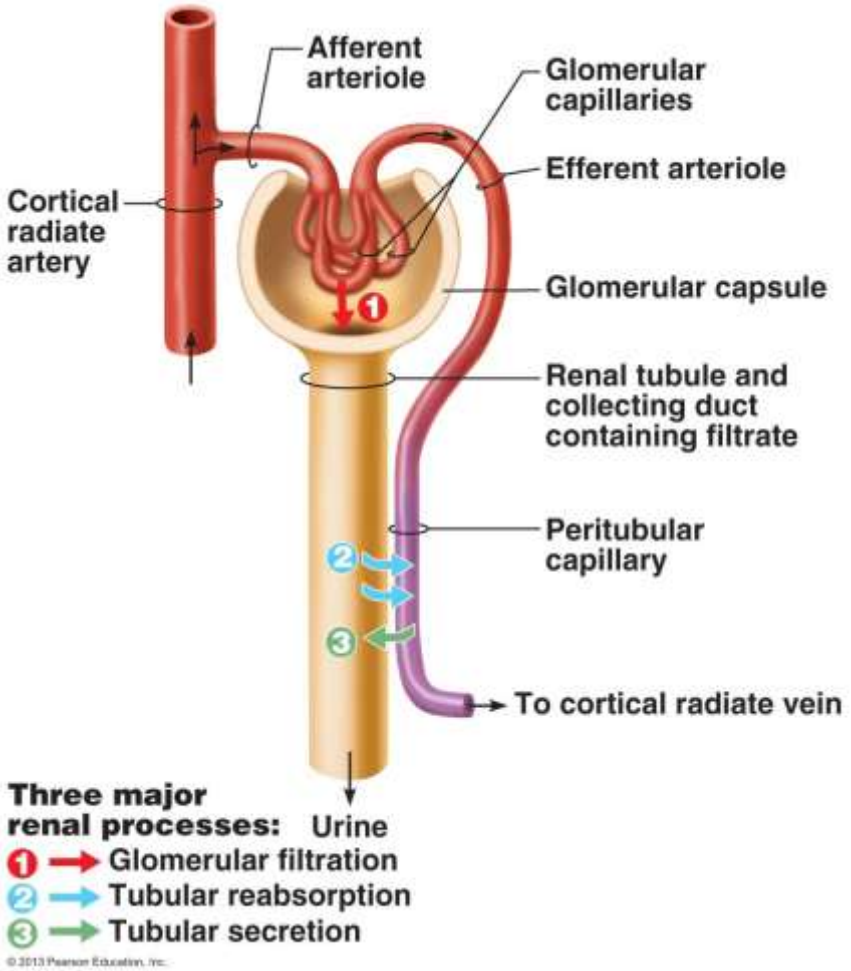
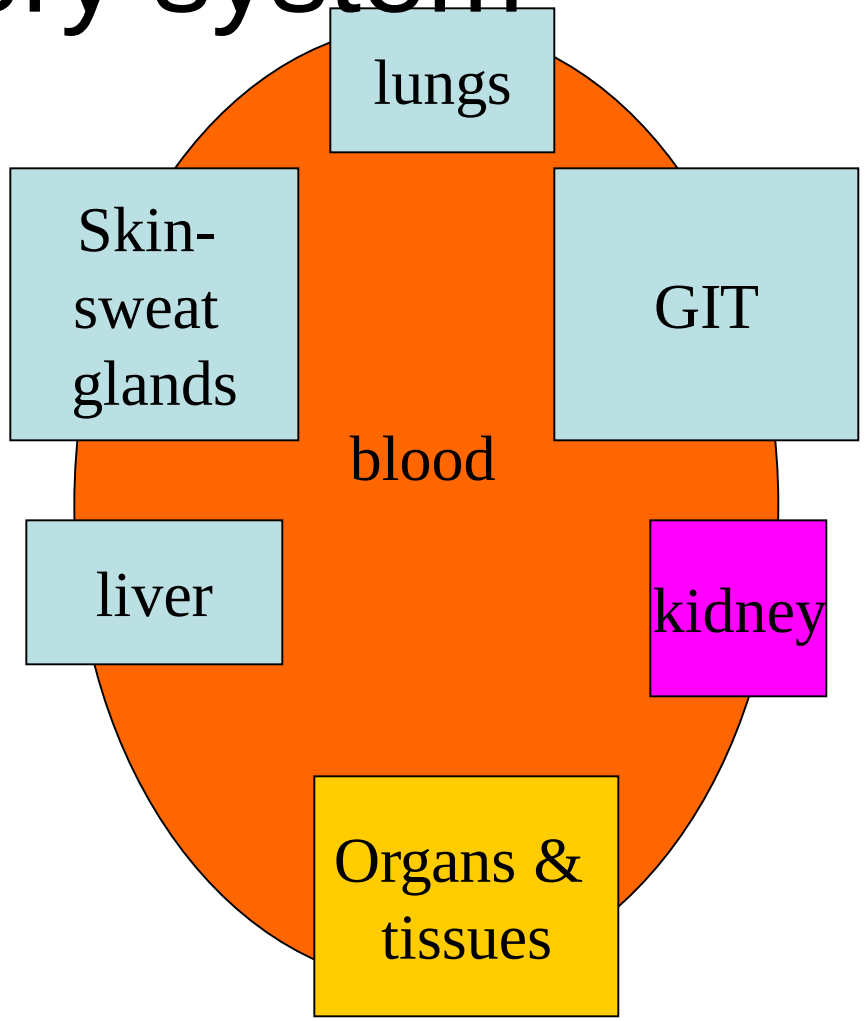
Lecture 31. Urinary system. Mechanisms of urine formation



Excretory system

- lungs - CO_2, H_2O vapour, ethers, chlorophorm
- Sweat glands- H_2O, salts, urea, uric acid, creatinin.
- Liver – bile pigments, products of haemoglobin break down
- GIT - H_2O, salts
- Kidney is the main organ of excretion



Kidneys functions

- *formation of urine*
- *water and electrolyte intake and metabolism*
- *excretion of water and solutes*
- elimination the waste products:

✓ urea (the main nitrogen-containing end-product of protein metabolism in humans)

✓ uric acid (an end-product of purine metabolism)

✓ creatinine (an end-product of muscle metabolism)

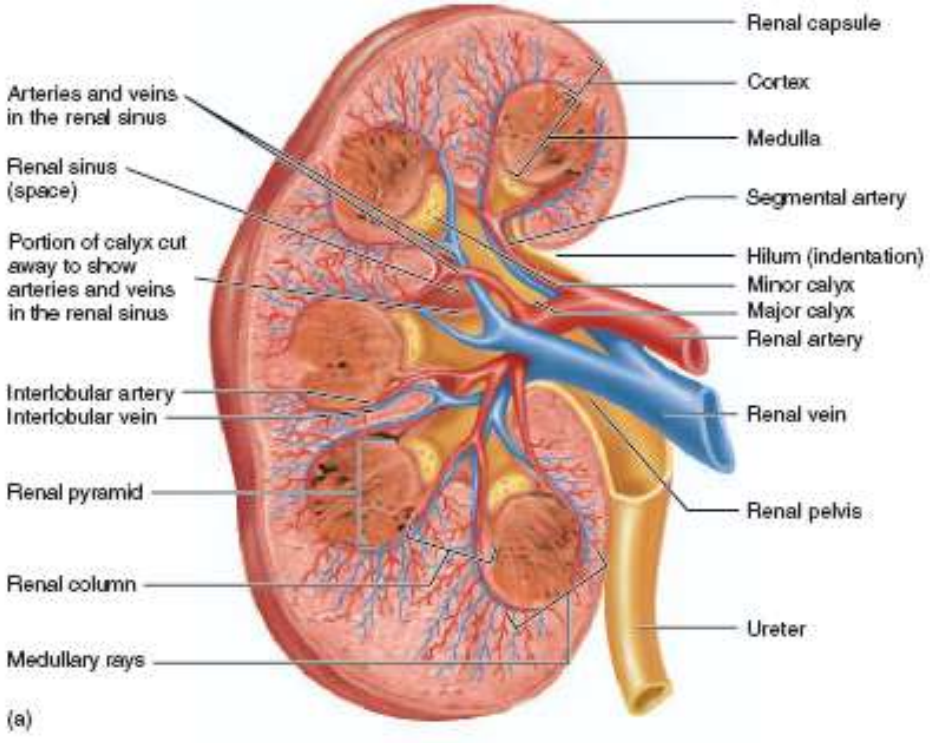
✓ drugs (e.g., penicillin) and foreign or toxic compounds

- *The volume of the extracellular fluid regulation* by controlling Na+ and water excretion;
- *The osmotic pressure (osmolality) of the body fluids regulation* by daily excreting of osmotically dilute or concentrated urine; *blood plasma ions concentration*
- *regulation* including Na+\ K+, Ca^{2+}, Mg^{2+}, Cl-, bicarbonate, phosphate and sulfate;
- *the formation and release of renin*

