparatus.
- **4- Distal Convoluted Tubule**: (DCT) The first part(diluting segment) continues from the ascending thick loop, then the distal segment which is both under the effect of Aldosterone for Na+-K+ exchange reabsorption.
- - **Collecting Duct:** cortical and medullary parts, both under the effect of Anti Diuretic Hormone ADH. Contain Principle cells(P-cells) for active Na+ reabsorption and Intercalated cells(I-cells) for H+ secretion.

- The nephrons in the inner portion of the cortex have long loops of Henle extending down into medullary pyramids and are called Juxta Medullary Nephrons, they form 15%.
- The nephron in the outer portion of the cortex have short loops of Henle and are called Cortical Nephrons which are 85%.

Cortical / Juxtamedullary Nephrons



- **Juxta glomerular apparatus:**
- The thick ascending limb of the loop of Henle reaches the glomerulus of the same nephron from which the tubule arose & passes close to its afferent arteriole, the wall of the afferent arteriole contain Renin – secreting Juxta Glomerular cells. At this point, the epithelium of the tubule is modified histologically to form Macula Densa.
- The juxta glomerular cells & the macula densa form the Juxta Glomerular Apparatus (JGA) which is a secretary structure secreting renin & erythropoietin.

- * The JGA achieves a regulatory process for Na ions by secreting renin enzyme, the enzyme secretion is stimulated by the sympathetic nerves when sodium is decreased in the blood.

- The renin enzyme converts the inactive form of Angiotensinogen (a protein synthesized in the liver) to Angiotensin I hormone which is converted to Angiotensin II by convertase enzyme in the blood.

Functions of Angiotensin II are:-

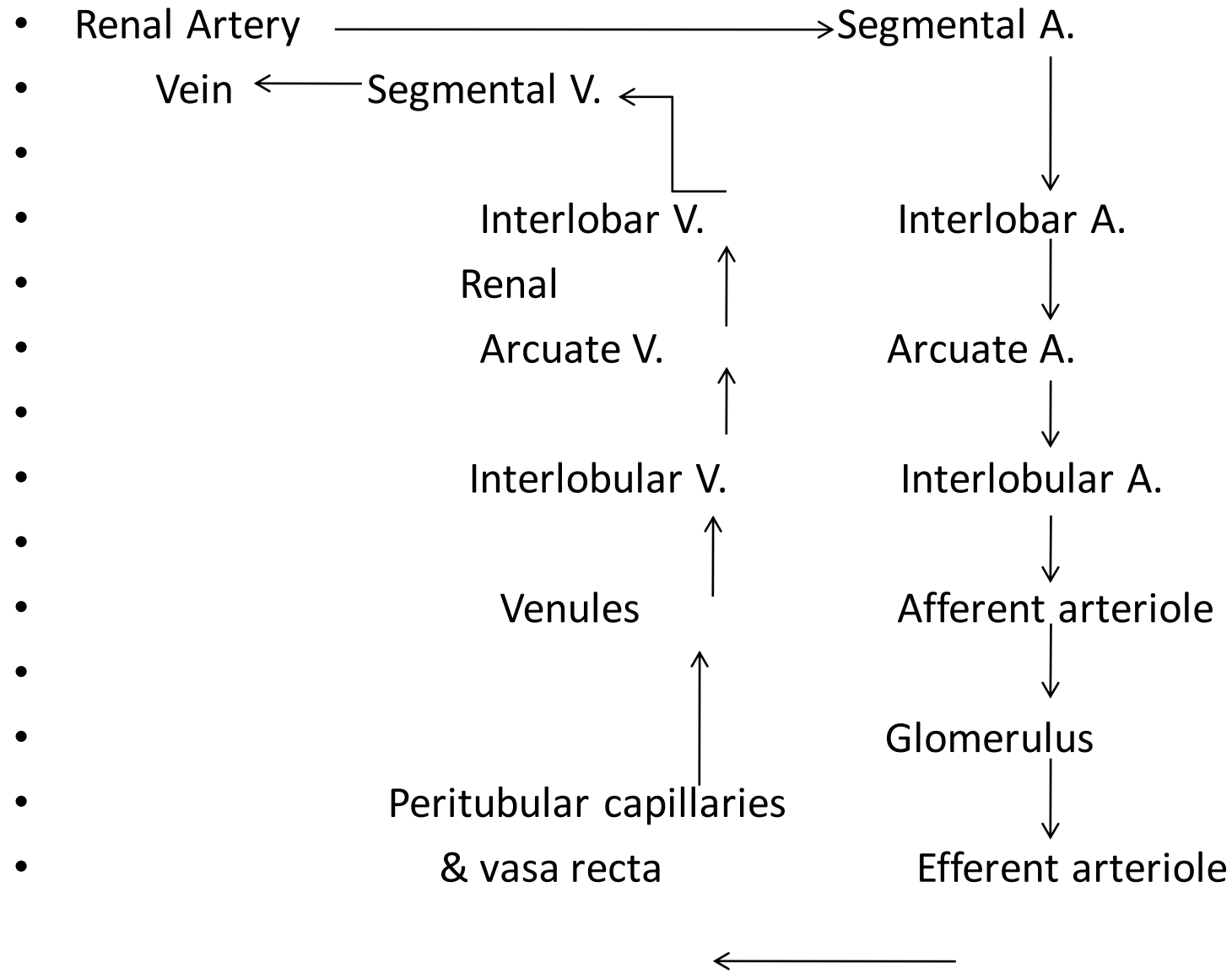
- **A. Short term:**
- 1. it's a potent vasoconstrictive agent due to increasing Blood Pressure(BP).
- 2. it also activates the heart which results in increasing the Cardiac Output(CO).
- **B. Long-term:**
- 1. stimulate secretion of Antidiuretic Hormone(ADH) from the Pituitary gland.
- 2. stimulate secretion of Aldosterone from the Adrenal cortex which regulates the sodium level in the blood.(Aldosteron stimulates reabsorption of Na+ ions & and water excretion in urine).
- Erythropoietin hormone is secreted in the kidney if either decreased BP or reduced O2 is carried in blood. This hormone stimulates erythropoiesis which increases Blood volume.

- *Other endocrine functions of the kidney:-*
- Secretion of prostaglandins (PGs): there are secretary cells called Type I medullary interstitial cells present in the interstitial tissue e.g. PGI2 & PGE2.
- Converting inactive vitamin D from the inactive form essential for regulation of Ca & Phosphorus in the body

- **The blood supply to the kidneys:**
- Your kidneys receive 20 -25 % of your total CO, in normal individuals about 1200ml of blood flows through the kidneys each minute.
- - each kidney receives blood from a *Renal Artery*. As it enters the renal sinus the renal artery provides blood to the *Segmental Arteries*. Segmental arteries further divide into a series of *Interlobar Arteries* that radiate outward between the renal pyramids. The Interlobar arteries supply blood to the *Arcuate Arteries*, which arch along the boundary between the cortex & medulla of the kidney.
- Each arcuate artery gives rise to a number of *Interlobular Arteries*, and branching from each interlobular artery are *Afferent Arterioles* (blood reaches the vascular pole of each *Glomerulus* through an afferent arteriole & leaves in an *Efferent Arteriole*).

