МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ

УЧРЕЖДЕНИЕ ОБРАЗОВАНИЯ
«ГОМЕЛЬСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ»

Кафедра биологии с курсами нормальной и патологической физиологии

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ФИЗИОЛОГИЯ ЧЕЛОВЕКА

Допущено Министерством образования
Республики Беларусь в качестве учебного пособия
для иностранных студентов
учреждений высшего образования по специальности «Лечебное дело»

В двух частях
Часть 2

HUMAN PHYSIOLOGY

In two parts
Part 2

Гомель
ГомГМУ
2021

УДК 612 (075.8)=111
ББК 28.707.3я73=432.1
М 48

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Мельник, В. А.
М 48 Физиология человека: учеб. пособие: в 2 ч. = Human physiology / В. А. Мельник, С. Н. Мельник, Ю. И. Брель; под ред. В. А. Мельника; пер. на англ. яз. М. В. Петренко, Ю. И. Брель, С. Н. Мельник, В. А. Мельника. — Гомель: ГомГМУ, 2021. — Ч. 2. — 316 с.
ISBN 978-985-588-211-5

Вторая часть учебного пособия содержит информацию о физиологии кровообращения, пищеварения, обмена веществ и энергии, терморегуляции, выделения, сенсорных систем и интегративной деятельности мозга. Каждый раздел заканчивается тестовым контролем. В конце учебного издания представлены базовые константы физиологических систем в Международной системе физических единиц (СИ).

Предназначено для студентов медицинских университетов, обучающихся на английском языке.

УДК 612 (075.8)=111
ББК 28.707.3я73=432.1

ISBN 978-985-588-211-5 (Ч. 2)
ISBN 978-985-588-209-2

CONTENTS

LIST OF ABBREVIATIONS

ACTH — adrenocorticotropic hormone

ADP — adenosine diphosphate

ANS — autonomic nervous system

AP — action potential

ATP — adenosine triphosphate

ATPase — adenosine triphosphatase

A-V — atrioventricular node

CC — cortex of cerebrum

CI – cardiac index

CNS — central nervous system

CO — cardiac output

CVS — cardiovascular system

ECG — electrocardiogram

EEG — electroencephalography

EFP — effective filtrational pressure

EG — endocrine glands

EPP — exciting postsynaptic potential

ERG — electroretinogram

ERV —expiratory reserve volume

ESR — erythrocyte sedimentation rate

FEF — forced expiratory flow

FEV — forced expiratory volume

FRC — functional residual capacity

FSH — follicle-stimulating hormone

FVC — forced vital capacity

GH — growth hormone

HNA — higher nervous activity

HR — heart rate

IPP — inhibitory postsynaptic potential

IRV — inspiratory reserve volume

LH — luteinizing hormone

MRP — membrane resting potential

MVL — maximal ventilation of lungs

NC — nerve center

ORE — osmotic resistance of erythrocytes

PEF — peak expiratory flow

PSNS — parasympathetic nervous system

RMV — respiratory minute volume

RP — receptor potential

RQ — respiratory quotient

RR — respiratory rate

S–A — synoatricular node

SNS — sympathetic nervous system

STH — somatotropic hormone

TLC — total lung capacity

TSH — thyroid-stimulating hormone

TV — tidal volume

VCL — vital capacity of lung

UNIT 1
PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

1.1. Physiology of the heart

1.1.1. Structure, properties of cardiac muscle (myocardium). Electrical manifestation of cardiac activity

1.1.1.1. Structural functional characteristics of the circulatory system

Blood can perform multiple life functions only during its continuous circulation, which is provided by the activity of the organs of the circulatory system — the heart and blood vessels.

During its circulation blood follows a complex path through the big (systemic) and small (pulmonary) circuits (Figure 1.1).

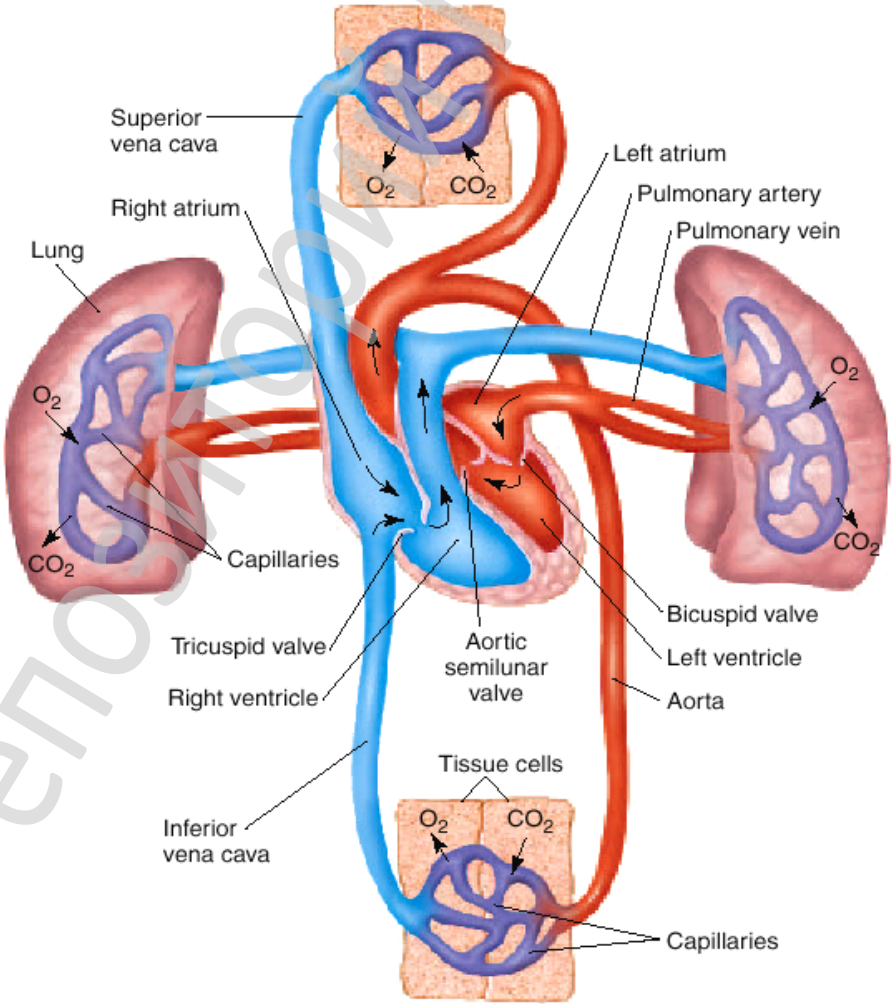


Figure 1.1 — Cardiovascular system (by Fox, 2006)

The big (systemic) circuit is the path of circulation between the heart and the other parts of the body (excluding the lungs). It starts from the left ventricle of the heart, includes the aorta, arteries, arterioles, capillaries, veins and ends with the venae cavae in the right atrium.

The small (pulmonary) circuit is the path of circulation between the heart and the lungs. It starts from the right ventricle, includes the pulmonary artery, its branches, arterioles, capillaries, veins and ends in the left atrium. While passing this path, the blood is released from the excess of CO_2 and is oxygenated.

1.1.1.2. Physiology of the heart. Structure, properties of cardiac muscle (myocardium)

The function of the heart is to pump blood rhythmically through arteries as a result of contraction (systole) and relaxation (diastole) of the myocardium (Figure 1.2).

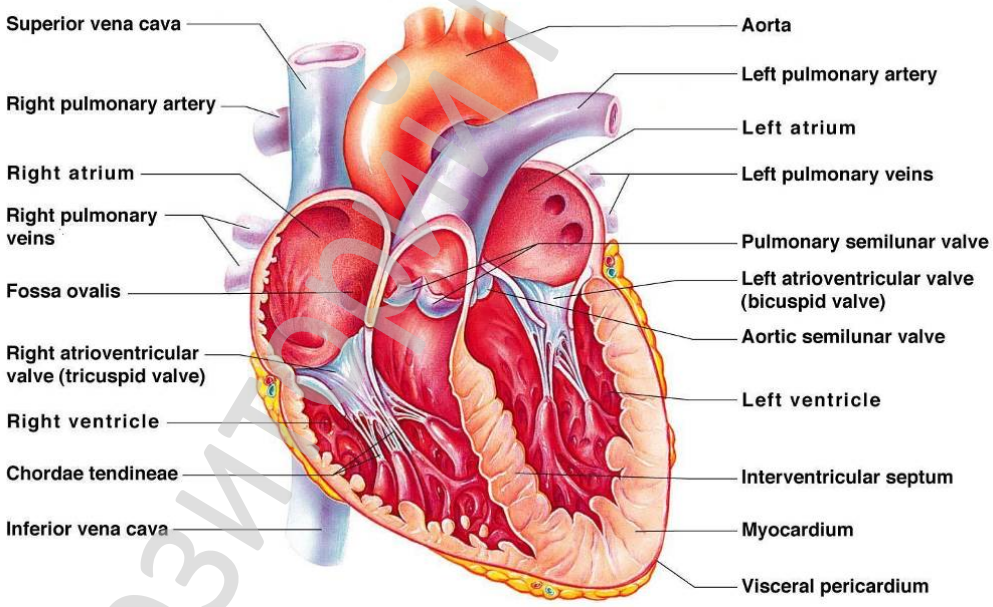


Figure 1.2 — Heart anatomy (by Elaine N. Marieb, 1989)

Normally, systole, diastole, and the general pause of the atria and ventricles are in concert with one another and organize the *cardiac cycle,* which lasts for 0.75–1.0 sec (0.8 sec). This cycle starts with atrial systole. Upon its termination, ventricular systole starts: the ventricles contract and pump the blood out of the heart into arteries. The atria at this time are in the diastole phase. Ventricular systole is followed by their diastole, during which the ventricles of the heart are relaxed, and the heart fills with blood. Just 0.1 sec before the end of the diastole phase, new atrial systole begins.

The heart in a human at rest works for 9 hrs 24 min a day and rests for 14 hrs 36 min.

The important parameter is the volume of the blood contained by the heart, on average it is 500–600 mL. The volume of the left ventricle is 120–130 mL.

The myocardium has an original constitution. The main portion of the working myocardium consists of transversely-striated irregularly organized fibers (Figure 1.3). Apart from the working myocardium, there is some accumulation of special cells called atypical *muscle tissue*: it contains a few myofibrils, a lot of sarcoplasm and weak striation. It forms the *cardiac conduction system*.

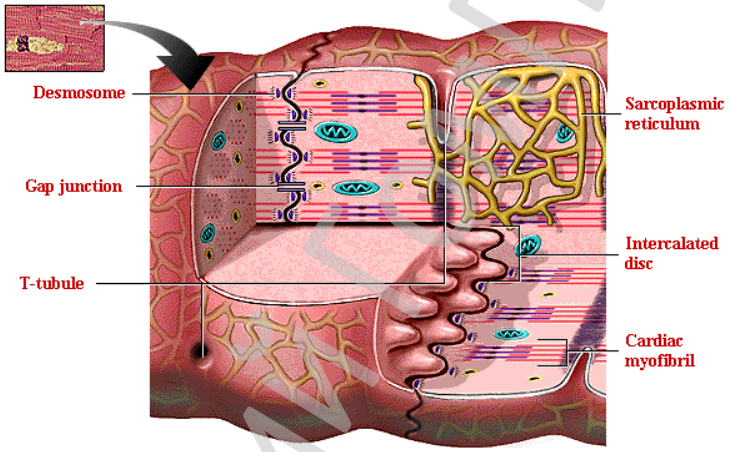


Figure 1.3 — Cardiac muscle cell (from biology.reachingfordreams.com)

The working myocardium and the conduction system of the heart are characterized by the presence of a large number of intercellular contacts — *nexuses*, through which excitation is capable to pass from one cardiomyocyte to another. These features of the intercellular interactions ensure synchronous cardiomyocyte contractions.

Properties of the myocardium

1. ***Excitability*** is the ability to respond to excitation. In excitation during systole excitability is reduced and disappears — this period of time is referred to as the refractory period (non-excitability). The refractory period helps the heart to pump blood into the blood vessels.

2. ***Conduction*** — ensures the propagation of excitation through the conduction system and myocardium.

3. ***Contraction*** and ***relaxation*** phenomena.

The force of a cardiac contraction depends on the initial length of muscle tissue (*the Frank — Starling's law* of the heart). When more blood comes to the heart, the ventricles get more stretched and their contractions become stronger (e.g., during physical work).

4. ***Automaticity*** is the ability of an organ (tissue) to get excited under the influence of impulses arising in it. Thus, the isolated heart of a frog placed into Ringer's solution can contract for a long time.

The atypical muscle tissue of the cardiac conduction system has the ability of self-excitation (automaticity). The conduction system of the heart also contains nerve cells which belong to the cardiac part of the metasympathetic nervous system.

In the cells of the sinoatrial node (the pacemaker of the heart), the membrane potential is not stable. There is a gradual decrease of the membrane potential during the phase of diastole — spontaneous slow depolarization (SD). When the critical level of the depolarization phase is reached (approximately — 50mV), there is a new action potential (AP) (the phases of fast depolarization and fast repolarization) (Figure 1.4).

This mechanism is the basis for automatic action of the pacemaker heart cells.

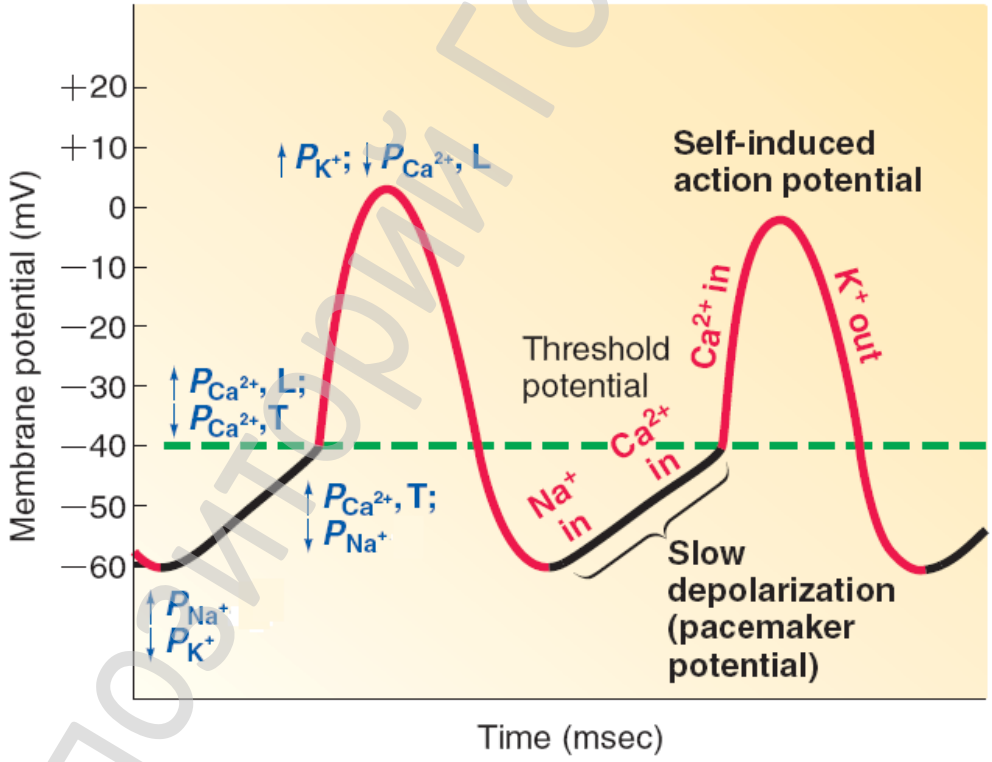


Figure 1.4 — Action potential of the pacemaker (from studylib.net)

T — transient-type channels; L — long-lasting channels; ↑↓ — opening or closing of voltage-gated channels

Ion mechanism of SD

At the peak of each AP after depolarization, the potassium channels open, which leads to repolarization. When potassium ion diffusion is reduced, the membrane begins to depolarize. The slow sodium channels and calcium channels of the two types are opened — transient-type calcium channels and long-lasting

calcium channels. The calcium influx through the transient-type calcium channels forms SD, the calcium influx through the long-lasting calcium channels creates AP.

The pacemaker cells are characterized by:

- the presence of the SD phase, which is smoothly replaced by the phase of fast depolarization;
- the AP of the pacemaker cells have no repolarization plateau;
- the membrane potential in the pacemaker cells is lower (-55–60 mV) than that in contractile cardiomyocytes (-90 mV).

1.1.1.3. Conduction system of the heart

The synoatrial (S-A) node is located in the right auricle in the region of the foramen of the venae cavae (Figure 1.5). The synoatrial node is the leading part of the heart and the pacemaker of the 1st order. It generates 60–80 impulses per minute.

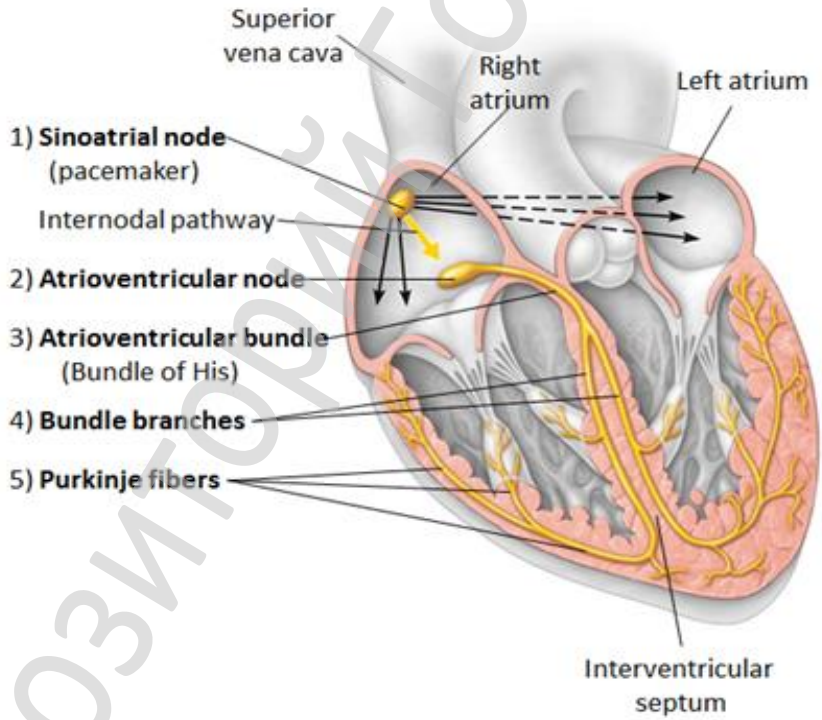


Figure 1.5 — Cardiac conduction system (by Elaine N. Marieb, 1989)

There are three conduction pathways from the S-A node:

— *Bachmann's pathway* goes from the S-A node to the myocardium of the left atrium and partially to the atrioventricular node (A-V node);

— *Wenckebach's pathway* connects the middle part of the S-A node with the A-V node;

— *Thorel's pathway* connects the posterior part of the S-A node with the A-V node.

Excitation is spread along the myocardium of the atria and reaches the **atrioventricular (A-V) node,** located in the right atrium in the region of the interatrial septum. This is the pacemaker of the 2nd order. The cells of the A-V node have the ability to generate impulses, but in normal conditions this ability is not manifested. The cells of the A-V node can start to generate action potentials when the action potentials from the S-A node do not propagate to them. The frequency of impulses generated by the A-V-node is 40–50 impulses per minute. In a healthy person impulses are normally generated only by the S-A node, and then are conducted by the conduction system to cardiomyocytes.

From the A-V node the **Bundle of His** starts connecting the atria with the ventricles (Figure 1.5). In the ventricles it is divided into the right and left **branches of the Bundle of His.** It forms the pacemaker of the 3rd order (Figure 1.5) and generates 30–40 impulses per minute. The final branching of the cardiac conduction system under the endocardium forms the **Purkinje fiber network** (20 impulses/minute). Hence, impulses which are formed in the S-A node are distributed along the conduction system contracting the myocardium and producing cardiac systole. First, the apex of the ventricles is contracted, then their base.

In the A-V-node excitation is conducted with some delay for 0.02–0.04 sec because of the small diameter of its muscle fibers and a small number of nexuses. Following this, the excitation reaches the Bundle of His once the atria have pumped blood into the ventricles.

From the S-A the signals propagate to the myocardium of the atria and to the A-V node at a rate of 1.0 m/sec;

— In the A-V node the rate of excitation conduction is 0.05 m/sec.

— In the bundle of His — 1.5 m/sec.

— In the Purkinje fibers — 3–5 m/sec.

The high rate of excitation conduction in the conduction system and myocardium promotes synchronous contractions of the ventricles, raises their force and pumping ability. Hence, the conduction system of the heart provides:

1) rhythmic generation of impulses;

2) sequence of contractions of the atria and ventricles;

3) synchronic contractions of myocardial fibers.

1.1.1.4 Relations of the excitability, excitation and contractions of the myocardium. Extrasystole

Myocardial action potentials (APs) of the different parts of the heart differ in shape, amplitude, and duration. The AP of the contractile ventricular myocardium includes several phases (Figure 1.6).

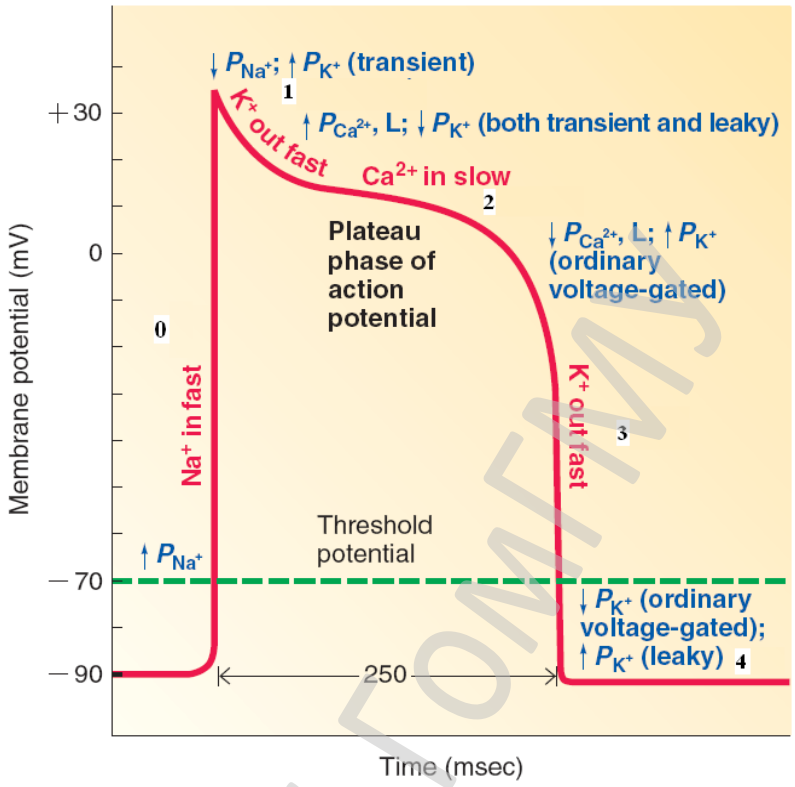


Figure 1.6 — Action potential of the contractile myocardium (from studylib.net)
0 — initial fast depolarization; 1 — initial fast repolarization; 2 — plateau; 3 — final fast repolarization; 4 — resting phase; ↑↓ — opening or closing of voltage-gated channels

1. The initial fast depolarization phase. It is associated with the entrance of Na+ ions into cells.

2. The initial fast repolarization phase is the result of the closure of sodium channels, the entrance of chlorine ions into cells and the exit of potassium ions out of them.

3. The phase of the plateau. During this phase, the membrane potential for some time remains at approximately the same level due to the interaction of the two ion currents: due to the slow opening of the potential-dependent calcium channels, Ca2+ ions enter cells together with sodium ions (depolarizing current), while the diffusion of potassium ions outside cells through the slow potassium channels is remained (repolarizing current);

4. The final fast repolarization phase. It occurs as a result of the closure of calcium and sodium channels and diffusion of potassium ions outside cells.

5. The resting phase. At this phase the membrane potential (–90 mV) is restored because of the exchange of potassium ions due to the functioning of the sodium-potassium pump.

The threshold stimulus initiates an action potential whose duration is about 0.3 sec. It spreads through cardiomyocytes and causes their contractions (Figure 1.7).

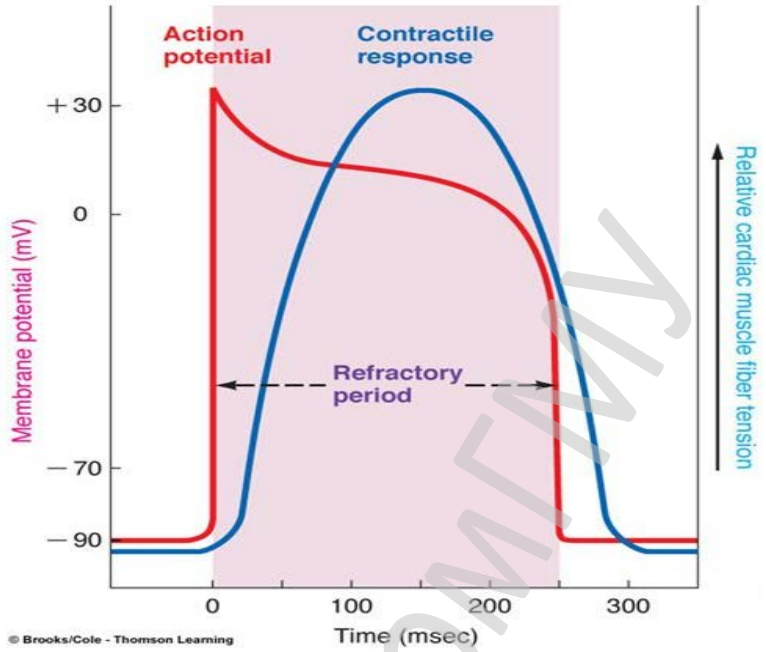


Figure 1.7 — Relations of myocardial excitation and contraction (from slideplayer.com)

During the phase of myocardial contractions (lasting about 0.33 sec), the excitability decreases (*the absolute refractory period* lasting for 0.27 sec, i.e. it is slightly shorter than the AP), and the heart does not respond to the effect of even the superthreshold stimulus. This condition is very important for the heart. If the prolonged absolute refractory period in cardiomyocytes was absent, the muscles of the heart would develop tetanus and would not be able to perform their functions.

As the relaxation phase begins, the excitability of cardiomyocytes starts to increase (*the relative refractory period* is 0.03 sec), and the heart can respond to the effect of the superthreshold stimulus. Then there comes a short period of *supernormal excitability* with the duration of about 0.03 sec (sodium channels by this time are practically reactivated, and the potential difference is close to the critical level of depolarization). At this time, the cardiac muscle can respond to the effect of the subthreshold stimulus by contracting.

The heart responds to stimulation along the **"all-or-none" law**. The heart responds to the effect of the threshold stimulus by excitement of all fibers, but it does not respond to the effect of the subthreshold stimulus. Therefore, the strength of the response is not changed if the strength of the superthreshold stimulus increases.

Cardiac muscle is contracted by the type of *single muscle contractions*, as the long absolute refractory period prevents the appearance of tetanic contractions.

During the conduction of the action potential along the membrane, *calcium ions come mainly from the intercellular medium*. Calcium, which enters the cell, extends the duration of the action potential and, as a result, the duration of the refractory period. Calcium is also a regulator of the force of myocardial contractions.

The force of myocardial contractions depends on:

1. The number of actin-myosin bridges, which are formed simultaneously. The more the fiber is stretched at rest, the more the force of the contraction is (the Frank — Starling's law).

2. The more calcium ions come into the sarcoplasm, the more the force of the contraction is.

3. The force of heart contractions is regulated by the duration of the action potential. The longer the action potential is, the more calcium ions enter cardiomyocytes.

Extrasystoles. The ability to generate rhythmic impulses, which is typical for the cells of the conduction system, is not revealed till the pacemaker's role is performed by the S-A node. However, the impulses can be frequently generated in other parts of the conduction system both in healthy and sick people. If the myocardium is excited during the phase of diastole when the excitability is recovered, there is a premature extra contraction — ***extrasystole*** (Figure 1.8).

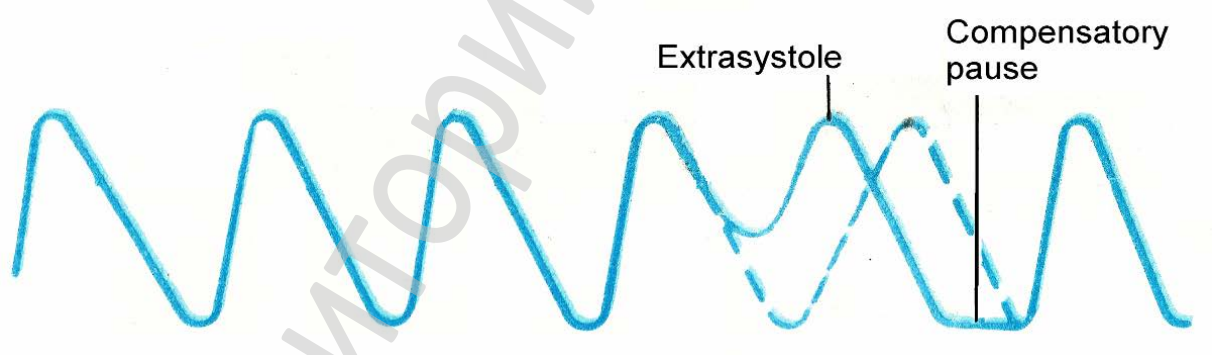


Figure 1.8 — Extrasystole (schematic illustration)

Extrasystoles can be: sinus, atrial, ventricular.

Impulses can be generated in the A-V node or near the node. Excitation reaches the Purkinje fibers quickly, spreads through the myocardium and causes its premature contraction. This extrasystole is called ventricular and it is accompanied by a complete compensatory pause. During the development of extrasystole, the S-A node sends another impulse to the ventricles. However, they are already contracted under the influence of the premature impulse from the A-V node, i.e. the ventricles are refractory (are not excitable), and the myocardium does not respond to the stimulation. At the end of the state of non-excitability, it takes some time before the next impulse comes from the S-A node. The loss of one ventricular contraction leads to a long compensatory pause.

Single extrasystoles are often found in healthy people and have no particular clinical significance (emotions, pain). Recurrent extrasystoles frequently arise in heart diseases.

1.1.1.5. Electrical manifestation of cardiac activity. Electrocardiography, its diagnostic significance

Excitation which appears in the pacemakers spreads along the conduction system and myocardium and is accompanied by the formation of a negative charge on the cell surface. The heart becomes a powerful generator of biological electricity. The cumulative potential of excited fibers is so huge that it can be registered far outside the heart. The application of electrodes to certain body spots makes it possible to record a curve reflecting the potential difference during the cardiac cycle. This curve, which has a complex character, is called the ***electrocardiogram*** (ECG), and the method of examination — ***electrocardiography***. Electrocardiography is a method based on the registration of the potential difference of the electric dipole of the heart within certain areas of the human body. When the myocardium is excited, an electric field is generated, which can be registered on the body surface.

To explain the mechanism of ECG formation, the **dipole theory** is used. It is a concept that assumes that the electric field of the heart is the result of the formation of electric dipoles in myocardial fibers and their subsequent summation.

An **electric dipole** is a combination of two electric charges equal in magnitude and opposite in sign, located at an infinitesimally small distance from each other. The main characteristic of the electric dipole is the ***dipole moment*** — a vector directed from a negative charge to a positive one. The positive pole of the dipole (+) is always directed towards the non-excited part of the cardiomyocyte, and the negative pole (–) — towards the excited one. The process of propagation of a depolarization/repolarization wave along a single muscle fiber can be conditionally represented as the movement of a double layer of the charges located on the border of the excited and (–) and non-excited (+) parts of the fiber. The myocardial fiber can be represented as an ***elementary electric dipole***. During one cycle of excitation/relaxation of the fiber, two dipoles are formed: depolarization dipole and repolarization dipole, the vectors of which are oppositely directed.

During the cardiac cycle, the excitation processes do not occur simultaneously in different areas of the heart. The conditional line connecting two points with the greatest potential difference is called the **electrical axis of the heart**. If the excitement spreads normally, the **electrical axis of the heart**

coincides with the anatomical axis. In certain periods, it is characterized by a different value and direction, i.e. it has the property of the vector value and is expressed by the value of the angle alpha (α).

The ECG is widely used as a diagnostic method allowing to define the nature of some cardiac disorders.

There are different ECG leads.

1. Leads from the extremities:
   a) Bipolar (Einthowen's) (Figure 1.9);
   b) Unipolar (Goldberger') (Figure 1.10).
2. Thoracal (pre-cardiac) leads:
   a) Bipolar (by Nab) (small thoracal triangle);
   b) Unipolar (by Wilson).