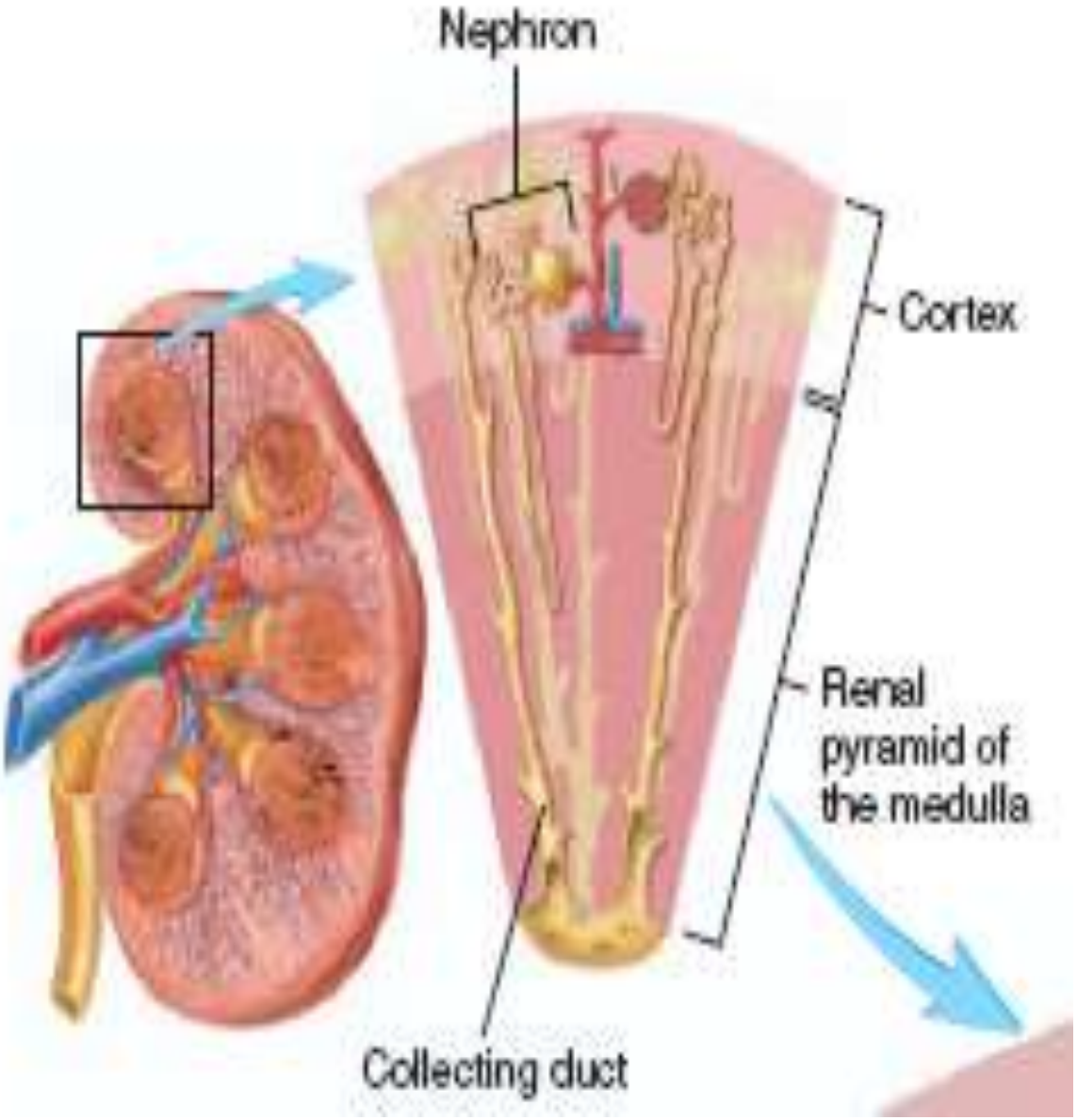
- *The formation and release of* erythropoietin;
- *vitamin D activation*;
- *gluconeogenesis.* The kidneys acquire the important ability to synthesize and secrete glucose produced from noncarbohydrate sources (glutamine) only in unusual circumstances such as prolonged starvation, chronic respiratory acidosis etc.;
- *acid-base balance regulation*

- the place of several polypeptide hormones including insulin, glucagon and parathyroid hormone biochemical degradation
- synthesize substances that affect renal blood flow and Na+ excretion including arachidonic acid derivatives (prostaglandins, thromboxane A2) and kallikrein (a proteolytic enzyme that results in the production of kinins

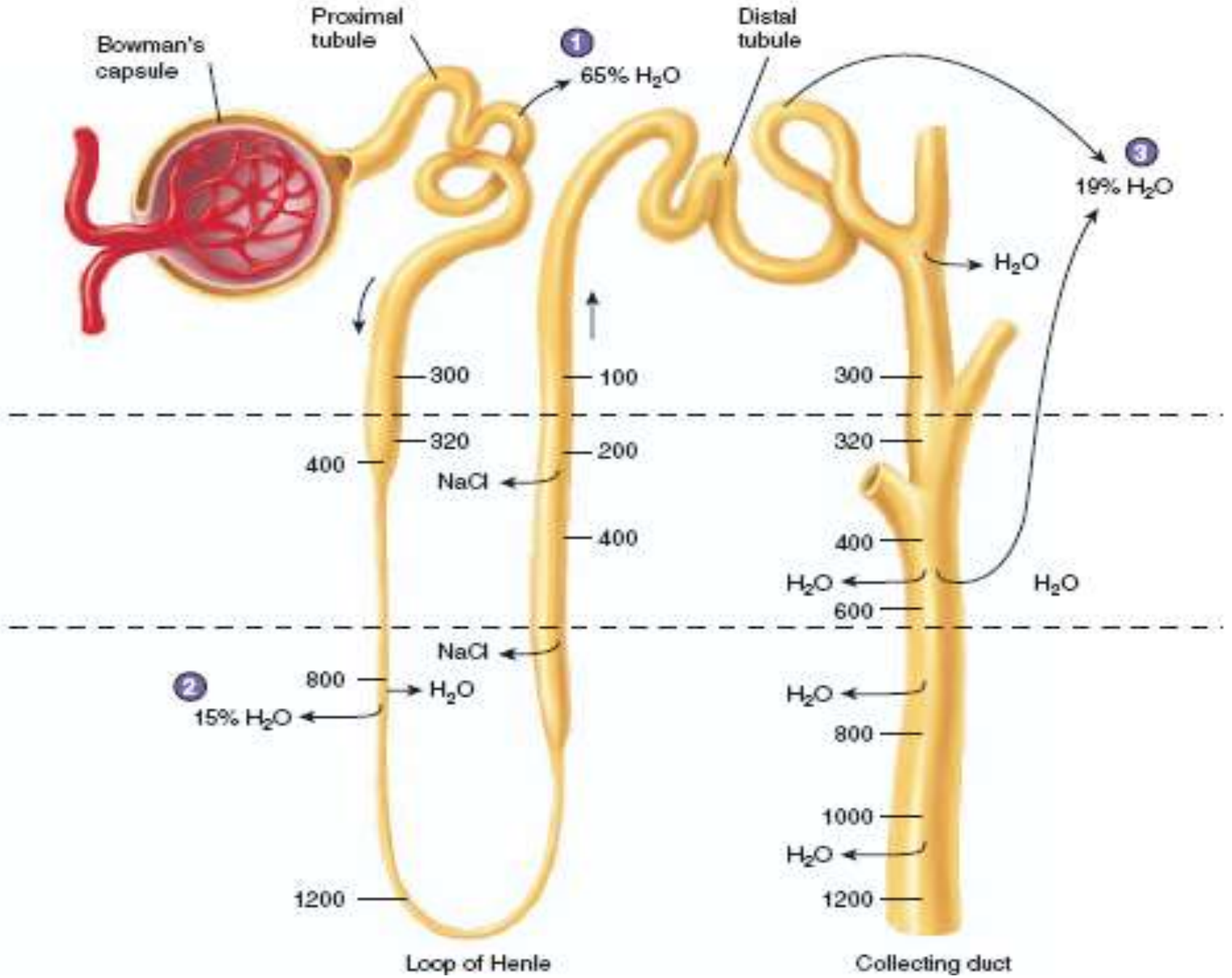
The Nephron Is the Functional Unit of the Kidney