- Blood travels from the efferent arteriole to form a capillary plexus, a net-work of *Peritubular Capillaries* (that supplies the PCT & DCT), The Peritubular capillaries provide a route for the pick-up or delivery of substances that are reabsorbed or secreted by these portions of nephrons

- In juxta medullary nephrons, the efferent arteriole & peritubular capillaries are connected to a series of long slender capillary that accompany the loops of Henle into the medulla, these capillaries are known as the *Vasa Recta*, which absorb & transport solutes and water reabsorbed into the medulla from tubular fluid in the loops of Henle & collecting ducts.(in the normal conditions the removal of solutes and water by the vasa recta balances the rate of solutes and water reabsorbed in the medulla).
- - from the peritubular capillaries & vasa recta, blood enters a network of venules and small veins that converge on the *Interlobular Veins* (in mirror image of the arterial distribution).


Renal Artery
Segmental A.
Vein
Segmental V.
Interlobar V.
Interlobar A.
Renal
Arcuate V.
Arcuate A.
Interlobular V.
Interlobular A.
Venules
Afferent arteriole
Glomerulus
Peritubular capillaries
& vasa recta
Efferent arteriole

- *kidneys receive around 20% of CO, 98% of which goes to the cortex & only 2% to the medulla.
- Innervation of the Kidneys:-
- The kidneys and ureters are innervated by the Renal Nerves. Most of the nerve fibers involved are sympathetic postganglionic fibers,
- the sympathetic innervation targets:-
- Juxtaglomerular apparatus.
- The smooth muscles in the walls of the afferent & efferent arterioles.
- Mesangial cells.
- ***Functions of the sympathetic innervation:**
- → Regulation of glomerular blood flow & pressure. through control of the diameters of the afferent & efferent arterioles and glomerular capillaries.
- → Stimulation of renin release from JGA.
- → Direct stimulation of water and sodium reabsorption.

Blood Cleaning by the Kidneys

The processes performed by the kidneys in order to filter (clean) blood.
are:

- **Glomerular Filtration** also called "Ultra-filtration",
- **Tubular Reabsorption** also called "Selective Re-Absorption" and
- **Tubular Secretion**.

Glomerular filtration

Glomerular Filtration—The First Step in Urine Formation

- Urine formation begins with the filtration of large amounts of fluid through the glomerular capillaries into Bowman's capsule.

- Like most capillaries, the glomerular capillaries are relatively impermeable to proteins, so the filtered fluid (called the glomerular filtrate) is essentially protein-free and devoid of cellular elements, including red blood cells.

- The concentrations of other constituents of the glomerular filtrate, including most salts and organic molecules, are similar to the concentrations in the plasma.

- Exceptions to this generalization include a few low-molecular-weight substances, such as calcium and fatty acids, that are not freely filtered because they are partially bound to the plasma proteins.

- Most of the water; Most of the salts; Most or all of the glucose; and Most or all of the urea.
- The above are filtered in preference to other components of blood based on particle size. (Water and solutes of relative molecular mass less than 68,000 form the filtrate.)
- Blood cells and plasma proteins are not filtered through the glomerular capillaries because they are relatively larger in physical size.
- The glomerular filtrate passes from the *renal corpuscle* to the renal tubule.

The glomerular filtration rate (GFR)

- is the volume of filtrate produced by both kidneys per minute.
- The GFR averages 115 ml per minute in women and 125 ml per minute in men.
- This is equivalent to 7.5 L per hour or 180 L per day (about 45 gallons)! Since the total blood volume averages about 5.5 L, this means that the total blood volume is filtered into the urinary tubules every 40 minutes.
- Most of the filtered water must obviously be returned immediately to the vascular system, or a person would literally urinate to death within minutes.

Determinants of the GFR

The GFR is determined by:

(1) the sum of the hydrostatic and colloid osmotic forces across the glomerular membrane, which gives the *net filtration pressure,* and

(2) the glomerular capillary filtration coefficient, Kf. The GFR equals the product of Kf and the net filtration pressure:

GFR = Kf * Net filtration pressure

The net filtration pressure

represents the sum of the hydrostatic and colloid osmotic forces that either favor or oppose filtration across the glomerular capillaries. These forces include

(1) hydrostatic pressure inside the glomerular capillaries (glomerular hydrostatic pressure, PG), which promotes filtration;

(2) the hydrostatic pressure in Bowman's capsule (PB) outside the capillaries, which opposes filtration

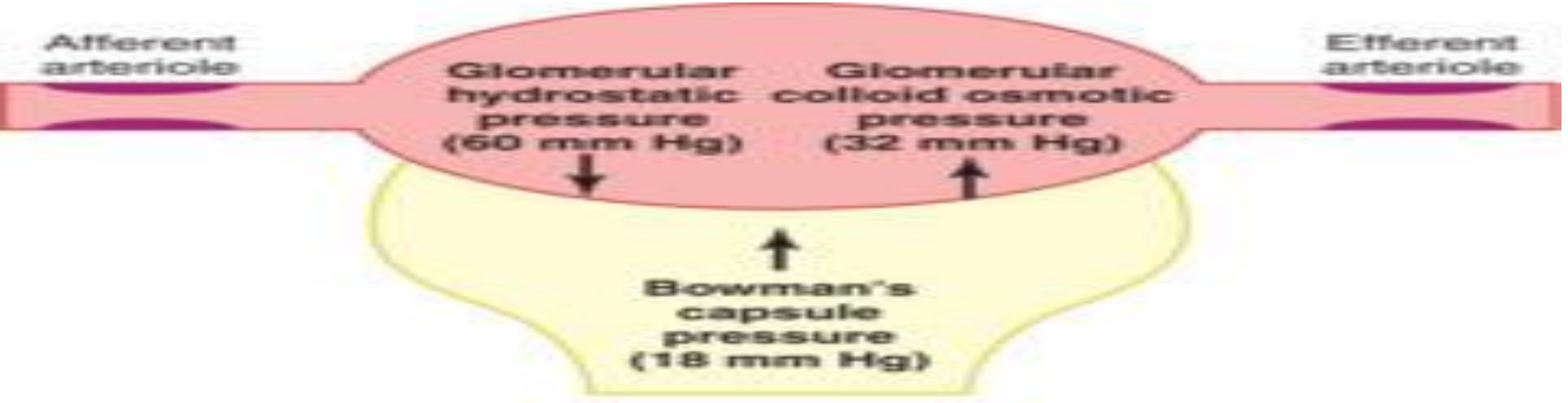
(3) the colloid osmotic pressure of the glomerular capillary plasma proteins (πG), which opposes filtration; and

(4) the colloid osmotic pressure of the proteins in Bowman's capsule (πB), which promotes filtration.

(Under normal conditions, the concentration of protein in the glomerular filtrate is so low that the colloid osmotic pressure of the Bowman's capsule fluid is considered to be zero.)

The GFR can therefore be expressed as

GFR = Kf * (PG – PB –(πG + πB))



Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) − Bowman's capsule pressure (18 mm Hg) − Glomerular oncotic pressure (32 mm Hg)

Net filtration pressure = 60 – 18 – 32 = +10 mm Hg

Some of these values can change markedly under different physiologic conditions, whereas others are altered mainly in disease states.

How can these determinant affecting GFR:

1- Increased Glomerular Capillary Filtration Coefficient Increases GFR

- The Kf is a measure of the product of the hydraulic conductivity and surface area of the glomerular capillaries.
- The Kf cannot be measured directly, but it is estimated experimentally by dividing the rate of glomerular filtration by net filtration pressure:
- Kf = GFR/Net filtration pressure
- Because total GFR for both kidneys is about 125 ml/ min and the net filtration pressure is 10 mm Hg, the normal Kf is calculated to be about 12.5 ml/min/mm Hg of filtration pressure.