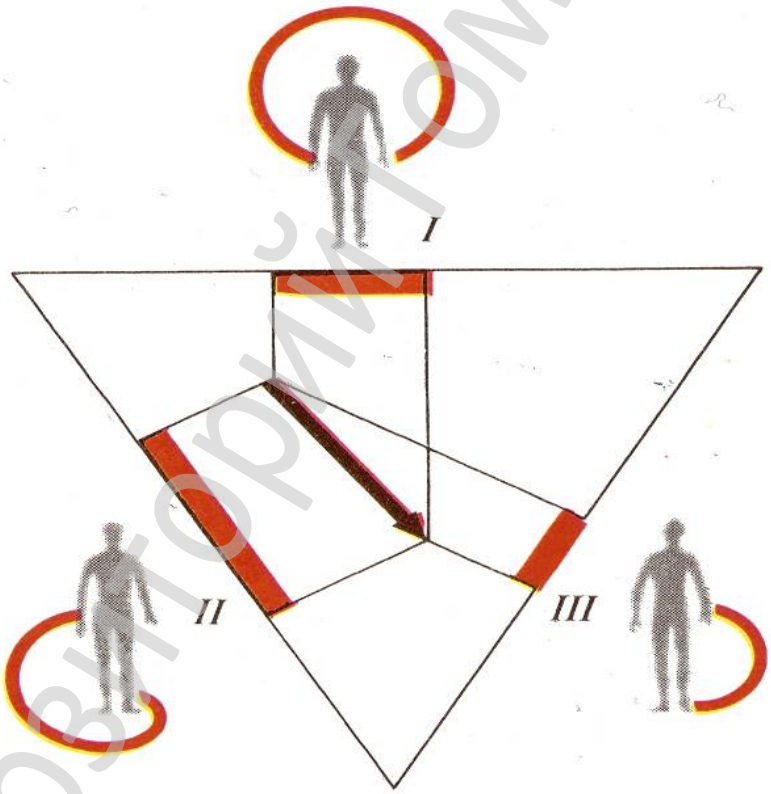


Figure 1.9 — Scheme which explains the difference between the amplitudes of the wave R in the three bipolar (standard) leads (I, II, III) from the extremities (Einthowen`s triangle) (by Korobkov A. V., Chesnokova S. A., 1986)

More often to register the ECG, the standard leads from the extremities by the method of the Einthowen triangle (bipolar leads) are used.

The three standard leads include:

I — the right hand — the left hand;

II — the right hand — the left leg;

III — the left hand — the left leg.

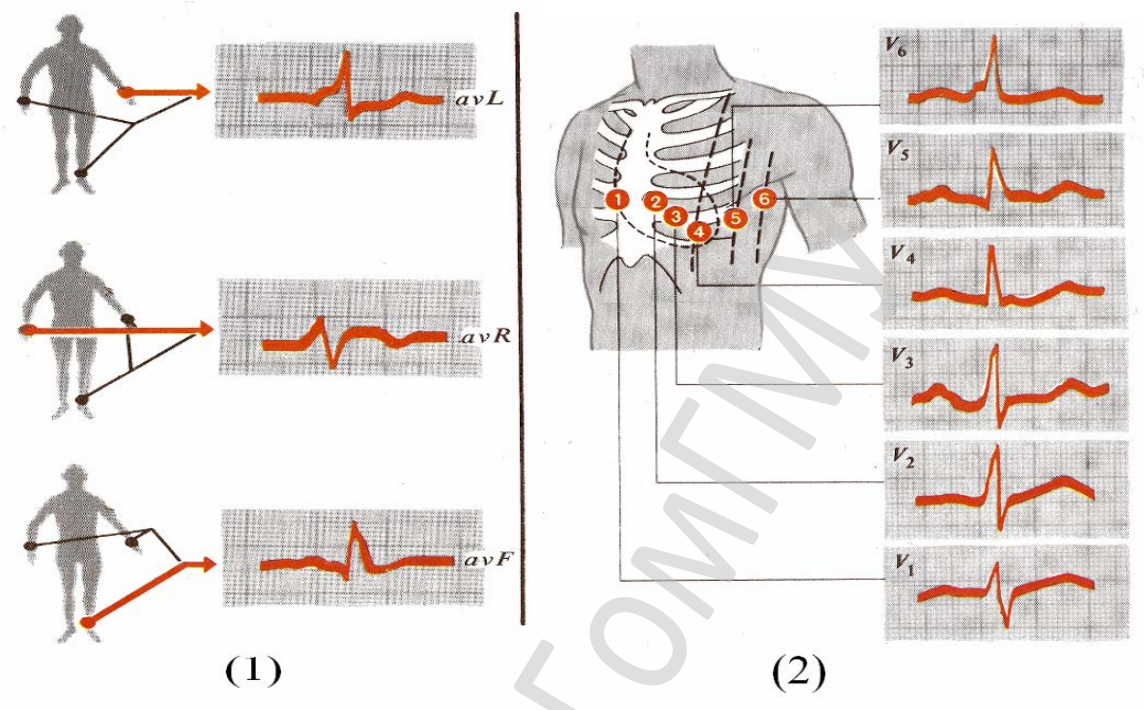


Figure 1.10 — Electrocardiography (unipolar leads)
(by Korobkov A. V., Chesnokova S. A., 1986)

Notes: (1) — Unipolar leads from the extremities (Goldberger's method); (2) — Unipolarthoracal (pre-cardiac) leads (Wilson`s method)

The typical ECG consists of 5 positive and negative oscillations-waves, conforming to the cycle of cardiac activity. They are marked with the Latin letters P, Q, R, S, T. The interspaces between the waves are named segments, the unity of a wave and a segment makes an interval. Three waves — P, R, T — are directed upwards, two small waves — Q and S — downwards (Figure 1.11, Table 6.1).

Table 6.1. — Amplitude and duration of the waves in the II standard lead

Waves of ECG	Amplitude of waves, mV	Duration of waves, sec
P	0.05-2.5	0.1
Q	0-0.3	0-0.03
R	1-2	0,03-0.09
S	0-0.6	0-0.03
T	0.2-0.5	0.12-0.16

The wave P reflects excitation of either atrium (right or left). The segment P-Q corresponds to the spread of excitation along the atrioventricular node. The interval P-Q reflects the duration of the conduction of excitation from the atria to the ventricles.

The QRS complex reflects the origination and conduction of excitation in the myocardium of the ventricles.

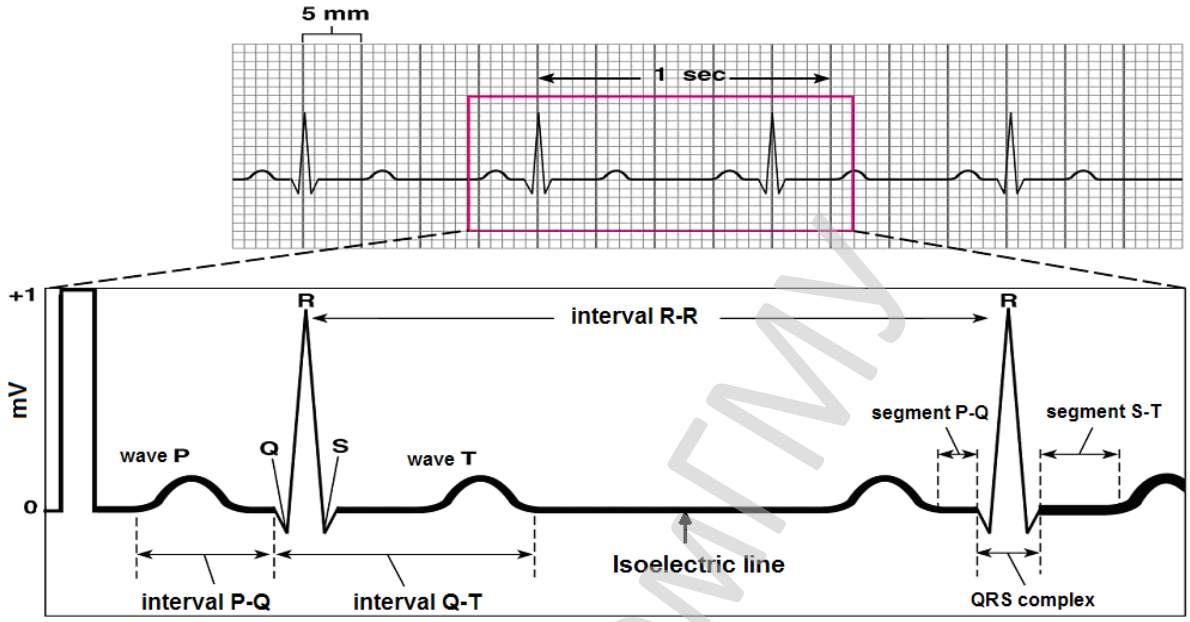


Figure 1.11 — Electrocardiogram (registered in the second standard lead)

The wave Q reflects the conduction of excitation of the interventricular septum and papillary muscles.

The wave R, the highest one, reflects the conduction of excitation along the main part of the ventricular myocardium (the walls of the right and left ventricles, apex of the heart).

The wave S is the period of the conduction of excitation in the ventricular bases and the external surface of the ventricles.

Then the total excitation of the ventricles comes, when their entire surface becomes electronegative, and the potential difference between the separate portions of the heart disappears. After the QRS complex **the segment ST** is registered.

The wave T represents myocardial repolarization. It is the most changeable since the repolarization process does not occur simultaneously in various areas of the myocardium.

The segment T-P is a quiescent period, general pause, and diastole. The interval QRST is called "electrical systole" of the heart, its duration is 0.36 sec.

There is a certain scheme of the ECG examination for its interpretation.

I. The analysis of the heart rhythm and conductivity:

1) assessment of the regularity of cardiac contractions;
2) measurement of the heart rate;
3) determination of the focus of excitation;
4) evaluation of the conduction function.

II. Evaluation of the electrical axis of the heart.

III. The analysis of the wave P.

IV. The analysis of the QRST complex:

1) analysis of the QRS complex;

2) analysis of the RS—T segment;

3) analysis of the wave T;

4) analysis of the Q—T interval.

V. ECG conclusion.

The ECG reveals the following manifestations of cardiac activity:

1. Heart rate — normally the heart at rest makes 60–80 contractions per minute. Low heart rate — 40–50 contractions per minute is called *bradycardia*. It is observed during the stimulation of the vagus nerve, injection of acetylcholine, in sportsmen at rest.

A rate of 90–100 and more contractions per minute at rest (*tachycardia*) is observed during excitation of the sympathetic nerve, in individuals in hot weather, after an adrenalin injection, under the effect of emotions, after coffee intake.

2. The source of the rhythm in the atria, A-V node, ventricles.

3. Rhythm disorder. Fluctuations of the tone of the nucleus of the vagus nerve during respiration causes respiratory arrhythmia. The intervals between the waves R-R change. At the end of expiration, the heart rate slows down, during inspiration it rises. As a norm arrhythmia can be observed in children.

4. Disorders of excitation conduction are reflected on the ECG. For example, an increase of the duration of the wave P reflects a decrease of the conduction rate in the atria, an increase of the PQ interval — a decrease of the conduction rate through the A-V-node.

5. Myocardial infarction in complete disturbance of the blood supply of the heart, etc.

However, the ECG analysis is not adequate for a final conclusion about heart diseases.

Review questions

1. What is the role of the cardiovascular system in an organism? List the circuits of blood circulation, give their characteristics.

2. What are the features of the myocardial structure? List the properties of the myocardium, explain them. Explain the mechanism of the action potential of the pacemaker cells.

3. What are the main structures of the conduction system of the heart? How does excitation propagate through the structures of the conduction

system? Give the definition of the "pacemaker". What does the cardiac conduction system provide?

4. What are the relations between the excitability, excitation, and contractions of the myocardium? What determines the force of myocardial contractions? Give the definition of "extrasystole". What are the types of extrasystole?

5. Explain the method of electrocardiography. What are the types of the standard leads? How are the ECG components formed? What manifestations of cardiac activity does the ECG reveal? What is its diagnostic value?

1.1.2. Cardiac function. Regulation of cardiac activity

1.1.2.1. Pumping function of the heart

The atria carry out the role of a reservoir. During ventricular systole they collect the blood from veins. Then it flows into the ventricles during their diastole. The ventricles carry out the role of a pump bringing the blood under pressure into the arterial system. According to the standard, the blood flow in the heart chambers is one-sidedly directed: from the atria into the ventricles and from the ventricles into the blood vessels. First, the atria contract and at the beginning of their contraction, the ostia of the veins are narrowed so the blood cannot come back to the veins. The ventricles at this time are relaxed, the pressure in them is lower than in the atria and the blood comes into them. The movement of the blood from the ventricles into the arteria is caused by the presence of the atrioventricular and the semilunar valves in the heart. The atrioventricular valves are located between the atria and ventricles:

— the tricuspid-valve in the right half of the heart;

— the bicuspid-valve, or mitral, in the left.

They prevent the return of the blood from the contracted ventricles into the atria. Tendinous chords do not allow the valves to be turned outside towards the atria.

The semilunar valves are located at the connections between the pulmonary artery and the right ventricle, and the aorta and the left ventricle. The aortic valve is located in the left ventricle, the pulmonary valve — in the right one.

During ventricular systole the blood pressure in the ventricles increases, the semilunar valves open, and the blood comes into arteries. When the ventricles are relaxed, the pressure in them becomes lower than in the blood vessels and, directing back into the ventricles, and the blood closes the semilunar valves.

70 % of ventricular filling with blood occurs during diastole. During atrial systole 30 % is added. The atria have a poor pumping function and are easily extended.

1.1.2.2. Sequence of the periods and phases of the cardiac cycle

The cardiac cycle starts with atrial systole, which lasts 0.1 sec. Upon its termination, ventricular systole begins, which lasts 0.33 sec. The atria at this time are in diastole, which lasts 0.7 sec. Ventricular systole is followed by its diastole, lasting for 0.47 sec. At its end 0.1 sec before the termination, the next atrial systole begins (Figure 1.12).

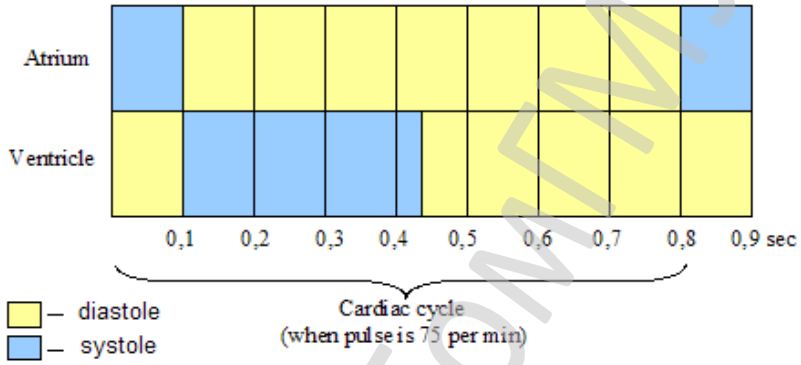


Figure 1.12 — Duration of systole and diastole of the atria and ventricles (during one cardiac cycle) (by Korobkov A. V., Chesnokova S. A., 1986)

After atrial systole there comes ventricular systole. It is divided into some periods and phases (Table 1.2).

Table 1.2 — Periods and phases of the cardiac cycle

Systole of the ventricles — 0.33 sec	Period of ***contraction*** — 0.08 sec	Phase of *asynchronous* contraction — 0.05 sec
		Phase of *isovolumetric* contraction — 0.03 sec
	Period of ***ejection***— 0.25 sec	Phase of r*apid ventricular ejection*— 0.12 sec
		Phase of *reduced* (slow) *ventricular ejection*— 0.13 sec
Diastole of the ventricles — 0.47 sec	***Protodiastolic*** period — 0.04 sec	
	Period of ***isovolumetric relaxation*** —0.08 sec	
	Period of ***filling*** of the ventricles with blood — 0.25 sec	Phase of *rapid blood filling* — 0.08 sec
		Phase of *reduced blood filling* — 0.17 sec
	Presystolic period — 0.1 sec	

The period of ***contraction*** includes the phases:

1. The phase of *asynchronous* contraction (0.05 sec). Excitation and contraction are distributed along the myocardium of the ventricles non-simultaneously, yet not all muscle fibers are covered with excitation. The pressure in the ventricles is close to 0. By the end of the phase, during the contraction of the whole myocardium, the fiber pressure increases rapidly.

2. The phase of *isometric* (isovolumetric) contraction. Under the pressure of the blood, the atrioventricular valves close, and the 1st heart sound arises —

systolic. During this phase, the pressure in the ventricles rises up to 70–80 mm Hg in the left ventricle, up to 15–20 mm Hg in the right one. The atrioventricular and semilunar valves are closed. Only the strain of the fibers (not the length) is increased. The blood volume does not change, it is constant. The pressure in the ventricles continues to increase, the left ventricle becomes spherical, and it strikes the internal surface of the thorax. It is accompanied by the apical thrust in the 5th intercostal space on the left from the medium clavicle lines (in men). By the end of the period, the pressure in the ventricles becomes higher than in the aorta and pulmonary artery. The cusps of the semilunar valves open and the blood comes into the vessels.

Next, the ***ejection*** period comes:

1. The phase of *rapid ventricular ejection*.
2. The phase of *reduced ventricular ejection*.

The pressure in the ventricles rises up to 120–130 mm Hg in the left and up to 25 mm Hg in the right ventricle.

At the end of the phase of reduced ventricular ejection, there comes relaxation of the ventricles. At the beginning of diastole, the pressure in the ventricles goes down. The blood goes back into the ventricles and closes the semilunar valves, there is the 2nd heart sound — ***diastolic***.

Ventricular diastole (0.47 sec) is divided into the following periods and phases.

The ***protodiastolic*** period (0.04 sec). This is the time from the beginning of the relaxation of the ventricles until the closure of the semilunar valves.

The period of ***isometric (isovolumic) relaxation*** (0.08 sec). The pressure in the ventricles is reduced to 0. The atrioventricular valves are still closed, the volume of the residual blood and the length of the myocardial fibers do not change. The pressure in the ventricles by the end of the period becomes lower than in the atria, the atrioventricular valves open, and the blood comes to the ventricles. There comes the next period.

The period of ***filling*** the ventricles with blood (0.25 sec). It includes:

1. The phase of *rapid* blood filling (0.08 sec).
2. The phase of *reduced* blood filling (0.17 sec), thus the 3rd heart sound appears.

Then there comes the ***presystolic*** period (0.1 sec), the atria contract and pump an additional portion of blood into the ventricles; the 4rd heart sound is formed.

1.1.2.3. Mechanical and sound manifestations of cardiac activity. Heart sounds

The apex during systole rises and puts pressure on the internal surface of the thorax. In the 5th intercostal space, the ***apical thrust*** can be palpated. The

work of the heart is also accompanied by sound phenomena. When the valves close, the vanes of the valves and the surrounding fluid vibrate under the influence of the pressure changes, and the heart sounds can be heard.

Heart sounds

During auscultation of the heart, two heart sounds can be detected: the first — systolic and the second — diastolic (Figure 1.13).

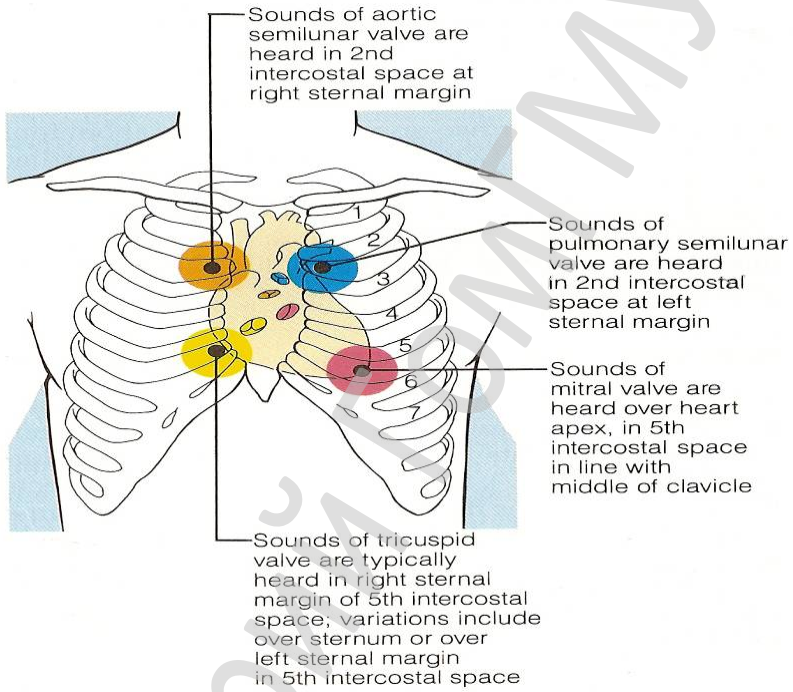


Figure 1.13 — Areas of the thoracic surface where the heart sounds can be best detected (by Elaine N. Marieb, 1989)

The ***systolic*** heart sound is low, prolonged (0.12 sec). It is caused by the closure of the A-V valves.

The characteristics of the 1st heart sound are determined by the vibrations of the atrioventricular valves, tendinous fibers, papillary muscles, walls of the ventricles.

The 1st heart sound is well heard in the 5th left intercostal space.

The 2nd heart sound is ***diastolic*** (high, short — 0.08 sec). It arises during the closure of the semilunar valves. The higher the pressure in the aorta and pulmonary artery is, the higher the heart sound is. It is well heard in the 2nd intercostal space on the right and on the left sternum.

The 3rd heart sound is formed by the oscillation of the walls of the ventricles during their rapid blood filling, the 4rd heart sound is formed during additional filling of the ventricles during atrial systole.

The heart sounds are auscultated with the help of a stethoscope or by placing an ear onto the thorax.

During incomplete closure of the valves or due to the turbulent blood flow, cardiac murmurs occur. Their detection has an important diagnostic value.

The heart sounds can be also recorded by ***phonocardiography*** — a diagnostic technique that creates a graphic record or phonocardiogram of the sounds produced by the heart (Figure 1.14). The 3rd and 4th heart sounds are usually not heard during auscultation with the stethoscope and are revealed on the phonocardiogram.

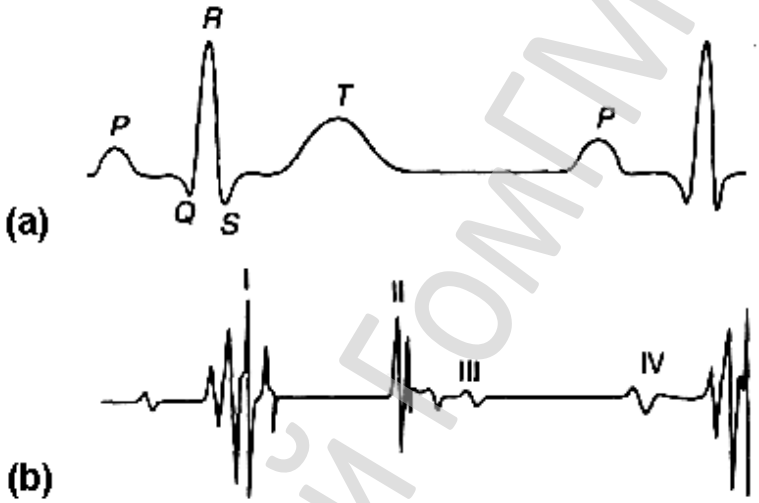


Figure 1.14— Simultaneous registration of ECG (a) and phonocardiography (b)

Notes: I, II, III, IV — heart sounds.

1.1.2.4. Stroke volume and cardiac output. Methods for the evaluation of cardiac activity

The amount of the blood ejected by the ventricle into an artery per minute is an important parameter of the functional state of the cardiovascular system (CVS) and is called the ***cardiac output***. It is identical for both the ventricles and at rest is 4.5–5.0 L.

During diastole the amount of blood in each ventricle is about 110 to 120 milliliters. This volume is called ***the end-diastolic volume***. Then, as the ventricles are emptied during systole, the volume decreases to nearly 70 milliliters, which is called ***the stroke volume*** **(SV)** *or* ***systolic volume***. The stroke volume in a healthy adult is equal to 65–70 mL at rest, and during physical work it increases up to 125 mL, and in sportsmen — up to 200 mL.

The remaining volume in each ventricle, about 40 to 50 milliliters, is called the ***end-systolic volume***. The fraction of the end-diastolic volume which is ejected is called ***the ejection fraction (EF).*** The normal EF is 50 to 75 per cent.

The *cardiac output* divided by the body surface area (S) in m^2 is defined as the ***cardiac index*** (CI, L/min·m^2), which reflects the pumping function of the heart.

$$CI = \frac{cardiacoutput}{S}, \text{ (L/min } m^2\text{);}$$

Normally, the CI is 3–4 L/min·m^2.

The whole complex of cardiac activity is registered by means of various physiological techniques, which are divided into:

— non-invasive methods — ECG, daily monitoring of the ECG and arterial pressure, transthoracic ultrasound cardiography (echocardiography), load tests (veloergometry), magnetic-resonance tomography, radionuclide methods. To determine cardiac output, the Fick`s formula is used. The Fick principle states that the cardiac output of the left and right ventricles is equal. The principle states that, in the steady state, the rate of oxygen consumption in the body must equal the amount of oxygen leaving the lungs via pulmonary vein minus the amount of oxygen returned to the lungs via the pulmonary artery, multiplied by the cardiac output. Since pulmonary blood flow of the right heart is equal to the cardiac output of the left heart, these measurements can be used to calculate cardiac output.

— invasive methods — electrophysiological examination of the heart, trans esophageal echocardiography, intravascular ultrasound examination, coronary angioraphy, etc.

1.1.2.5. Regulation of cardiac activity (intracardiac, extracardiac, humoral)

When the body is at rest, the human heart pumps about 10 tons of blood into the arterial system per day, 4,000 tons per year, and about 300,000 tons during the whole life. At the same time, a healthy heart always responds to the changing needs of an organism precisely and supplies organs and tissues with the necessary amount of blood.

The adjustment of cardiac activity to the changing human body needs occurs by means of the following basic regulatory mechanisms:

1. Intracardiac regulatory mechanisms (myogenic regulation and intracardiac peripheral reflexes).

2. Extracardiac regulatory mechanisms: nervous and humoral.

Intracardiac regulation. Myogenic autoregulation. The mechanisms of myogenic autoregulation are determined by the properties of muscle fibers. There are endocellular and intercellular mechanisms of regulation.

The endocellular mechanisms of regulation lie in the fact that in every cardiomyocyte there are mechanisms regulating protein synthesis. Thus,

increased load on the heart (for example, during regular muscle work) leads to increased synthesis of the contractive proteins of the myocardium (working hypertrophy of the myocardium, e.g., in sportsmen).

The intercellular mechanisms of regulation are connected with the presence of nexuses, which provide the conduction of excitation from cell to cell, transport of substances, interaction of myofibrils. Inhibition of intercellular interactions leads to asynchronous excitation of myocardial cells and occurrence of arrhythmia.

Some autoregulation mechanisms are connected with reactions which occur if the initial length of myocardial fibers changes — ***heterometric regulation.*** The reactions which are not connected with the change of the initial length of myocardial fibers are called ***homeometric regulation***.

The concept of heterometric regulation was formulated by Frank and Starling. This mechanism is called the **Frank — Starling's law**: the force of cardiac contractions depends on the initial length of muscle tissue. Therefore, the stronger the stretching of the myocardium during diastole (corresponding to the increased blood flow) is, the stronger the cardiac contraction will be during the next systole. Such a correlation is revealed when the fibers are stretched not more than 45 % from their initial length.

The mechanisms (***homeometric regulation***) of autoregulation also include the effects connected with the changes of the pressure in the aorta (the effect of Anrep) and changes of the rhythm of cardiac contractions (the effect or stairs of Bowditch).

The effect of Anrep is an autoregulation method in which myocardial contractility increases proportionally with the increased resistance in the aorta, which occurs in increased arterial pleasure. The heart, pumping out the same volume of blood associated with the increased resistance in the aorta, performs more work. In these conditions the working and energy requirements of the ventricles rise sharply.

The effect of Bowditch lies in the fact that a high heart rate increases the force of myocardial contractions. This effect is also called "the phenomenon of stairs", or the law of homometric regulation. It was revealed on the isolated heart of a frog. If to expose the isolated, stopped heart of a frog to rhythmic stimulation with a constantly increasing frequency, the amplitude of contractions increases gradually with every next stimulus. The mechanism of this phenomenon consists in the fact that during frequent stimulation calcium ions are not completely removed from the sarcoplasm, which creates conditions for more intensive interactions between myosin and actin fibers.

The intracardiac peripheral reflexes provide self-control of the work of the heart due to reflexes whose arch is located in the heart, i. e. the bodies of

the neurons which form the reflex arch and are situated in the intracardiac ganglia (i. e., during stimulation of the stretching receptors of the right atrium the contraction of the left ventricle becomes stronger).

The extracardiac mechanisms of regulation are subdivided into nervous and humoral. They are the highest level of the regulation of cardiac activity and are carried out due to structures situated outside the heart (the CNS, extracardial vegetative ganglia, endocrine glands).

Nervous regulation is carried out through the sympathetic and vagus nerves.

The influence of the vagus nerve. From the nucleus of the vagus nerve, located in the medulla oblongata, come axons, which form synapses on the motor neurons of the intramural ganglia (Figure 1.15). In the terminals of the vagus nerve ***acetylcholine*** is formed. Acetylcholine interacts with muscarinic cholinoreceptors (M- cholinoreceptors).

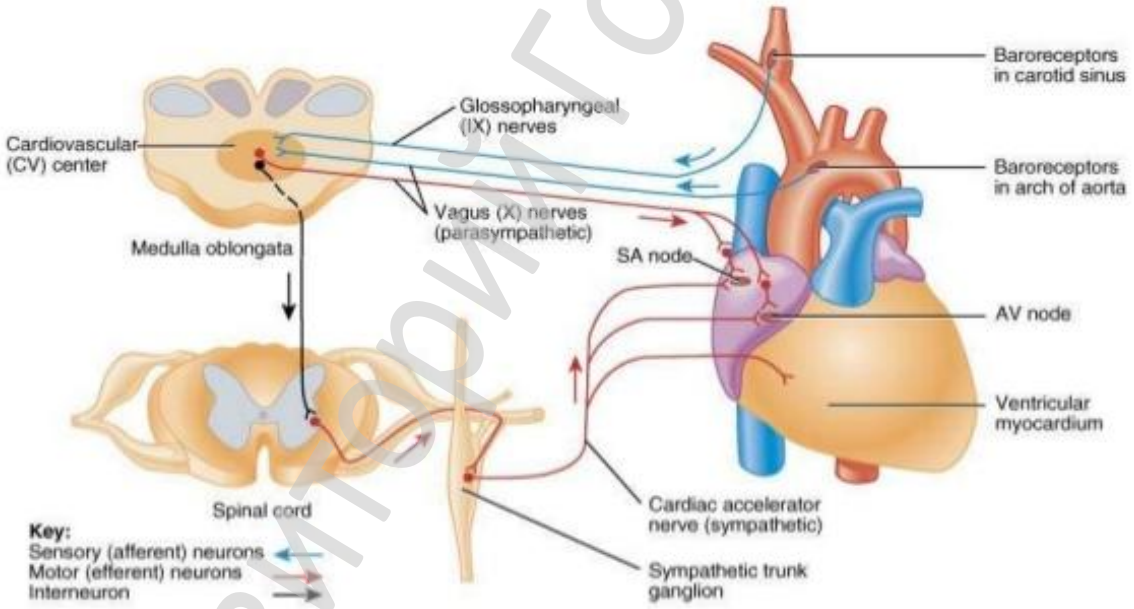


Figure 1.15 — Sympathetic and parasympathetic innervation of the heart (from biology.reachingfordreams.com)

The research of the Weber brothers (1845) detected an inhibiting influence of these nerves on cardiac activity.

During the stimulation of the peripheral end of the cut vagus nerve, the following changes can be revealed:

1. Negative chronotropic effect — a decrease of the contraction rhythm.
2. Negative inotropic effect — a decrease of the contraction amplitude (force).
3. Negative bathmotropic effect — a decrease of the excitability of the myocardium.

4. Negative dromotropic effect — a decrease of the excitation conduction rate in cardiomyocytes.

5. Negative tonotropic effect — a decrease of heart muscle tone.

The stimulation of the vagus nerve can cause a complete stop of cardiac activity. However, as the stimulation continues, the heart restores its contractions again, and the ***"escape of the heart from the vagus influence"*** is observed. This occurs because there is a high concentration of acetylcholinesterase in the region of the pacemaker, and the mediator is quickly destructed.

The influence of the sympathetic nerve. The neurons of the sympathetic nerves are located in the lateral horns of the 3 superior segments of the thoracic part of the spinal cord (Figure 1.15). The preganglionic fibers of these neurons go to the cervical sympathetic ganglia and form synapses on the ganglionic neurons. Signals in these synapses propagate with the help of acetylcholine. The postganglionic fibers go to all the parts of the heart, and the effects of the sympathetic system are provided by the release of ***noradrenaline*** and β-adrenergetic stimulation.

The first scientists who investigated the above influence on the heart were I. F. Tsion, (1867), I. P. Pavlov, U. Gaskell. They discovered the opposite influence of the sympathetic nerves on heart activity:

1. Positive chronotropic effect — acceleration of heart contractions.

2. Positive inotropic effect — an increase of the contraction amplitude (force).

3. Positive bathmotropic effect — an increase of the excitability of the myocardium.

4. Positive dromotropic effect — an increase of the excitation conduction rate.

5. Positive tonotropic effect — an increase of heart muscle tone.

During simultaneous stimulation of the sympathetic and vagus nerves, the effect of the vagus nerve prevails. Despite the opposite effects of the sympathetic and vagus nerves, they are functional synergists.

Acetylcholine, released from the vagus nerve endings, increases the permeability of the conductive fiber membranes to potassium ions greatly, which allows rapid leakage of potassium out of the fibers and causes hyperpolarization. In the sinus node, the state of hyperpolarization decreases the resting membrane potential to a level considerably more negative than usual. Therefore, it takes the initial rise of the sinus nodal membrane potential, caused by the sodium and calcium leakage, much longer to reach the threshold potential for excitation. This slows the rhythmicity rate of these nodal fibers. If the vagal stimulation is strong enough, it is possible to stop the rhythmical self-excitation of this node completely. In the A-V node, the state of hyperpolarization caused by the vagal stimulation delays the conduction of the impulse.