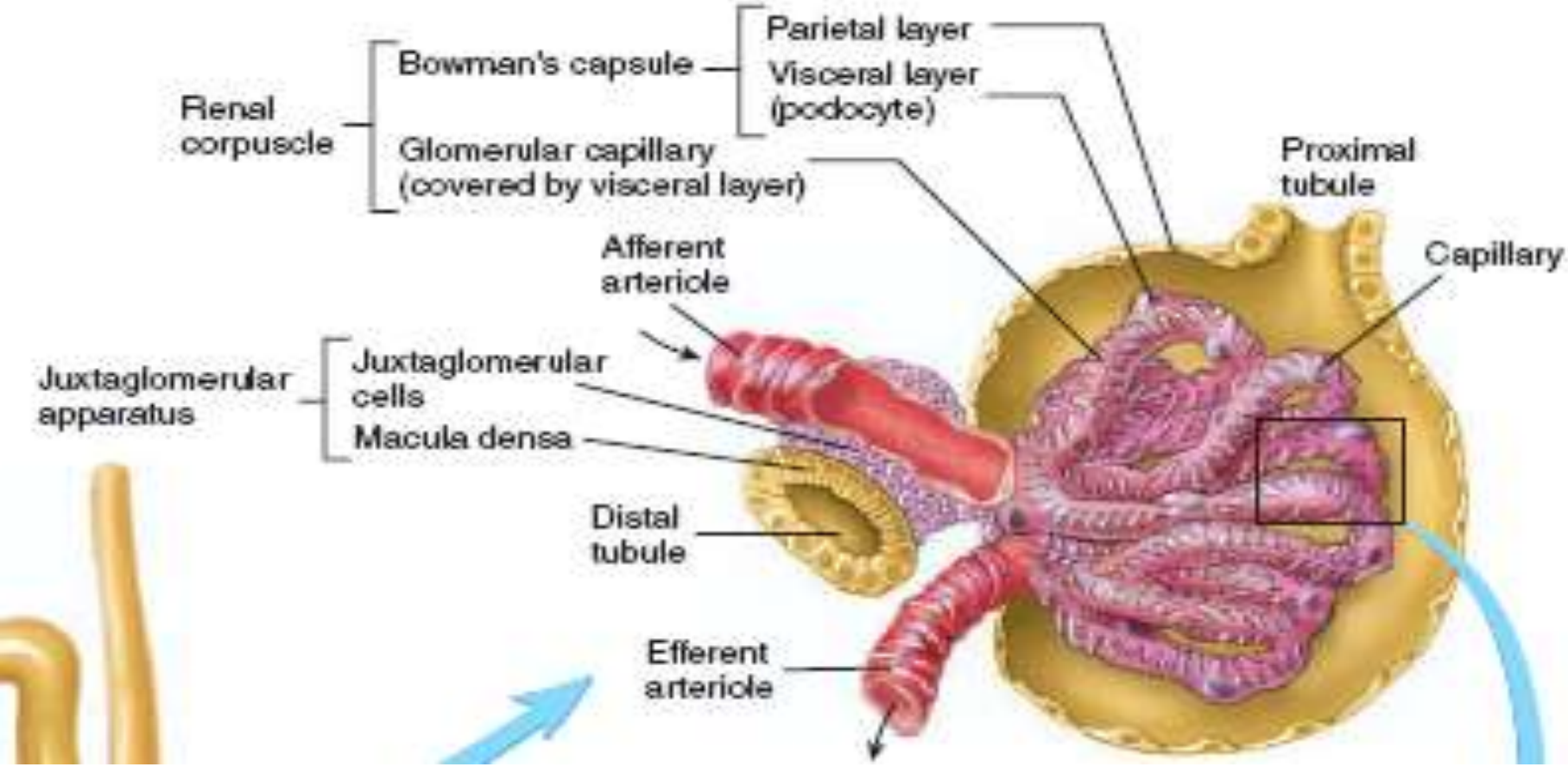


- Each kidney in the human contains about 1 million nephrons, each capable of forming urine. The kidney cannot regenerate new nephrons. Therefore, with renal injury, disease, or normal aging, there is a gradual decrease in nephron number.

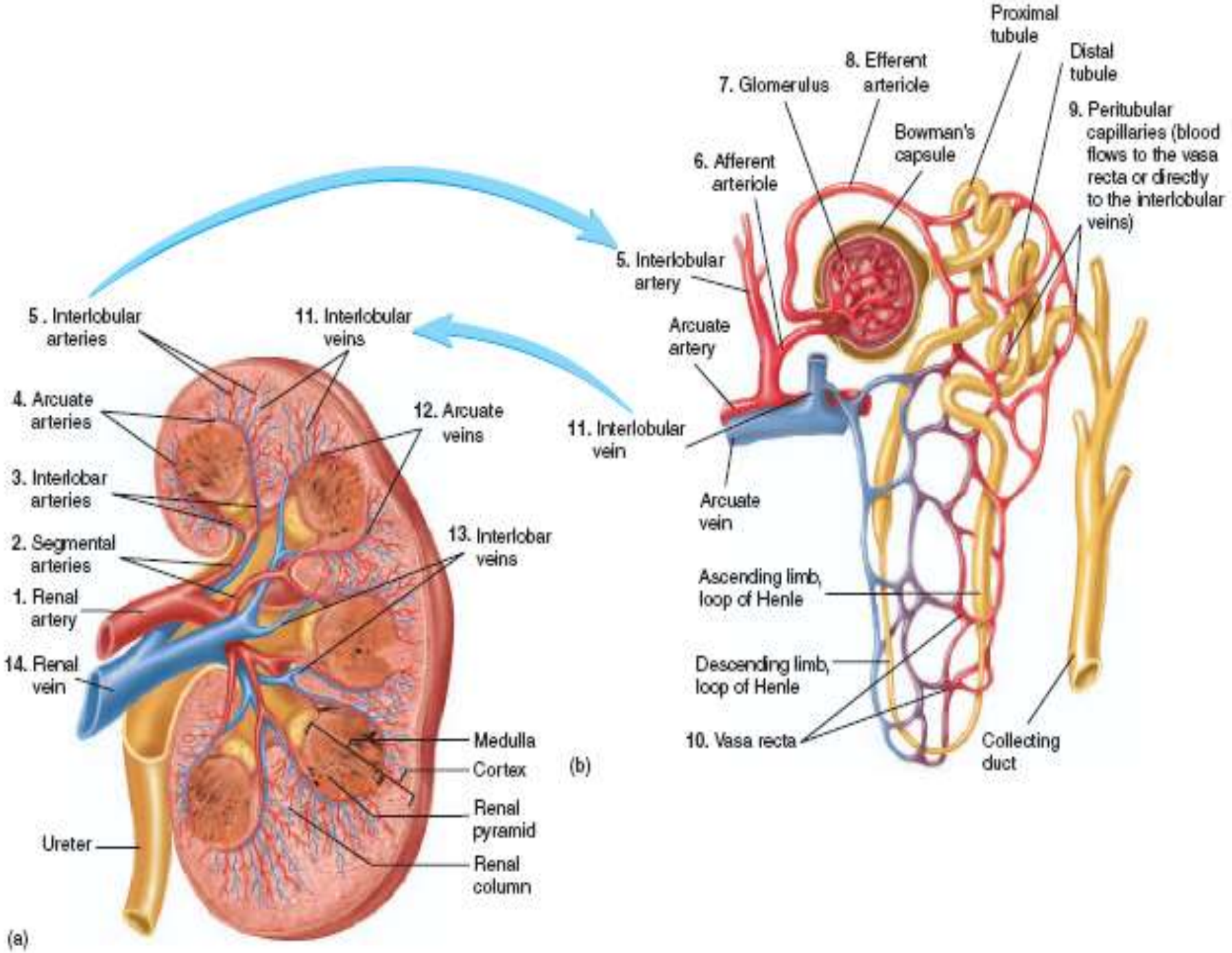


- Each nephron contains a tuft of glomerular capillaries called the glomerulus, through which large amounts of fluid are filtered from the blood, and a long tubule in which the filtered fluid is converted into urine on its way to the pelvis of the kidney.


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



- Juxtaglomerular cells - the macula densa plays an important role in controlling nephron function. Beyond the macula densa, fluid enters the distal tubule that, like the proximal tubule, lies in the renal cortex.

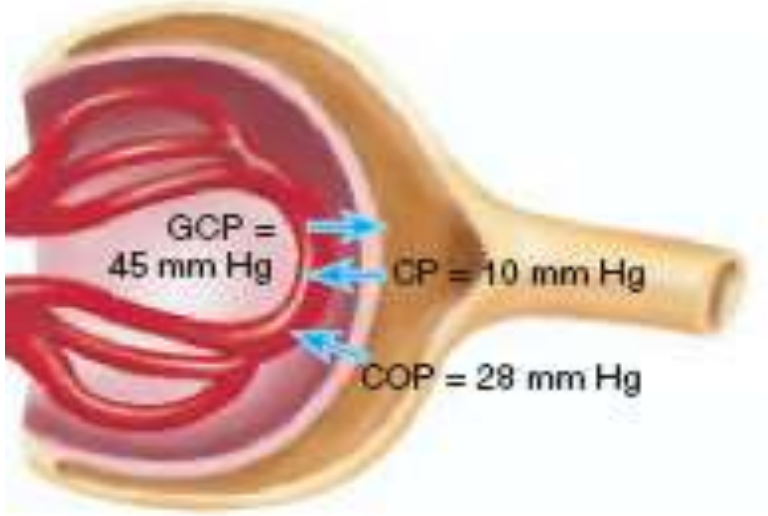

5. Interlobular arteries
11. Interlobular veins
4. Arcuate arteries
12. Arcuate veins
3. Interlobar arteries
2. Segmental arteries
13. Interlobar veins
1. Renal artery
14. Renal vein
Medulla
Cortex
Renal pyramid
Ureter
Renal column
(a)
Proximal tubule
Distal tubule
8. Efferent arteriole
7. Glomerulus
9. Peritubular capillaries (blood flows to the vasa recta or directly to the interlobular veins)
Bowman's capsule
6. Afferent arteriole
5. Interlobular artery
Arcuate artery
11. Interlobular vein
Arcuate vein
Ascending limb, loop of Henle
Descending limb, loop of Henle
10. Vasa recta
Collecting duct
(b)

Factors responsible for high blood pressure in the glomerulus

- **Short renal artery receding from abdominal aorta**
- **The afferent arteriole is wider then efferent arteriole**

PHYSIOLOGIC CONTROL OF GLOMERULAR FILTRATION AND RENAL BLOOD FLOW

- The determinants of GFR that are most variable and subject to physiologic control include the glomerular hydrostatic pressure and the glomerular capillary colloid osmotic pressure.
- These variables, in turn, are influenced by the sympathetic nervous system, hormones and autacoids (vasoactive substances that are released in the kidneys and act locally), and other feedback controls that are intrinsic to the kidneys.