2-Increased Bowman's Capsule Hydrostatic Pressure Decreases GFR:

- Direct measurements, using micropipettes, of hydrostatic pressure in Bowman's capsule and at different points in the proximal tubule suggest that a reasonable estimate for Bowman's capsule pressure in humans is about 18 mm Hg under normal conditions.

- Increasing the hydrostatic pressure in Bowman's capsule reduces GFR, whereas decreasing this pressure raises GFR.

- In certain pathological states associated with obstruction of the urinary tract, Bowman's capsule pressure can increase markedly, causing a serious reduction of GFR. For example, precipitation of calcium or uric acid may lead to "stones" that lodge in the urinary tract, often in the ureter, thereby obstructing the outflow of the urinary tract and raising Bowman's capsule pressure.
- This reduces GFR and eventually can damage or even destroy the kidney unless the obstruction is relieved.

3-Increased Glomerular Capillary Colloid Osmotic Pressure Decreases GFR

The reason for this is that about one-fifth of the fluid in the capillaries filters into Bowman's capsule, thereby concentrating the glomerular plasma proteins that are not filtered causes in decreasing of GFR.

4-Increased Glomerular Capillary Hydrostatic Pressure Increases GFR

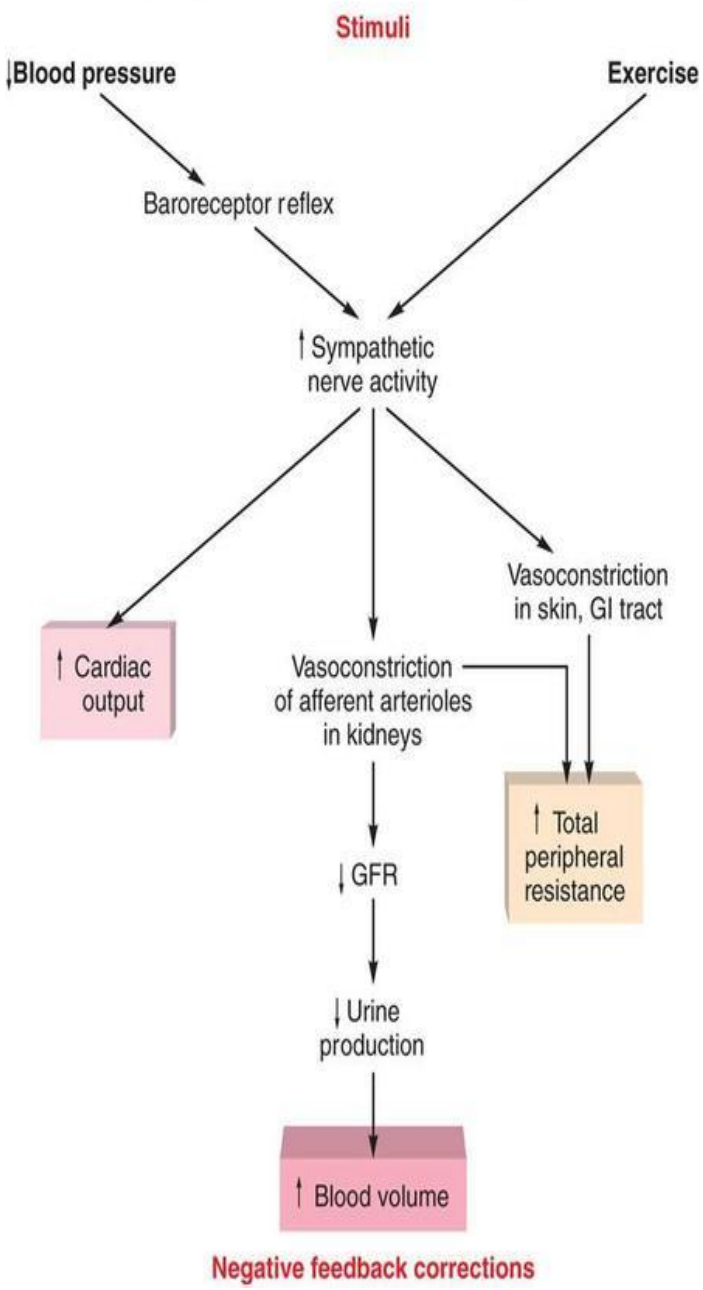
- The glomerular capillary hydrostatic pressure has been estimated to be about 60 mm Hg under normal conditions. Changes in glomerular hydrostatic pressure serve as the primary means for physiologic regulation of GFR.
- Increases in glomerular hydrostatic pressure raise GFR, whereas decreases in glomerular hydrostatic pressure reduce GFR.

Regulation of Glomerular Filtration Rate:

- Vasoconstriction or dilation of afferent arterioles affects the rate of blood flow to the glomerulus, and thus affects the glomerular filtration rate.
- Changes in the diameter of the afferent arterioles result from both **extrinsic regulatory mechanisms** (produced by sympathetic nerve innervation), and **intrinsic regulatory mechanisms** (those within the kidneys, also termed ***renal autoregulation***).
- These mechanisms are needed to ensure that the GFR will be high enough to allow the kidneys to eliminate wastes and regulate blood pressure, but not so high as to cause excessive water loss.

Sympathetic Nerve Effects (extrinsic)

- An increase in sympathetic nerve activity, as occurs during the fight-or-flight reaction and exercise, stimulates constriction of afferent arterioles. This helps to preserve blood volume and to divert blood to the muscles and heart.
- The decreased GFR and the resulting decreased rate of urine formation help to compensate for the rapid drop of blood pressure under these circumstances.



Renal Autoregulation (intrinsic)

- The ability of the kidneys to maintain a relatively constant GFR in the face of fluctuating blood pressures is called **renal autoregulation.**
- Renal autoregulation is achieved through the effects of locally produced chemicals on the afferent arterioles.
- When systemic arterial pressure falls toward a mean of 70 mmHg, the afferent arterioles dilate, and when the pressure rises, the afferent arterioles constrict.
- Blood flow to the glomeruli and GFR can thus remain relatively constant within the autoregulatory range of blood pressure values.
- Autoregulation is also achieved through a negative feedback relationship between the afferent arterioles and the volume of fluid in the filtrate.

- An increased flow of filtrate is sensed by a special group of cells called the *macula densa in the thick portion* of the ascending limb When the macula densa senses an increased flow of filtrate, it signals the afferent arterioles to constrict.
- This lowers the GFR, thereby decreasing the formation of filtrate in a process called **tubuloglomerular feedback.**