The stimulation of the *sympathetic nerves* releases noradrenalin on the sympathetic nerve endings. Noradrenalin stimulates the beta-1 adrenergic receptors, which causes a rise in the permeability of the fiber membrane to sodium and calcium ions. In the sinus node, an increase of the sodium-calcium permeability causes a more positive resting potential and also an increased rate of the upward drift of the diastolic membrane potential toward the threshold level for self-excitation, thus accelerating self-excitation and, therefore, increasing the heart rate.

In the A-V node the increased sodium-calcium permeability makes it easier for the action potential to excite each succeeding portion of the conductive fiber bundles, thereby decreasing the time of the conduction from the atria to the ventricles.

The increase in the permeability to calcium ions is partially responsible for the increase in the contractile force of cardiac muscle under the influence of the sympathetic stimulation, because calcium ions play a leading role in the excitement of the contractile process of the myofibrils.

The nervous centers of the medulla oblongata, from which the vagus nerves extend to the heart, are in the state of constant tone. Constant inhibiting influences come from them to the heart. The transection of both the vagus nerves leads to acceleration of heart contractions. Breathing bears influence on the tone of the nuclei of the vagus nerve: during inspiration the tone of the nucleus of vagus nerve decreases, during expiration the tone rises, and the activity of the heart slows down (respiratory arrhythmia).

The regulation of cardiac activity is carried out by the hypothalamus, limbic system, cortex of the cerebrum.

An important role in the regulation of the heart is played by the receptors of the vascular system, forming the vascular reflexogenic zones.

The most significant ***reflexogenic zones*** are: aortal zone, sinocarotid zone, zone of the pulmonary artery, the heart itself. Mechano- and chemoreceptors, which are a part of these zones, participate in the stimulation or inhibition of cardiac activity, which results in high or low blood pressure.

The excitation from the receptors of the foramen of the venae cavae leads to an accelerated force of heart contractions, which is connected with the decreased tone of the vagus nerve and the increased tone of the sympathetic nerve – the *reflex of Beinbridge*. The r*eflex of Golts* is also one of the classical vagus reflexes: due to mechanical pressure on the stomach or intestines of a frog, a cardiac arrest (the influence of the vagus nerve) is observed. It can also be found on the anterior abdominal wall in a person during a stroke.

Danini-Achner's ocular-cardiac reflex. During the pressing on the eyeballs the heart rate decreases by 10–20 per minute (the influence of the vagus nerve).

Higher force of heart contractions is observed under the effects of pain, emotions and during muscle work.

The participation of the cortex of the cerebrum in the regulation of the heart is proved by the method of conditioned reflexes. If to combine a conditioned stimulus (sound) with the pressure on the eyeballs repeatedly, the heart rate slows down, after some time only the conditioned stimulus will produce the same reaction. This phenomenon is called the Danini-Achner's conditional ocular-cardiac reflex.

The rhythm of heart contractions can change under the influence of excitation from thermoreceptors. A high body or environmental temperature leads to the acceleration of heart contractions. Cooling of a body after immersion into cold water leads to a lower heart rate.

Humoral regulation is carried out by the hormones and ions of the intercellular fluid. Catecholamines (adrenaline and noradrenaline) increase the force and rhythm of contractions.

Adrenaline cooperates with beta-receptors, adenylatecyclase is activated, cyclic adenosine monophosphate is formed, inactive phosphorylase turns into active, glycogen is split, glucose is formed, and as a result of these processes energy is released. Adrenaline raises the permeability of the membranes to Ca^{2+}, which participates in the processes of cardiomyocyte contractions. The force of the contractions is in the same way influenced by *glucagon, corticosteroids (aldosterone), angiotensin, serotonin, thyroxine.* Ca^{2+} raises the excitability and conduction of excitation in the myocardium.

Acetylcholine, hypoxemia, hypercapnia, acidosis, K^+, HCO_3^-, H^+ suppress cardiac activity.

Electrolytes are of great importance for normal cardiac activity. The concentrations of K^+ and Ca^{2+} ions influence the automaticity and contractile properties of the heart. The excess of K^+ causes a slow heart rate, low force of contractions, poor excitability, and conductivity. Washing of the isolated heart of animals with the concentrated solution of K^+ leads to myocardial relaxation and cardiac arrest in diastole.

Ca^{2+} ions increase the heart rate, force of cardiac contractions, excitability, and conductivity. The excess of Ca^{2+} leads to the cardiac arrest in systole. The lack of Ca^{2+} weakens cardiac contractions.

1.1.2.6. Endocrine function of the heart

Atrial natriuretic peptide or atrial natriuretic factor is a hormone that is produced primarily by the myocytes of the heart atria. It increases the excretion of Na^+ and Cl^- by the kidneys, glomerular filtration, lowers the secretion of renin, effect of angiotensin II, aldosterone, relaxes smooth myocytes of small vessels, which leads to low blood pressure.

Review questions

1. Give the comparative description of the pumping function of the right and left ventricles. What is the role of the heart valves?

2. What are the periods and phases of the cardiac cycle? Give their description.

3. What are the mechanical and sound manifestations of cardiac activity? List the heart sounds. When do they arise? Give their description.

4. Give the definition of the "stoke volume", "cardiac output". What are the methods for the diagnosis of cardiac activity?

5. List the mechanisms of the regulation of the activity of the heart. What regulation mechanisms are related to the intracardiac regulation? Give their description.

6. How does the sympathetic and parasympathetic nervous system influence the heart? What are the reflexogenic zones? What reflexes are associated with them? Name the hormones that activate and reduce cardiac activity. What is the endocrine function of the heart?

1.2. Physiology of the vascular system

1.2.1. Fundamentals of hemodynamics. Blood pressure. Arterial pulse

1.2.1.1. Fundamentals of hemodynamics

The science studying the blood circulation in the blood vessels is known as hemodynamics. Its laws are similar to those of hydrodynamics (the doctrine of the flow of fluids). According to the law of hydrodynamics, the fluid flow in the vessels is determined by two forces:

1. The pressure (P) under which a fluid flows, i. e. the difference of the pressure at the beginning and the end of a pipe. This force promotes the circulation.

2. The resistance (R) which a fluid has due to viscosity, friction against the vascular walls and vortex motion. The resistance interferes the circulation.

The relation of the difference of the pressure to the resistance determines the volume velocity of the fluid flow.

The volume velocity rate of the fluid flow is expressed by the equation:

$$Q = \frac{P_1 - P_2}{R},$$

where Q — volume velocity, L/min; P_1–P_2 — the difference of the pressure at the beginning and the end of a pipe, mm Hg; R — resistance to the flow, Pa s/cm^3.

If to apply it to the vascular system, then, taking into account, that at its end (venae cavae) the pressure is close or equal to zero, it is possible to write down the equation in such a way:

$$Q = \frac{P}{R},$$

where Q — cardiac output L/min; P — average pressure in the aorta mm Hg; R — vascular resistance Pa s/cm^3.

From this it follows that the pressure in the aorta is in a direct proportional relation to the cardiac output pumped out by the heart and the peripheral resistance (R):

$$P = Q \times R$$

It is possible to measure the pressure in aortic cardiac output. Knowing these values, it is possible to calculate the peripheral resistance (R):

$$R = \frac{8 \times L \times \eta}{\pi \times r^4},$$

where R — peripheral resistance defined by the formula of Poiseuille, Pa s/cm^3; L — length of a pipe (vessel), m; η — viscosity of a flowing fluid, cP; π — relation of the circumference to the diameter (3,14); r — radius of a pipe, m.

The peripheral resistance is the major parameter of the state of the vascular system.

For a separate part of a vessel it can be defined by the formula:

$$R = \frac{P_1 - P_2}{Q},$$

where R — peripheral resistance, Pa s/cm^3.; P1, P2 — pressure at the beginning and at the end of a vessel, mm Hg; Q — amount of the blood flowing through the vessels per second, L/min.

To calculate the volume velocity of blood flow, the Hagen–Poiseuille law is used:

$$Q = \frac{\pi \times r^4 \times (P_1 - P_2)}{8L\eta},$$

where P_1-P_2 — the pressure difference, mm Hg; r — the radius of the vessel, cm; L — the length of the vessel, cm; η — blood viscosity, cP; π — relation of the circumference to the diameter (3.14).

Peripheral resistance is formed by the resistance of each vessel. At rest only a small number of capillaries are open. A great number of them are included into the bloodstream in parallel. Therefore, their traction resistance will be much less than in arteries. Blood viscosity determines resistance but it is changeable in different areas of vascular channels. The lesser the diameter of a vessel is, the lesser its viscosity is. The basic vessels of resistance, or resistive vessels, are arteries and arterioles. They have a small diameter (15–70 microns), a thick layer of ring smooth muscles, which during contractions, can considerably decrease the diameter and raise the resistance of the blood flow. Thus, the arterial pressure in them rises. A decreased tone of arterioles promotes the blood outflow from arteries and decreases their arterial pressure. Hence, a change of the diameter of arterioles is the main regulator of the general arterial pressure level. In working organs, the tone of the arteriolar walls goes down, the blood supply is improved. In non-working organs it does not occur. It supports the necessary level of arterial pressure.

The heart, pumping blood into the vessels, forms the pressure necessary for the blood flow. The pressure determines the blood flow rate and promotes the overcoming of the resistance. The higher the resistance is, the more force is necessary to ensure the blood flow. In large and average arteries the pressure is reduced only by 10 %, in arterioles and capillaries — by 85 %.

The important condition for normal blood circulation is its interrelation in arteries and veins (Figure 1.16):

— arteries contain 17 % of blood;

— veins — 67 %.

The basic parameters of hemodynamics are:

1. Volume velocity of the blood flow.
2. Linear velocity of the blood flow (velocity of blood circulation).
3. Pressure in different parts of vascular channels.

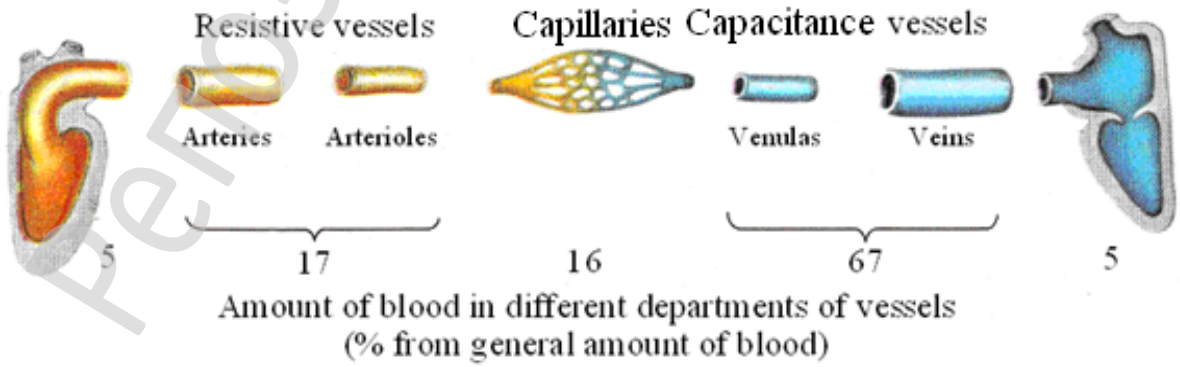


Figure 1.16 — Distribution of blood in different departments of the vascular system (by A. V. Korobkov, S. A. Chesnokova, 1986)

1.2.1.2. Volume and linear types of the blood flow velocity in various areas of the blood vessels

Volume velocity is the amount of blood passing through cross-section of a vessel per unit of time (1 min). Normally, the blood outflow from the heart is equal to its inflow to the heart. It means that the volumetric rate is constant.

Linear velocity is the blood flow rate along the vessel. It varies in different areas of vascular channels and depends on the total amount of the cross-section area of a certain part of vascular channels.

In the aorta, the cross-section is 8 cm^2, the rate of blood flow is 50–70 cm/sec. In capillaries the total section of all the vessels is 8,000 cm^2, the rate of blood flow is 0.05 cm /sec (Figure 1.17).

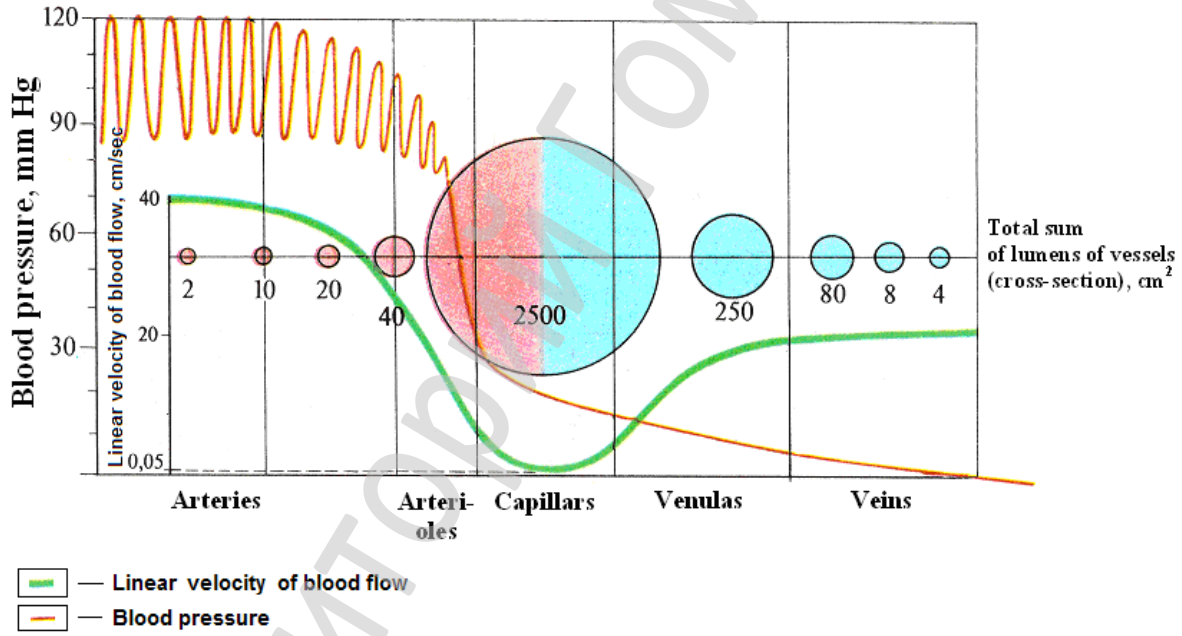


Figure 1.17 — Blood pressure level, total number of the vessel lumens, and linear velocity in different departments of the vascular system (by Korobkov A. V., Chesnokova S. A., 1986)

In arteries the blood flow rate is 20–40 cm/sec, in arterioles — 0.5–10 cm/sec, in the venae cavae — 20 cm/sec.

Due to the output of blood from the heart to the vessels by separate portions, the blood flow in arteries has a pulsating character.

The continuity of the flow in the whole system of the blood vessels is provided by the elastic properties of the aorta and arteries. During systole the heart produces basic kinetic energy necessary for the blood flow. One part of this energy is spent on pumping blood, the other turns into the potential energy of the wall distension of the aorta and arteries during systole. During diastole this energy turns into the kinetic energy of the blood flow.

1.2.1.3. Factors ensuring blood circulation in the high pressure blood vessels

All blood vessels inside are covered with epithelium forming a smooth surface (Figure 1.18). Normally, it prevents blood coagulation. Moreover, except capillaries, the blood vessels contain elastic collagen and smooth muscle fibers.

Elastic fibers are easily stretched and produce elastic force counteracting blood pressure.

Collagen fibers resist distention, form folds and counteract pressure when the blood vessels are greatly stretched.

Smooth muscle fibers create the tone of the vascular walls and change the lumens of the blood vessels if necessary. Some smooth muscular cells are able to contract spontaneously (regardless the nervous system), which sustains the constant tone of the vessel walls.

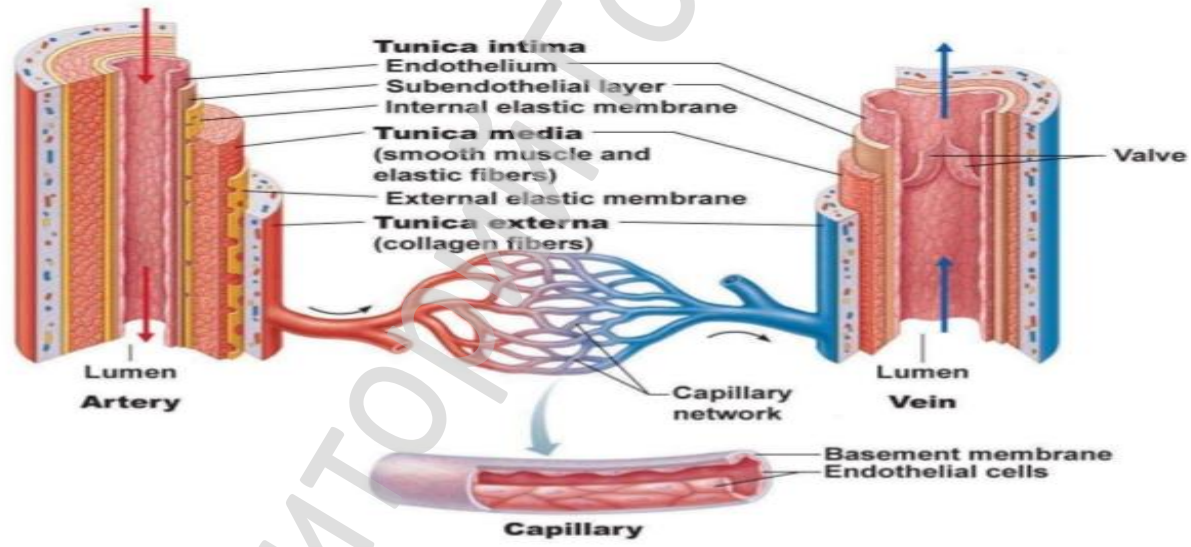


Figure 1.18 — Structure of the blood vessel (from slideplayer.com)

1.2.1.4. Blood pressure, its kinds and determining factors. Measurement methods

The blood pressure level is determined by a set of different factors:

1. Pumping force of the heart;

2. Peripheral resistance of the blood vessels;

3. Volume of circulating blood.

Blood pressure is measured in mm Hg.

The major factor of the maintenance of the level of arterial pressure is the work of the heart. The blood pressure in arteries constantly changes. Its rise during systole determines the ***maximal (systolic)*** pressure. In a middle-aged

person in the brachial artery (and in the aorta) it is 110–139 mm Hg. The pressure decrease during diastole corresponds to the ***minimal (diastolic)*** pressure, which is equal to 80 mm Hg on average (60-89 mm Hg). It depends on the peripheral resistance of the blood vessels and heart rate. The difference between systolic and diastolic pressure compounds ***pulse pressure*** (40–50 mm Hg). It is proportional to the systolic volume. These values are the main parameters of the functional state of the whole cardiovascular system.

If arterial pressure is higher than the normal value, it is referred to as *hypertension*, if it is lower, it is called *hypotension*. Under the influence of various factors arterial pressure can considerably vary. Thus, emotions lead to a dramatic rise of arterial pressure (during examinations, sport competitions). Daily fluctuations of arterial pressure can be observed: it is higher in the day-time, in quiet sleep it is a little lower (20 mm Hg). Pain is accompanied with a rise of arterial pressure, but due to the long influence of a pain stimulus arterial pressure may decrease.

Hypertension arises:

— in high cardiac output;

— in high peripheral resistance;

— when both the factors are combined.

The second factor determining the level of arterial pressure is the peripheral resistance caused by the state of the resistive vessels.

The third factor is the amount of circulating blood and its viscosity. During transfusion of a large amount of blood, arterial pressure rises, if there is some blood loss, it drops down. Arterial pressure depends on the venous return (e. g., during muscle work).

Methods for the measurement of blood pressure

Two types of methods of the measurement of arterial pressure are used.

Direct methods (invasive, or intravascular) are carried out by the introduction of a catheter into a blood vessel, the catheter is connected with a recorder.

Indirect methods.

Palpation method, offered by Riva-Rocci (1896). It is used in the clinic in humans. The main device for measuring blood pressure is a sphygmomanometer. A rubber inflatable cuff is placed on the arm above the elbow. When air is pumped into the cuff, it compresses the brachial artery, stopping blood flow in it. The pulse in the radial artery disappears. While releasing air from the cuff, the monitoring of the appearance of the pulse is performed. At moment when pulse appears, the pressure value is registered with the help of a manometer. This method (palpation method) allows to determine only the systolic pressure.

Auscultatory method. In 1905 I. S. Korotkov offered *the auscultatory method* to measure arterial pressure by means of auscultation of the sounds (Korotkov's tones) in the brachial artery below the cuff with the help of a stethoscope. When the valve opens, the blood pressure under the cuff goes down and when it becomes lower than systolic pressure, short, clear tones (systolic pressure) appear in the artery. Systolic pressure is marked on a manometer. Then the tones become louder and further fade, thus determining diastolic pressure (Figure 1.19).

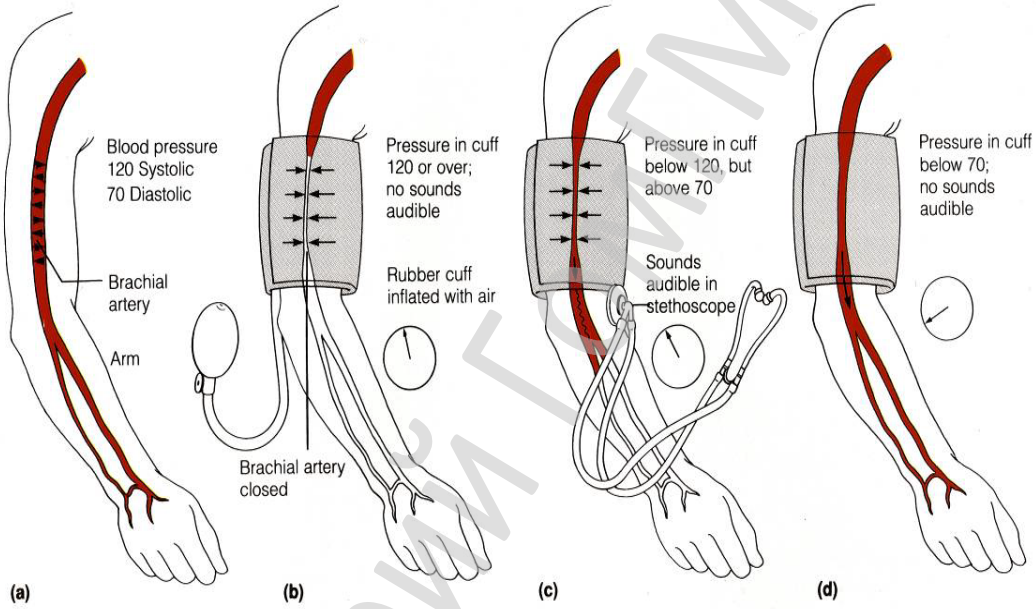


Figure 1.19 — Measurement of blood pressure (from studylib.net)

1.2.1.5. Functional classification of the blood vessels

Amortizing (elastic) vessels are the aorta, pulmonary artery, other large arteries. They contain elastic elements, reduce arterial pressure during systole and contribute to the blood flow during diastole.

Distribution vessels are medium and small arteries of the muscular type; their function is the distribution of blood flow to all the organs and tissues.

Resistant vessels are arteries and arterioles. The thick smooth muscular walls of these vessels are capable to variate the diameter of the vessels considerably, they regulate the blood supply to the organs.

The vessels ***sphincters*** are the last area of pre-capillary arterioles. By changing the diameter of arterioles, they determine the number of functioning capillaries.

Exchange vessels are capillaries. Their thin walls are characterized by permeability, they promote the exchange between blood and tissues.

Capacitance vessels are venulas, veins. Their walls are thinner than those of arteries, and they are easily stretched; large veins have valves. They contain a big volume of blood (especially the veins of the liver).

Shunt vessels (anastamoses) connect arteries with veins bypassing capillaries. They participate in the regulation of the flow of peripheral blood, the temperature of body parts. These are the vessels of ears, noses, feet, etc.

The vessels returning blood to the heart are represented by medium and large veins and venae cavae.

1.2.1.6. Arterial pulse, its nature and characteristics

The pulse is rhythmic oscillations of the walls of the vessels connected with the pumping of blood by the heart into the blood vessels and changing of their pressure during systole and diastole of the left ventricle. The amount of the blood pumped out into the aorta during systole produces an increase of the pressure and stretches its walls (Figure 1.20).

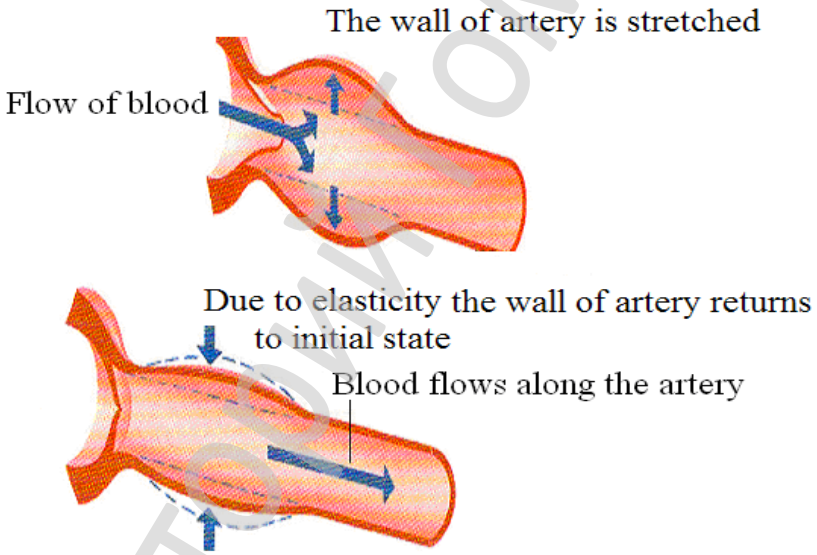


Figure 1.20 — Formation of a pulse wave (from picgalleria.com)

Due to their elasticity, the walls of the aorta tend to restore the initial state and push the blood forward where the walls are extended, a "compensatory chamber" appears. Such processes occur in the next areas of the blood vessels, gradually weaken and fade in arterioles and capillaries. Accordingly, the blood flow has a pulsating character. These pulse variations of the blood flow, blood pressure, and blood volume are distributed as the pulse wave at a certain rate. With years, the rate increases. When arterial pressure rises, the walls of the blood vessels are strained and their extensibility is reduced, the rate of the pulse wave distribution is increased. Hence, the wave distribution of the pulse rate reflects the elasticity of the vessel walls.

The arterial pulse can be palpated on the radial and temporal arteries, common carotid artery, etc. (Figure 1.21.).

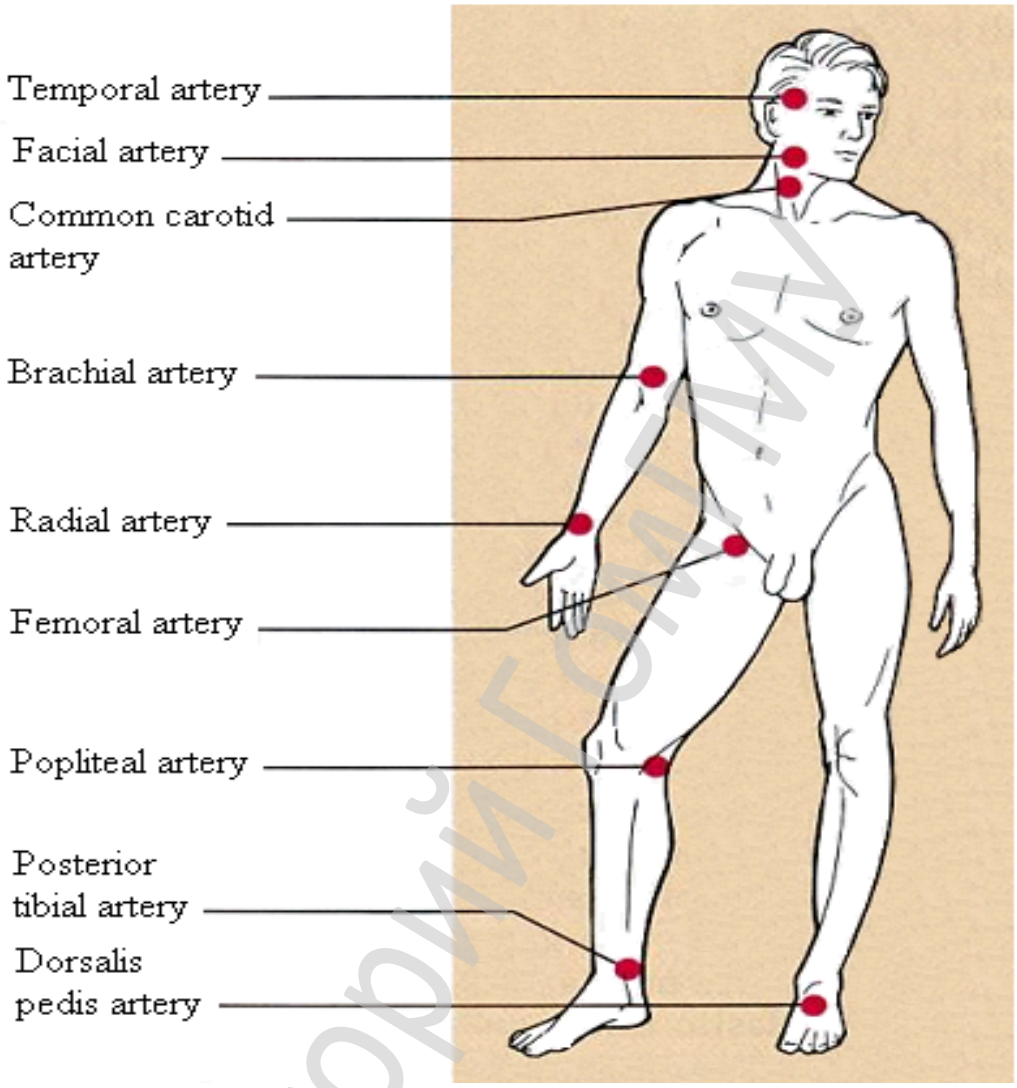


Figure 1.21 — Body sites where the pulse is most easily palpated (by Elaine N. Marieb, 1989)

Characteristics of the pulse

The pulse can be examined by means of simple palpation. They distinguish:

1. ***Heart rate***: *slow, high, normal*. In children at rest the pulse is more rapid. In newborns the average pulse is 140 beat per minute, influenced only by the sympathetic nerve. In sportsmen the pulse at rest is slower due to the predominant influence of the vagus nerve and the increased stroke blood volume.

2. ***Rhythm***: *rhythmic, arrhythmic*. Normally, pulsations follow at equal intervals of time (rhythmic pulse). Respiration (respiratory arrhythmia) influences the rhythm. During inspiration the pulse goes up, during expiration it slows down.3. ***Filling*** (height): *good, satisfactory, weak, thready pulse*. Filling depends on the systolic volume and volume velocity of the blood flow during diastole, on the elasticity of the vessel walls.

4. ***Pulse velocity***: normal, rapid, slow pulse. It is determined by the velocity of the ascending and descending of the arterial wall. Rapid pulse can reflect the insufficiency of the aortic valve. The increased amount of blood is pumped out, some part of the blood returns into the ventricle. Slow pulse can be observed in aortic stenosis when the blood comes slower to the aorta.

5. ***Pulse tension*** (strain): moderate, firm, mild pulse. It is determined by the pressing on an artery till the pulse disappears under the fingers located next to the pressed spot.

With the help of a sphygmograph it is possible to register the form of the pulse wave — ***sphygmogram*** (Figure 1.22). Its components are as follows:

• ***Anacrota***. This initial sharp rise of the curve is caused by the opening of the semilunar valve and the blood outflow into the aorta. The pressure rises, the walls of the aorta are stretched.

• ***Catacrota***. It is the recession of the curve. The ventricle is relaxed, the pressure in it becomes lower than in the aorta, the blood flow is directed to the ventricle, the pressure in the aorta is reduced, the walls of the aorta return into the initial state.

• ***Dicrotic wave (notch)***. The reverse blood flow to the ventricle closes the semilunar valve (on sphygmogram *incisure* is fixed), which creates a secondary wave of increased pressure stretching the aorta.

• ***Smoothed*** dicrota is indicative of the insufficiency of the aortal valve.