Filtration pressure = GCP – COP – CP

45 mm Hg GCP (glomerular capillary pressure)
–28 mm Hg COP (colloid osmotic pressure)
–10 mm Hg CP (capsule pressure)

7 mm Hg filtration pressure

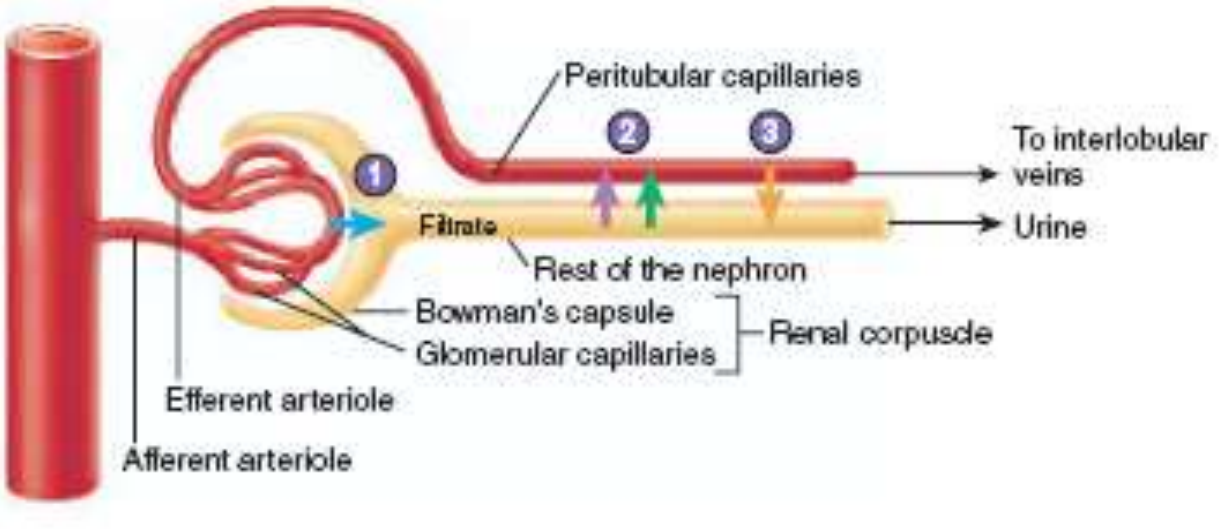
Filtration Pressure

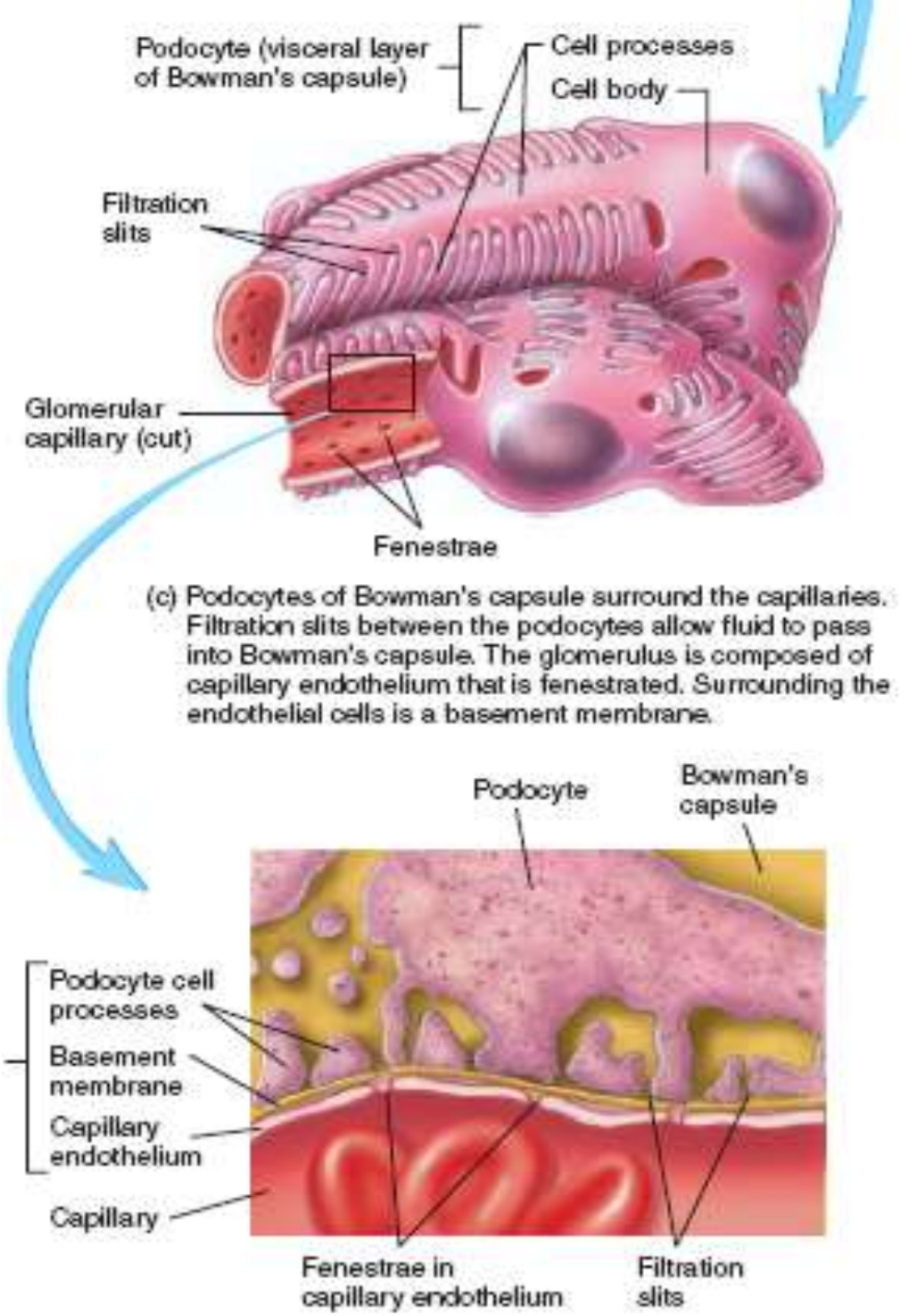
GFR

- The normal range of GFR, adjusted for body surface area, is 100–130 average 125 mL/min/1.73m^2 in men and 90–120 mL/min/1.73m^2 in women younger than the age of 40. In children, GFR measured by inulin clearance is 110 mL/min/1.73 m^2 until 2 years of age in both sexes, and then it progressively decreases. After age 40, GFR decreases progressively with age, by 0.4–1.2 mL/min per year.
- In case < 60 ml/min – Chronic kidney disease

URINE FORMATION

- The rates at which different substances are excreted in the urine represent the sum of three renal processes, (1) glomerular filtration, (2) reabsorption of substances from the renal tubules into the blood, and (3) secretion of substances from the blood into the renal tubules.
- Expressed mathematically,
- Urinary excretion rate = Filtration rate
- - Reabsorption rate + Secretion rate





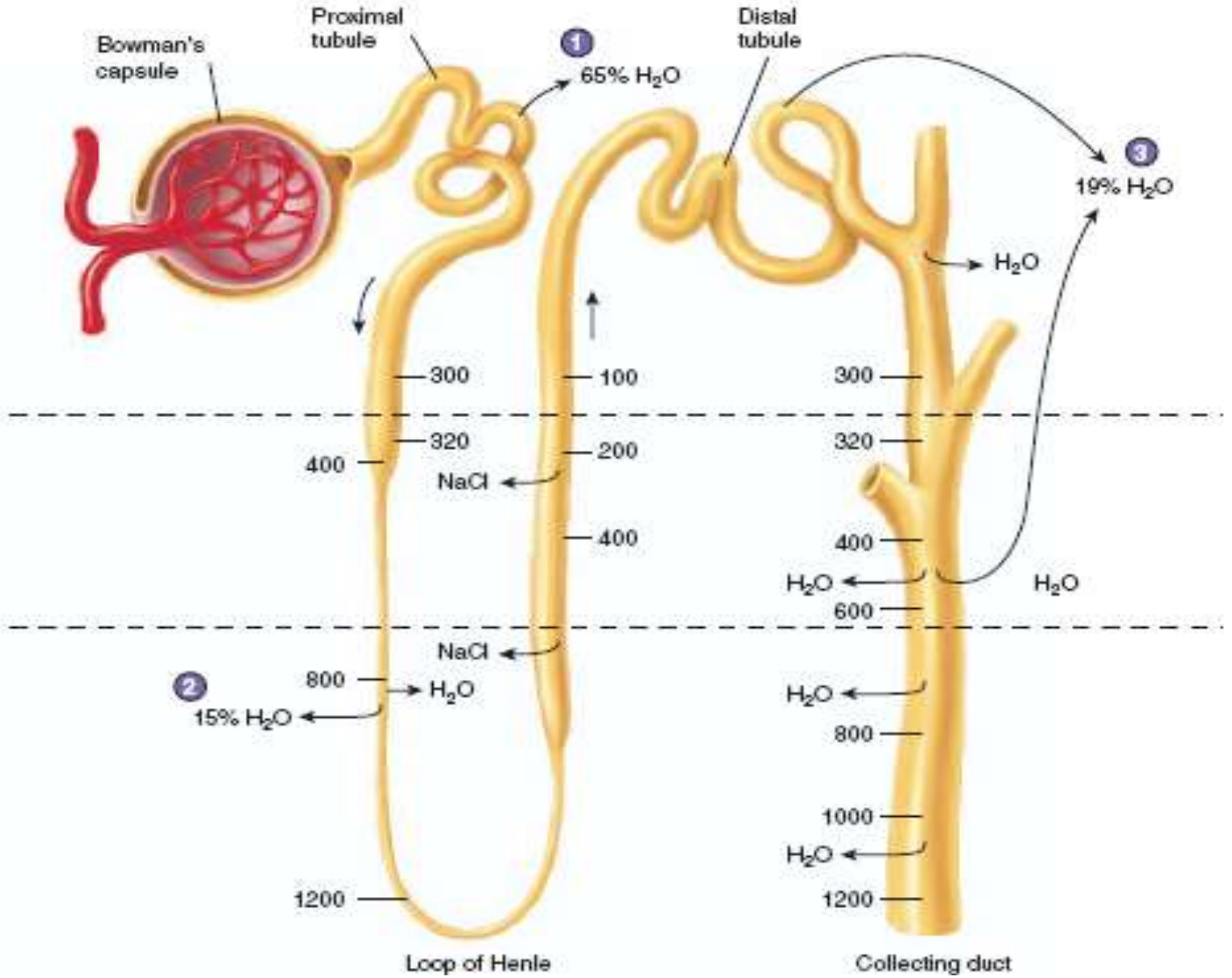
- Urine formation begins with filtration from the glomerular capillaries into Bowman's capsule of a large amount of fluid that is virtually free of protein.
- Most substances in the plasma, except for proteins, are freely filtered so that their concentrations in the glomerular filtrate in Bowman's capsule are almost the same as in the plasma.

Podocytes

- The final part of the glomerular membrane is a layer of epithelial cells (podocytes) that encircle the outer surface of the capillaries.
- The foot processes are separated by gaps called slit pores through which the glomerular filtrate moves. The epithelial cells, which also have negative charges, provide additional restriction to filtration of plasma proteins.