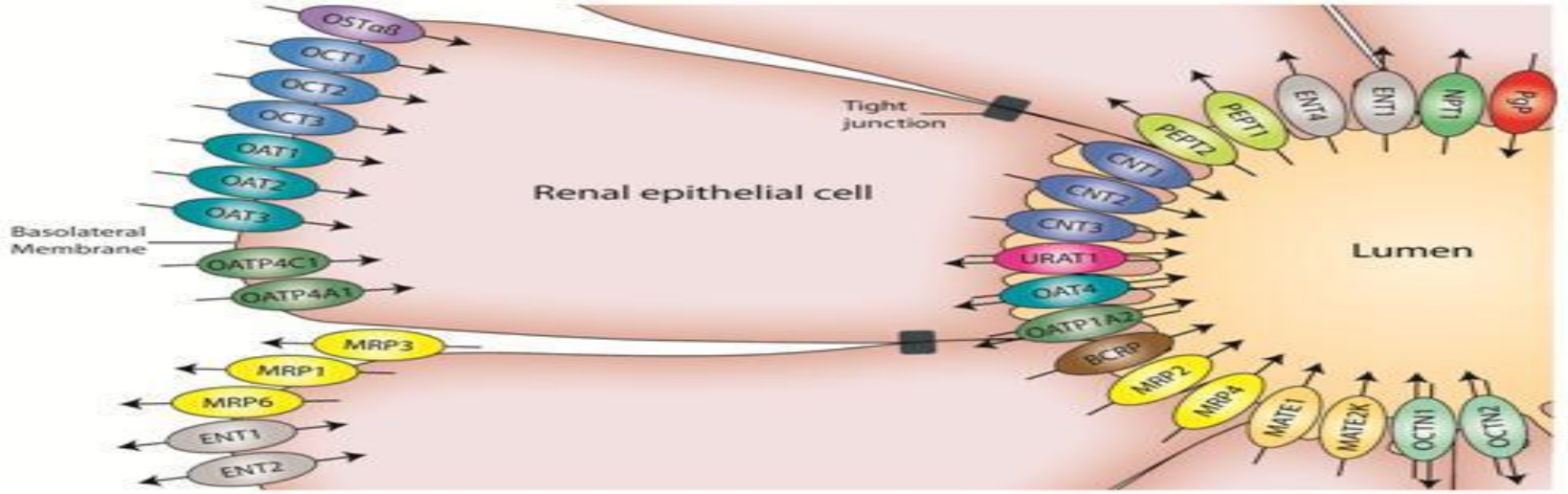
Tubular Reabsorption

- is the flow of glomerular filtrate from the proximal tubule of the nephron into the peritubular capillaries, or from the urine into the blood.
- It is termed "reabsorption" because this is technically the second time that the nutrients are being absorbed into the blood, the first time being from the small intestine into the villi.

- This happens as a result of sodium transport from the lumen into the blood by the Na+/K+ ATPase in the basolateral membrane of the epithelial cells.
- Thus, the glomerular filtrate becomes more concentrated, which is one of the steps in forming urine.
- In this way, many useful solutes (primarily glucose and amino acids), salts, and water that have passed in the proximal convoluted tubule through the Bowman's capsule return to circulation.
- Small proteins and some peptide hormones are reabsorbed in the proximal tubules by endocytosis.
- Other substances are secreted or reabsorbed in the tubules by passive diffusion between cells and through cells by facilitated diffusion down chemical or electrical gradients or active transport against such gradients.
- Reabsorption varies according to the body's needs, enabling the body to retain most of its nutrients.

Na+ and Cl– Reabsorption:

- ✓ The reabsorption of Na+ and Cl– plays a major role in body electrolyte and water metabolism.
- ✓ In addition, Na+ transport is coupled to the movement of H+, other electrolytes, glucose, amino acids, organic acids, phosphate, and other substances across the tubule walls.
- ✓ The tubular cells are connected by tight junctions at their luminal edges, but there is space between the cells along the rest of their lateral borders.



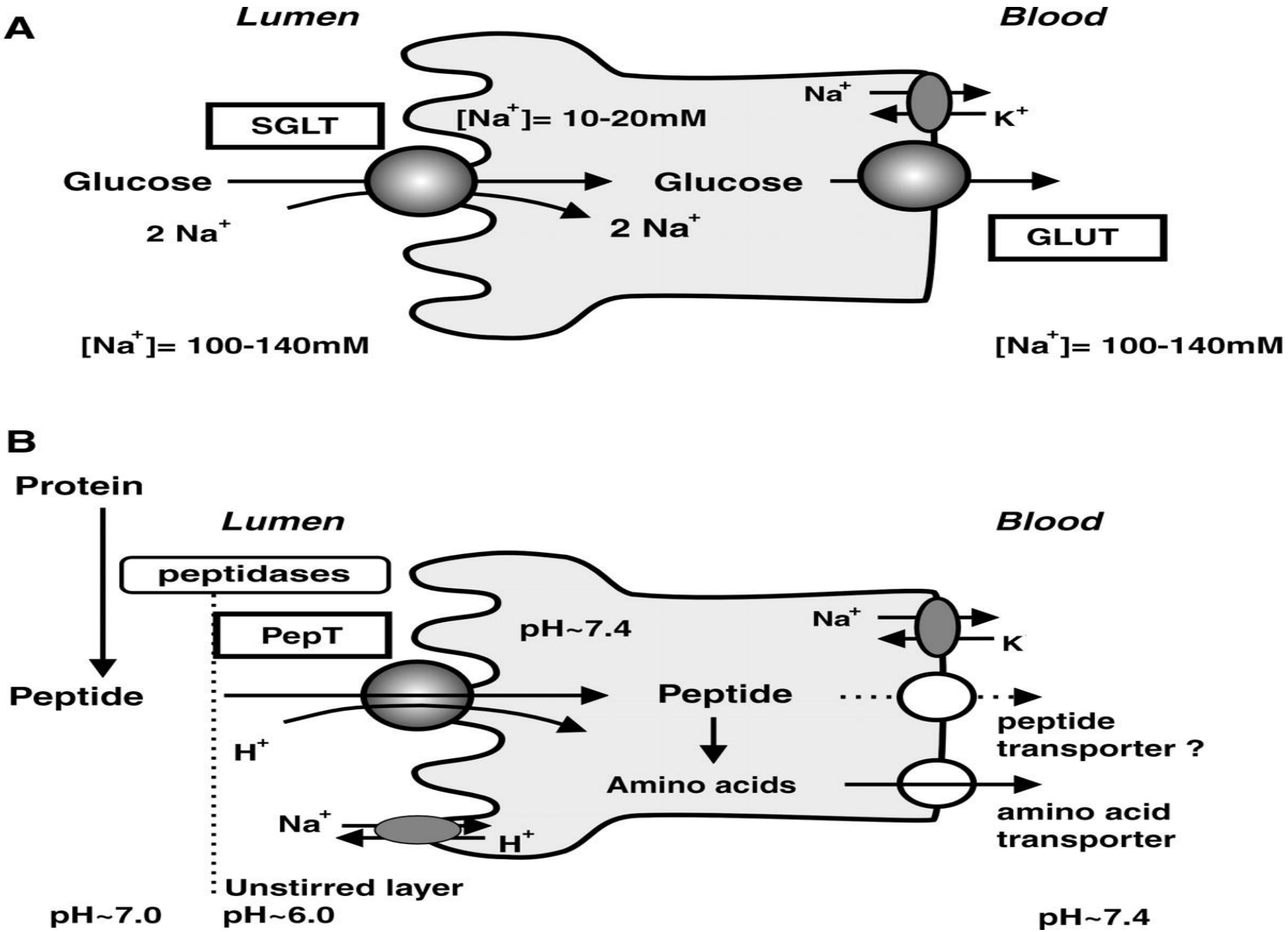
- Much of the Na+ is actively transported into these extensions of the interstitial space, the lateral intercellular spaces Normally about 60% of the filtered Na+ is reabsorbed in the **proximal tubule**, primarily by the **Na+–H+ exchange**. Another 30% is absorbed via the **Na+–2Cl––K+** cotransporter in the **thick ascending limb of the loop of Henle**, and about 7% is absorbed **by Na+–Cl–** cotransport in the **distal convoluted tubule**.