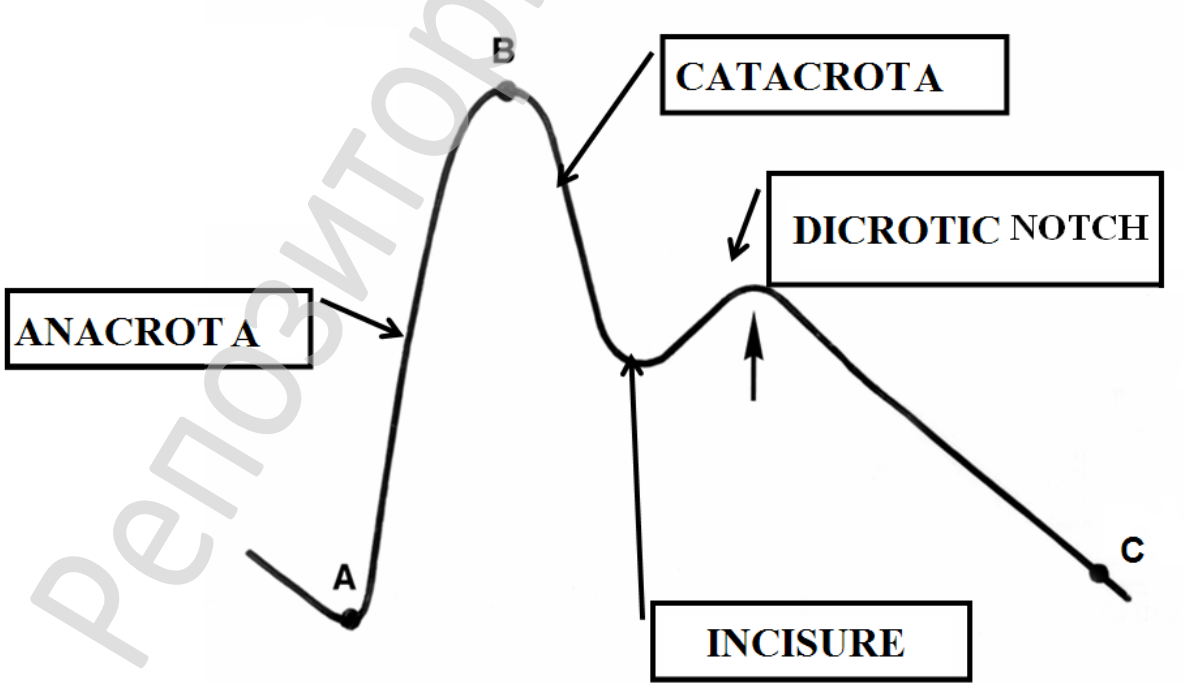


Figure 1.22 — Sphygmogram and its components

1.2.1.7. Blood flow in the low pressure blood vessels. Venous pulse

Veins are related to capacitance vessels. Their walls are more elastic, therefore they accumulate a big amount of blood (70–80 %).

Veins determine the amount of the blood which returns to the heart, systolic volume, cardiac output. In veins blood flows from the region of higher pressure to the region of lower pressure. The blood pressure in venules is 12–18 mm Hg. In the veins outside the thorax it is 5–9 mm Hg. When it flows into the right atrium, it is almost equal to atmospheric pressure and changes depending on the phases of respiration: during inspiration — below atmospheric and during expiration — 2–5 mm Hg higher. The damage of the veins located close to the thoracic cavity (for example, the jugular vein) is life-threatening. During inspiration, when the pressure in veins becomes negative, the atmospheric air penetrating into the vein cavity can cause air embolism. Air bubbles in the blood cause occlusion of the arterioles and capillaries and can result in death.

The pressure in the right atrium forms ***central venous pressure***. Generally, it varies synchronically with the respiratory and cardiac rhythms.

An increase of venous pressure up to 20–35 cm of the water column is a sign of a cardiovascular disorder. It is observed if the activity of the right ventricle is low, in disturbance of the tricuspid valve.

The blood flow in veins is ensured by the extra factors:

1. Suction action of the thorax. During inspiration the pressure in the thorax decreases, which promotes venous distention, thus inducing the effect of blood sucking from the adjacent vessels. The diaphragm, moving down, increases the intra-abdominal pressure, which promotes the venous inflow to the heart from the vessels of the abdominal cavity.

2. **"*Muscular pump*"** (Figure 1.23). During contractions the skeletal muscles compress the veins and thus push the blood to the heart. The presence of the valves on the internal surface of some veins prevents the backflow of blood. These mechanisms work in active movements.

3. Suction action of the heart. The atrioventricular septum during ventricular systole is shifted downwards and creates the suction effect of the blood to the heart from the veins.

4. Peristaltic contractions of the walls of some veins are 2–3 times per minute.

In small and medium veins, the pulse fluctuation of blood pressure is absent. The blood flow in large veins close to the heart has a pulsating character.

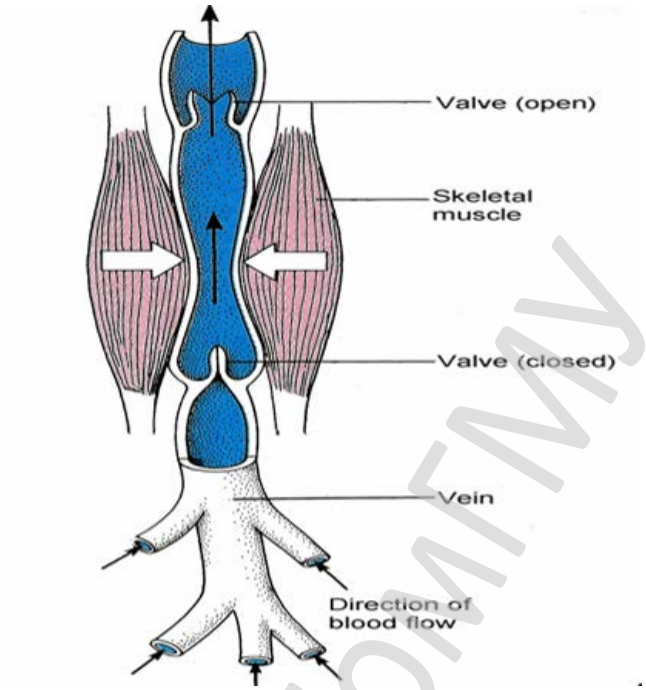


Figure 1.23 — Relations between the activity of skeletal muscle and function of the venous valve (by Elaine N. Marieb, 1989)

Venous pulse. The pulse wave in veins is of other origin than in arteries. It is formed when the pressure in veins stretching the vascular wall increases, the blood outflow from the veins during systole of the heart is terminated.

The curve of the venous pulse, the ***phlebogram*** (Figure 1.24), distinguishes 3 waves:

The a-wave reflects an increase of the pressure in the venae cavae during atrial systole when the blood outflow from the vein is terminated;

The c-wave is ensured by an increase of the pressure in the venae cavae during the contraction of the ventricle. The atrioventricular valve is stuck out into the right atrium increasing the pressure in it, which complicates the blood outflow from the veins. Then, during blood expulsion, the valve is displaced to the apex of the ventricles, a fast decrease of the venous pressure follows.

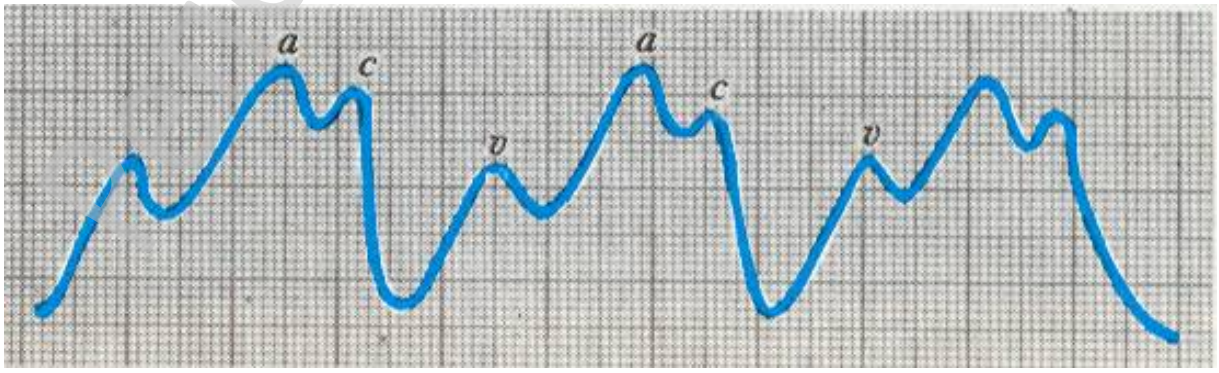


Figure 1.24 — Phlebogram and its components (a-wave, c-wave, v-wave)

The v-wave is ensured by an increase of the pressure in the vein due to the termination of the blood outflow from the vein at the end of atrial diastole, after the blood filling of the atria. The changes of the venous pulse curve are important parameters in diagnostics since they reflect the tricuspid valve insufficiency.

The total circulation time through systemic and pulmonary circulation in a human is about 20–25 sec at a heart rate of 70–80 bpm.

Review questions

1. What forces determine hemodynamics? How are they related? Write the appropriate formulas. What is the value of the peripheral resistance in the blood circulation?

2. Give the definitions of "linear velocity of the blood flow", "volume velocity of the blood flow". How does the linear velocity of the blood flow change from the aorta to the venae cavae?

3. What factors determine the blood circulation in high pressure blood vessels?

4. List the types of blood pressure. What are the normal values of blood pressure? What are the methods for the measurement of blood pressure? Describe them.

5. List the blood vessels according to their functional classification.

6. Give the definition of the "arterial pulse". How is it formed? What are the characteristics of the pulse? What is the sphygmogram? Give its analysis.

7. What factors determine the blood flow in low pressure vessels? What is central venous pressure?

8. Give the definition of the "venous pulse". How is it formed? What is the phlebogram? Give its analysis.

1.2.2. Microcirculation. Regulation of the blood flow in the blood vessels

1.2.2.1. Microcirculation. Capillary blood flow and its features. Factors influencing the processes of microcirculation

Capillaries are the most important, in the functional respect, regions of the vascular system. They are related to exchange vessels and participate in the supply of cells with nutrient, plastic substances and excretion of metabolic waste products. This process is also present in venules.

In a person at rest blood circulates only in 25–35 % of all capillaries. Arterioles, metarterioles, venules participate in the regulation of the capillary blood flow (Figure 1.25). A set of the blood vessels from arterioles to venules is called a microcirculation bed. They compose a general functional unit.

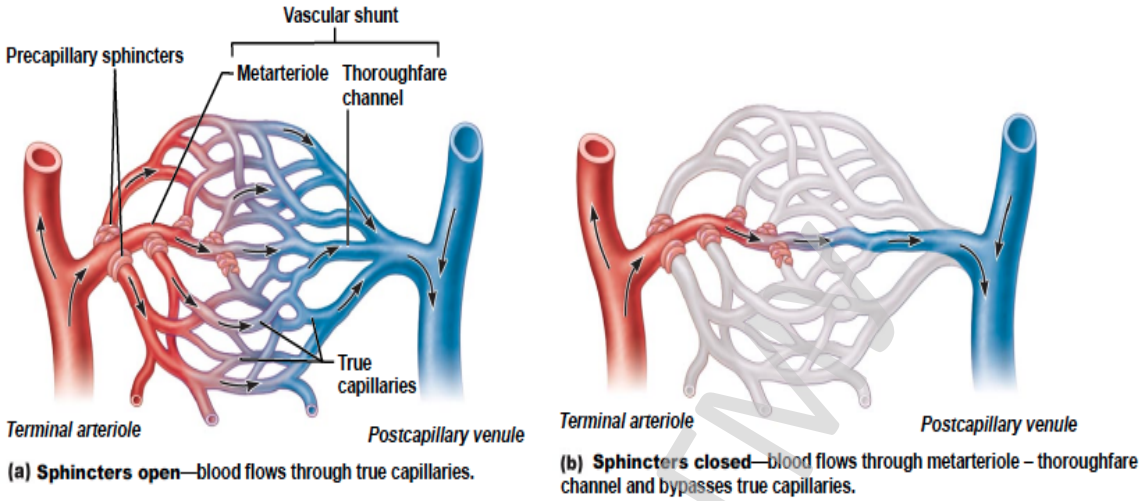


Figure 1.25 — Functioning of the capillary bed (from bianoti.com)

The density of capillaries in different organs considerably varies. A large number of them are contained in the myocardium, brain, liver, kidneys (up to 2,500–3,000 capillaries per 1 mm^2). This number is less in osteal, adipose, connective tissues. The blood in the capillaries contacts a very big surface over rather a long time.

The diameter of capillaries is 4-8 μm.

The general surface of all capillaries is about 1,000 m^2.

The wall of capillaries represents the semipermeable membrane closely connected functionally and morphologically with the surrounding connective tissue, that is, capillaries are inseparable from the organs, they are components of the organs. There are squamous, loop capillaries, they are easily stretched according to the diameter of erythrocytes.

The walls of capillaries consist of 2 membranes: internal — endothelial and external — basal. Depending on the ultrastructure of the capillary walls, they can be divided into 3 types (Figure 1.26):

1. ***Somatic*** type — has a continuous endothelial and basal envelope, a great number of the smallest pores (4–5 nm in diameter). They are permeable to water and mineral substances. Such capillaries are present in skeletal and smooth muscles, adipose and connective tissue, lungs, cerebral cortex.

2. ***Visceral*** type — has fenestration (holes) with a diameter of 50–80 nm. Fenestrations are frequently covered with the thinnest membrane. They are permeable to water, dissolved salts, macromolecules. Such capillaries are present in the kidneys, digestive canal, endocrine glands.

3. ***Sinusoid*** type — the basal membrane is partially absent, the endothelial envelope is irregular, with big interstitial lumens. Fluids, blood cells, macromolecules pass through them. Such capillaries are located in the liver, spleen, bone marrow.

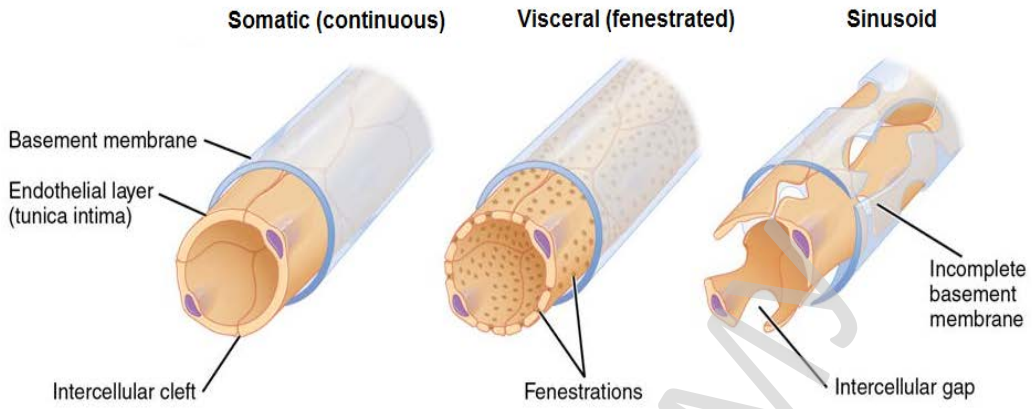


Figure 1.26— Types of capillaries (from bianoti.com)

The function of capillaries depends on their blood flow rate, the permeability of their walls, values of hydrostatic and oncotic pressures, number of perfused capillaries. The average linear rate in capillaries is 0.5–1 mm/s. Each blood cell remains in a capillary for approximately 1.0 sec.

The hydrostatic pressure in capillaries depends on the resistance of arteries and arterioles. In capillaries it continues to decrease and constitutes in the arterial end 30–35 mm Hg, in the venous end — 15–20 mm Hg.

The flow of fluids and various substances through the walls of capillaries is carried out by *diffusion, filtration,* and *osmosis*.

Diffusion is provided by the difference of the substance concentrations, it has a double-direction nature, its rate is very high. Passing through a capillary, the fluid of plasma 40 times completely exchanges with the interstitial fluid. Through the general exchange on the body surface the diffusion rate is approximately equal to 60 L/min, within 24 hours it makes 85,000 L on average.

During *filtration* blood plasma and dissolved substances pass through the capillary wall to the interstitial fluid. The main force of the filtration is the hydrostatic pressure in the capillary.

Reabsorption is the process of the return of the fluid from the interstitium into the capillary. The main force of reabsorption is the oncotic pressure of blood plasma.

According to the theory of **E. Starling**, at the arterial end of a capillary, the hydrostatic pressure of blood (HPB) is 35 mm Hg, the hydrostatic pressure of tissues (HPT) — 1 mm Hg, the oncotic pressure of blood (OPB) — 24 mm Hg; the oncotic pressure of tissues (OPT) — 2 mm Hg.

At the venous end of the capillary:

HPB =15 mm Hg, HPT = 1 mm Hg,
OPB = 24 mm Hg, OPT = 2 mm Hg.

The effective filtration pressure= (HPB + OPT) – (HPT + OPB) = (35 mm Hg + 2 mm Hg) — (1 mm Hg + 24 mm Hg) = 12 mm Hg.

The effective reabsorption pressure = (HPB + OPT) – (HPT + OPB) = (15 mm Hg + 2 mm Hg) — (1 mm Hg + 24 mm Hg) = – 8 mm Hg

At the arterial end of the capillary, the effective filtration pressure is 12 mm Hg. At the venous end, the effective reabsorption pressure is 8 mm Hg.

At the arterial end of the capillary the positive filtration pressure is created, under the influence of which the filtration of water and dissolved substances occurs.

At the venous end of the capillary, the HPB decreases to 15 mm Hg, and the OPB remains constant. Due to this filtration, the pressure in this part of the capillary becomes negative (–8 mm Hg) and its action is aimed at the return (reabsorption) of water from the interstitium to blood.

Normally, the filtration rate is practically equal to the reabsorption rate. Only a small part of intercellular fluid gets into the lymphatic vessels. The filtration rate is about 20 L/day, reabsorption rate — 18 L/day, 2 L of fluid a day gets into the lymphatic vessels (Figure 1.27).

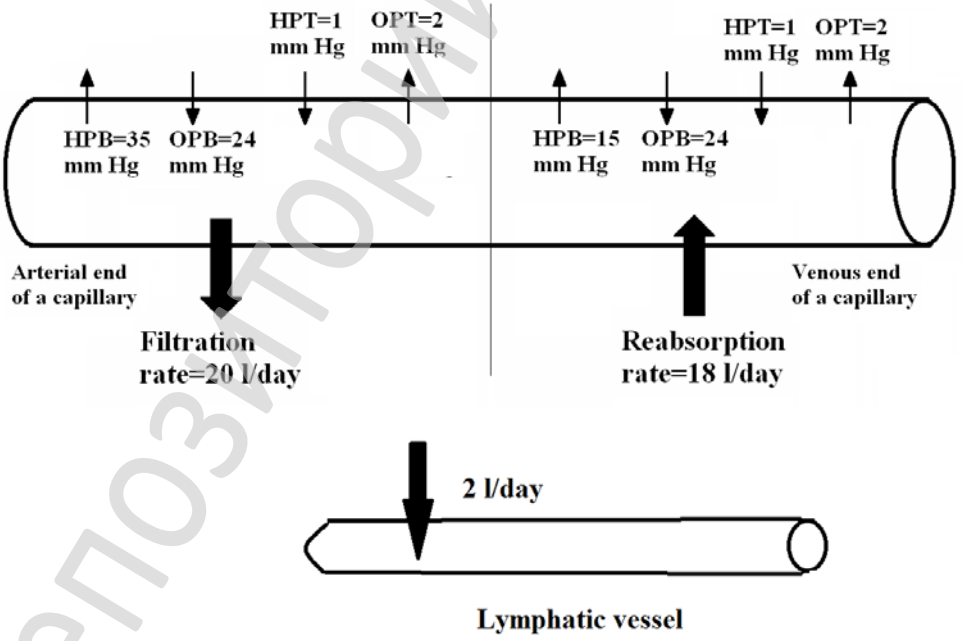


Figure 1.27 — Forces which determine the direction of the fluid flow in capillaries

Notes: **HPB** = hydrostatic blood pressure in the capillary; **OPB** = oncotic blood pressure in the capillary; **HPT** = hydrostatic pressure of tissues (in the interstitial fluid); **OPT** = oncotic pressure of tissues (in the interstitial fluid); Small arrows show the direction of the action of the pressure. Big arrows show

the direction of the fluid flow. Notice that the filtration rate is 20 L/day and reabsorption rate is 18 L/day, and 2 L of fluid per day gets into the lymphatic vessels.

1.2.2.2. Regulation of the blood flow in the blood vessels

The mechanisms of the regulation of the blood flow in the blood vessels can be divided into two constituent parts:

1. Central, determining the value of arterial pressure and systemic circulation.

2. Local, regulating the blood flow in separate organs and tissues.

Local mechanisms of the regulation of vascular tone. Substances formed during metabolism are capable to dilate arterioles and to enlarge the number of functioning capillaries. A decrease of the smooth muscle tone leading to *vasodilatation* occurs under the influence of the increased concentration of H^+, CO_2, the decrease of O_2.

The smooth muscles of the blood vessels constantly keep some level of contractions — muscle tone. The leading role in its maintenance belongs to myogenic regulation. The tone is preserved even in the complete absence of nervous and humoral influences and is called *basal* or *peripheric*.

However, the local mechanisms, being the important component of the blood flow regulation, yet are insufficient for the provision of fast and significant changes of the blood flow if necessary. More precise regulation of the blood flow is reached by the coordination of the local and central neuro-humoral mechanisms.

Central mechanisms of the regulation of the vascular tone (neuro-humoral regulation of the blood flow).

Neural regulation

The mechanisms of neural regulation include some parts:

1. The afferent (receptor) part.
2. The central part.
3. The efferent part.

Afferent (receptor) part. There are several types of receptors located in the blood vessels (angioreceptors):

- ***baroreceptors*** — respond to the rate and degree of the distention of the vascular walls. They are mechanoreceptors by the mechanism of action.
- ***chemoreceptors*** — are sensitive to the amounts of O_2, CO_2, H^+ in the blood.

Angioreceptors are located in the blood vessels of the whole system of circulation forming the receptive field which is composed of reflexogenic zones (the places of maximum accumulation of the receptors). The most important reflexogenic zones are aortal, sinocarotid, pulmonary arteries, and others.

Aortal zone*.* It is located in the wall of the aortic arch. Its receptors are the endings of the afferent fibers of the aortic nerve (the branch of the vagus nerve). It is the depressor nerve.

Synocarotid zone*.* It is located in the place of the branching of the common carotid artery into internal and external. It is connected with the vasomotor center by the sinus nerve, which is also knowns as Hering's nerve (the branch of the glossopharyngeal nerve).

Central part. It carries out the regulation by the nervous structures which make the vasomotor center. It includes various levels of the CNS, where all the lower structures are controlled by the higher ones.

Spinal level. The centers of the sympathetic nervous system are located in the thoracic and lumbar parts of the spinal cord. They send axons to the neurons of the prevertebral and paravertebral ganglia and directly innervate the smooth myocytes of the blood vessels, and also regulate the work of the heart by modulating the activity of the neurons of the cervical ganglia. The neurons of the sympathetic nervous system of the spinal cord are effector neurons. Through them the centers of the higher levels of the CNS (medulla oblongata, pons varolii, midbrain, hypothalamus) influence the vascular tone and heart function.

The main center of the maintenance of the vessel tone and regulation of blood pressure is ***the vasomotor center of the medulla*** (discovered by F. V. Ovsyannikov in 1871). It is a part of the cardiovascular center of the CNS (which controls both the vascular tone and cardiac activity). The vasomotor center consists of 2 zones:

The depressor zone is responsible for low activity of the sympathetic nervous system, vasodilation, it reduces the peripheral resistance, activates the parasympathetic mechanisms.

The pressor zone is responsible for high vascular tone, cardiac output, and peripheral resistance, and as a result the blood pressure level increases. Between the pressor and depressor zones there are reciprocal relations: if the depressor area is excited, this leads to the inhibition of the pressor area and vice versa.

When the arterial pressure *in the aorta* increases, the walls of the aorta are stretched, the baroreceptors are excited, and along the fibers of the aortal nerve the excitation reaches the vasomotor center of the medulla. It promotes high nucleus vagal tone, the tone of the vasoconstrictor center reduces, the blood pressure is low, because the vessels are dilated and cardiac activity decreases.

When the arterial pressure decreases, the frequency of pulses in the depressor decreases, the center of the vagus nerve is inhibited, the sympathetic part is activated. The vessels are narrowed, the activity of the heart increases, and blood pressure increases. So, the self-regulation of the constant level of arterial pressure is carried out.

When the arterial pressure *in the carotid artery* increases, the baroreceptors are excited, which reflexively reduces the tone of the vasomotor vasoconstrictor center and increases the tone of the vagus nerve. The blood pressure in the vessels reduces due to the dilation of the blood vessels and a low heart rate.

When the blood pressure in the carotid artery decreases, the intensity of impulsions from the baroreceptor decreases. The vascular tone increases, the peripheral resistance increases, and blood pressure becomes normal (Figure 1.28).

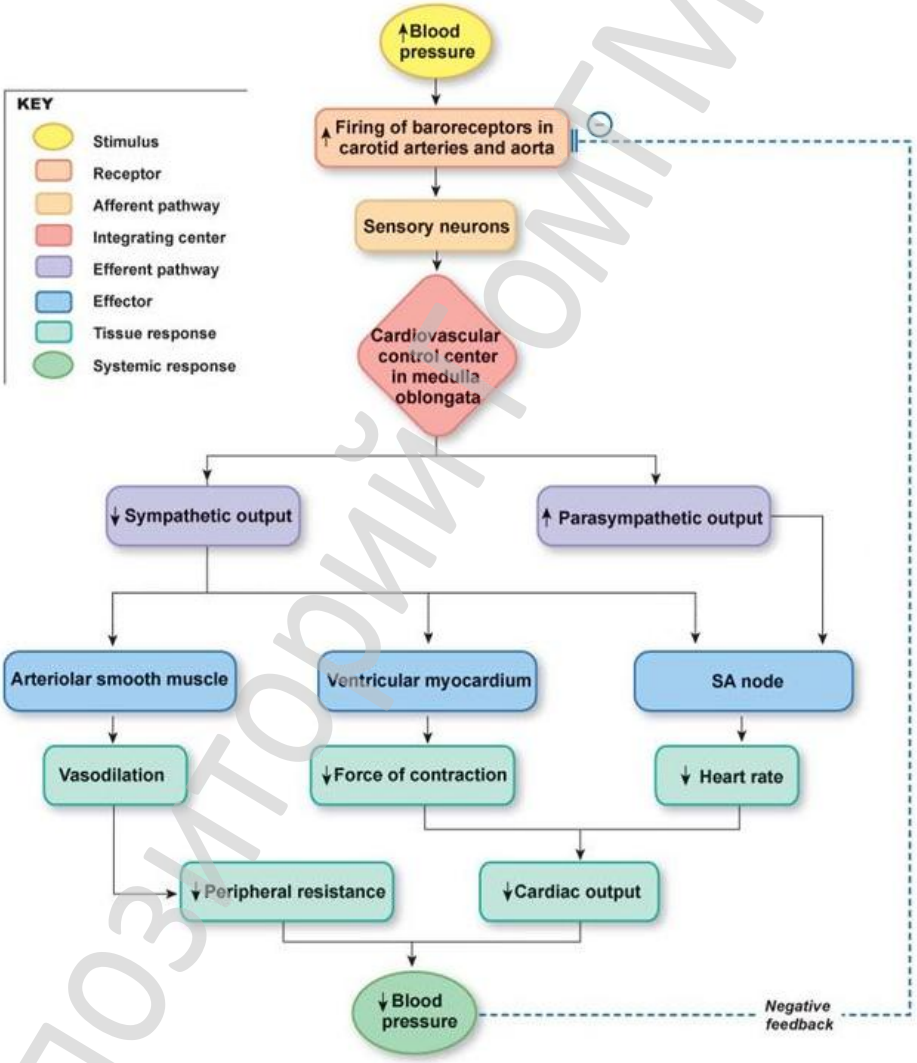


Figure 1.28 — Baroreceptor reflex pathways (from slideplayer.com)

The sinocarotid and aortal zones contain chemoreceptors which are sensitive to the blood levels of CO_2, H^+ and to O_2 deficiency. From these receptors, excitation through the afferent nerve fibers is transmitted to the vasomotor center and causes an increase of its tone. As a result, the vessels are narrowed and the pressure increases. At the same time, there is excitation of the respiratory center.

Thus, the excitation of the chemoreceptors of the aorta and carotid artery causes vascular pressor reflexes, and the excitation of mechanoreceptors – depressive reflexes.

In the vessels of the pulmonary circle, an increase of arterial pressure also leads to bradycardia, hypotension, and dilatation of the spleen vessels (*Parin's reflex*). The congestion of the blood in the lungs is eliminated.

In the **hypothalamus,** there are the pressor and depressor zones which perform functions similar to those of the medulla.

The influence of the **cortex of the cerebrum** on the changes of the vascular tone and, consequently, on the blood flow, is examined by the method of conditioned reflexes. If to combine the warming or cooling of a part of the skin changing the lumen of the vessels repeatedly, with sound or light, after some time one indifferent conditioned stimulus (sound) produces the same vascular reaction as an unconditioned stimulus (warmth, cold).

Efferent part. The nervous mechanism of the efferent part is realized through sympathetic and parasympathetic nerve fibers. Sympathetic fibers are the main vasoconstrictors, they support the vascular tone and constant blood pressure level.

The parasympathetic nerves (vagus, chorda tympani, glossopharyngeal, pelvic nerves) cause vascular vasodilation. But not all parasympathetic nerves cause the same effect, in the heart the narrowing of the blood vessels is observed. The sympathetic nerves dilate the vessels of the heart and skeletal muscles. Vasodilatation can occur if there is a decrease in the vasoconstrictor activity of the nerve fibers.

Humoral regulation

The important role in the humoral regulation of the vessel tone is played by the hormones of the adrenal medulla, neurohypophysis, juxtaglomerular apparatus of the kidneys.

Vasoconstriction substances

Angiotensin is the most powerful vasoconstricting substance which narrows arteries, arterioles and to a lesser extent veins. It is a component of the renin-angiotensin-aldosterone system (Figure 1.29).

Renin-angiotensin-aldosterone system. A decrease of the arterial pressure in the kidneys (below 100 mm Hg) causes increased production of renin by the juxtaglomerular apparatus. The secretion of renin into the blood depends on the concentration of K^+, Na^+ and sympathetic effects.

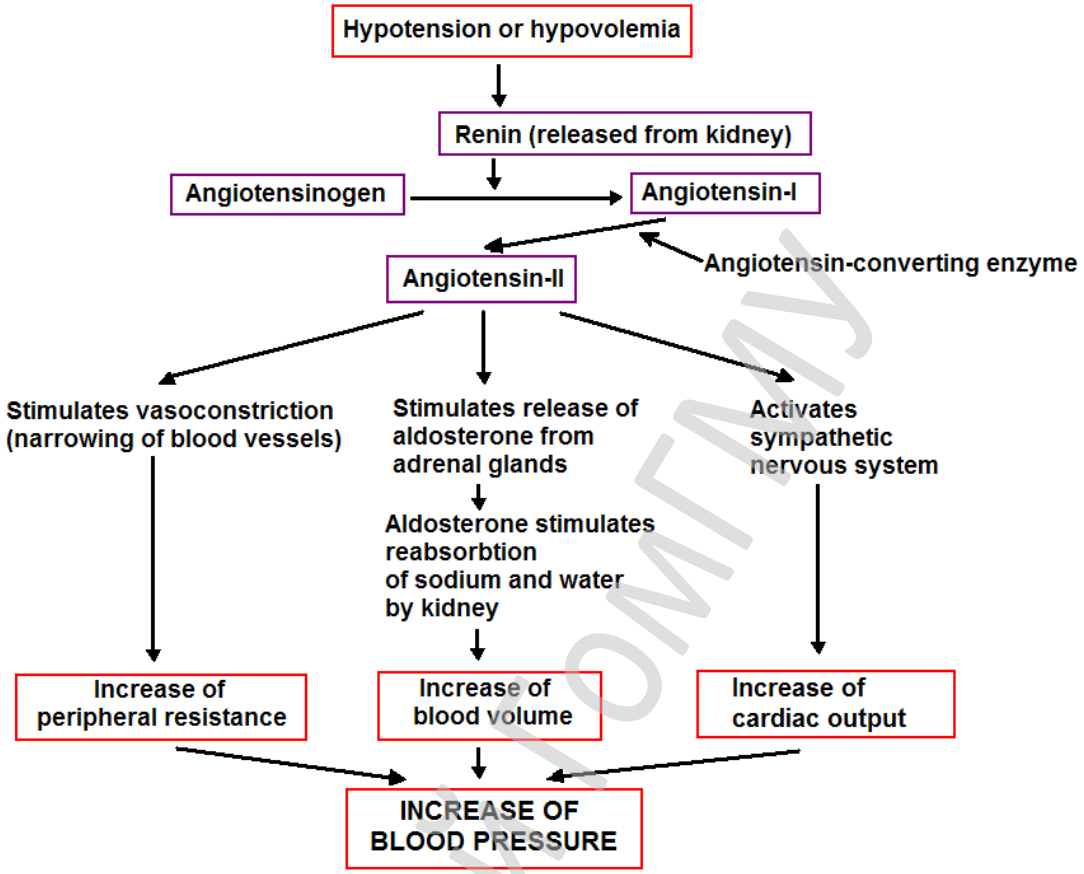


Figure 1.29 — Renin-angiotensin-aldosterone system and its role in the regulation of arterial pressure (from slideplayer.com)

Renin itself has no vasoconstrictor effect, however, it affects angiotensinogen (α_2-globulin of plasma), turning it into angiotensin I, which under the action of the angiotensin-converting enzyme of the plasma becomes a powerful vasoconstrictor — angiotensin II. Under its influence the vessels are narrowed, and blood pressure increases. Angiotensin II stimulates the secretion of aldosterone. Aldosterone increases the reabsorption of Na^+ and water in the kidneys. Water is retained in the vessels, and both blood volume and blood pressure increase. Thus, angiotensin II acts directly, aldosterone — indirectly. A large amount of renin is produced when the arterial pressure is low, and the kidneys are supplied with less blood, and more renin is produced. The fact of the discovery of renin explained the cause of hypertension in kidney disease (renal hypertension).

Some substances which are produced by endothelium, have a vasoconstrictor effect — endothelins, thromboxanes, endothelium-derived contracting factor (EDCF).