Filtration, Reabsorption, and Secretion of Different Substances

- In general, tubular, reabsorption is quantitatively more important than tubular secretion in the formation of urine, but secretion plays an important role in determining the amounts of potassium and hydrogen ions and a few other substances that are excreted in the urine.
- Most substances that must be cleared from the blood, especially the end products of metabolism such as urea, creatinine, uric acid, and urates, are poorly reabsorbed and are, therefore, excreted in large amounts in the urine.
- Certain foreign substances and drugs are also poorly reabsorbed but, in addition, are secreted from the blood into the tubules, so that their excretion rates are high.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15% H_2O
H_2O
800
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H_2O
1200
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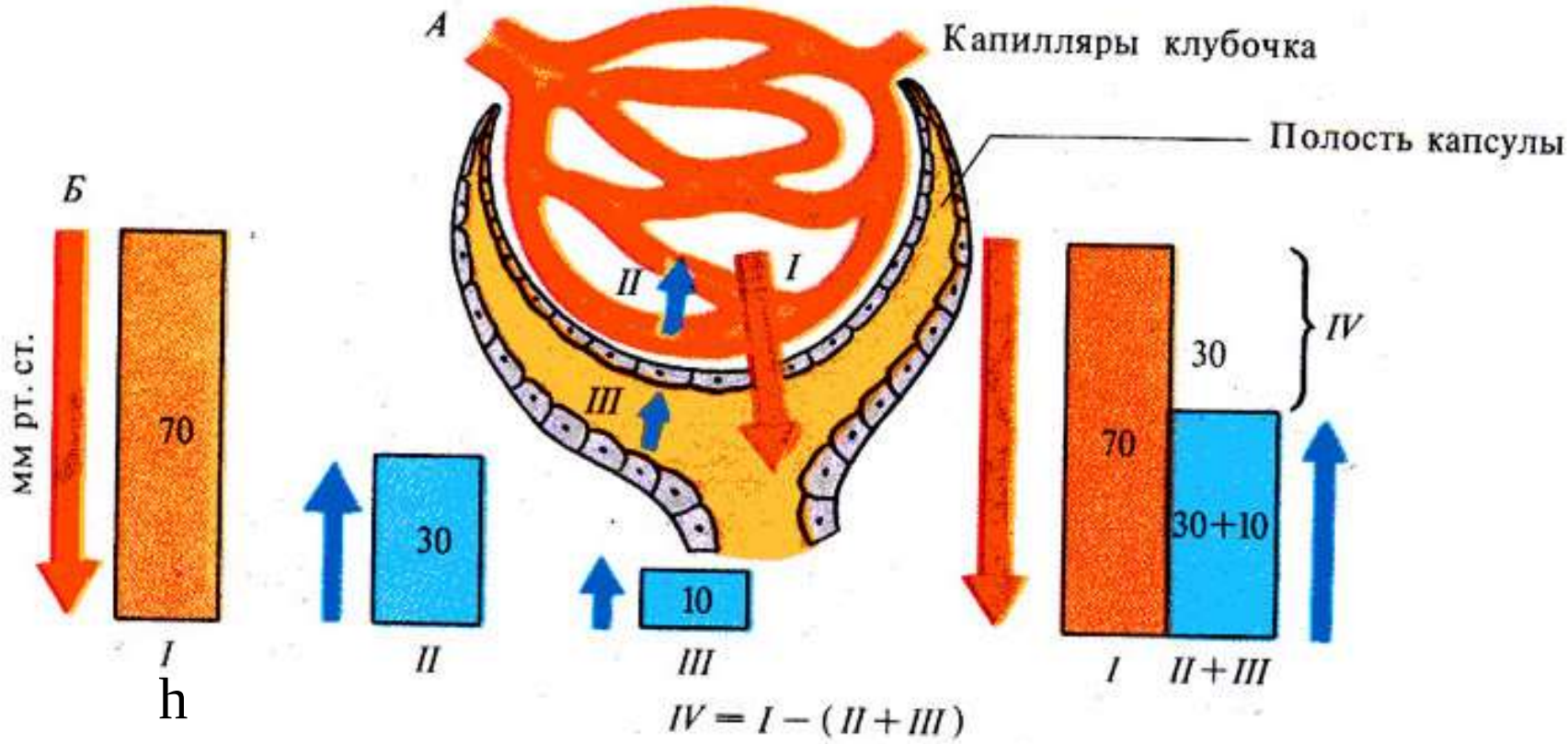
Loop of Henle
Collecting duct

Filtration, Reabsorption, and Secretion of Different Substances

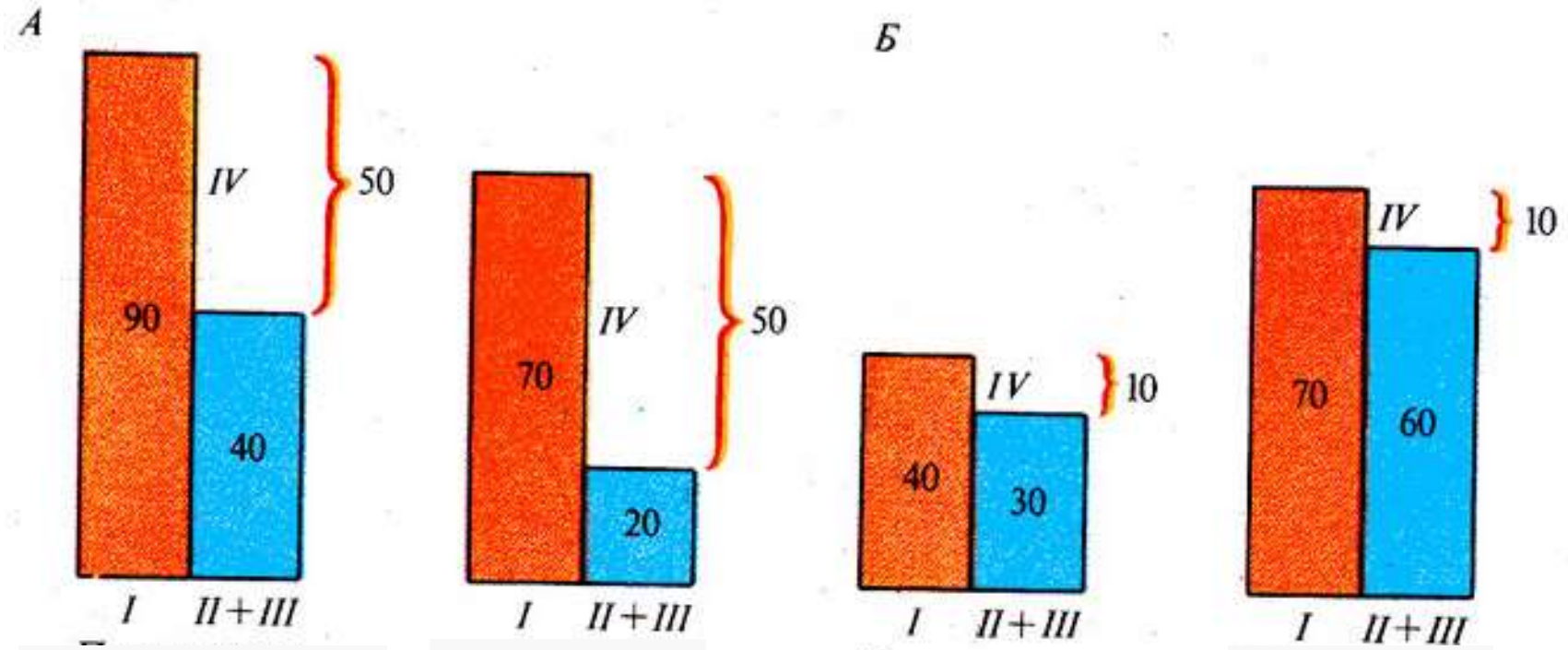
- Nutritional substances, such as amino acids and glucose, are completely reabsorbed from the tubules and do not appear in the urine even though large amounts are filtered by the glomerular capillaries. Each of the processes - glomerular filtration, tubular reabsorption, and tubular secretion - is regulated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