- The remainder of the filtered Na+, about 3%, is absorbed via the **ENaC (epithelial sodium channels)** in the **collecting ducts**, and this is the portion that is regulated by aldosterone and angiotensin II for homeostatic adjustments in Na+ balance.

Glucose Reabsorption

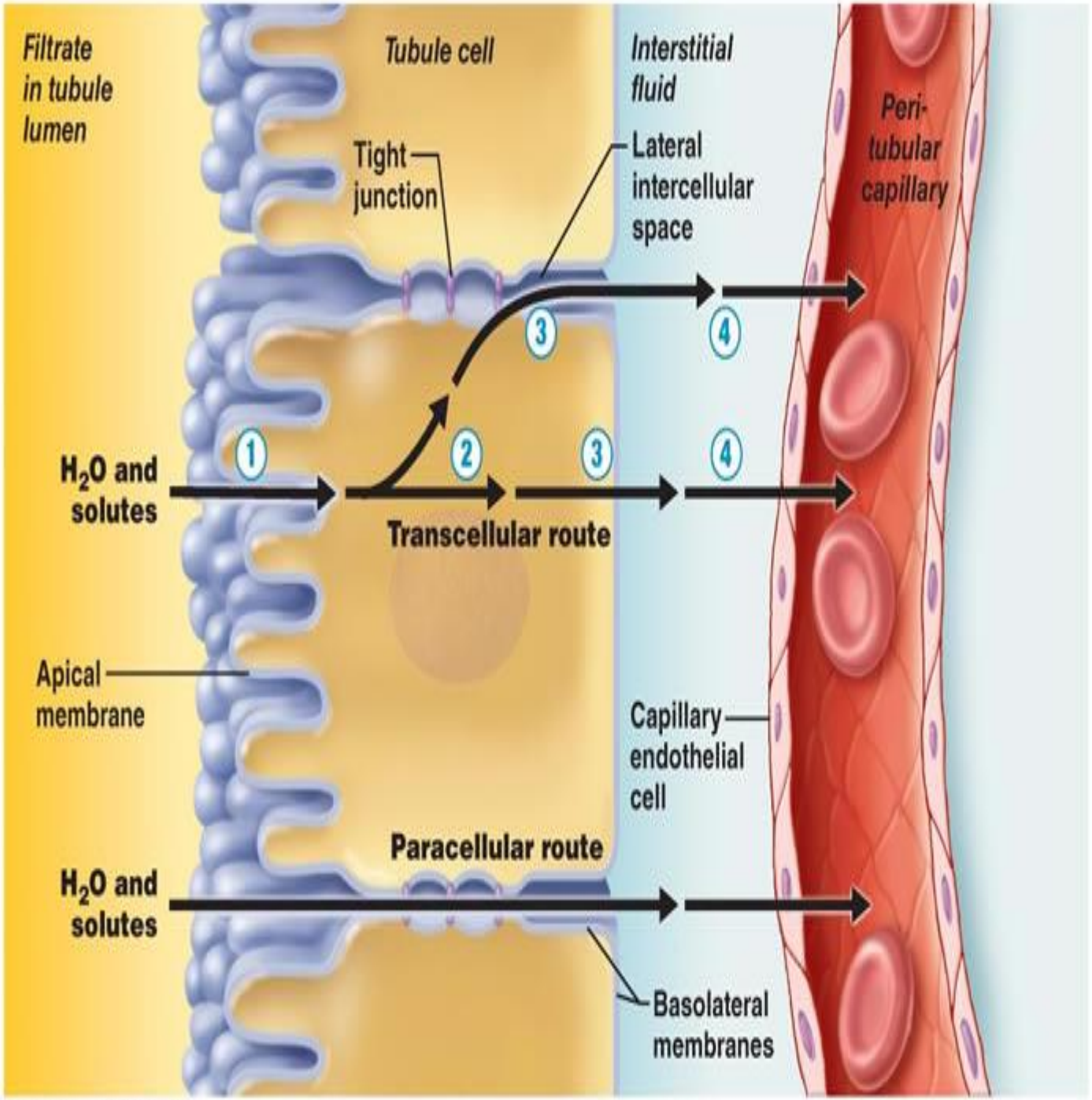
Glucose, amino acids, and bicarbonate are reabsorbed along with Na+ in the early portion of the proximal Tubule Farther along the tubule, Na+ is reabsorbed with Cl–. Glucose is typical of substances removed from the urine by secondary active transport. Essentially all of the glucose is reabsorbed, and no more than a few milligrams appear in the urine per 24 hours.

Glucose reabsorption in the kidneys is similar to glucose reabsorption in the intestine . Glucose and Na+ bind to the common carrier SGLT 2 (sodium glucose cotransporter 2)in the luminal membrane and glucose is carried into the cell as Na+ moves down its electrical and chemical gradient. The Na+ is then pumped out of the cell into the lateral intercellular spaces, and the glucose is transported by GLUT 2(glucose transporter 2) into the interstitial fluid.


A
Lumen
Blood
SGLT
[Na+]= 10-20mM
Na+
K+
Glucose
Glucose
2 Na+
2 Na+
GLUT
[Na+]= 100-140mM
[Na+]= 100-140mM
B
Protein
Lumen
Blood
peptidases
PepT
pH~7.4
Na+
K+
Peptide
Peptide
peptide transporter ?
H+
Amino acids
Na+
H+
amino acid transporter
Unstirred layer
pH~7.0
pH~6.0
pH~7.4

- **Water Reabsorption**
- The proximal tubule reabsorbs 67% of the filtered water.
- The driving force for water reabsorption is a transtubular osmotic gradient established by reabsorption of solute (e.g., NaCl, Na^+-glucose). Reabsorption of Na^+ along with organic solutes, HCO_3^-, and Cl^- from tubular fluid into the lateral intercellular spaces reduces the osmolality of the tubular fluid and increases the osmolality of the lateral intercellular space.
- Because the proximal tubule is highly permeable to water, water is reabsorbed via osmosis.
- Because the apical and basolateral membranes of proximal tubule cells express aquaporin water channels, water is primarily reabsorbed across the proximal tubular cells.
- Some water is also reabsorbed across the tight junctions.

- An important consequence of osmotic water flow across the proximal tubule is that some solutes, especially K^+ and Ca^{++}, are entrained in the reabsorbed fluid and thereby reabsorbed by the process of solvent drag .
- Reabsorption of virtually all organic solutes, Cl^- and other ions, and water is coupled to Na^+ reabsorption.
- Therefore, changes in Na^+ reabsorption influence the reabsorption of water and other solutes by the proximal tubule.



The transcellular route involves:

1. Transport across the apical membrane.
2. Diffusion through the cytosol.
3. Transport across the basolateral membrane. (Often involves the lateral intercellular spaces because membrane transporters transport ions into these spaces.)
4. Movement through the interstitial fluid and into the capillary.

The paracellular route involves:

- Movement through leaky tight junctions, particularly in the PCT.
- Movement through the interstitial fluid and into the capillary.

Tubular secretion:

- The third process by which the kidneys clean blood (regulating its composition and volume) is called **tubular secretion** and involves substances being added to the tubular fluid.
- This removes excessive quantities of certain dissolved substances from the body, and also maintains the blood at a normal healthy pH .
- The substances that are secreted into the tubular fluid (for removal from the body) include:

- Potassium ions (K^+),
- Hydrogen ions (H^+),
- Ammonium ions (NH_4^+),
- creatinine,
- urea,
- some hormones, and
- some drugs (e.g. penicillin).