Endothelins. There are three types of endothelins (ET-1, -2, -3). The most active is ET-1. It binds with the receptors ET_A and ET_B. It is suggested that

disorders of endotheliocyte functions and a long-term increase of ET1 can be a cause of hypertension in humans and vasospasm of some body parts.

The endothelium-derived contracting factor (EDCF) is formed from arachidonic acid in the damaged endothelium. It can stimulate the receptors of thromboxane A_2 and prostaglandin H_2 causing an increased calcium level, contraction of smooth myocytes and vasoconstriction.

Noradrenalin cooperates basically with α-adrenergic receptors, whose excitation promotes vasoconstriction.

Vasopressin (antidiuretic hormone) is produced in the neurohypophysis. The vasoconstrictor effect is observed only when the concentration of this hormone in the blood exceeds a physiologically normal level.

Vasodilatation substances

Histamine causes dilatation of arterioles and venules and increases the permeability of capillaries. It is released mainly when the skin and mucous membranes of the walls of the stomach and intestines, skeletal muscles are damaged. Intensive formation and action of histamine produce the reaction of skin redness.

Natriuretic hormone is produced in the atria of the heart and causes vascular dilatation by relaxation of the smooth muscles of small arteries.

Acetylcholine is released from the postganglionic fibers of the parasympathetic nervous system. Its vasodilator effect is short-term because of the fast destruction by acetylcholinesterase. One of the mechanisms of its vasodilator effect is stimulation of NO formation.

The kallikrein–kinin system. Two peptides promoting vasodilatation (bradykinin and kallidin) are formed from the protein called kininogen under the action of proteases which are named kallikreins.

Kinins cause:

- relaxation of the smooth cells of vessels and decreasing of AP;
- contraction of the smooth muscle cells of the internal organs;
- increased permeability of capillaries;
- increased blood flow in the sweat and salivary glands and exocrine part of the pancreas.

Endothelial regulators

The endothelial cells of vessels under the action of different substances and conditions synthesize *nitric oxide,* which influence the tone of vessels and AP. The aminoacid L- arginine is the endogenous source of NO. Under the effect of NO the formation of cyclic GMP is stimulated through guanylate cyclase. NO participates in the regulation of AP on the peripheral level due to the local dilatation of vessels, and also at the CNS level by decreasing the sympathetic activity.

Substances with double action on the blood vessels

Adrenaline activates α- and β-adrenergic receptors. Excitation of α-receptors causes vasoconstriction, and excitation of β-receptors — vasodilatation. Low concentrations of adrenaline cause vasodilatation, and its high concentrations — vasoconstriction. It is explained by the fact that the sensitivity of β-receptors is higher than that of α-receptors, and due to this the physiological concentrations of adrenaline activate only β-receptors, which leads to vasodilatation. In emotional strain or blood loss the adrenaline concentration in the blood can increase to such a degree that vasoconstriction becomes the prevailing effect due to the simultaneous activation of β- and α-receptors. It is explained by the fact that in different vessels of the body there are more α-receptors than β-receptors.

Adrenaline constricts the arteries and arterioles of the skin, digestive system, kidneys, lungs (α-receptors prevail). It relaxes the vessels of the skeletal muscles, bronchial smooth muscles (β-receptors prevail).

Serotonin is synthesized by the epithelium of the mucous membrane of the intestines, neurons of some parts of the brain, thrombocytes. Serotonin causes contractions of the smooth myocytes of the main arterioles and narrowing of the blood vessels. If a vessel is damaged, serotonin is released from destructed thrombocytes, provides the constriction of the vessel and stops the bleeding. The character of serotonin influences the vessel diameter depending on the initial tone of the smooth myocytes of the vascular wall. If the initial tone is low, serotonin causes vasoconstriction, if high — the vasoconstrictor effect can be absent.

Prostaglandins (PG) are biologically active substances formed from arachidonic acid. They are found in almost all tissues and are synthesized most actively in the kidneys. Among them there are vasoconstrictor and vasodilator substances (prostacyclin PGI_2, *e*ndothelium-derived hyperpolarizing factor (EDHF) — vasodilatation; thromboxanes, endothelium-derived contracting factor (EDCF) — vasoconstriction.

Review questions

1. What are the types of capillaries? What factors influence the processes of microcirculation? What pressure affects the transmembrane movement of liquids?

2. List the mechanisms of the regulation of the blood flow in vessels. Give the concept of the vasomotor center. What are the main reflex zones? How does the regulation take place with the help of these zones?

3. Name the hormones with vasoconstrictor and vasodilator effects. Characterize the renin-angiotensin-aldosterone system. What is its role in the regulation of blood pressure?

Multiple Choice Questions
PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

1.Synchronous cardiomyocyte contractions are provided by...

Variants of answers:

a) intracardial peripheral reflexes;
b) features of intercellular interactions (nexuses);
c) intracellular regulation;
d) the influence of vagus nerve;
e) the influence of sympathetic nerves.

2. How is the process of periodic spontaneous excitation of the heart called?

Variants of answers:

a) automaticity;
b) conduction;
c) refracterity;
d) contraction;
e) irritability.

3. Spontaneous impulses in the synoatrial node arise in a person at rest with a rate...

Variants of answers:

a) 20 impulses/minute;
b) 40–50 impulses/minute;
c) 30–40 impulses/minute;
d) 60–80 impulses/minute;
e) 100–120 impulses/minute.

4. What is extrasystole?

Variants of answers:

a) the next contraction of the heart;
b) a cardiac contraction with an increased force;
c) an extra contraction of the heart;
d) the next contractions of the atrium;
e) an atrium contraction with increased force.

5. In which extrasystole is the complete compensatory pause present?

Variants of answers:

a) ventricular;

b) atrial;
c) sinus;
d) any of the mentioned;
e) atrial and sinus.

6. What is the main reason of the second heart sound?
Variants of answers:
a) closure of the atrioventricular valves;
b) closure of the semilunar valves;
c) ventricular contractions;
d) atrial contractions;
e) all the answers are correct.

7. Electrocardiography is a method of the evaluation of...
Variants of answers:
a) the work of the heart;
b) the force of cardiac contractions;
c) excitation of the heart;
d) sound manifestations of cardiac activity;
e) mechanical manifestations of cardiac activity.

8. The phenomenon of the «Bowditch staircase » is...
Variants of answers:
a) a decrease of the force of cardiac contractions under rhythmic simulation with increasing frequency;
b) an increase of the frequency of cardiac contractions under rhythmic action of identical stimuli;
c) an increase of the force of cardiac contractions under rhythmic simulation with increasing frequency;
d) an increase of the excitability of the heart under rhythmic action of identical stimuli;
e) a stop of cardiac contractions under the rhythmic effect of identical stimuli.

9. The strengthening of the contractions of the left ventricle in the moderate stretching of the walls of the right atrium is provided by...
Variants of answers:
a) intercellular interaction;
b) intracellular regulation;
c) intracardial peripheral reflex;
d) influence of adrenaline;
e) influence of the vagus nerve.

10. The chronotropic effect on the action of the heart is a change of...

Variants of answers:

a) the force of cardiac contractions;
b) the excitability of the myocardium;
c) the rhythm of cardiac contractions;
d) the conduction rate of excitation in the myocardium;
e) all the answers are correct.

11. The inotropic effect on the action of the heart is a change of...

Variants of answers:

a) the excitability of the myocardium;
b) the rhythm of cardiac contractions;
c) the rate of the conduction of excitation in the myocardium;
d) the force of cardiac contractions;
e) all the answers are correct.

12. The bathmotropic effect on the action of the heart is a change of...

Variants of answers:

a) the rhythm of cardiac contractions;
b) the rate of the excitation conduction in the myocardium;
c) the excitability of the myocardium;
d) the force of cardiac contractions;
e) all the answers are correct.

13. The dromotropic effect on the action of the heart is a change of...

Variants of answers:

a) the force of cardiac contractions;
b) the excitability of the myocardium;
c) the heart rate;
d) the heart conductivity;
e) all the answers are correct.

14. Which effects do the vagus nerves produce on cardiac muscle?

Variants of answers:

a) positive inotropic, negative chronotropic;
b) negative inotropic, positive chronotropic;
c) negative inotropic, negative chronotropic;
d) positive inotropic, positive chronotropic;
e) the vagus nerves do not influence cardiac muscle.

15. Which effects do sympathetic nerves produce on cardiac muscle?

Variants of answers:

a) positive inotropic, negative chronotropic;

b) positive inotropic, positive chronotropic;

c) negative inotropic, positive chronotropic;

d) negative inotropic, negative chronotropic;

e) sympathetic nerves do not influence heart muscle.

16. The phenomenon of the heart escaping from the influence of the vagus nerve consists in...

Variants of answers:

a) the renewal of the contractions of the heart stopped under the action of the sympathetic nerve;

b) the renewal of the contractions of the heart stopped under the action of the vagus nerve;

c) the stop of cardiac contractions under the action of the vagus nerve;

d) a decrease of the rhythm of cardiac contractions under the action of the vagus nerve;

e) an increase of the frequency of cardiac contractions under the action of the vagus nerve.

17. How does the sympathetic nerve influence the excitability and conductivity of the heart?

Variants of answers:

a) the sympathetic nerve reduces them;

b) the sympathetic nerve does not influence them;

c) the sympathetic nerve increases them;

d) the sympathetic nerve increases excitability and decreases conductivity;

e) the sympathetic nerve decreases excitability and increases conductivity.

18. If to cut the sympathetic and parasympathetic nerves, which will innervate the heart...

Variants of answers:

a) the heart will stop contracting;

b) the heat rate will decrease;

c) the heart rate will increase;

d) the rhythm of the atrioventricular node will appear;

e) the heart rate will not change.

19. What is the neurotransmitter of the sympathetic nerves of the heart?

Variants of answers:

a) acetylcholine;
b) histamine;
c) noradrenaline;
d) serotonine;
e) dopamine.

20. What is the neurotransmitter of the vagus nerve of the heart?

Variants of answers:

a) adrenaline;
b) serotonine;
c) histamine;
d) acetylcholine;
e) dopamine.

21. Which changes of heart rate are observed during pressing on the eyeballs (reflex of Danini-Achner)?

Variants of answers:

a) it increases;
b) it decreases;
c) the rhythm does not change;
d) it causes arrhythmia;
e) at first it does not change, and then becomes more frequent.

22. With the help of which reflex is it possible to decrease the rate of cardiac contractions temporarily?

Variants of answers:

a) Danini-Achner's reflex;
b) Anrep's reflex;
c) Starling's reflex;
d) effect of Bowditch;
e) reflex of Bainbridge.

23. Which humoral factor stimulates the work of the heart?

Variants of answers:

a) acetylcholine;
b) adrenaline;
c) potassium ions;
d) endothelin;
e) all the answers are correct.

24. The greatest resistance in the systemic circle of blood circulation is observed at the level of...

Variants of answers:

a) large arteries;

b) middle-sized arteries;

c) capillaries;

d) arterioles;

e) vascular anastomoses.

25. How does the volume velocity of the blood flow change in different parts of the vascular system?

Variants of answers:

a) it is higher in arteries and less in veins;

b) it is the greatest in the aorta and large arteries;

c) it is constant in all blood vessels;

d) it is the greatest in the venae cavae;

e) it is the greatest in capillaries.

26. How does the linear velocity of the blood flow change from the aorta up to hollow veins?

Variants of answers:

a) it remains constant in all the levels of the vascular system;

b) it rises up to the level of capillaries, then it reduces;

c) it reduces to the level of capillaries, then rises;

d) it is gradually reducing in all the levels of the vascular system;

e) it is gradually rising in all the levels of the vascular system.

27. At which level of the vascular system is the minimal linear velocity of the blood flow observed?

Variants of answers:

a) arteries;

b) veins;

c) capillaries;

d) arterioles;

e) aorta.

28. In which case will the linear velocity of the blood flow increase?

Variants of answers:

a) if the total cross-section of all blood vessels increases;

b) if the volumetric rate of the blood-flow decreases;

c) if the total cross-section of all blood vessels decreases;
d) if the pressure decreases;
e) all the answers are correct.

29. How does blood pressure change in the vascular system from the aorta up to the venae cavae?

Variants of answers:
a) it remains constant along the whole vascular system;
b) it is decreasing along the whole vascular system;
c) it is decreasing to the level of capillaries, then rises;
d) it rises up to the level of capillaries, then decreases;
e) it is gradually rising at all the levels of the vascular system.

30. At which level of the vascular system is the lowest blood pressure observed?

Variants of answers:
a) venules;
b) capillaries;
c) arteries;
d) venaecavae;
e) arterioles.

31. Which example is the highest value of pulse pressure?

Variants of answers:
a) 120/80 mm of Hg;
b) 130/90 mm of Hg;
c) 110/60 mm of Hg;
d) 140/95 mm of Hg;
e) 110/70 mm of Hg.

32. In which blood pressure do tones disappear if to measure arterial pressure by Korotkov's method?

Variants of answers:
a) in diastolic pressure;
b) in systolic pressure;
c) in pulse pressure;
d) in average pressure;
e) in osmotic pressure.

33. Compare the linear velocity of the blood flow and the velocity of the pulse wave?

Variants of answers:

a) the linear velocity of the blood flow is higher;

b) they are identical;

c) the linear velocity of the blood flow is less;

d) in the aorta, the linear velocity of the blood flow is higher, and in the venae cavae the velocity of the pulse wave is higher;

e) in the aorta, the linear velocity of the blood flow is less, and in the venae cavae, the velocity of the pulse wave is less.

34. How is the registration method of the rhythmic oscillations of the walls of arteries called?

Variants of answers:

a) phlebography;

b) sphygmography;

c) phonocardiography;

d) electrocardiography;

e) radiography.

35. The dicrotic notch on the catacrota of the sphygmogram is caused by…

Variants of answers:

a) the reflected wave after the closing of the aortal valve;

b) the opening of the semilunar valve;

c) the phenomenon of «aortal compressive chamber»;

d) dilation of the venae cavae;

e) all the answers are correct.

36. Which departments of the cardiovascular system contain up to 60–70 % of the whole blood volume?

Variants of answers:

a) arteries;

b) capillaries;

c) veins;

d) aorta;

e) arterioles.

37. Which wave of the phlebogram is related to the systole of atria?

Variants of answers:

a) C-wave (the second wave);

b) V-wave (the third wave);
c) A-wave (the first wave);
d) waves C and V (the second and the third waves);
d) all the waves.

38. According to the Starling scheme, the filtration of fluids from capillaries into tissues will be higher, if...

Variants of answers:

a) the concentration of proteins (especially albumins) in blood plasma is decreased;
b) all the answers are correct;
c) the hydrostatic pressure in the capillaries increases;
d) the hydrostatic pressure in the interstitial fluid decreases;
e) the concentration of albumins in the interstitial fluid increases.

39. The basal tone of the vascular wall is the level of its contractions...

Variants of answers:

a) caused by neurogenic and humoral influences;
b) kept after the elimination of neurogenic and hormonal influences;
c) caused by the influence of adrenaline and noradrenaline;
d) caused by the influence of thyroxin and vasopressin;
e) caused by the influence of the vagus nerve.

40. In which department of the central nervous system is the cardiovascular center located?

Variants of answers:

a) in the spinal cord;
b) in the hypothalamus;
c) in the medulla oblongata;
d) in the thalamus;
e) in the basal nuclei.

41. Which effect will be observed if the pressor zone of the vasomotor center is stimulated?

Variants of answers:

a) dilatation of arteries, low arterial pressure, depression of work of the heart;
b) there will be no changes of the vessel tone, arterial pressure and work of the heart;

c) narrowing of arteries, high arterial pressure, stimulation of the work of the heart;

d) the effect of Bowditch;

e) the effect of Bainbridge.

42. How will the tone of the depressor zone of the vasomotor center change if the pressure in the carotid sinus increases?

Variants of answers:

a) it will not change;

b) it will rise;

c) it will decrease;

d) at first it will fall sharply, and then it will rise;

e) all the answers are correct.

43. Which variant lists the effects of angiotensin II correctly?

Variants of answers:

a) expressed vasodilatation, depression of the secretion of aldosterone by the adrenal glands;

b) expressed vasoconstriction, simulation of the secretion of aldosterone by the adrenal glands;

c) angiotensin II essentially does not influence the tonus of vessels;

d) angiotensin II is not vasoactive substance;

e) expressed vasodilatation, depression of the secretion of adrenaline by the adrenal glands.

44. How will arterial pressure change after the constriction of renal arteries?

Variants of answers:

a) it will not change;

b) it will increase (the renin-angiotensin-aldosterone system is stimulated);

c) it will decrease because of vasodilatation;

d) it will decrease (the renin-angiotensin-aldosterone system is stimulated);

e) all the answers are correct.

45. Which humoral factor provides only the vasoconstrictor effect?

Variants of answers:

a) adrenaline;

b) noradrenaline;

c) prostaglandins;
d) adrenaline and noradrenaline;
e) all the answers are correct.

46. The SA node acts as a pacemaker of the heart because …

Variants of answers:
a) it is capable of generating impulses spontaneously;
b) it has rich sympathetic innervations;
c) it has poor cholinergic innervations;
d) it generates impulses at the highest rate;
e) it generates impulses at the lowest rate.

47. The highest conduction rate in the conduction system of the heart is observed in…

Variants of answers:
a) the SA node;
b) the AV node;
c) the bundle of His;
d) the Purkinje fibers;
e) the conduction rate is identical in all the parts of the conducting system.

48. The least conduction velocity is found in…

Variants of answers:
a) the AV node;
b) the Purkinje fibers;
c) the bundle of His;
d) the ventricular myocardial fibers;
e) the conduction rate is identical in all the parts of the conduction system.

49. The cardiac output in L/min divided by the heart rate equals …

Variants of answers:
a) diastolic pressure;
b) mean stroke volume;
c) cardiac index;
d) mean arterial pressure;
e) systolic pressure.

50. The cardiac output in an adult in nearly…

Variants of answers:
a) 7.5 L/min;

b) 5 L/min;
c) 12 L/min;
d) 10 L/min;
e) 1 L/min.

51. The cardiac index is defined as...

Variants of answers:

a) stroke volume /body surface area;
b) cardiac output per unit of body surface area;
c) systolic pressure/ body surface area;
d) end diastolic volume / body surface area;
e) diastolic pressure/ body surface area.

52. The termination of the isometric relaxation phase coincides with…

Variants of answers:

a) the opening of the AV valves;
b) the T-wave in ECG;
c) the R-wave of ECG;
d) the closing of the semilunar valves;
e) the opening of the semilunar valves.

53. During the cardiac cycle the opening of the aortic valve takes place during …

Variants of answers:

a) the beginning of systole;
b) the end of presystolic period;
c) the end of diastole;
d) the end of isometric relaxation;
e) the end of isovolumetric contraction.

54. Which of the following correlates with the isometric contraction phase…

Variants of answers:

a) the opening of the AV valves and closure of the aortic and pulmonary valve;
b) the closure of the AV valves and opening of the aortic and pulmonary valve;
c) both the valves are closed;
d) both the valves are open;
e) the aortic valve is open and the pulmonary valve is closed.

55. Which of the following statements is true about the fourth heart sound?

Variants of answers:

a) it can be heard by a human ear;

b) its frequency is high**;**

c) it is formed during atrial systole;

d) it is formed during the ventricular ejection phase;

e) it is formed during the isometric contraction phase.

56. The distribution of the blood flow is mainly regulated by the…

Variants of answers:

a) arteries;

b) arterioles;

c) capillaries;

d) venules;

e) aorta.

57. Which of the following statements about capillaries is not correct?

Variants of answers:

a) they are the greatest cross sectional area;

b) they contain 85% of blood;

c) they contain less blood than veins;

d) they have a single layer of cells bounding the lumen;

e) they provide the exchange of substances between blood and tissues.

58. Blood pressure is defined as the product of…

Variants of answers:

a) systolic pressure x pulse;

b) diastolic pressure x pulse rate;

c) pulse pressure x pulse rate;

d) cardiac output x peripheral resistance;

e) cardiac output x pulse rate.

59. Which of the following promotes the filtration at the arteriolar end of the capillary bed?

Variants of answers:

a) decrease in the hydrostatic pressure of capillaries;

b) increase in the hydrostatic pressure of capillaries;

c) increase in the oncotic pressure of capillaries;

d) decrease in the oncotic pressure of interstitium;

e) decrease in the hydrostatic pressure of capillaries and oncotic pressure of interstitium.

60. All of the following causes vasodilation except…

Variants of answers:

a) angiotensin II;
b) acetylcholine;
c) bradykinin;
d) nitric oxide;
e) histamine.

CORRECT ANSWERS
PHYSIOLOGY OF CARDIOVASCULAR SYSTEM

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	b	16	b	31	c	46	d
2	a	17	c	32	a	47	d
3	d	18	c	33	c	48	a
4	c	19	c	34	b	49	b
5	a	20	d	35	a	50	b
6	b	21	b	36	c	51	b
7	c	22	a	37	c	52	a
8	c	23	b	38	b	53	e
9	c	24	d	39	b	54	c
10	c	25	c	40	c	55	c
11	d	26	c	41	c	56	b
12	c	27	c	42	b	57	b
13	d	28	c	43	b	58	d
14	c	29	b	44	b	59	b
15	b	30	d	45	b	60	a

UNIT 2
PHYSIOLOGY OF DIGESTION

2.1. Physiological bases of hunger and satiety. Types of digestion

Human organism needs various materials and a great deal of energy for its vital activity. Substances satisfying the plastic and energy requirements of the body should come from the environment. Obviously, insufficient supply with nutrients affects homeostasis and is incompatible with life. At the same time, the human body is not able to assimilate proteins, fats, carbohydrates, and a number of other substances from food without its prior processing. This major body function is carried out by the digestive system (Figure 2.1).

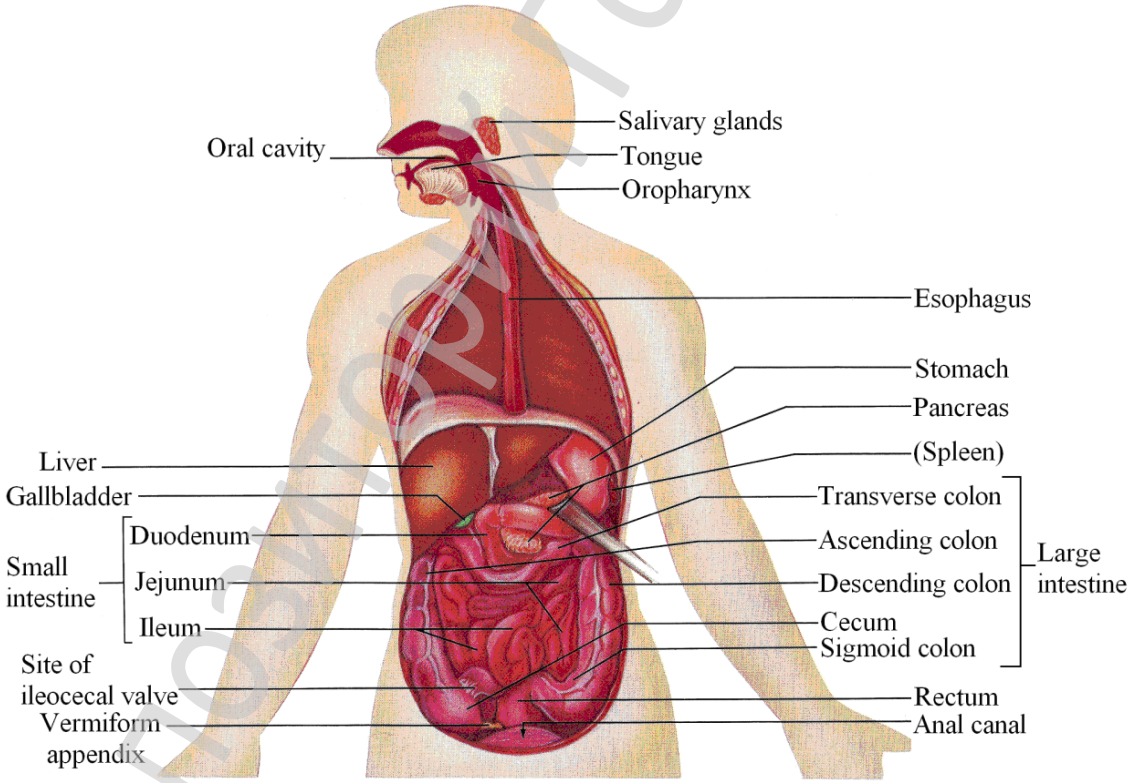


Figure 2.1 — Organs of the alimentary canal and accessory digestive organs (by Elaine N. Marieb, 1989)

Physical and chemical processing of food is called **digestion**.

Hunger as a physiological state is an expression of the organism`s needs for nutrients of which it has been deprived for some time, which has resulted in a decreased amount of these substances in the blood.

The subjective manifestations of hunger, known as hunger contractions or hunger pangs, are unpleasant sensations: “burning sensations”, sinking sensations in the abdominal region, nausea, sometimes giddiness, headache, lack of energy.

The external objective manifestation of hunger is the behavioral reaction to procure food and thus eliminate the cause of hunger.

The subjective and objective manifestations of hunger are caused by the excitation of neurons of various parts and levels of the CNS. Academician I. P. Pavlov named all these neurons as the feeding center. Its functions are to form feeding behavior aimed at the search and intake of food, and also at the regulation and functional integration of the digestive organs.

The feeding center is a compound hypothalamolimbic and reticulocortical complex. The main part which activates all feeding centers is the lateral nuclei of the hypothalamus. Destruction of these nuclei results in the refusal to eat food (aphagia), while their stimulation leads to voracious eating (hyperphagia). The lateral nuclei of the hypothalamus, being a part of the feeding center, are called the center of hunger.

Destruction of the ventromedial nuclei of the hypothalamus leads to hyperphagia and their stimulation — to aphagia. The ventromedial nuclei, a part of the feeding center, are the satiety center.

The hypothalamic nuclei of the feeding center are excited or inhibited depending on the level of nutritional substances in the blood and also signals from various peripheral receptors.

The theories of the origin of the sensation of hunger:

- **Glucostatic theory** according to which the sensation of hunger is determined by a low blood glucose level.
- **Aminoacidostatic theory** according to which the excitability of the neurons of the feeding center is determined by the amino acid level in the blood.
- **Lipostatic theory** considers that the stimulus of the hypothalamic nuclei is the insufficiency of metabolites formed during fat mobilization.
- **Thermostatic theory** assumes suppression of the feeding center due to a rise in the temperature of the blood washing it, which happens during meals.
- **Hydrostatic theory** connects the sensation of hunger with the organism`s water resources: their decrease reduces food consumption.
- **Metabolic theory** unites all the above theories.

Eating induces the state of ***satiety*** opposite to hunger. It precedes the coming of digestion products into the blood. This satiety is called ***sensory (initial) satiety***. It implies inhibition of the feeding center and has a complex reflex nature. Sensory satiety is replaced with ***metabolic (secondary, or true) satiety,*** whose basic mechanism is the entry of digestion products into the blood.

However, to have nutrients come into the blood to be utilized by the organism, food has to undergo complex mechanical and chemical digestion in the gastrointestinal tract. The basis of the functioning of the digestive system is the *conveyor principle* — a certain sequence of food digestion in various departments of the gastrointestinal tract.

Types of digestion

Depending on the origin of hydrolytic enzymes, there are three types of digestion:

1. Self-digestion — is carried out by enzymes which are synthesized by macroorganisms (the enzymes of saliva, gastric and pancreatic juices, epithelium of the small intestine).

2. Symbiotic — hydrolysis of nutrients due to enzymes which are synthesized by the symbionts of macroorganisms (bacteria and protozoa of the digestive tract). This type of digestion in humans is carried out in the large intestine (for example, cellulose fiber splitting). The role of symbiotic digestion in humans is relatively not significant as self-digestion is developed.

3. Autolytic — is carried out due to exogenic hydrolases, which enter the organism with ingested food. The role of this digestion becomes significant if self-digestion is insufficiently developed (for example, in newborns, nutrients from the mother's milk are digested by the enzymes which come into the baby`s digestive tract with the mother's milk).

Depending on the localization of the hydrolysis process on nutrients, digestion is divided into:

1 **Intracellular digestion** — substances transported into cells by phagocytosis and pinocytosis are split up by cellular enzymes into cytosol or digestive vacuole. This process plays a significant role in intestinal digestion during the period of early postnatal development.

2. **Extracellular digestion** is subdivided into:

— **distant (cavitary) digestion**;

— **contact (parietal, membrane) digestion**.

Distant digestion is carried out in a medium located away from the place where enzymes are produced (for example, in the cavity of the stomach, intestines).

Parietal digestion occurs in the small intestine on a very big surface formed by the folds, villi, and microvilli of its mucous membrane. Hydrolysis of nutrients is carried out by enzymes located in the membranes of the microvilli. The feature of parietal digestion is the integration of final food splitting and absorption of the final products due to close localization of transmembrane transport proteins.

2.2. Digestion in the oral cavity

Food processing begins in the oral cavity. Here grinding of food, its moistening by saliva, analysis of gustatory properties, initial hydrolysis of some nutrients and formation of a food lump take place. On average, food stays in the oral cavity for 15–18 sec.

Food stimulates gustatory, tactile, and temperature receptors of the oral cavity. Signals from these receptors along the centripetal nerve fibers of trigeminal, facial and glossopharyngeal nerves reach the nerve centers of several reflexes. Centrifugal impulses from these centers excite the secretion of salivary, gastric and pancreas glands, release bile into the duodenum, change the motor activity of the stomach. Thus, despite the fact that food stays in the mouth for a short time, this part of the digestive tract influences all the stages of food digestion.

2.2.1. Salivation

At the initial stage of digestion, the role of saliva is great. It is produced by the three pairs of large salivary glands: **parotid (admaxillary)**, **submandibular**, and **sublingual** glands and a number of smaller glands on the surface of the tongue, in the mucous membranes of the palate and cheeks (Figure 2.2). From the glands through the excretory ducts saliva comes into the oral cavity. Depending on the produced secret, the salivary glands can be of three types: ***serous*** (produce a fluid secret without mucus); ***mixed*** (produce a serous-mucous secret) and ***mucous*** glands (produce saliva rich in mucin). The serous glands are the parotid gland and the small glands of the lateral surfaces of the tongue. The mucous gland are the glands located at the root of the tongue and palate. The mixed glands are the submandibular (serous-mucosal), sublingual (mucosal-serous) glands.

Without food intake saliva is secreted on average 0.24 mL/min for humidification of the oral cavity, during mastication — 3–3.5 mL/min (about 200 mL/h) depending on the type of food. Responding to incoming citric acid, salivation can reach 7.4 mL/min. The normal daily production of saliva varies between 0.5 and 2.0 liters.

2.2.2. Composition and properties of saliva

Saliva is a viscous fluid with a density of 1.001–1.017. The composition of saliva depends on the rate of its secretion, the pH of mixed saliva is 5.8–7.8.

Mixed saliva contains 99.4–99.5 % water, the rest is dry residual. The inorganic components of saliva are: chlorides, carbonates, phosphates, and other salts of sodium, potassium, calcium, magnesium, etc. (Table 2.1).

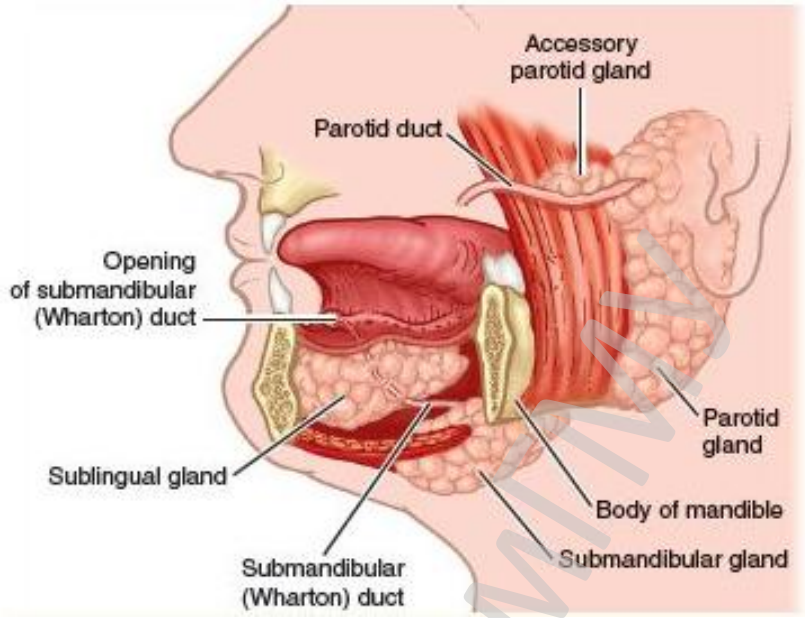


Figure 2.2 — Salivary glands (by C. Guyton and John E. Hall, 2016)

Table 2.1 — Composition of saliva

Organic components			**Inorganic components**
Digestive enzymes		**Other organic substances**	
Name of the enzymes	**Role of the enzymes**	Mucin Lysozyme Callecrein Proteins Amino acids Creatinine	Na^+ K^+ Ca^{2+} Mg^{2+} Chlorides, Carbonates Phosphates (and others)
Alpha-amylase	It splits carbohydrates (polysaccharides — starches, glycogen) with formation of dextrines, disaccharides (maltose and partially glucose)		
*Proteinases (*cathepsines, salivain, glandulain), *lipase*, *alkaline and acidic phosphatases*	The activity of these enzymes in saliva is insignificant		

Saliva contains organic substances the content of which is 2–3 times as high as that of mineral salts. Organic substances are products of the secretory activity of the salivary glands. The composition of saliva includes various proteins, free amino acids, some carbohydrates, ammonia, creatinine, and other substances. Saliva contains mucin, which gives it viscosity. Due to the presence of mucin, a saliva-saturated food lump is easily swallowed.