Glomerular diuresis



hydro

Factors influencing filtration pressure

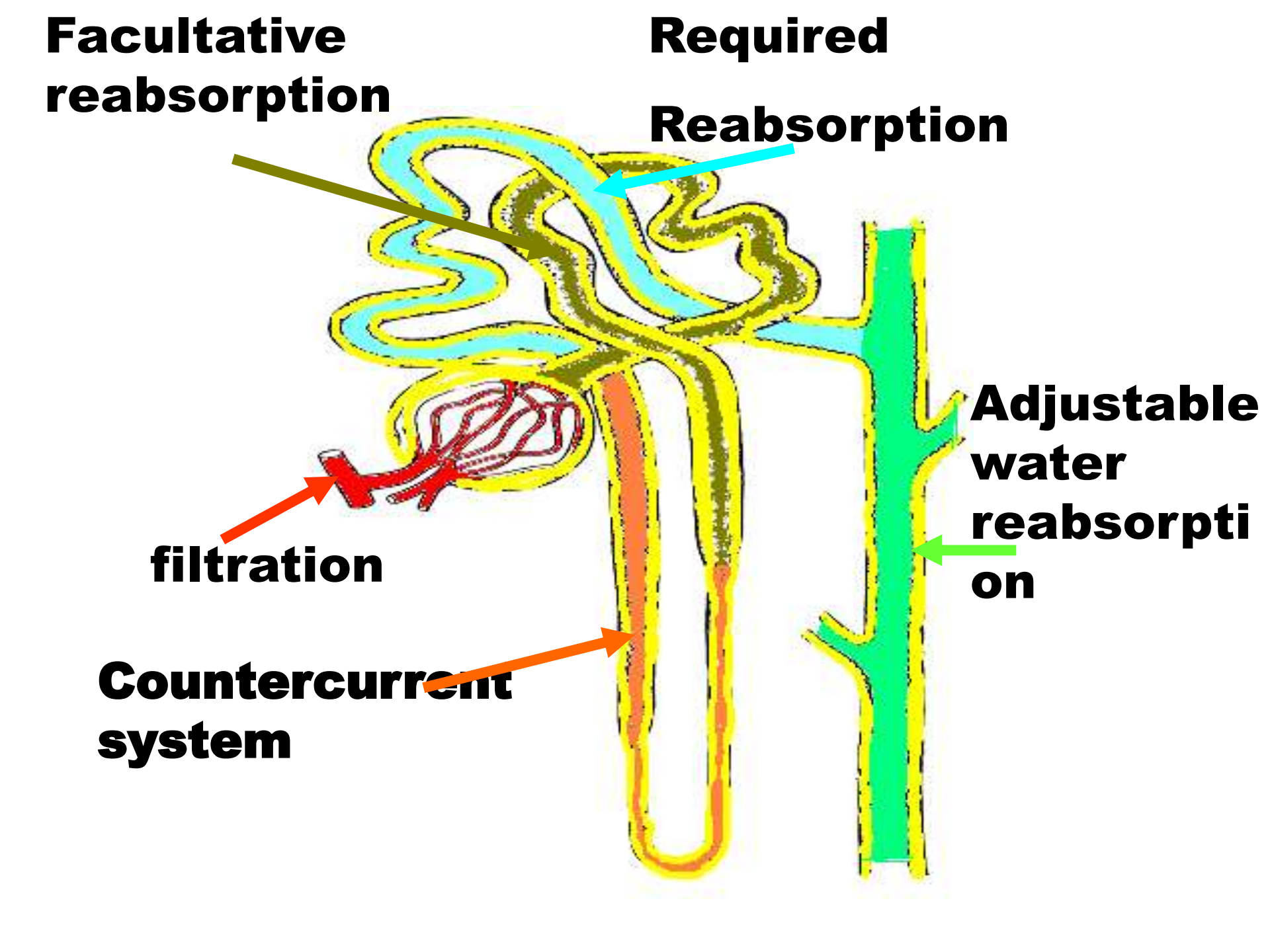


Increase in hydrostatic pressure

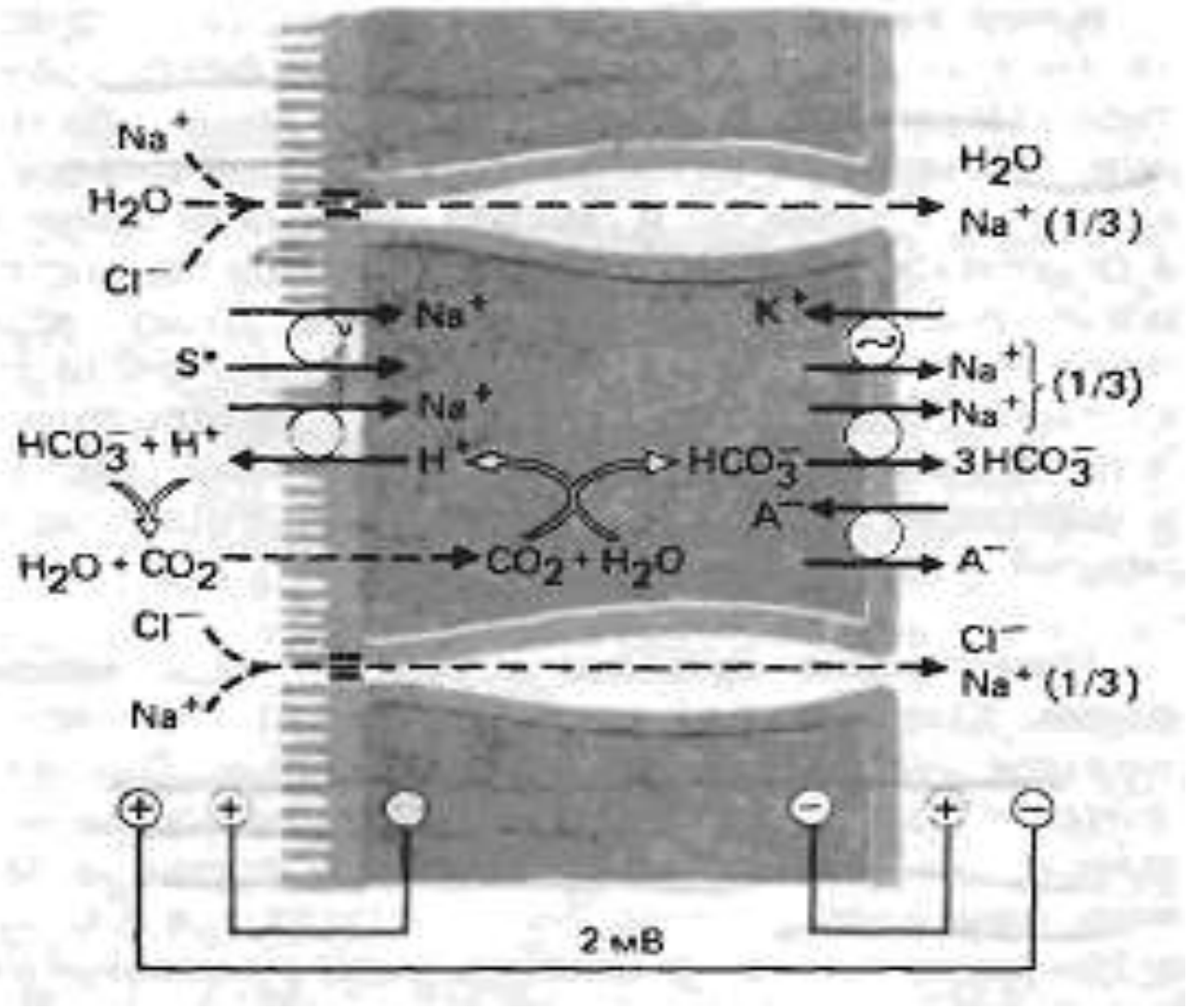
Decrease in oncotic pressure

Increase in hydrostatic pressure

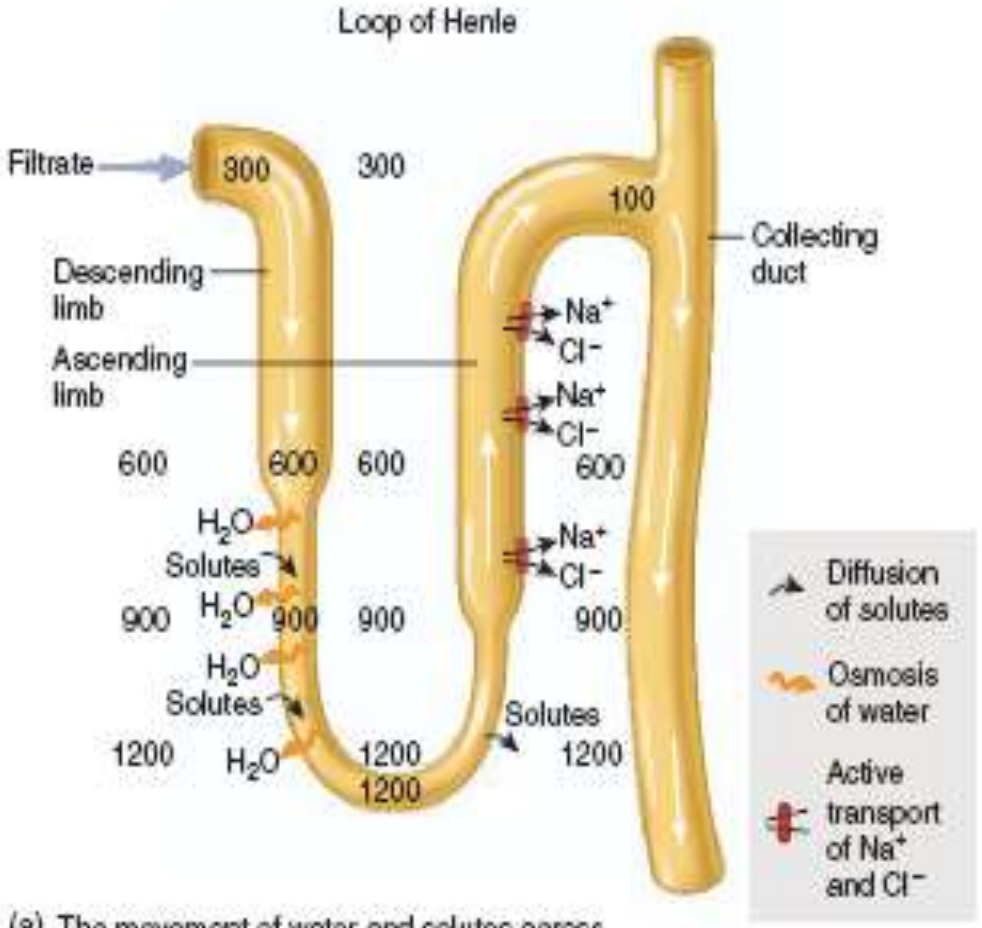
Increase in oncotic pressure


Facultative reabsorption
Required Reabsorption
Adjustable water reabsorption
filtration
Countercurrent system