- ... and finally
- Urine formed via the three processes outlined previously and trickles into the kidney pelvis. At this final stage it is only approx. 1% of the originally filtered volume but includes high concentrations of urea and creatinine, and variable concentrations of ions.

Water excretion:

➢ Proximal Tubule

Many substances are actively transported out of the fluid in the proximal tubule, but fluid remains essentially isosmotic to the end of the proximal tubule Therefore, in the proximal tubule, water moves passively out of the tubule along the osmotic gradients set up by active transport of solutes, and isotonicity is maintained.

➢ Loop of Henle

The descending limb of the loop of Henle is permeable to water, but the ascending limb is impermeable.

➢ Distal Tubule

- The distal tubule, particularly its first part, is in effect an extension of the thick segment of the ascending limb.
- It is relatively impermeable to water, and continued removal of the solute in excess of solvent further dilutes the tubular fluid. About 5% of the filtered water is removed in this segment.

➢ Collecting Ducts

- The collecting ducts have two portions: a cortical portion and a medullary portion.
- The changes in osmolality and volume in the collecting ducts depend on the amount of vasopressin acting on the ducts. This antidiuretic hormone from the posterior pituitary gland increases the permeability of the collecting ducts to water.

- ❖ Water excretion by the kidneys is regulated primarily by ADH (vasopressin).
- ❖ ADH is released by the posterior pituitary and results in increased water reabsorption in the distal nephrons.
- ❖ ADH release is stimulated by any of the following:

- •Increased serum osmolality
- •Decreased blood volume
- •Decreased BP
- •Stress

ADH release may be impaired by certain substances (eg, ethanol, and central diabetes insipidus. Water intake decreases serum osmolality. high serum osmolality inhibits ADH secretion, allowing the kidneys to produce dilute urine.

Water intake :

- The average daily fluid intake is about 2.5 L. The amount needed to replace losses from urine and other sources is about 1 to 1.5 L/day in healthy adults.
- However, an average young adult with normal kidney function may ingest as little as 200 mL of water each day to excrete the nitrogenous and other wastes generated by cellular metabolism.
- More is needed in people with any loss of renal concentrating capacity in

•The elderly

•People with diabetes insipidus, certain renal disorders, hypercalcemia, chronic overhydration,

•People who ingest ethanol.

•People with osmotic diuresis (eg, due to high-protein diets or hyperglycemia)

- Other obligatory water losses are mostly insensible losses from the lungs and skin, averaging about 0.4 to 0.5 mL/kg/h or about 650 to 850 mL/day in a 70-kg adult.

- With fever, another 50 to 75 mL/day may be lost for each degree C of temperature elevation above normal.

- gastrointestinal (GI) losses are usually insignificant except when marked vomiting, diarrhea, or both occur.

- Sweat losses can be significant during environmental heat exposure or excessive exercise.

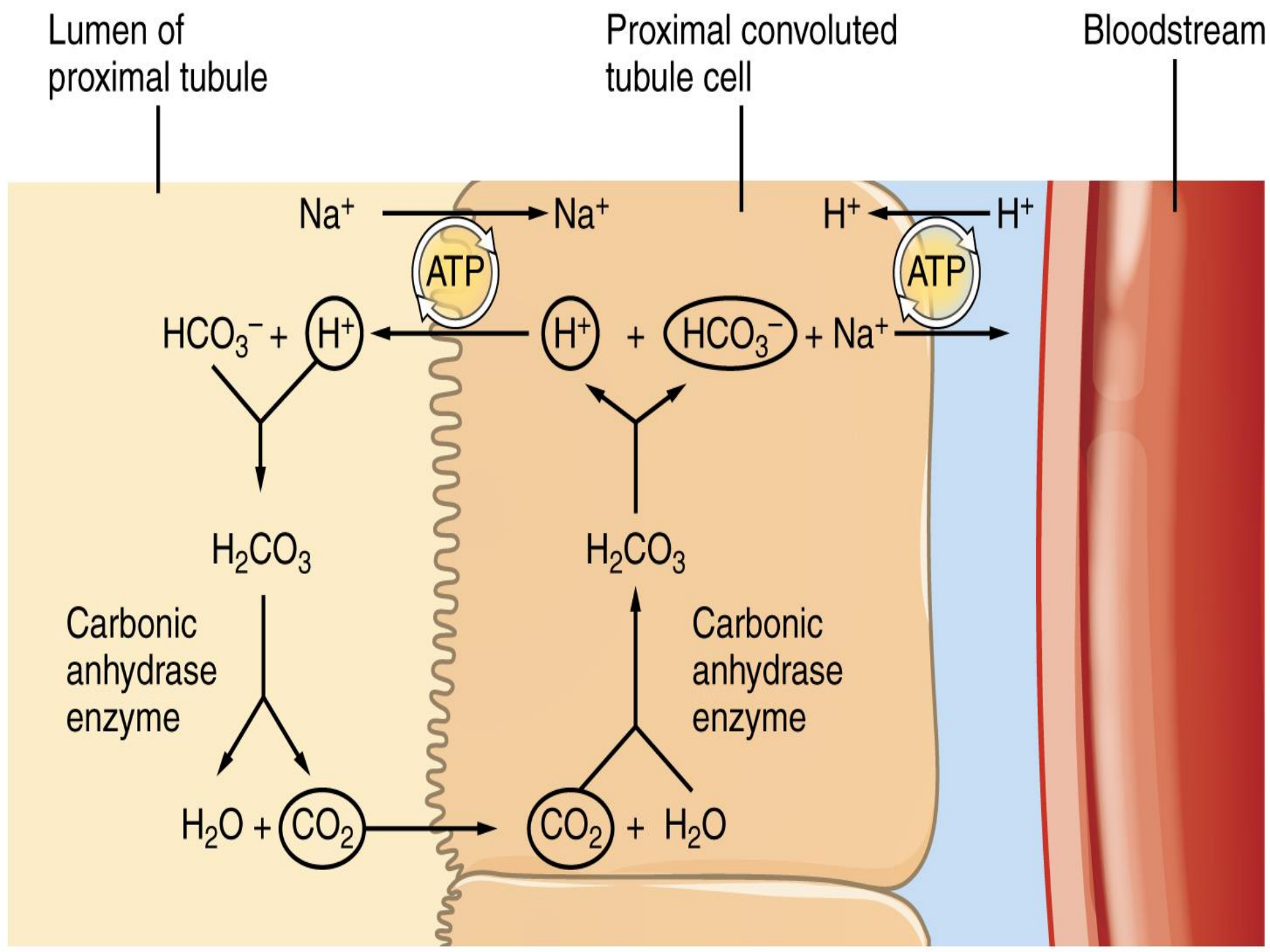
- Water intake is regulated by thirst. Thirst is triggered by receptors in the hypothalamus that respond to increased serum osmolality (as little as 2%) or decreased body fluid volume.

Hydrogen secretion :

- Glomerular filtered bicarbonate is reabsorbed in the proximal tubule via the following mechanism:

the filtered HCO_3^- and secreted H^+ from the tubular cell (Na-H exchanger) forms with the help of luminal carbonic anhydrase H_2CO_3, which dissociates to CO_2 ad H_2O.

- The CO_2 enters easily into the tubule cell and binds with OH^- (remnants of the H^+ secretion) to bicarbonate (HCO_3^-).
- With the help of the Na^+/HCO_3^--cotransporter in the basal membrane, bicarbonate is returned into the blood.
- In the case of alkalosis, bicarbonate can be secreted to balance the acid-base homeostasis.