Saliva is rather rich in enzymes though the amount of some of them is insignificant. Human saliva has the ability of active carbohydrate hydrolysis. It is carried out by ***alpha-amylase,*** splitting polysaccharides (starches, glycogen)

with the formation of dextrines and then disaccharide (maltose) and partially glucose.

Salivary amylase starts its activity in the oral cavity, but it is insignificant due to the short stay of food there. Carbohydrate hydrolysis by the enzymes of saliva continues in the stomach till acidic gastric juice gets into the deep layers of the food contents. Gastric juice inactivates the enzymes of saliva. Saliva contains a number of other enzymes: *proteinases* (cathepsines, salivain, glandulain), *lipases,* alkaline, and acidic *phosphatases.* They take part in digestion, but their activity is insignificant. Saliva has bactericidal properties due to the presence of the enzyme *lysozyme*. Saliva contains callecrein, which dilates the blood vessels and increases blood supply to the salivary gland.

The physiological role of saliva:

1. It moistens and dilutes food.
2. It promotes gustatory approbation of food.
3. The enzymes of saliva provide carbohydrate hydrolysis.
4. It protects the mucous membrane from drying out and maintains its integrity.
5. Due to mucin a food lump is formed.
6. Lysozyme has a bacteriostatic effect (factor of nonspecific protection).
7. Saliva partially neutralizes acidic products when it gets into the oral cavity.
9. Saliva contains biologically active substances — callecrein, parotin.
10. Saliva delivers minerals (calcium, phosphate, etc.) and microelements (fluorine, etc.) to the tooth enamel and maintains its optimal chemical composition (mineralization function).
11. Saliva participates in the excretion of metabolic products (urea, uric acid, etc.), as well as the salts of the heavy metals, pharmacological preparations from the organism.

The enzymic composition and properties of saliva change with age, depend on a diet and type of food. The dryer the food is, the more viscous is saliva. Acids, a bitter taste require a significant amount of more liquid saliva. The amount and composition of saliva due to food ingestion are determined by the regulatory influence on the salivary glands.

2.2.3. Regulation of salivation

Ingestion of food stimulates salivation. Salivation proceeds all the phases of eating and stops once it is finished.

From the receptors of the oral cavity signals are sent to the CNS along the afferent fibers of the trigeminal, facial, glossopharyngeal, and vagus nerves.

The basic salivation center is situated in the *medulla*. Signals from the oral cavity get here and also into the lateral horns of the superior thoracal segments of the spinal cord. From here the influences along the efferent parasympathetic and sympathetic nerve fibers go to the salivary glands.

The parasympathetic innervation of the salivary glands begins from the nuclei of the medulla (Figure 2.3). **Parasympathetic** fibers stimulate the formation of a great **amount** of fluid saliva with a **low content of organic substances.** *The sympathetic innervation* of the salivary gland is carried out from the lateral horns of II–IV thoracal segments of the spinal cord. **Sympathetic** fibers stimulate the formation of a **small amount of saliva rich in organic substances**.

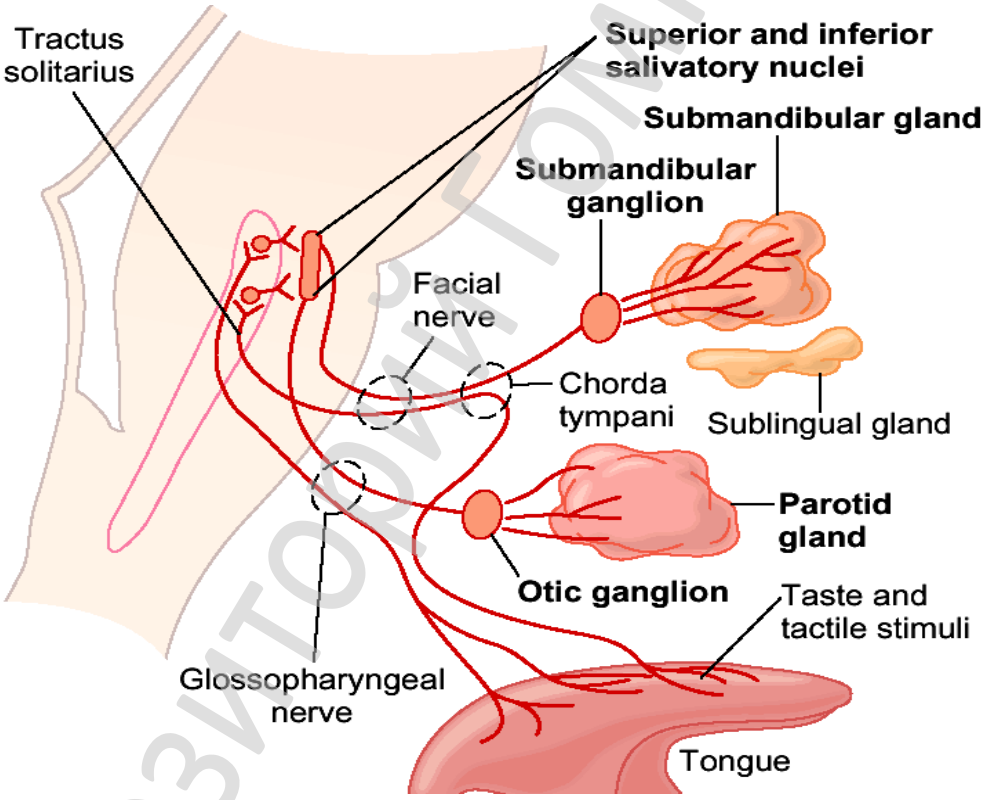


Figure 2.3 — Regulation of salivary secretion (parasympathetic) (by C. Guyton and John E. Hall, 2016)

Salivation *begins by the type of conditioned reflexes* — in response to the sight and smell of food.

Salivation can also be inhibited by pain, negative emotions, body dehydration. All these effects reduce the activity of the feeding center and its part — the satiety center. The inducers of the latter can be some humoral substances. For example, excessive salivation is observed in asphyxia due to the stimulation of the satiety center by carbonic acid.

2.2.4. Swallowing

The process of swallowing consists of voluntary (buccal) and involuntary (pharyngeal-esophageal) phases (Figure 2.4).

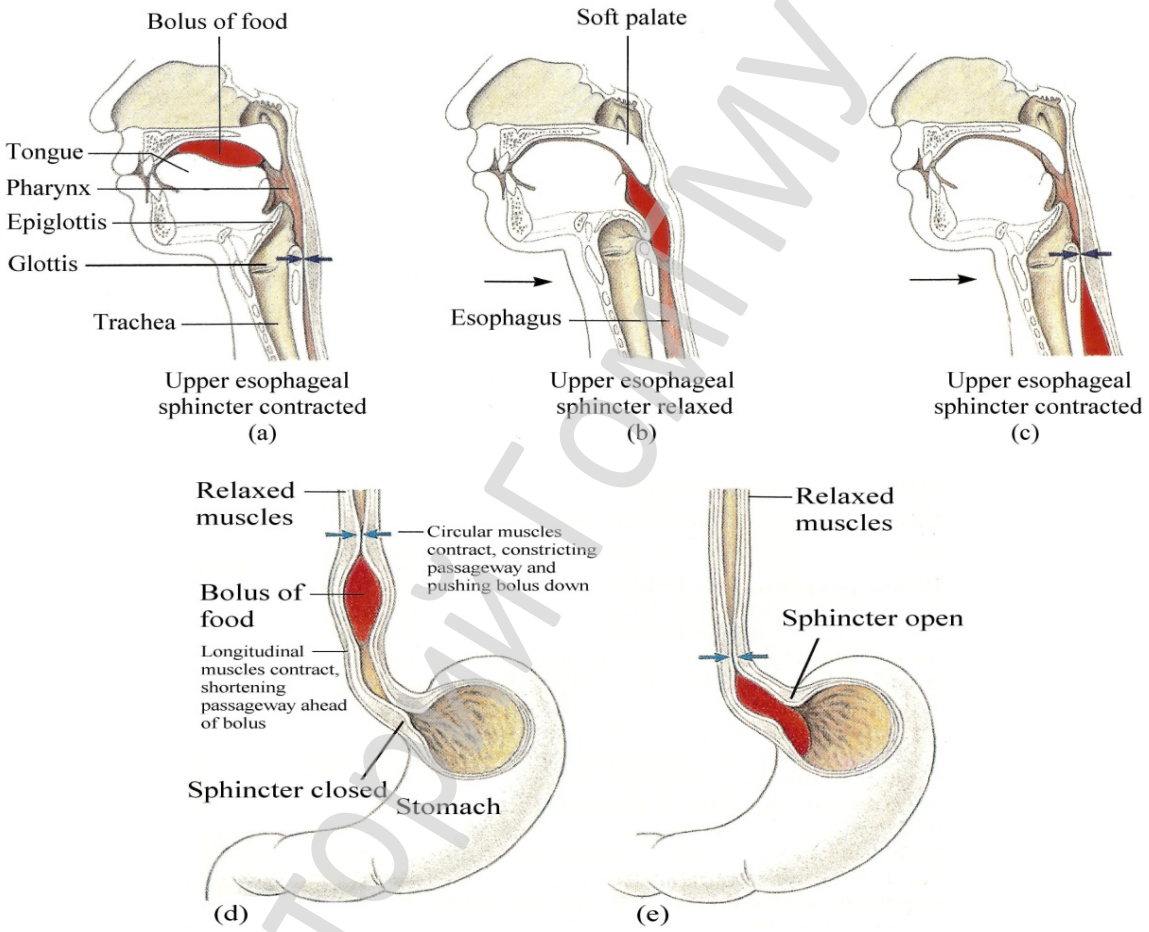


Figure 2.4 —Swallowing (by Elaine N. Marieb, 1989)

During the buccal phase, the tongue rises and presses against the hard palate; doing so, it forces the food bolus into the oropharynx (Figure 2.4, «a»). Once the food enters the pharynx, the involuntary phase of swallowing begins. The food passage into the respiratory passageways is prevented by the rising of the uvula and larynx and relaxation of the upper esophageal sphincter, which makes it possible for the food to enter the esophagus (Figure 2.4, «b»,). The constrictor muscles of the pharynx contract forcing the food into the esophagus inferiorly, and the upper esophageal sphincter contracts once the food has entered (Figure 2.4, «c»). The food is pushed along the length of the esophagus to the stomach by peristaltic waves (Figure 2.4, «d»). The gastroesophageal sphincter opens, and the food enters the stomach (Figure 2.4, «e»).

2.3. Digestion in the stomach

The stomach (Figure 2.5) performs a number of digestive and non-digestive functions.

Non-digestive functions of the stomach:

1. It participates in the regulation of the processes of erythropoiesis (produces Castle's intrinsic factor necessary for B_{12} vitamin absorption).
2. It participates in the mechanisms of pH regulation and hemopoesis (homeostatic function).
3. It performs the excretory function (excretion of heavy metals, some medical substances and drugs from the organism).
4. It performs the endocrine function (there are a number of endocrine cells which form the peptides of the digestive system).
5. It performs the protective function (secreted HCl is bactericidal for microorganisms).

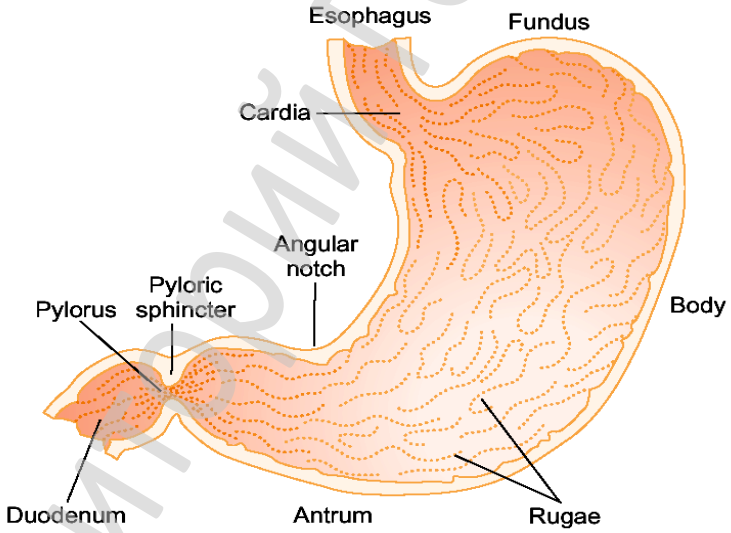


Figure 2.5 — Anatomy of the stomach (from studylib.net)

Digestive functions:

1. Deposition of food.
2. Mixing of food.
3. Food is exposed to chemical (enzymatic) digestion.
4. Portion evacuation into the duodenum.
5. Absorption of some substances (for example, water).

The enzymes of acidic gastric juice may influence food proteins only in a relatively narrow zone of the food contents which is either in direct contact with the mucous membrane of the stomach or close to it, where gastric juice is able to diffuse and is not neutralized due to the buffer properties of the food.

The whole mass of the food in the stomach is not mixed with the juice. As the food is chemically processed and becomes more fluid, its layer adjacent to the mucous membrane is moved to its antral part by motions of the stomach and is further evacuated into the intestines.

2.3.1. Secretory activity of the stomach

Gastric juice is produced by the gastric glands located in the mucous membrane. The glands in the fornix of the stomach contain several types of cells (Figure 2.6):

— *main glandulocytes (chief cells),* which produce pepsinogens;

— *parietal glandulocytes (coating cells),* which synthesize and excrete hydrochloric acid;

— *mucocytes (additional cells),* which excrete mucoid secret.

In the pyloric parts of the stomach, there are no parietal glandulocytes. Due to the difference in the structure of the fundus and pyloric glands, they produce juice of different composition. The leading role in gastric digestion is played by the gastric juice of the fundus.

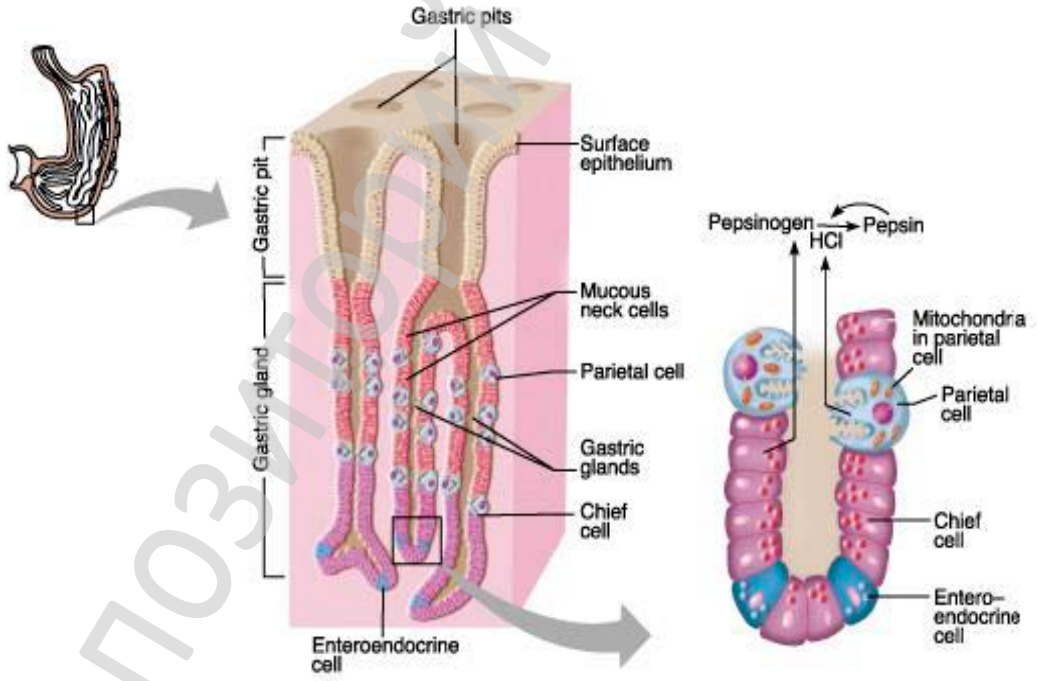


Figure 2.6 — Structure of the gastric glands (from bianoti.com)

The human stomach secretes 2.0–2.5 liters of gastric juice per day. It represents a transparent fluid containing hydrochloric acid (0.3–0.5 %) and therefore has an acid reaction (pH 1.5–1.8). The pH level of the chyme in the stomach is much higher, as the juice of the glands of the fundus is partially neutralized by the ingested food. The faster the gastric juice is secreted, the lesser it is neutralized and the higher its acidity is.

HCl performs the following functions:

1. Activation of pepsinogen into pepsin.
2. Denaturation and swelling of proteins (promotes protein hydrolysis).
3. Antibacterial function.
4. Stimulation of gastric motor activity.
5. Stimulation of hormone formation (HCl comes into the duodenum, causes production of the hormones of secretin and cholecystokinin. These hormones are absorbed into the blood, approach the pancreas and stimulate it).
6. Evacuation of the chyme (obturative pyloric reflex).

2.3.2. Composition and properties of gastric juice

Gastric juice contains many inorganic substances: chlorides, sulphates, bicarbonate of sodium, potassium, calcium and magnesium, ammonia (Table 2.2.). The osmotic pressure of gastric juice is higher than that of blood plasma.

Table 2.2 — Composition of gastric juice

<table>
<tr><th colspan="3">Organic components</th><th>Inorganic components</th></tr>
<tr><th colspan="2">Digestive enzymes</th><th>Other organic substances</th><td rowspan="6">Hydrochloric acid
Na^+
K^+
Ca^{2+}
Mg^{2+}
Chlorides
Sulphates,
Bicarbonates
(and others)</td></tr>
<tr><th>Name of the enzyme</th><th>Role of the enzyme</th><td rowspan="5">Mucoids
Castle's intrinsic factor
Urea
Urinary acid
Lactic acid
Amino acids
Polypeptides</td></tr>
<tr><td>Pepsin and gastricsin
(they are secreted in inactive form — pepsinogens — and act in the presence of HCl)</td><td>They split proteins with the formation of large polypeptides</td></tr>
<tr><td>Chymosin</td><td>It coagulates milk proteins. It can be found in gastric juice mainly in children.</td></tr>
<tr><td>Gelatinase</td><td>It splits gelatin</td></tr>
<tr><td>Lipase</td><td>It splits fats (especially the emulsified fat of milk during breast feeding).
The activity of this enzyme in gastric juice of adults is insignificant</td></tr>
</table>

The organic components of gastric juice are represented by a large number of nitrogen-bearing substances (200–500 mg/L): urea, urinary and lactic acids, amino acids, polypeptides. The organic substances are the products of the secretory activity of the gastric glands and metabolism in the mucous membrane of the stomach. Enzymes have a special value for digestion.

The main *glandulocytes* of the gastric glands synthesize and secrete **pepsinogens of two groups** (Figure 2.7). The pepsinogens of the first group (5 of them) are formed in the fornix of the stomach, the second group (2 of

them) — in the pyloric part of the stomach. Actually, pepsins are considered to be enzymes hydrolyzing proteins at the maximal rate at a pH level of 1.5–2.0. Their other fraction hydrolyzes proteins at the optimum pH level of 3.2–3.5 and is called *gastricsin.* Pepsin and gastricsin influence different kinds of proteins. Pepsins are able to coagulate milk proteins. The ability of pepsins to operate at many pH levels is of great importance in gastric proteolysis, which occurs at different pH levels depending on the volume and acidity of gastric juice, buffer properties, and amount of the ingested food. The proteases of gastric juice split up proteins into large polypeptides. The proteins subjected to the preliminary action of gastric proteases form fragments of protein molecules, which then can be easier split by the proteases of the juice of the pancreas and the small intestine.

Gastric juice in an adult has low *lipolytic* activity. This lipolytic activity has an important value for babies during their breast feeding (breakdown of emulsified milk fat).

The important component of gastric juice is *mucoids.* Mucus, containing mucoids, protects the membrane of the stomach from mechanical and chemical stimulations.

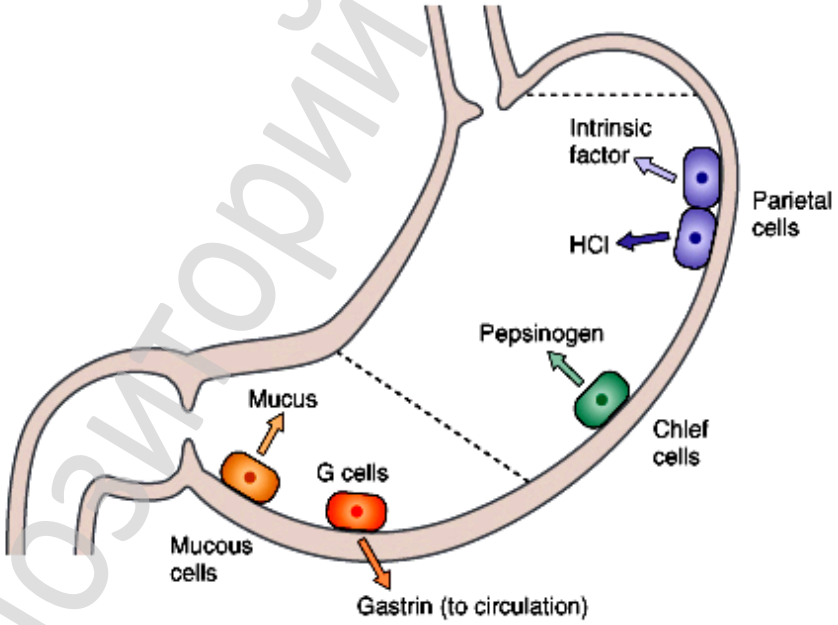


Figure 2.7 — Main types of the stomach cells and the predominant areas of their localization (by C. Guyton and John E. Hall, 2016)

The glands of the pyloric parts of the stomach secrete a small amount of juice of the alkalescent reaction with a big proportion of mucus. The secret of the pyloric glands has low proteolytic, lipolytic, and amylolytic effects. The alkaline pyloric secret partially neutralizes the acidic contents of the stomach evacuated from the stomach into the duodenum.

2.3.3. Regulation of gastric secretion

Without digestion the glands of the human stomach secrete a small amount of gastric juice. Food intake sharply enlarges the secretion by the glands of the stomach body (but not the pyloric glands) as a result of the stimulation of the gastric glands by nervous and humoral mechanisms.

The main and parietal *glandulocytes, mucocytes* of the gastric glands, are stimulated by the secretory fibers included into the structure of the *vagus nerve*. The terminals of these fibers secrete acetylcholine, which stimulates the gastric glands. Dissection of the vagus nerves results in low gastric secretion (this operation is sometimes performed in order to normalize the secretion during its augmentation). *The sympathetic nerves* have an inhibiting effect on the gastric glands reducing the volume of secretion. However, the combination of the sympathetic influences with other factors stimulating the gastric glands leads to the secretion of juice with a high amount of pepsin, since the sympathetic fibers in the main glandulocytes strengthen the synthesis of pepsinogen.

The potent stimulator of the gastric glands is gastrin. It is liberated from G-cells, the majority of which are in the mucous membrane of the pyloric parts of the stomach. The secretion of gastrin is increased by the influence of the vagus nerve and also by the local mechanical and chemical stimulation of this part of the stomach. If the pH in the pyloric part of the stomach goes down (if the secretion of hydrochloric acid by the gastric glands rises), the release of gastrin decreases and at a pH level of 1.0 it ceases. Thus, gastrin takes part in the self-regulation of the gastric secretion depending on the volume of the pH of the pyloric parts of the stomach.

The stimulator of the gastric glands is histamine, which is formed in the mucous membrane of the stomach. It stimulates the secretion of a great amount of highly acidic juice.

Secretin and cholecystokinin inhibit the secretion of hydrochloric acid stimulated by gastrin (less by histamine), but strengthen the secretion of pepsins.

Other intestinal hormones *(neurotensin, somatostatin, serotonin)* also inhibit the secretion of hydrochloric acid in the stomach. The acidity of the duodenal contents inhibits the secretion of hydrochloric acid by the glands of the stomach (self-regulation) due to the reflex principle and duodenal hormones.

The secretion of gastric juice includes three phases.

2.3.4. Phases of gastric secretion

The initial secretion of gastric juice is stimulated by food intake. Excitation comes to the glands as conditioned reflexes in response to the stimulation of the receptors of the eye, ear, and nose induced by the sight and smell of food, sounds of the whole surroundings related to food intake. They are joined with unconditioned reflexes arising during the stimulation of

the receptors of the oral cavity and esophagus. Nervous influences have starting effects. This gastric secretion is called **the first,** or **«cephalic» phase of secretion** (Table 2.3, Figure 2.8).

Table 2.3 — Phases of gastric secretion

Phase of stomach secretion	Mechanism of the stimulation of secretion	Example of an experiment which proves the presence of the phase	Physiological role of the phase	Reflex arc
«cephalic» phase	conditioned reflexes	Sight and smell of food lead to the secretion of gastric juice which can be received in dogs with the fistula of the stomach	The stomach is prepared for food intake	1) visual, auditory, olfactory receptors; 2) cortex of the cerebrum; 3) hypothalamus; 4) nuclei of the vagus nerve in the medulla; 5) gastric glands
	unconditioned reflexes	The so-called false feeding of dogs which have undergone esophagostomy with the fistula of the stomach (in this dog food does not get into the stomach, but, 5–10 min after the beginning of feeding the secretion of gastric juice begins)	The stomach is prepared for food intake	1) receptors of the oral cavity, esophagus; 2) nuclei of the vagus nerve in the medulla; 3) gastric glands
gastric phase	unconditioned reflexes, humoral regulation	Ingestion of food or some solutions into the stomach through the fistula, or stimulation of the mechanoreceptors of the stomach produce the secretion of gastric juice	Correction of the amount and composition of gastric juice according to the properties of the ingested food	1) chemoreceptors and mechanoreceptors of the mucous membrane of the stomach; 2) nuclei of the vagus nerve in the medulla; 3) gastric glands; 4) regulation of the secretion of the gastric glands is made by nerve and humoral (gastrin) mechanisms
intestinal phase	unconditioned reflexes, humoral regulation	Ingestion of some kinds of food (meat bouillon, cabbage juice, hydrolysates of proteins) into the small intestine produces the secretion of gastric juice	Correction of the amount and composition of gastric juice according to the properties of partially digested food which came into the intestines	1) chemoreceptors and mechanoreceptors of the mucous membrane of the intestine; 2) nuclei of the vagus nerve in the medulla; 3) gastric glands. The regulation of the secretion of the gastric glands is made by nerve and humoral (secretin and cholecystokinin) mechanisms

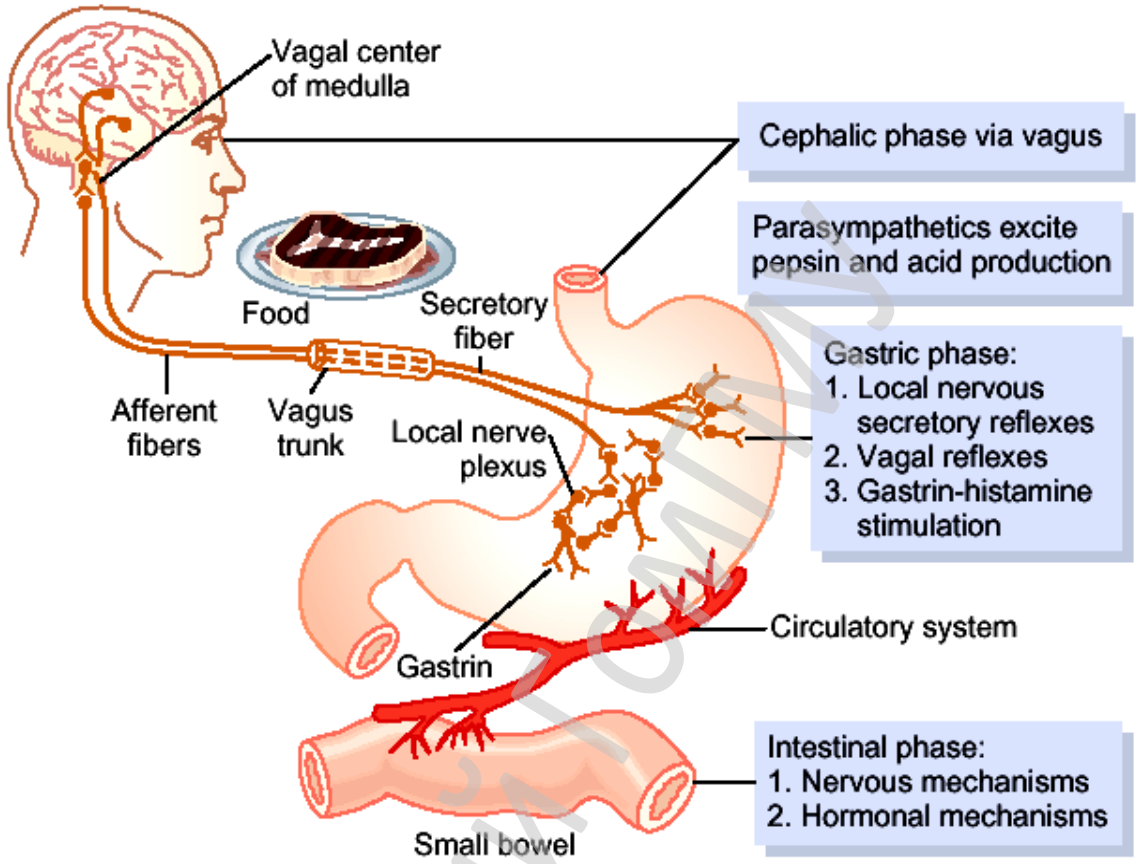


Figure 2.8 — Phases of gastric secretion (by C. Guyton and John E. Hall, 2016)

The fact that proves the presence of the first phase of gastric secretion is the experience of the so-called false feeding of dogs which have undergone esophagostomy with the fistula of the stomach. During feeding of such dogs, the food drops out of the esophagus and does not get into the stomach, however, 5–10 min after the beginning of the imaginary feeding, the secretion of gastric juice begins.

The juice produced in the stomach and caused by the smell and sight of food, chewing and swallowing was called «appetizing» by Academician I. P. Pavlov. Owing to its secretion, the stomach is ready for food intake.

The conditionally-reflectory secretion of gastric juice is induced by the sight of food, sounds accompanying eating (sounds of plates and forks), etc. The reflex influences on the gastric glands are transferred through the vagus nerves.

The secretion during the «cephalic» phase is easily inhibited by the influence of external (poor table setting, unpleasant odour) and internal factors.

The first phase of the secretion is overlaid by **the second phase,** called **the gastric phase,** as it is produced by the action of the digestive contents on the mucous membrane of the stomach.

The presence of the given phase of the secretion is proved by the fact, that the introduction of food into the stomach through the fistula, introduction of some solutions through it or a probe into the stomach, and, finally, stimulation of the mechanoreceptors of the stomach produce the secretion of gastric juice. The volume of the secret thus is 2–3 times less than that during natural ingestion of food. Gastric secretion in the second phase is intensified due to the reflexes arising under the effect of the stomach contents on the receptors of the stomach and also by the neurohumoral way.

Some kinds of food (meat bouillon, cabbage juice, hydrolysates of proteins) when administered into the small intestine produce the secretion of gastric juice. Afferent influences from the intestines on the glands of the stomach stimulate their secretion in **the third phase,** called **the intestinal phase.** The stimulating and inhibiting influences from the duodenum and jejunum on the glands of the stomach are carried out by nervous and humoral mechanisms. The secretion of gastric juice is stimulated by the entering of the insufficiently digested chyme of low acidity into the duodenum. The hydrolysis products, which are absorbed in the intestines, also stimulate gastric secretion. If the acidic chyme gets into the intestines, the secretion of gastric juice is inhibited. The inhibition of the secretion is caused by the products of hydrolysis of fats, starch, polypeptides, amino acids, which are found in the intestines.

2.3.5. Motor function of the stomach

The contractions of the smooth muscles of the stomach walls perform the motor function of the stomach. It provides *deposition* of the ingested food in the stomach, *its mixing* with gastric juice, *transporting of the gastric contents* and, finally, *portion evacuation* of the *gastric contents* into the duodenum.

During meals and soon after them the stomach is relaxed — *digestive receptive relaxation*. After a while, depending on the kind of ingested food, the contractions increase.

The regulation of gastric motor activity is carried out by nervous and humoral mechanisms. The influences coming along the efferent fibers of the vagus nerves strengthen the motility of the stomach: they increase the rate and force of the contractions, the rate of the peristaltic waves, accelerate evacuation of the gastric contents.

The influences going through the sympathetic nerves reduce the rate and force of the contractions and also the rate of the peristaltic waves.

Gastrointestinal hormones play an important role in the regulation of gastric motor activity. The motility of the stomach is forced by gastrin, motilin, serotonin, and insulin. Secretin and cholecystokinin cause inhibited gastric motor activity.

Transition of food from the stomach into the intestines. Mixed food in the stomach of an adult may stay for about 6–10 hours. Foods heavy in carbohydrates empty fastest, followed by high-protein foods. Fatty food is evacuated from the stomach at the slowest rate. Fluids start to pass into the intestines immediately after they enter the stomach.

2.3.6. Vomiting

Vomiting is a complex reflex motor act arising from contractions of the small intestine. As a result of these contractions, some part of the contents of the intestines is pushed out into the stomach. After 10–20 sec the stomach start to contract opening the entrance into it, the muscles of the abdominal wall and diaphragm are strongly contracted owing to which the contents of the stomach at the moment of expiration are expelled through the esophagus into the oral cavity.