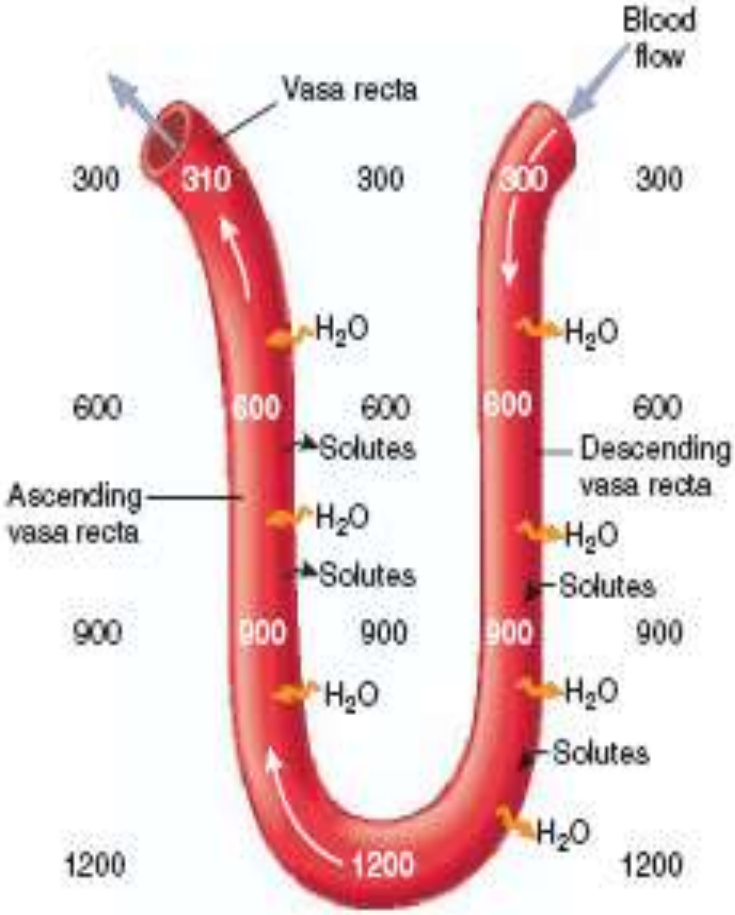
Scheme of transport mechanisms in the proximal tubule



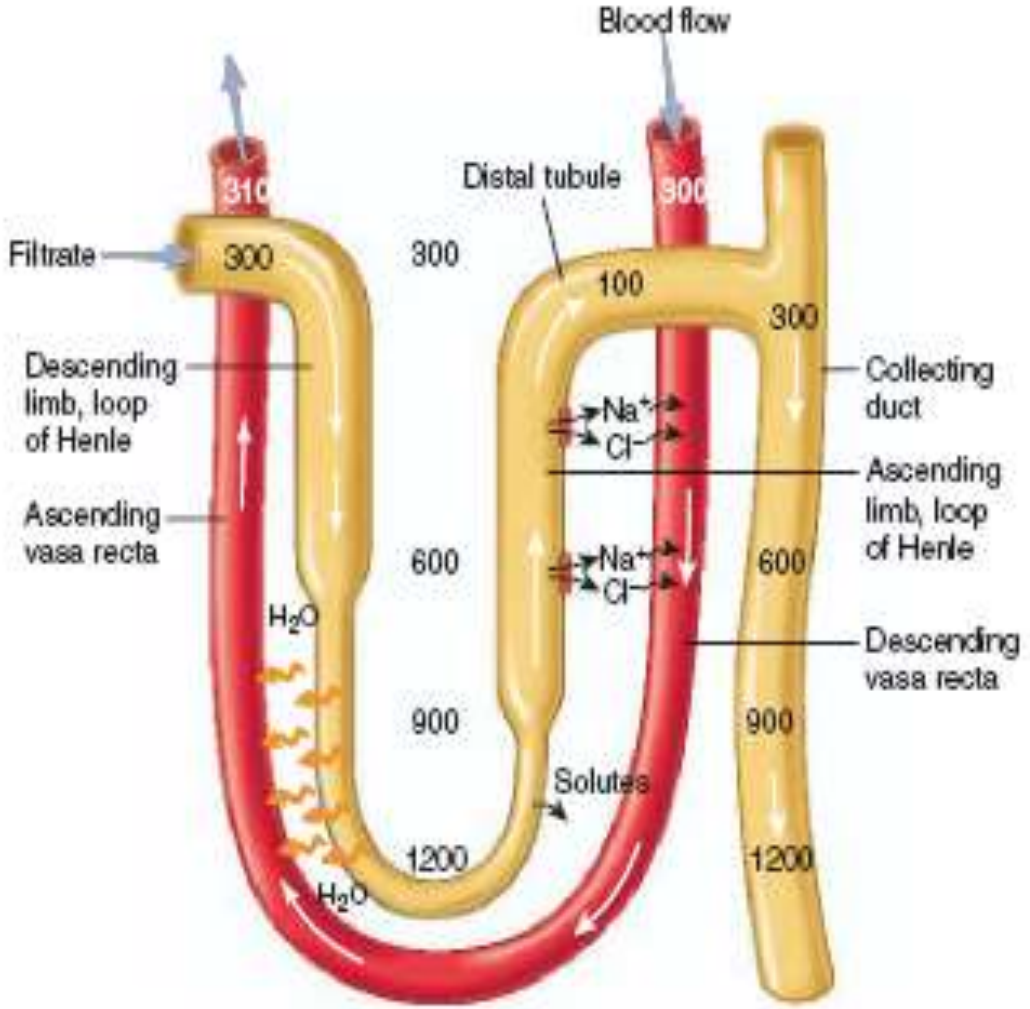
Countercurrent mechanism and concentration of urine



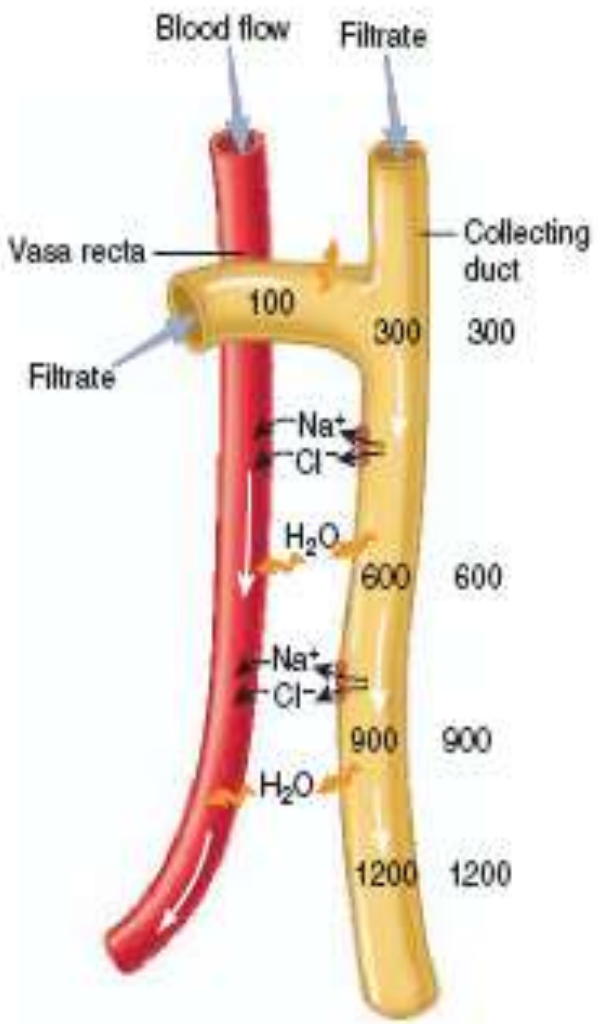
(a) The movement of water and solutes across the wall of the loop of Henle.



(b) The movement of water and solutes across the wall of the vasa recta.



(c) The loop of Henle and the vasa recta function together. Water moves out of the descending limb of the loop of Henle and enters the vasa recta. Solutes diffuse out of the ascending thin segment of the loop of Henle and enter the vasa recta, but water does not. Solutes transported out of the thick segment of the ascending limb of the loop of Henle enter the vasa recta. Excess water and solutes are carried away from the medulla without reducing the high concentration of solutes. The concentration of the filtrate is reduced to 100 mOsm/kg by the time it reaches the distal tubule.



(d) Water and solutes move out of the collecting duct into the vasa recta.

Countercurrent mechanism and concentration of urine

- ***The descending part of Henle's loop is covered with a flat epithelium, poor mitochondria and can not provide active sodium transport, but passes water.***
- ***The ascending part of Henle's loop is covered with cubic epithelium, rich in mitochondria and provides active sodium transport, but does not allow water to pass through.***
- ***Sodium in the parenchyma of the medulla layer increases the osmotic pressure and draws water from the descending knee and from the collecting tubules***

RENAL CLEARANCE

- *Clearance* is a measure of the volume of plasma completely freed of a given substance per minute by the kidneys. It is the *efficiency* with which the plasma is cleared of a given substance.

- Renal clearance of a given substance is the ratio of the renal excretion rate of the substance to its concentration in the blood plasma

$$C_x = U_x \cdot \frac{\dot{V}}{P_x}$$

- where Cx — is the clearance of the substance (ml/min);
- Ux and Px — concentration (mg/ml) of the substance in urine and plasma, respectively;
- V — urine minute volume or volume of urine output per minute (ml/min);
- Ux ♦ V — amount of substance excreted per unit time (mg/min)