Lumen of proximal tubule
Proximal convoluted tubule cell
Bloodstream
Na+
Na+
ATP
H+
H+
ATP
HCO3− + H+
H+ + HCO3− + Na+
H2CO3
H2CO3
Carbonic anhydrase enzyme
Carbonic anhydrase enzyme
H2O + CO2
CO2 + H2O

Role of Urea

- Urea contributes to the establishment of the osmotic gradient in the medullary pyramids and the ability to form concentrated urine in the collecting ducts.
- Urea transport is mediated by urea transporters, presumably by facilitated diffusion.
- There are at least four isoforms of the transport protein UT-A in the kidneys (UTA1 to UT-A4).
- The amount of urea in the medullary interstitium and in the urine varies with the amount of urea filtered, and this in turn varies with the dietary intake of protein.
- Therefore, a high-protein diet increases the ability of the kidneys to concentrate the urine

Water Diuresis

- The feedback mechanism controlling vasopressin secretion and the way vasopressin secretion is **stimulated by a rise and inhibited by a drop in the effective osmotic pressure of the plasma**.
- The water diuresis produced by drinking large amounts of hypotonic fluid begins about 15 minutes after ingestion of a water load and reaches its maximum in about 40 minutes.
- The act of drinking produces a small decrease in vasopressin secretion before the water is absorbed, but most of the inhibition is produced by the decrease in plasma osmolality after the water is absorbed.

Osmotic diuresis :

is increased urination caused by the presence of certain substances in the small tubes of the kidneys.

- The excretion occurs when substances such as glucose enter the kidney tubules and cannot be reabsorbed (due to a pathological state or the normal nature of the substance).
- The substances cause an increase in the osmotic pressure within the tubule, causing retention of water within the lumen, and thus reducing the reabsorption of water, increasing urine output (i.e. diuresis).
- The same effect can be seen in therapeutics such as mannitol, which is used to increase urine output and decrease extracellular fluid volume.

- Substances in the circulation can also increase the amount of circulating fluid by increasing the osmolarity of the blood.

- This has the effect of pulling water from the interstitial space, making more water available in the blood and causing the kidney to compensate by removing it as urine.

- In hypotension, often colloids are used intravenously to increase circulating volume in themselves, but as they exert a certain amount of osmotic pressure, water is therefore also moved, further increasing circulating volume.

- As blood pressure increases, the kidney removes the excess fluid as urine.
- Sodium, chloride, and potassium are excreted in Osmotic diuresis, originating from Diabetes Mellitus (DM).
- Osmotic diuresis results in dehydration from polyuria and the classic polydipsia (excessive thirst) associated with DM.

What are the symptoms of an osmotic diuresis?

Osmotic diuresis does not cause symptoms unless dehydration occurs. Symptoms of dehydration include faintness, dizziness, rapid pulse, and dry mouth.

URINE ACIDIFICATION

Source of acids

Carbonic acids and Non carbonic acids

Source of H+ :

- Diet
- CO_2
- produced as the end of metabolism
- Secretion of H by renal tubules

The majority of urine acidification occurs in DCT AND PCT. Three main buffers remove free H

1. Bicarbonate system.
2. Phosphate system.
3. Ammonia system

- **Buffer systems in the kidney**
- **The bicarbonate system** secreted H in PCT react with HCO3 to form H2CO3 and help in HCO3 reabsorption

1. No net H secretion occurs.
2. therefore pH remains unchanged
3. H secreted in excess is buffered by two other systems

- **phosphate systems**

H secreted is buffered with HPO4

H is secreted in exchange for Na and N

1. 70%-75% of filtered HPO4 is reabsorbed
2. 25% available for buffering a 2 HPO4 into Na H2PO4
3. Na H2PO4 excreted in urine

Ammonia system

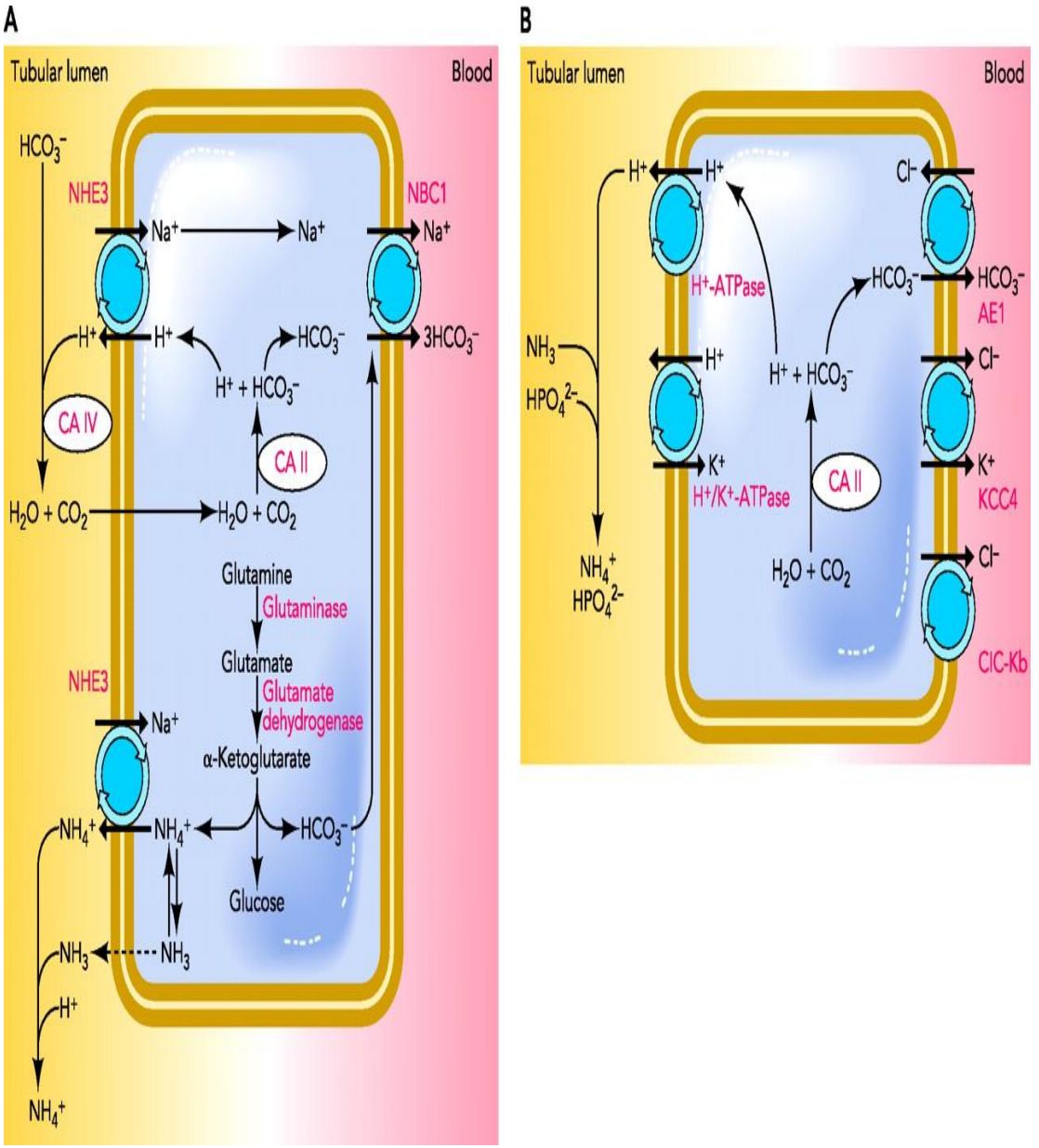
Site (DCT and PCT)

Secreted and synthesized not by filtrate

Formation of ammonia

Mainly form glutamine

NH3 diffuses from tubular cells into the lumen where it combines with H to form NH4 is lipid insoluble and, therefore remains in the lumen



Uremia or uremia: is a term used to loosely describe the illness accompanying kidney failure (also called renal failure), in particular the nitrogenous waste products associated with the failure of this organ.