Vomiting has a protective value and *arises reflexively* as a result of the stimulation of the receptors of the root of the tongue, pharynx, mucous membrane of the stomach, intestines, vestibular apparatus (in travel-sickness or sea-sickness). Vomiting may be caused by olfactory and gustatory stimulations producing the sensation of disgust (conditioned reflex vomiting). Vomiting is caused by some substances (for example, alkaloid apomorphin) which influence *the nerve center of vomiting*, situated in the medulla.

Review questions

1. Give the definitions of "hunger" and "satiety". What are the objective and subjective manifestations of hunger? Where are the centers of hunger and satiety located? List the theories of hunger. What are the types of satiety? What are the types of digestion?

2. Name the three pairs of the large salivary glands. What are the components and properties of saliva? What is the physiological role of saliva? How does the sympathetic and parasympathetic nervous system affect salivation?

3. What are the phases of swallowing? Characterize them.

4. List the digestive and non-digestive functions of the stomach. What types of glandular cells are present in the stomach? What are the composition and properties of gastric juice? What is the physiological role of hydrochloric acid in the stomach? Name the enzymes of gastric juice and their functions. What are the features of the juice of the pyloric glands?

5. What are the phases of the regulation of gastric secretion? Describe them.

6. What does the motor function of the stomach provide? How is the gastric motility regulated?

2.5. Digestion in the small intestine

Digestion in the small intestine provides depolymerization of nutrients up to the stage (basically of monomers) in which they are absorbed from the intestines into the blood and lymph. The digestive process in the small intestine takes place first in its cavity *(cavitary digestion)* and then in the region of the intestinal epithelium with the help of enzymes fixed on its microvilli and in glycocalix *(parietal digestion).*

Cavitary and parietal digestion are carried out by the enzymes of pancreatic juice and intestinal enzymes; the important role in intestinal digestion is played by bile.

2.5.1. Secretory activity of the pancreas. Composition and properties of pancreatic juice

The human pancreas secretes 1.5–2.0 liters of juice a day. This juice is a product of the activity of secretory pancreacytes. It is a colorless transparent fluid, its pH is 7.8–8.4. The alkalinity of the juice is caused by the presence of sodium bicarbonates. The juice also contains sodium and potassium chlorides. Pancreatic juice is rich in enzymes which digest proteins, fats, and carbohydrates (Table 2.4). *Amylase, lipase,* and *nucleases* are secreted by the pancreas in the active state and proteases are formed by zymogen-like cells which are activated by the action of other enzymes.

Table 2.4 — Composition of pancreatic juice

<table>
<tr><th colspan="2">Organic components</th><th>Inorganic components</th></tr>
<tr><td colspan="2">Digestive enzymes</td><td rowspan="9">Bicarbonates (cause the alkalinity of juice)
Chlorides
Na^+
K^+</td></tr>
<tr><td>Name of enzyme</td><td>Role of enzymes</td></tr>
<tr><td>Trypsin (synthesized in an inactive form — trypsinogen, which turns into trypsin in the duodenum under action of its enzyme enterokinase; Ca^{2+} accelerate the process)</td><td rowspan="3">They split proteins and large polypeptides with the formation of small peptides and amino acids</td></tr>
<tr><td>Chymotrypsin (synthesized in inactive form — chymotrypsinogen, which is activated by trypsin)</td></tr>
<tr><td>Elastase (synthesized in inactive form — proelastase, which is activated by trypsin)</td></tr>
<tr><td>Carboxypeptidases A and B. (synthesized in inactive form — procarboxypeptidases A and B, which are activated by trypsin)</td><td>They split ends of proteins and peptides</td></tr>
<tr><td>Lipase</td><td rowspan="3">They split fats (emulsified by the action of salts of bile acids) with the formation of mono-glycerides and fatty acids</td></tr>
<tr><td>Phospholipase</td></tr>
<tr><td>Esterase</td></tr>
</table>

Organic components		Inorganic components
Alpha-amylase	It splits carbohydrates: (polysaccharides) with the formation of oligosaccharides, disaccharides, monosaccharides	
Ribonuclease and dezoxyribonuclease	They split nucleic acids with the formation of nucleotides	

Trypsinogen of pancreatic juice in the duodenum under the effect of its enzyme *enterokinase* turns into *trypsin* (Figure 2.9). The process is accelerated by Ca^{2+} ions.

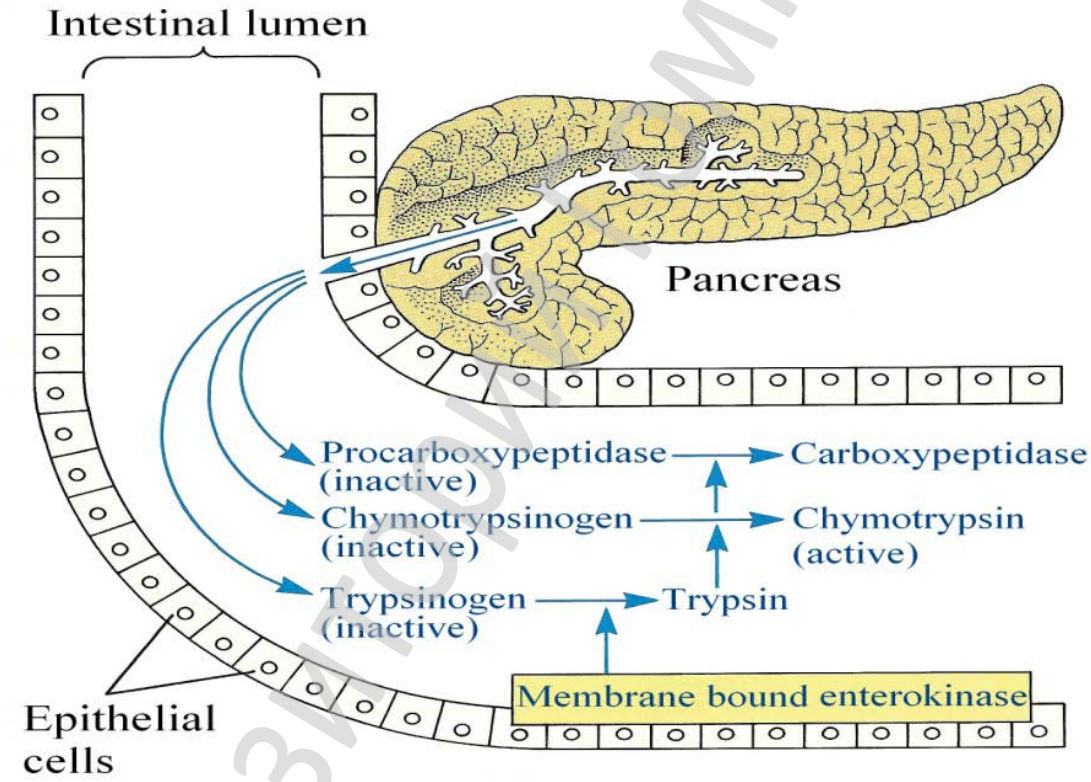


Figure 2.9 — Activation of pancreatic proteases in the small intestine (by Elaine N. Marieb, 1989)

The second enzyme from the group of pancreatic proteases — *chymotrypsin* — is also synthesized in an inactive form as *chymotrypsinogen,* which is activated by trypsin. The pancreas synthesizes *procarboxypeptidases A and B and others.* They are activated by trypsin with the formation of the corresponding peptidases.

Pancreatic juice is rich in ά-amylase, splitting polysaccharides. Pancreatic lipase splits fats into monoglycerides and fatty acids. The hydrolysis of fats with lipase requires the presence of bile (salts of bile acids) and Ca^{2+} ions.

2.5.2. Regulation of pancreatic secretion

The secretion of the pancreas is regulated by the nervous and humoral mechanisms.

The initial secretion of the pancreas is produced by the sight, smell of food, other stimuli *(conditioned stimuli),* and also chewing and swallowing *(unconditioned stimuli).* The nervous signals which are formed in the receptors of the oral cavity and pharynx, reach the medulla, and then efferent influences along the fibers of the vagus nerve reach the gland and produce its secretion.

The stimulation of the vagus nerve causes the secretion of a small amount of pancreatic juice rich in enzymes. The sympathetic fibers innervating the pancreas inhibit its secretory activity. Therefore, after the section of the celiac nerves in a dog, pancreatic secretion increases. The sympathetic influences strengthen the synthesis of organic substances included into pancreatic juice.

Inhibition of pancreatic secretion is observed in pain reactions, during sleep, intense physical and mental work.

The humoral regulation has the leading value in the stimulation of pancreatic secretion.

The introduction of hydrochloric acid into the duodenum produces excessive secretion of pancreatic juice. Under the influence of hydrochloric acid in the duodenum the hormone called *secretin* is formed.

Secretin produces the secretion of a great amount of pancreatic juice rich in bicarbonates but poor in enzymes.

The second hormone intensifying the secretion of the pancreas is *cholecystokinin,* which stimulates the secretion of the pancreas and release of bile into the duodenum (Figure 2.10).

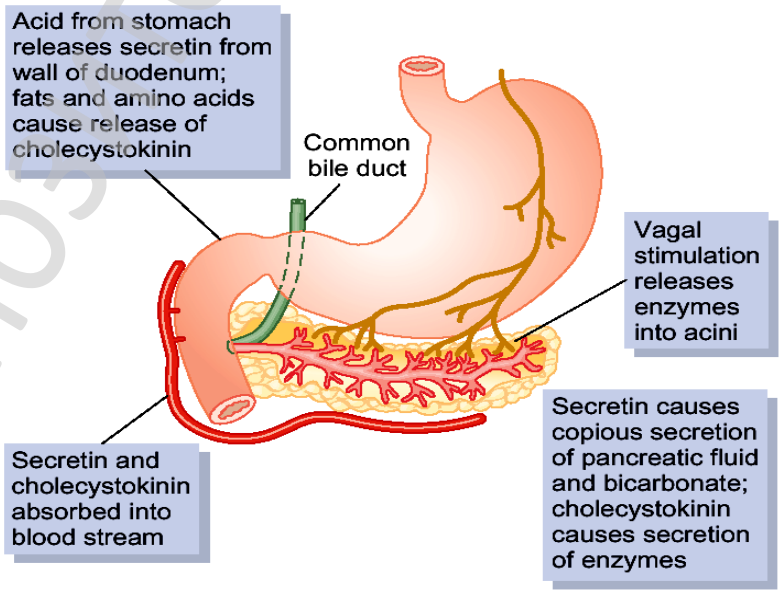


Figure 2.10 — Action of the vagus, cholecystokinin, and secretin on pancreatic secretion (by C. Guyton and John E. Hall, 2016)

Nervous influences during food ingestion provide *only starting effects on the gland,* however in the correction of pancreatic secretion a big role is played by the humoral mechanisms.

The phases of pancreatic secretion during its stimulation by food intake are similar to those of gastric secretion, however, the hormonal influences on the pancreas, especially during the intestinal phase, are more expressed.

2.5.3. Bile, its composition and participation in digestion

Bile is a product of the activity of the liver. Its participation in digestion is manifold. The arrest of bile secretion into the intestines (in obstruction of the common cholic duct) essentially disturbs the process of digestion in the organism and results in severe metabolic disorders.

Functions of bile:

1. Emulsification of fats promoting their hydrolysis (Figure 2.11).
2. It strengthens the action of lipolytic enzymes. It helps to fix enzymes on the surface of enterocytes and thus improves membrane digestion.
3. It strengthens the motility of the intestines.
4. It participates in neutralization of acidic products which have come from the stomach.
5. It promotes absorption of fatty acids, liposoluble vitamins, cholesterin, amino acids, and salts of calcium.
6. It inhibits decay process in the intestines.
7. Protective function (has a bacteriostatic action).
8. It stimulates bile formation (the more bile is released from the organism, the more bile is formed).
9. Excretion of bilirubin.

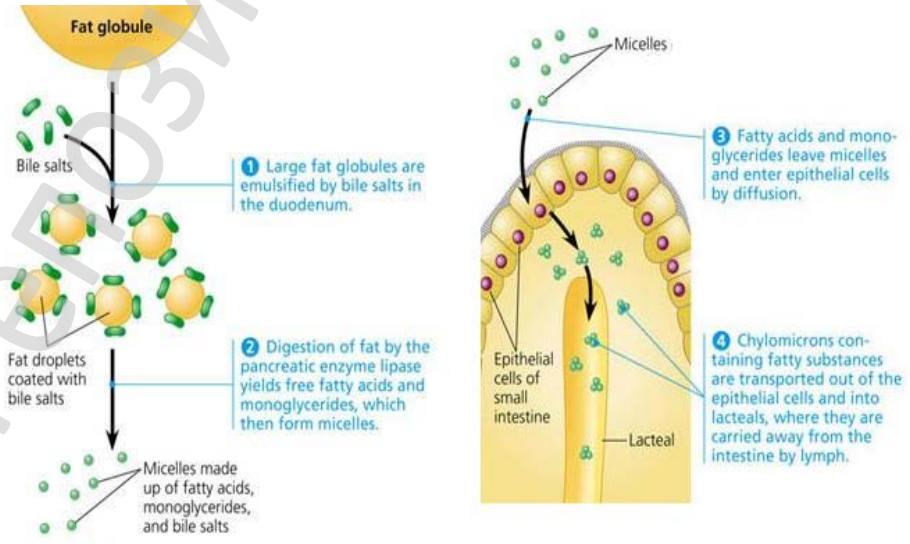


Figure 2.11 —Role of bile in fat digestion and absorption (from studylib.net)

About 500–1500 mL of bile is produced in humans every day. The process of bile formation goes continuously, entering of bile into the duodenum — *biliary secretion* — periodically, basically during meals. If the stomach is empty, bile does not reach the intestines, but goes to the gall bladder, where it becomes concentrated and slightly changes its composition. Therefore, there are two kinds of bile — hepatic and cystic.

Bile contains amino acids, vitamins, and other substances. Bile has low catalytic activity; the pH of hepatic bile is 7.3–8.0.

The main components of bile are water and bile acids. C*holic* and *chenodeoxycholic acids* (**primary**) are formed in the human liver, and they are secreted into the ileum with bile. The basic amount of bile acids and their salts is contained in bile as compounds of glycine and taurine. In human bile, *glycocholic* acids are about 80 %. Bile acids and their salts determine the basic properties of bile as of an alimentary secret (Table 2.5). Up to 20 % of primary bile acids are converted into **secondary** (*deoxycholic and lithocholic*) under the influence of anaerobic intestinal bacteria and are excreted through the gastrointestinal tract (Figure 2.12).

Table 2.5 — Composition and functions of bile

Organic components of bile	**Inorganic components of bile**	**Functions of bile**
Bile acids — cholic and chenodeoxycholic acids — and their salts (in bile they are contained as compounds with glycine and taurine; glycocholic acids — 80% and taurocholic acids — 20%) *Bile pigments* (bilirubin and biliverdin) *Cholesterol* *Phospholipids* *Mucin* *Amino acids*	Na^+ K^+ Ca^{2+} Mg^{2+} Chlorides Bicarbonates (HCO_3^-) Phosphates (and others)	1. Emulsification of fats which promote their hydrolysis. 2. It strengthens action of lipolytic enzymes. 3. It strengthens the motility of the intestines. 4. It participates in neutralization of acidic products which have come from the stomach. 5. It promotes absorption of fatty acids, liposoluble vitamins, cholesterin, amino acids and salts of calcium. 6. It inhibits decay process in the intestines. 7. Protective function (bile has a bacteriostatic effect). 8. It stimulates bile formation. 9. Excretion of bilirubin.

About 85–90 % bile acids secreted into the intestines with bile are absorbed from the small intestine into the blood. The bile acids absorbed into the blood are brought to the liver and included into the composition of bile. Other 10–15 % bile acids are excreted from the organism basically as part of excrements. This loss of bile acids is supplied with their synthesis in the liver.

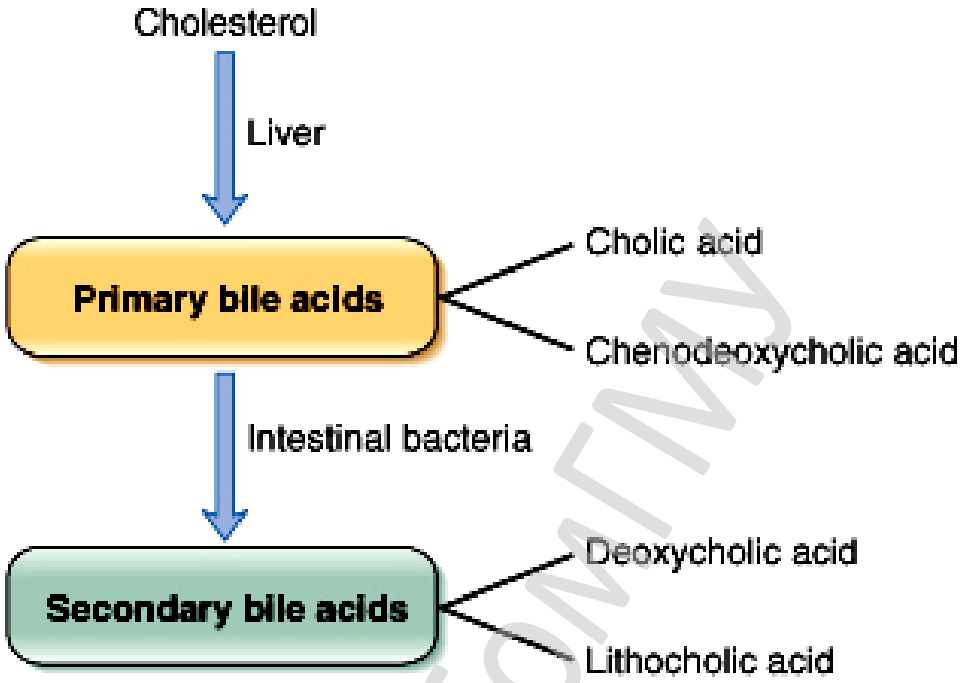


Figure 2.12 — Primary and secondary bile acids (from slideplayer.com)

Bile pigments are liver-secreted final products of the breakdown of hemoglobin and other derivative porphyrins. The basic bile pigment — *bilirubin* is of the yellow color responsible for the typical color of hepatic bile. The other pigment — *biliverdin* — is contained at insignificant amounts in human bile (it is of green color).

Cholesterol in bile is in a dissolved state, mainly due to the salts of bile acids.

Bile formation occurs by means of the active secretion of its components (bile acids) by hepatocytes, active and passive transport of some substances from the bloodstream (water, glucose, creatinine, electrolytes, vitamins, hormones, etc.) and reabsorption of water and of some substances from bile capillaries, ducts, and gallbladder. Bile formation is stimulated by eating and varies depending on different kinds of food.

Bile itself also participates in the humoral regulation of bile formation (Figure 2.13). The more bile acids come from the small intestine into the blood of the portal vein, the more of them are secreted in the composition of bile and less bile acids are synthesized by hepatocytes. If less bile acids enter the bloodstream, their deficiency is refilled by the intensified synthesis of bile acids in the liver. Secretin increases biliary secretion; biligenesis is weaker stimulated by glucagon, gastrin, and cholecystokinin.

The stimulation of the vagus nerves, the secretion of bile acids into the intestines and high protein foods increase not only bile formation but also the secretion of organic components.

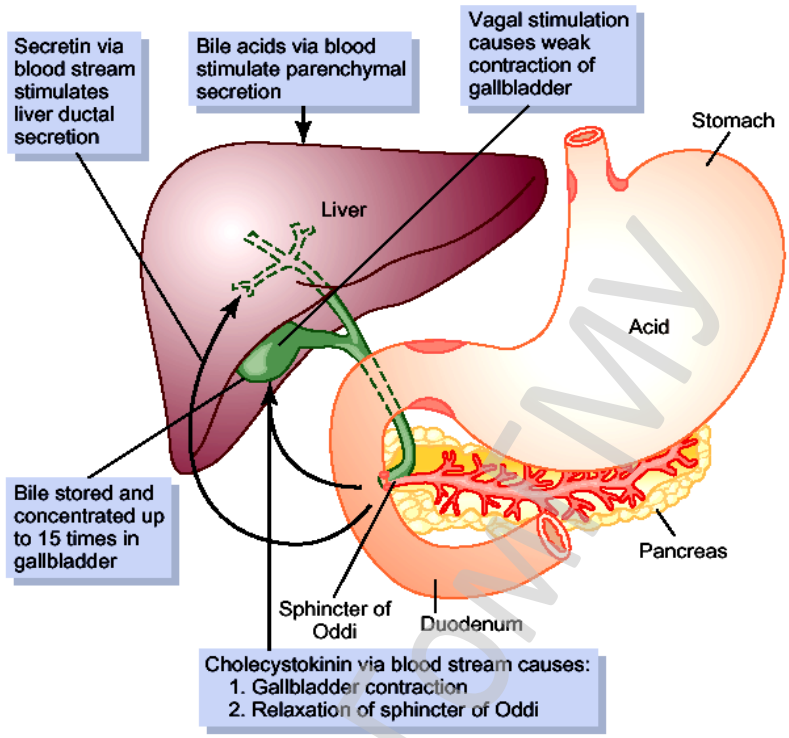


Figure 2.13 — Regulation of bile secretion and gallbladder emptying (by C. Guyton and John E. Hall, 2016)

2.5.4. Intestinal secretion

Intestinal juice represents a turbid, enough viscous fluid. It is a product of the activity of all the mucous membranes of the small intestine. The intestinal glands are situated in the mucous membrane of the duodenum and the whole small intestine (Figure 2.14).

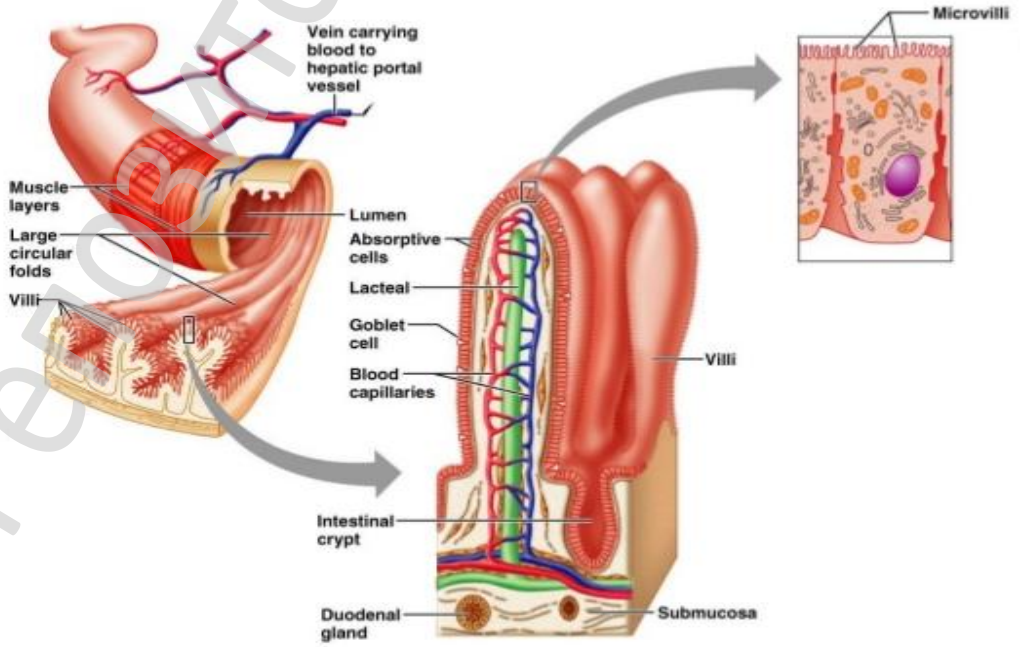


Figure 2.14 — Structure of the intestinal walls (from bianoti.com)

In the mucous membrane of the superior part of the duodenum, there are a large number of the duodenal glands. By the structure and functions, they are similar to the glands of the pyloric part of the stomach. The juice of the duodenal glands is a colorless fluid of alkaline reaction, it has low proteolytic, amylolytic and lipolytic activity (Table 2.6).

Table 2.6 — Composition of the juice of the small intestine

<table>
<tr><th colspan="2">Organic components</th><th rowspan="2">Other organic substances</th><th>Inorganic components</th></tr>
<tr><th colspan="2">Digestive enzymes</th><td rowspan="7">Mucus
Proteins
Amino acids
Urea
Non-destructed epithelial cells and fragments of cells</td><td rowspan="7">Na^+
K^+
Ca^{2+}
Chlorides
Bicarbonates
Phosphates</td></tr>
<tr><th>Name of enzyme</th><th>Role of enzyme</th></tr>
<tr><td>Protein-digesting enzymes: enterokinase, peptidases (dipeptidase, aminopeptidase)</td><td>They split small peptides, dipeptides with the formation of mainly aminoacids</td></tr>
<tr><td>Carbohydrate-digesting enzymes: amylase, lactase, saccharase</td><td>They split dextrins and oligosaccharides with the formation of the main monosaccharides</td></tr>
<tr><td>Fat-digersting enzymes: lipase, phospholipase</td><td>They split fats with the formation of monoglycerides and fatty acids</td></tr>
<tr><td>Alkaline phosphatase</td><td>It splits the residue of phosphoric acid from the organic ether compounds of phosphoric acid</td></tr>
<tr><td>Nuclease</td><td>It splits nucleotides with the formation of N-containing bases, ribose, deoxyribose, phosphate</td></tr>
</table>

During centrifugation intestinal juice is divided into fluid and dense parts. The fluid part of the juice is formed by water solutions of inorganic and organic substances transported from the blood, and by partially destroyed cells of the intestinal epithelium. Among inorganic substances there are chlorides, bicarbonates, and phosphates of sodium, potassium, calcium; the pH of the secret is 7.2–7.5. Organic substances of the fluid part of the juice include mucus, proteins, amino acids, urea, and other metabolic products of the organism. The dense part of the juice is yellow and grey mass. It looks like mucous lumps, consists of non-destructed epithelial cells, their fragments and mucus, or the secret of goblet cells. In the mucous membrane of the small intestine there is a continuous change of the layers of the superficial epithelium cells.

The dense part of the juice has much greater catalytic activity than the fluid one. The basic part of enzymes is synthesized in the mucous membrane of the intestines but some of them are transported from the blood. *Intestinal juice*

has more than 20 various enzymes participating in digestion (Table 2.6). The basic enzymes among them are: *enterokinase,* some *peptidases, alkaline phosphatase, nuclease, lipase, amylase, lactase, saccharase.* In natural conditions they are fixed in the region of the brush border and carry out parietal digestion. The secretion of the intestinal glands is intensified during meals, during local mechanical and chemical stimulation of the intestines and under the influence of some intestinal hormones.

The leading value of intestinal secretion belongs to local mechanisms. During the mechanical stimulation of the mucous membrane of the small intestine, the secretion of the fluid part of the juice increases sharply. The chemical stimulators of the small intestine are the products of the digestion of proteins, fats, pancreatic juice, hydrochloric acid (and other acids). The products of the digestion of nutrients under their local action produce the secretion of intestinal juice rich in enzymes.

Depending on location, the processes of nutrient digestion in the small intestine can be carried out both in the cavity of the small intestine (**distant or cavitary digestion**), and on the surface of the intestinal wall mucosa and on the enterocyte membrane. Here within the area of the brush border, enzymes are fixed to the microvilli, which carries out **contact (parietal, membrane)** digestion. Parietal digestion was discovered in 1957 by A. M. Ugolev.

Parietal digestion has a number of advantages over cavitary digestion:

1) in parietal digestion, the optimal orientation of enzymes and their substrates increases the rate of hydrolysis thus ensuring the maximum activity of enzymes;

2) it prevents the development of a pathogenic microflora, the absorption of substances occurs from the sterile zone;

3) digestion is isolated from a competing microflora (conditionally pathogenic microorganisms which live in the intestine cannot pass through the spaces between the microvilli);

4) parietal digestion increases the "lifetime" of enzymes (cavitary enzymes are removed with the chyme).

2.5.5. Motor activity of the small intestine

The motor activity of the small intestine provides the *mixing of alimentary contents* with alimentary secrets, *passing of the chyme* into the intestines, change of the layer of the chyme and its mucous membrane, *high intraintestinal pressure* promoting absorption of some components of the chyme from the intestinal cavity into the blood and lymph.

The contractions of the small intestine occur as a result of coordinated movements of the longitudinal (external) and transversal (circulatory, i.e.

internal) layers of smooth muscles. According to the functional principle, all the contractions are divided into two groups:

1) local, they provide the mixing of the contents of the small intestine;

2) aimed at the removal of the intestinal contents.

There are some types of contractions:

1. Rhythmic segmentation (Figure 2.15)

2. Pendulum.

3. Peristaltic (very slow, slow, fast, prompt) (Figure 2.15).

4. Tonic.

5. Antiperistaltic (as a rule, they are not observed).

Rhythmic segmentation is provided mainly by the contractions of the circulatory layer of muscles. The intestinal contents are separated into parts. The following contraction forms a new segment of the intestines which contains parts of the former segment. This causes mixing of the chyme.

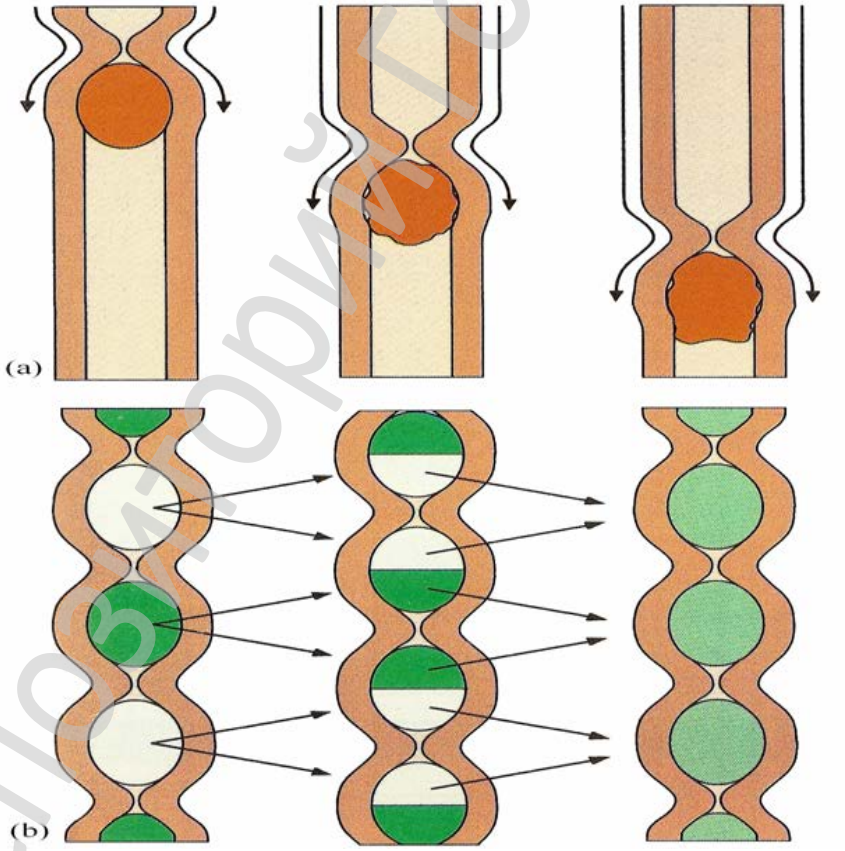


Figure 2.15 — Peristalsis and segmentation (by Elaine N. Marieb, 1989)

Notes: (a) During peristalsis the adjacent segments of the intestines (or other alimentary tract organs) contract and relax alternately, which results in the movement of food through the tract distally;м (b) During segmentation, the nonadjacent segments of the intestines contract and relax alternately. As the active segments are separated by inactive regions, the food is moved forward and then backward; this results in mixing of the food rather than food propulsion.

Pendulum contractions are provided by the contractions of the longitudinal layer of muscles with the participation of the circulatory one. These contractions induce back-and-forth movements of the chyme and weak forward movements.

During **peristalsis** due to the contraction of the circular *layer* of muscles above the chyme an intercepting is formed; below the chyme as a result of the contraction of the longitudinal muscles the intestinal cavity is dilated. These interceptings and dilations move through the intestines and move the chyme portion before the intercepting. Several peristaltic waves move through the intestines simultaneously.

Tonic contractions can have a very low rate and sometimes are not distributed at all, considerably narrowing the intestinal lumen along a big distance.

During **antiperistaltic contractions** the wave goes in the inverse (oral) direction. Normally the small intestine does not contract *antiperistaltically* (e. g. during vomiting).

The motility of the small intestine is adjusted by the nervous and humoral mechanisms, the role of the myogenic mechanisms which are the basis for properties of the automaticity of smooth muscles is highly significant.

The parasympathetic nerve fibers mainly provoke, and sympathetic — inhibit the contractions of the small intestine. Both the fibers provide the reflex regulation of the motility of the small intestine. Food intake by conditional and unconditional reflexes at first inhibits for a while, and then increases the motility.

The important role of the cerebral cortex and the second signaling system in the regulation of the intestinal motility is proved by the fact that while talking or even thinking about delicious food the motility *of the intestines* strengthens, and if there is some disgust at food, the motility is inhibited. It is also inhibited under the effect of anger, fear, and pain. Sometimes caused by some strong emotions, for example fear, rough peristalsis of the intestines («nervous diarrhea») can be observed.

The motor activity of the intestines depends on the physical and chemical properties of the chyme. Rough food and fats raise its activity (brown bread, vegetables, etc.).

2.6. Digestion in the large intestine

From the small intestine a portion of the chyme through the *ileocecal sphincter* passes into the large intestine. The sphincter performs the role of a valve passing the contents of the intestines only in one direction.