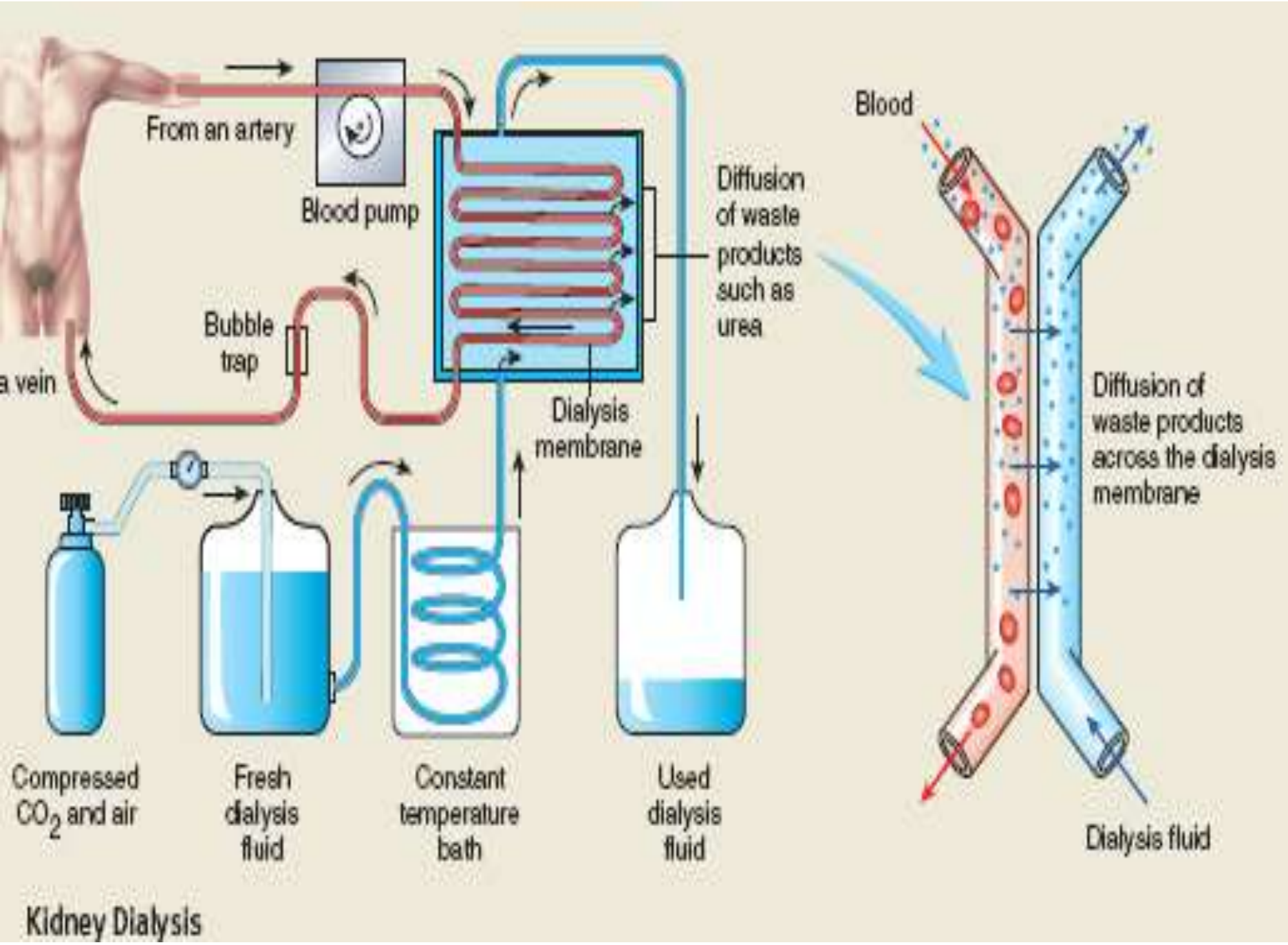
- *Filtration fraction* — the fraction of the renal plasma flow that gets filtered. About 1/5 of the plasma entering the kidneys becomes glomerular urine.
- *Urinary excretion rate* is the amount of a substance appearing in the final urine per unit time. It might be explained by the following equation (mass/volume) (volume/time) = mass/time.
- *Fractional excretion* (FE) is the ratio of clearance of interested substance X to inulin clearance (Cx/CIn) and defines which fraction of the filtered quantity of X was excreted

The *filtration coefficient* (FC)

- The *filtration coefficient* (FC) of the glomerular membrane is a function of the capillary surface area and the membrane permeability.

GFR = FC x EFP

- the *phenomenon of the arterial pressure autoregulation* allows GFR and RBF to remain quite constant in a wide range of the renal arterial pressure (from 80 till 180 mm Hg).



Kidney Dialysis

Sympathetic Nervous System Activation Decreases GFR

- Strong activation of the renal sympathetic nerves can constrict the renal arterioles and decrease renal blood flow and GFR.
- Moderate or mild sympathetic stimulation has little influence on renal blood flow and GFR. For example, reflex activation of the sympathetic nervous system resulting from moderate decreases in pressure at the carotid sinus baroreceptors or cardiopulmonary receptors has little influence on renal blood flow or GFR. Moreover, because the baroreceptors adapt within minutes or hours to sustained changes in arterial pressure, il is unlikely that these reflex mechanisms have an important role in longterm control of renal blood flow and GFR.
- The renal sympathetic nerves seem to be most important in reducing GFR during severe, acute disturbances, lasting for a few minutes to a few hours, such as those elicited by the defense reaction, brain ischemia, or severe hemorrhage. In the healthy resting person, there appears to be little sympathetic tone to the kidneys.

Angiotensin II Constricts Efferent Arterioles

- A powerful renal vasoconstrictor, angiotensin II, can be considered as a circulating hormone as well as a locally produced autacoid because it is formed in the kidneys as well as in the systemic circulation. Because angiotensin II preferentially constricts efferent arterioles, increased angiotensin II levels raise glomerular hydrostatic pressure while reducing renal blood flow.
- It should be kept in mind that increased angiotensin II formation usually occurs in circumstances associated with decreased arterial pressure or volume depletion, which tend to decrease GFR
- Increased angiotensin II levels that occur with a low-sodium diet or volume depletion help to preserve GFR and to maintain a normal excretion of metabolic waste products, such as urea and creatinine, that depend on glomerular filtration for their excretion.

Hormonal and Autacoid Control of Renal Circulation

- Norepinephrine, Epinephrine, and Endothelin Constrict Renal Blood Vessels and Decrease GFR. Hormones that constrict afferent and efferent arterioles, causing reductions in GFR and renal blood flow, include norepinephrine and epinephrine released from the adrenal medulla.
- The endothelin may contribute to hemostasis (minimizing blood loss) when a blood vessel is severed, which damages the endothelium and releases this powerful vasoconstrictor. Plasma endothelin levels also are increased in certain disease states associated with vascular injury, such as toxemia of pregnancy, acute renal failure, and chronic uremia.

Endothelial-Derived Nitric Oxide Decreases Renal Vascular Resistance and Increases GFR

- A basal level of nitric oxide production appears to be important for preventing excessive vasoconstriction of the kidneys and allowing them to excrete normal amounts of sodium and water.
- Administration of drugs that inhibit the formation of nitric oxide increases renal vascular resistance and decreases GFR and urinary sodium excretion, eventually causing high blood pressure.
- In some hypertensive patients, impaired nitric oxide production may contribute to renal vasoconstriction and increased blood pressure.

Prostaglandins and Bradykinin Tend to Increase GFR

- Hormones and autacoids that cause vasodilation and increased renal blood flow and GFR include the prostaglandins (PGE_2 and PG_{12}) and bradykinin.
- By opposing vasoconstriction of afferent arterioles, the prostaglandins may help to prevent excessive reductions in GFR and renal blood flow.
- Under stressful conditions, such as volume depletion or after surgery, the administration of nonsteroidal anti-inflammatory agents, such as aspirin, that inhibit prostaglandin synthesis may cause significant reductions in GFR.

AUTOREGULATION OF GFR AND RENAL BLOOD FLOW

- Feedback mechanisms intrinsic to the kidneys normally keep the renal blood flow and GFR relatively constant, despite marked changes in arterial blood pressure. These mechanisms still function in blood-perfused kidneys thal have been removed from the body, independent of systemic influences. This relative constancy of GFR and renal blood flow is referred to as autoregulation.
- The primary function of blood flow autoregulation in most other tissues besides the kidneys is to maintain delivery of oxygen and nutrients to the tissues at a normal level and to remove the waste products of metabolism, despite changes in the arterial pressure. In the kidneys, the normal blood flow is much higher than required for these functions. The major function of autoregulation in the kidneys is to maintain a relatively constant GFR and to allow precise control of renal excretion of water and solutes. The GFR normally remains autoregulated (that is, remains relatively constant), despite considerable arterial pressure fluctuations that occur during a person's usual activities. In general, renal blood flow is autoregulated in parallel with GFR, but GFR is more efficiently autoregulated under certain conditions.

Myogenic Autoregulation of Renal Blood Flow and GFR

- A second mechanism that contributes to the maintenance of a relatively constant renal blood flow and GFR is the ability of individual blood vessels to resist stretching during increased arterial pressure, a phenomenon referred to as the myogenic mechanism.
- Stretch of the vascular wall allows increased movement of calcium ions from the extracellular fluid into the cells, causing them to contract through the mechanisms. This contraction prevents overdistention of the vessel and at the same time, by raising vascular resistance, helps to prevent excessive increases in renal blood flow and GFR when arterial pressure increases.

Control of kidney activity

Humoral control

- *ADH* produced in the supra-optical nucleus of hypothalamus *intensifies the reabsorption of water in the distal part of nephron and decreases the diuresis*

*(*Deficiency of the posterior pituitary lobe cases *diabetes insipidius).*

- The mineralocorticoids secreted by the adrenal cortex (*aldosterone, desoxycorticosterone*) increase the renal reabsorption for Na+ and secretion for K+, H+.

- *Adrenaline is cause constriction of the efferent arterial vessels (vas efferens),* increase of the glomerular filtration pressure (amount of urine will increase). Large doses of adrenaline (at pain, stress) also constrict the afferent vessels, which reduces blood flow to the glomeruli and suppresses diuresis.
- The *thyroid and parathyroid (PTH) hormone increase salts in urine, urine secretion,* increases renal Ca^{2+} reabsorption, inhibits renal phosphate reabsorption

Nervous control

- Constriction of the renal vessels is observed when the sympathetic nerves innervated the kidneys are stimulated. If the afferent arteriole is constricted, filtration pressure falls and formation of filtrate is reduced. But if the efferent arterioles are narrowed, pressure in the glomeruli rises and filtration is increase

- *Strong sympathetic activation* (pain) cause stoppage of urine production (*pain anuria)*

- Cortical control of the urine formation by conditioned reflexes is possible too

The end