- This is not to be confused with uricemia, or hyperuricemia, a build-up of uric acid in the blood.
- In kidney failure, urea and other waste products, which are normally excreted into the urine, are retained in the blood.
- Early symptoms include anorexia and lethargy, and late symptoms can include decreased mental acuity and coma.
- Other symptoms include fatigue, nausea, vomiting, cold, bone pain, itch, shortness of breath, and seizures.
- Because uremia mostly is a consequence of kidney failure, its signs and symptoms often occur concomitantly with other signs and symptoms of kidney failure, such as hypertension due to volume overload, hypocalcemia tetany, and anemia due to erythropoietin deficiency.

- Many individuals who have uremia need to be hospitalized. Doctors treat the condition with dialysis, a medical procedure in which a machine filters and purifies the blood.
- Medical practitioners might also make recommendations regarding dietary changes or prescribe medication to control the symptoms.
- Patients who have uremia occasionally develop acute tubular necrosis, a condition in which the tissues in the kidneys become severely damaged.
- These patients might eventually develop acute kidney failure, a condition where the kidneys suddenly stop working. Other patients with uremia might have convulsions, heart failure, or coma.
- Untreated uremia can be fatal.

Acidosis is a condition in which there is too much acid in the body fluids. It is the opposite of alkalosis (a condition in which there is too much base in the body fluids).

Causes

The kidneys and lungs maintain the balance (proper pH level) . Acidosis occurs when acid builds up or when bicarbonate (a base) is lost.

- Acidosis is classified as either **respiratory acidosis** or **metabolic acidosis.**

❖ **Metabolic acidosis:** develops when too much acid is produced or the kidneys cannot remove enough acid from the body. There are several types of metabolic acidosis:

✓ **Diabetic acidosis** (also called diabetic ketoacidosis and DKA) develops when substances called ketone bodies (which are acidic) build up during uncontrolled diabetes.

- ✓ **Hyperchloremic acidosis** is caused by the loss of too much sodium bicarbonate from the body, which can happen with severe diarrhea.

- ✓ **Lactic acidosis** is a buildup of lactic acid. This can be caused by: Alcohol, Cancer, Liver failure, Low blood sugar (hypoglycemia) ,Medications , Prolonged lack of oxygen from shock, heart failure, or severe anemia.

Other causes of metabolic acidosis include:
Kidney disease (distal renal tubular acidosis and proximal renal tubular acidosis) and Severe dehydration.

Micturition: is the process where the urinary bladder empties after being filled.

-**Micturition reflex:** mediated through the pelvic nerves (S2-S3) which contain sensory fibers for the detection of bladder wall stretching and the motor fibers (parasympathetic) ending on bladder wall ganglion cells that send postganglionic fibers to the detrusor muscles of the bladder.

The urinary bladder begins to fill up to 100-150 ml and issues a first desire to urinate due to stretch receptors in the wall of the urinary bladder causing a reflex contraction. After some time, the contraction disappears.

When the volume reaches 400-500 ml, the reflex contraction increases & if the pressure builds more than the external sphincter (voluntary control), the opening of the bladder neck occurs and leads to another reflex through the pudendal nerve (S1-S2) to inhibit the external sphincter. If this inhibition overcomes the voluntary control, urination occurs

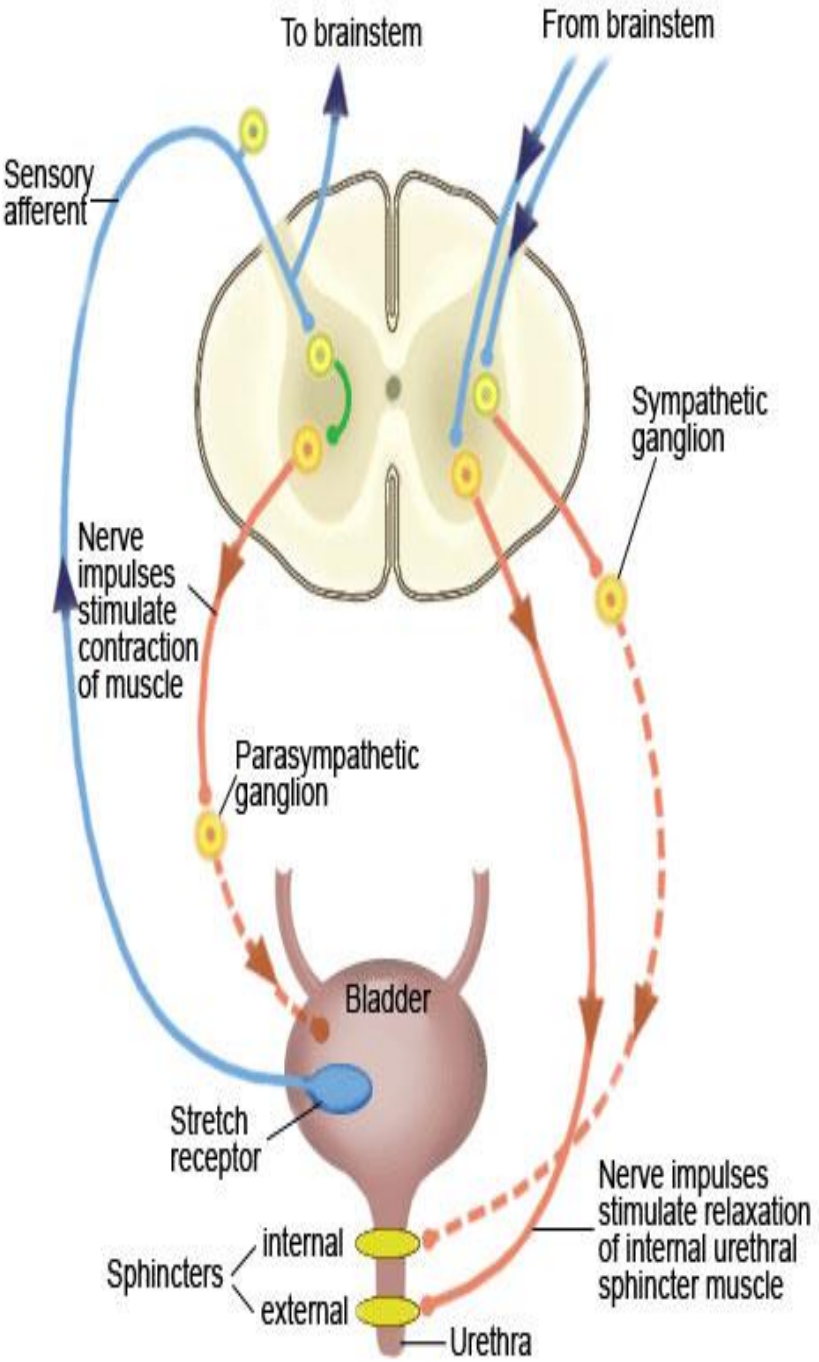


Image adapted from McGill Molson Medical Informatics Project