Without digestion the ileocecal sphincter is closed. 1–4 minutes after a meal every half a minute the valve opens reflectively and small portions of the chyme (up to 0.015 L) pass from the small intestine into the caecum. The peristaltic wave of the small intestine causes high pressure there and opens the valve. The high pressure in the large intestine raises the tone of the muscles of the ileocecal sphincter and inhibits the passing of the contents of the small intestine into the large intestine. During digestion the large intestine plays the secondary role, as food is digested and absorbed almost completely in the small intestine, except for some substances, for example vegetable fibers. A small amount of food and digestive juices is exposed to hydrolysis in the large intestine under the influence of the enzymes which have come from the small intestine, and also the juice of the large intestine.

The juice of the large intestine is secreted at a very small amount when there is no mechanical stimulation. It contains fluid and dense parts, the juice has an alkaline reaction (pH 8.5–9.0). The dense part looks like mucous lumps and consists of desquamated epithelial cells and mucus, produced by goblet cells.

The majority of enzymes are contained in the dense part of the juice. Enterokinase and saccharase are absent in the juice of the large intestine. The concentration of alkaline phosphatase is 15–20 times as low as that in the small intestine. There is cathepsine, peptidases, lipase, amylase, and nucleases at small amounts.

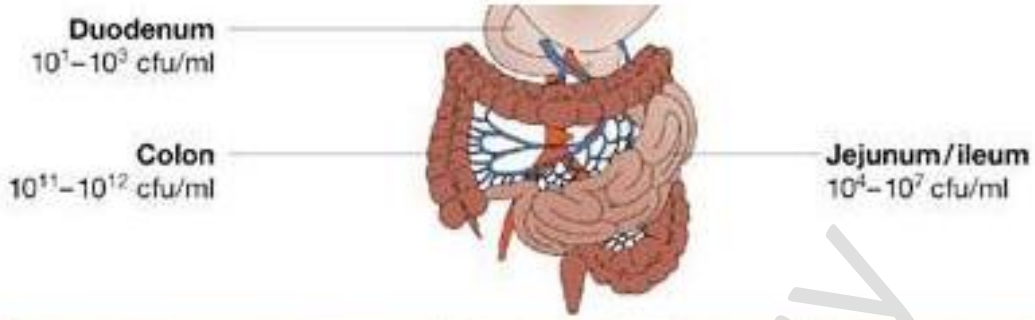
The juice secretion in the large intestine is caused by local mechanisms. During mechanical stimulation the secretion increases by 8–10 times.

In humans, about 400 g of chyme comes from the small intestine into the large intestine a day. In its proximal part only some substances are digested. In the large intestine there is intense adsorption of water, which to a greater extent is provided by the motility of the large intestine. The chyme gradually turns into excrements, 150–250 g of which are produced and excreted daily. There are more excrements after intake of vegetable food than mixed or meat food.

2.6.1. Vital role of the microflora of the large intestine

The bacterial flora of the gastrointestinal path is a prerequisite for normal existence of the organism. The number of microorganisms in the stomach is minimal compared to a much greater number in the small intestine (especially in its distal portion). The number of microorganisms in the large intestine is rather high — up to 10 billion per 1 kg of contents.

90 % of the whole flora of the human large intestine consists of sporeless anaerobe bacteria of Bifidum bacterium, Bacteroides. The rest 10 % are Lactobacilli, Colon Bacilli, Streptococci, and others (Figure2.16).



Protective functions	Structural functions	Metabolic functions
Pathogen displacement	Barrier fortification	Ferment non-digestible dietary residue and endogenous epithelial-derived mucus
Nutrient competition	Induction of IgA	Metabolize dietary carcinogens
Receptor competition	Apical tightening of tight junctions	Synthesize vitamins e.g., biotin, folate
Production of anti-microbial factors e.g., bacteriocins, lactic acids	Immune system development	

Figure 2.16 — Bacterial density and functions of the intestinal flora (from slideplayer.com)

The physiological role of the microflora of the large intestine:

1. Final decomposing of the residuals of undigested food and components of digestive secrets (the enzymes of bacteria split vegetable fibers, undigested in the small intestine).

2. Building of an immune barrier (inhibition of pathogens). Normal microflora *depresses pathogenic microorganisms,* prevents the host`s infection. Damage to normal microflora in diseases or as a result of a long-term intake of antibacterial preparations is often followed by complications caused by rough breeding of yeast, Staphylococci, and other microorganisms in the intestine.

3. Synthesis of some vitamins, enzymes, and other physiologically active substances (the intestinal flora *synthesizes K* and *B vitamins)*.

4. Participation in the metabolism of the organism. Due to the participation of the microflora of the intestines the exchange of proteins, phosphatides, bile and fatty acids, bilirubin, cholesterol occurs in the organism.

2.6.2. Motor activity of the large intestine

The process of digestion lasts for about 1–3 days and most of the time is spent on the removal of the food residuals in the large intestine. The motility of the large intestine provides:

1. Reservoir function.
2. Accumulation of the intestinal contents.

3. Absorption of some substances (basically water) from the intestines.

4. Formation of excrement masses and their removal from the intestines.

There are some kinds of the contractions of the large intestine:

1. Small and big pendulum-like contractions provide the mixing of the contents, its condensation by water adsorption.

2. Peristaltic and antiperistaltic contractions perform the same functions.

3. Strong propulsive contractions advance the contents in the caudal direction (3–4 times a day).

The large intestine possesses automaticity, but it is less expressed than in the small intestine.

The sympathetic nerve fibers inhibit, and parasympathetic stimulations stimulate the motility of the large intestine. The motility increases during meals by the mechanism of the conditioned reflex and also during stimulations of the esophagus, stomach, and duodenum by the unconditioned reflex. Local mechanical and chemical stimulations have an important role in the stimulation of the motility of the large intestine.

2.7. Absorption

Absorption is the transfer of various substances into the blood and lymph from the surface, from the cavities or hollow organs of the body through cells, their membranes or intercellular ducts. Cellular membranes have unequal permeability for various substances (Table 2.7).

Table 2.7 — Absorption of substances in the intestines

Duodenum	Ca, Mg, Fe, monosaccharides, glucose, galactose
Jejunum	fat-soluble vitamins, fats, fatty acids, monoglycerides, water-soluble vitamins, proteins and amino acids, bile salts
Ileum	Vitamin B_{12}, sodium, water, chlorides, bases, fatty acids
Colon	water

Transport of macro- and micro molecules. Macro-molecules are transported by phagocytosis and pinocytosis, called *endocytosis.* Some substances can be transported by intercellular spaces (Figure 2.17).

In the gastrointestinal tract mainly micromoleculas (monomers of nutrients and ions) are absorbed into the blood and lymph. This transport is divided into passive transport, facilitated diffusion, and active transport. Passive transport includes *diffusion, filtration,* and *osmosis.* It is carried out by concentration, osmotic, and electrochemical gradients. The facilitated diffusion is possible by means of special membranous carrier agents. Active transport is the transfer of

substances through membranes in the direction opposite the concentration, osmotic and electrochemical gradients with energy consumption.

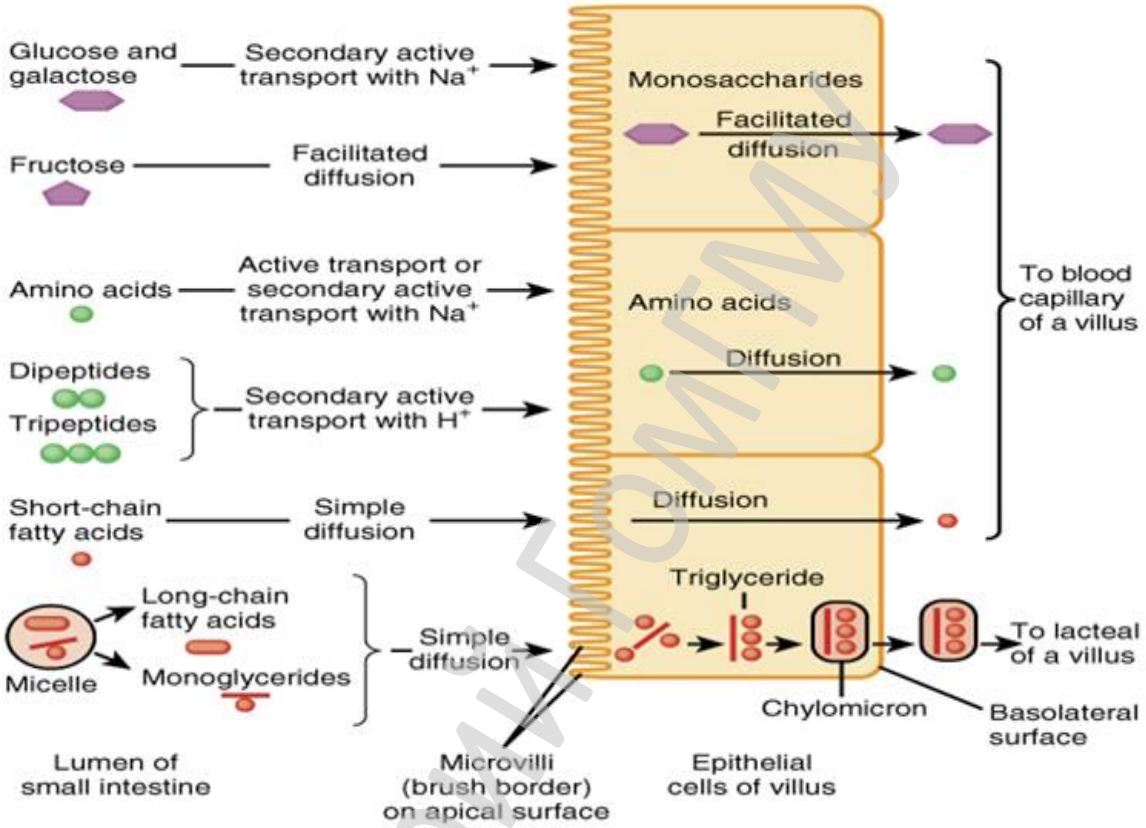


Figure 2.17 — Mechanisms of nutrient absorption in the intestines (from studylib.net)

Mechanisms of absorption

Passive transport – transport by gradients without energy expenditure.

1) Filtration (water, electrolytes)

2) Osmosis (water)

3) Diffusion:

— *Simple diffusion* (urea, alcohols, glycols, salts);

— *Facilitated diffusion* — with the help of molecules-carriers (large molecules are transported):

• Exchange diffusion — **antiport** (2Na+ to Ca^{2+});

• **Symport** – combined transport of Na+ and glucose; Na+ and amino acids (secondary active transport, or co-transport).

Active (primary) transport – transport against gradients using energy (large organic molecules — oligopeptides, fatty acids and micelles, etc., as well as electrolytes (Na^{+}, Ca^{2+}, Mg^{2+}, etc.) using ATPases).

Review questions

1. Name the end products of the breakdown of nutrients in the intestines.

2. What are the amount and composition of pancreatic juice? How is the secretion of pancreatic juice regulated?

3. What is the role of the liver in digestion? What are the composition and properties of bile? How are the formation and excretion of bile regulated?

4. What are the composition and properties of the juice of the small intestine? How is the secretion of intestinal juice regulated?

5. What are the types of the contractions of the small intestine? How is the motor activity of the small intestine regulated?

6. Explain the physiological role of the digestion in the large intestine. What is the physiological role of the microflora of the large intestine? What are the types of the contractions of the large intestine? How is the motor activity of the large intestine regulated?

7. Name the substances absorbed in the different departments of the gastrointestinal tract. What are the mechanisms of the absorption of substances?

Multiple Choice Questions
PHYSIOLOGY OF DIGESTION

1. What properties of food substances are remained after their hydrolysis in the gastrointestinal tract?

Variants of answer:

a) specific individuality;
b) antigenic properties;
c) energetic and plastic value;
d) constant molecular composition;
e) all the answers are correct.

2. Which principle is the basis for the functioning of the digestive system?

Variants of answer:

a) independent functioning of separate organs;
b) synthetic principle;
c) conveyor principle;
d) analytic principle;
e) all the answers are correct.

3. The stage of satiety which appears before the products of food hydrolysis get into the blood is called…

Variants of answer:

a) sensory satiation;
b) metabolic satiation;
c) true satiation;
d) humoral satiation;
e) catalytic satiation.

4. The stage of satiety which appears when the products of food hydrolysis get into the blood is called…

Variants of answer:

a) imaginary satiation;
b) true satiation;
c) sensory satiation;
d) humoral satiation;
e) catalytic satiation.

5. The basic type of digestion in humans is …

Variants of answer:

a) symbiotic;
b) autolytic;
c) hemotrophic;
d) own digestion;
e) there is no basic type.

6. In which type of digestion is the hydrolysis of substances carried out by the enzymes of microorganisms?

Variants of answer:

a) autolytic;
b) all types;
c) symbiotic;
d) own digestion;
e) hemotrophic.

7. In which department of the gastrointestinal tract does membrane digestion take place?

Variants of answer:

a) in the stomach;
b) in the large intestine;
c) in the oral cavity;
d) in the small intestine;
e) in all the above departments.

8. What is the basic role of membrane (parietal) digestion?

Variants of answer:

a) realization of initial stages of the hydrolysis of nutrients;
b) hydrolysis of fats and carbohydrates;
c) absorption of vitamins;
d) final hydrolysis and absorption of nutrients;
e) all the answers are correct.

9. Which function does not refer to the functions of the digestive system?

Variants of answer:

a) secretory function;
b) hemopoietic function;
c) excretory function;
d) respiratory function;
e) endocrine function.

10. What are the non-digestive functions of the digestive system?

Variants of answer:

a) hydrolysis of food substances;

b) participation in hemopoiesis, excretory function;

c) absorption of the products of hydrolysis;

d) motor function;

e) deposition of food.

11. Which department of the gastrointestinal tract carries out the function of food deposition?

Variants of answer:

a) the small intestine;

b) the stomach;

c) the large intestine;

d) the rectum;

e) the oral cavity.

12. The enzymes of saliva mainly split up …

Variants of answer:

a) fibers;

b) fats;

c) carbohydrates;

d) vitamins;

e) all the answers are correct.

13. In which department of the CNS is the center of satiety situated?

Variants of answer:

a) in the intermediate brain;

b) in the medulla oblongata;

c) in the midbrain;

d) in the spinal cord;

e) in the cerebellum.

14. Secretion of a big volume of not-concentrated saliva is observed during the stimulation of …

Variants of answer:

a) the accessorius nerve;

b) the sympathetic nerve;

c) the parasympathetic nerve;

d) the facial nerve;

e) the sublingual.

15. Secretion of a small volume of concentrated saliva is observed during the stimulation of…

Variants of answer:

a) the accessorius nerve;
b) the sympathetic nerve;
c) the parasympathetic nerve;
d) the trigeminal nerve;
e) the glossopharyngeal nerve.

16. After the removal of a significant part of the stomach, anemia develops due to the lack of …

Variants of answer:

a) Hageman factor;
b) fibrin stabilisating factor;
c) Kastl's intrinsic factor;
d) pepsinogen;
e) lipase.

17. Which food substances are basically digested by enzymes in the stomach?

Variants of answer:

a) only fats;
b) only proteins;
c) proteins, emulsified fats, and insignificant amount of carbohydrates;
d) only carbohydrates;
e) only nucleic acids.

18. Pepsinogen is synthesized in the stomach by…

Variants of answer:

a) parietal cells;
b) mucocytes;
c) chief cells;
d) G-cells;
e) all the answers are correct.

19. What do the parietal cells of the mucous membrane of the stomach produce?

Variants of answer:

a) pepsinogens;
b) mucin;

c) lysozyme;
d) hydrochloric acid;
e) lipase.

20. The denaturation and breakdown of proteins in the stomach is caused by …

Variants of answer:
a) pepsin;
b) pepsinogen;
c) lipase;
d) carbonic acid;
e) hydrochloric acid.

21. Which condition is necessary for the transformation of pepsinogens into pepsins?

Variants of answer:
a) presence of mucins;
b) absence of gastric lipase;
c) presence of hydrochloric acid;
d) absence of carbohydrates;
e) presence of nucleic acids.

22. What happens to the proteolytic enzymes of gastric juice in an alkaline medium?

Variants of answer:
a) they are activated;
b) they are destroyed;
c) they do not change their properties;
d) their synthesis is increased,
e) their composition is changed.

23. Gastric juice has the greatest acidity during the digestion of …

Variants of answer:
a) fats;
b) proteins;
c) carbohydrates;
d) vitamins;
e) nucleic acids.

24. In which condition is fat present in mother's milk? How does it influence digestion?

Variants of answer:

a) in emulsified condition, which increases the action of lipase;

b) in hydrolyzed condition, which raises its consumption;

c) in emulsified condition, which accelerates the action of amylase;

d) in emulsified condition, which accelerates the action of pepsin;

e) in emulsified condition, which accelerates the action of chymotrypsin.

25. Which component of gastric juice protects the mucous membrane of the stomach from self-digestion?

Variants of answer:

a) pepsin;

b) lipase;

c) gastricsin;

d) mucin;

e) hydrochloric acid.

26. What is the effect of the stimulation of the vagus nerve on gastric secretion?

Variants of answer:

a) sharply decreased secretion;

b) termination of secretion;

c) increased secretion;

d) the vagus nerve does not influence gastric secretion;

e) it provides various effects.

27. What are the phases of gastric secretion?

Variants of answer:

a) cephalic, gastric, intestinal;

b) cephalic, pancreatic, intestinal;

c) cephalic, gastric, pancreatic;

d) cephalic, hepatic, intestinal;

e) gastric, hepatic, pancreatic.

28. Which phase of gastric secretion takes place in a person when they see and smell food?

Variants of answer:

a) gastric;

b) cephalic;

c) gastric and intestinal;

d) intestinal;
e) pancreatic.

29. Which phase of gastric secretion can be studied during the experience of false feeding?

Variants of answer:
a) gastric and cerebral phases;
b) cephalic phase;
c) intestinal phase;
d) cerebral, gastric, intestinal phases;
e) pancreatic.

30. How is the motor activity of the stomach changed under the influence of gastrin?

Variants of answer:
a) it is decreased;
b) it is not changed;
c) it is increased;
d) it is stopped;
e) motor activity is changed diversely.

31. Which substances are evacuated from the stomach at the lowest speed?

Variants of answer:
a) carbohydrates;
b) fats;
c) proteins;
d) vitamins;
e) nucleic acids.

32. Which enzymes of the pancreas are secreted in an active condition?

Variants of answer:
a) trypsinogen, chymotrypsinogen;
b) procarboxypeptidases;
c) proteases;
d) amylase, nucleases;
e) proelastase, prophospholipase.

33. Which enzymes of the pancreas are secreted in the form of zymogens (inactive precursors)?

Variants of answer:

a) amylase;

b) trypsinogen, chymotrypsinogen;

c) nucleases;

d) lipase;

e) ribonuclease, deoxyribonuclease.

34. Which enzymes of the pancreas do not participate in protein hydrolysis?

Variants of answer:

a) carboxypeptidase A;

b) trypsin;

c) chymotrypsin;

d) amylase, lipase;

e) carboxypeptidase B.

35. Trypsinogen is activated under the influence of …

Variants of answer:

a) secretin;

b) hydrochloric acid;

c) enterokinase;

d) gastrin;

e) cholecystokinin.

36. Which enzymes of the pancreas are activated by trypsin?

Variants of answer:

a) only trypsinogen;

b) all the enzymes, except trypsinogen;

c) amyase;

d) trypsinogen, prophospholipase A, proelastase, procarboxypeptidases A and B, chymotrypsinogen;

e) lipolitic enzymes.

37. What is the influence of the stimulation of the sympathetic nerves on pancreatic secretion?

Variants of answer:

a) increased secretion;

b) decreased secretion;

c) the sympathetic nerves do not influence pancreatic secretion.

d) the secretion is stopped;

e) pancreatic secretion changes diversely.

38. What is the influence of adrenaline and acetylcholine on the motor activity of the small intestine?

Variants of answer:

a) adrenaline increases the motor activity, acetylcholine decreases it;

b) adrenaline does not influence the motor activity, acetylcholine decreases it;

c) adrenaline decreases the motor activity, acetylcholine does not influence it;

d) adrenaline decreases the motor activity, acetylcholine increases it;

e) both of them decrease the motor activity.

39. Fats in the duodenum are emulsified by…

Variants of answer:

a) bile;

b) lipase;

c) mucus;

d) hydrochloric acid;

e) enterokinase.

40. Which process constantly takes place in the liver…

Variants of answer:

a) production of bile;

b) secretion of bile;

c) production and secretion of bile;

d) production of mucin;

e) production of trypsin.

41. Decreased secretion of bile into the duodenum affects the digestion of…

Variants of answer:

a) proteins;

b) carbohydrates;

c) proteins and carbohydrates;

d) fats;

e) vitamins.

42. What is the difference between the composition of hepatic and cystic bile?

Variants of answer:

a) hepatic bile is more concentrated;

b) essentially do not differ;

c) gall bladder bile is more concentrated;

d) hepatic bile contains more enzymes;

e) gall bladder bile is more light.

43. What is the normal pH of the intestinal secret?

Variants of answer:

a) neutral;

b) alkaline;

c) acid;

d) there is no right answer;

e) all the answers are correct.

44. What processes mainly occur in the large intestine?

Variants of answer:

a) intensive absorption of water, formation of fecal masses, synthesis of vitamins;

b) intensive hydrolysis of food substances;

c) intensive membrane digestion;

d) secretion of hydrochloric acid;

e) hydrolysis of proteins, fats, and carbohydrates.

45. What is the positive role of the microflora of the intestines?

Variants of answer:

a) formation of the organism`s immunological barrier;

b) synthesis of the vitamins of groups B and K;

c) partial digestion of vegetable fibers;

d) all the answers are correct;

e) inactivation of enzymes.

46. Hydrolysis of vegetable fibers in the large intestine goes under the influence of the enzymes of…

Variants of answer:

a) vegetable fibers are not hydrolyzed in the body;

b) microflora;

c) pancreatic juice;

d) enterocytes;

e) trypsin.

47. Which type of contractions is not characteristic for the small intestine?

Variants of answer:

a) peristaltic contractions;

b) pendulum contractions;

c) rhythmic segmentation;

d) antiperistaltic contractions;

e) all the answers are correct.

48. Which regulatory mechanisms play the leading role during the digestion in the large intestine?

Variants of answer:

a) local;

b) humoral;

c) nervous;

d) nervous, humoral, local;

e) all the answers are correct.

49. Can absorption be carried out in the oral cavity?

Variants of answer:

a) only some substances can be absorbed;

b) absorption begins only in stomach;

c) absorption begins only in the small intestine;

d) absorption begins only in the large intestine;

e) all the substances can be absorbed.

50. The main department of the gastrointestinal tract, where the absorption of the products of food hydrolysis and water occurs, is…

Variants of answer:

a) the stomach;

b) the small intestine;

c) the rectum;

d) the large intestine.

e) the oral cavity.

51. Iron is actively absorbed in…

Variants of answer:

a) the stomach;

b) the duodenum and proximal jejunum;
c) the large intestine;
d) the ileum;
e) all the answers are correct.

52. Vitamin B_{12} is absorbed in…
Variants of answer:
a) the duodenum;
b) the jejunum;
c) the ileum;
d) the stomach;
e) all the answers are correct.

53. Which of the following statements about secretin is not correct?
Variants of answer:
a) it increases the secretion of pancreatic juice rich in bicarbonate ions;
b) it inhibits gastric acid secretion;
c) it increases gastric acid secretion;
d) it causes the contractions of the pyloric sphincter;
e) all the answers are correct.

54. The longest transit time in the gastrointestinal tract is found in…
Variants of answer:
a) the stomach;
b) the jejunum;
c) the colon;
d) the ileum;
e) the transit time is identical in all the parts of the gastrointestinal tract.

55. The chyme is moved down into the small intestine by…
Variants of answer:
a) segmentation;
b) haustrations;
c) tonic contractions;
d) peristalsis;
e) all the answers are correct.

56. Which of the following statements is true about gastric emptying…
Variants of answer:
a) it is decreased by cholecystokinin;

b) it is decreased by gastrin;
c) it is increased by secretin;
d) it is decreased by insulin;
e) all the answers are correct.

57. The mechanism that protects the pancreas from autodigestion is…
Variants of answer:
a) the secretion of biocarbonate;
b) protease inhibitors present in plasma;
c) proteolytic enzymes secreted in inactive form;
d) the resistance of pancreatic cells;
e) the secretion of insulin.

58. Which of the following types of secretion has a very high pH level?
Variants of answer:
a) gastric juice;
b) pancreatic juice;
c) bile in the gall bladder;
d) saliva;
e) all the answers are correct.

59. The enzyme secreted by the exocrine part of the pancreas is…
Variants of answer:
a) somatostatin;
b) pepsin;
c) glucagon;
d) insulin;
e) chymotrypsin.

60. Bile acids are synthesized from…
Variants of answer:
a) cholesterol;
b) amino acids;
c) bilirubin;
d) protein;
e) glycogen.

CORRECT ANSWERS
PHYSIOLOGY OF DIGESTION

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	16	c	31	b	46	b
2	c	17	c	32	d	47	d
3	a	18	c	33	b	48	a
4	b	19	d	34	d	49	a
5	d	20	e	35	c	50	b
6	c	21	c	36	d	51	b
7	d	22	b	37	b	52	c
8	d	23	b	38	d	53	c
9	d	24	a	39	a	54	c
10	b	25	d	40	a	55	d
11	b	26	c	41	d	56	a
12	c	27	a	42	c	57	c
13	b	28	b	43	b	58	b
14	c	29	b	44	a	59	e
15	b	30	c	45	d	60	a

UNIT 3
METABOLISM AND ENERGY

3.1. Exchange of proteins, fats and carbohydrates

Metabolism is a set of processes which substances undergo from the moment of their absorption into the gastrointestinal tract till the formation of final decay products, which promote *growth, survival, and reproduction* of a human being.

Nutrients are unique sources of energy for humans. Nutrients also play the ***plastic role*** because structural components of cells and tissues are formed from them after complex chemical transformations.

The human need for nutrients varies depending on genetic constitution, body size, age, sex, state of the endocrine system, physical activity, reproductive function, etc.

In the human body, including its organs, tissues, and cells, there is a continuous process of the formation of complex substances from simple ones. Simultaneously, there is the breakdown, oxidation of complex organic substances into CO_2 and H_2O.

Growth and replacement of body cells are possible only if O_2 and nutrients (building material) continuously enter the body.

Metabolism is all physical, chemical, and physiological processes providing the intake and delivery of energy to cells, organs, and tissues from exo- and endogenous sources, satisfying of the plastic needs with the purpose of body part regeneration and excretion of metabolic waste products from the body.

Metabolism includes 2 interconnected processes: catabolism (dissimilation) and anabolism (assimilation) (Figure 3.1).

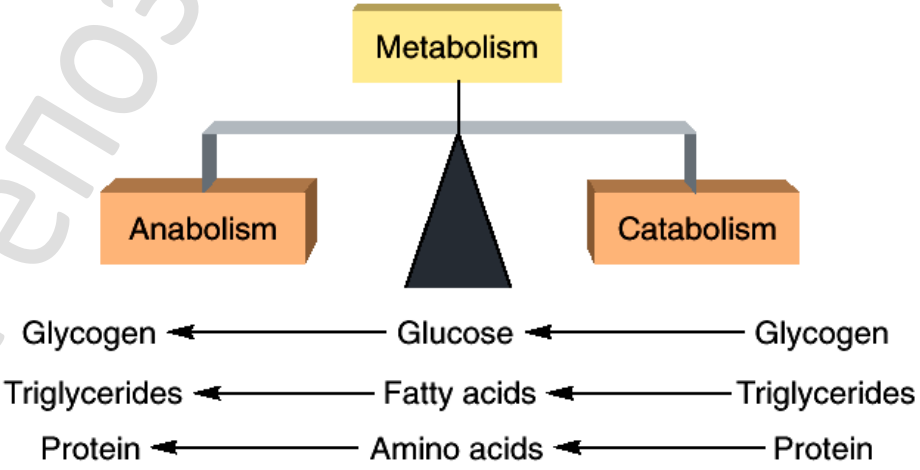


Figure 3.1 —Anabolism and catabolism (from slideplayer.com)

Catabolism is the enzymic breakdown of large organic molecules of nutrients into smaller ones during the process of oxidative reactions (the breaking down of complex organic substances is accompanied by energy liberation) to CO_2 and H_2O, i.e. these two processes are interconnected.

Anabolism is the enzymic synthesis of large-molecular cell components — polysaccharides, nucleic acids, proteins, lipids — from simple organic molecules, i.e. the sum of processes by which living organized substance is built up and maintained.

3.1.1. Exchange of proteins

Among organic elements proteins take a special place in metabolism as they transfer genetic information.

The functions of proteins are diverse:

Proteins maintain the oncotic pressure, viscosity, participate in the maintenance of the pH value of blood (buffer properties), they maintain constant water-salt exchange, etc.

1. The plastic, or **structural** value of proteins — being a part of all cells and intercellular structures, cytoplasm, hemoglobin, blood plasma, they provide body growth and development due to the biosynthesis processes (they are a reserve for construction of tissue proteins).

2. The catalytic activity of proteins aids and adjusts the rate of biochemical reactions that take place within and outside cells. Thus, enzymes determine all the aspects of metabolism and energy formation. Proteins are a part of many hormones.

3. The protective function consists of the formation of immune proteins — antibodies. Proteins are capable of binding toxins and poisons; they provide blood coagulation (hemostasis).

4. The transport function — transport of oxygen and carbon dioxide with hemoglobin; binding and transport of some ions (iron, copper, hydrogen), medicinal substances, toxins.

5. The energy function of proteins is defined by their ability to release energy during oxidation: 1 g of protein accumulates 17.1 kilojoules (4.0 kilocalories) of energy.

Proteins also supply energy, particularly if carbohydrate and fat intake is inadequate or if protein intake exceeds the body needs.

The need in proteins is especially great in the periods of growth, pregnancy, breastfeeding, recovery after a serious illness, injury or surgery.

In the digestive tract proteins are split up to amino acids and elementary polypeptides (Figure 3.2). From amino acids cells of various tissues and organs

(in particular, the liver) synthesize specific proteins which are used for the regeneration of destroyed cells and growth of new cells and for the synthesis of enzymes and hormones.

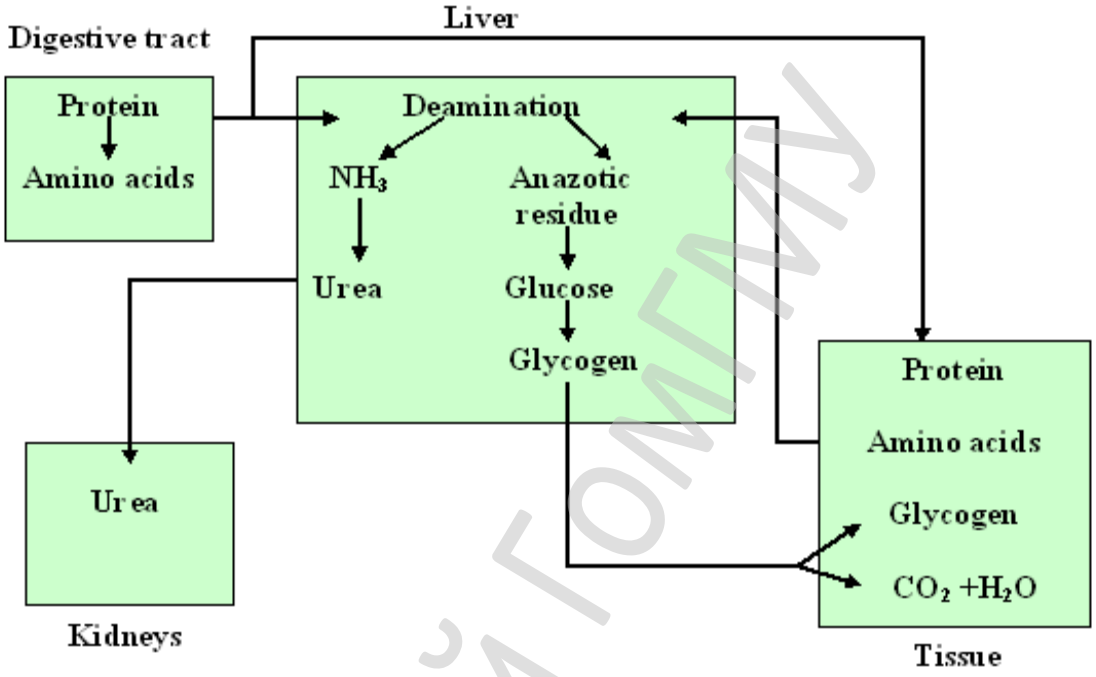


Figure 3.2 — Protein exchange (by A. Ginetsinskiy, 1986)

Biological value of amino acids

Proteins are organ-, tissue-, and species-specific. Proteins are irregular polymers whose monomers are amino acids. Out of 80 amino acids, only 20 are basic. For normal metabolism not only the absolute amount of protein received by humans is important but also its qualitative structure, namely, essential and non-essential amino acids. Amino acids which can be synthesized by the body itself from other amino acids are ***non-essential*** (alanine, cysteine, glutamic and aspartic acid, thyroxin, proline, serine, glycine, and conditionally arginine and histidine).

Amino acids which cannot be synthesized but necessarily should be taken in with food are called ***essential*** (leucine, isoleucine, valine, methionine, lysine, threonine, phenylalanine, tryptophan; conditionally: arginine, and histidine)**.**

Food proteins which contain all essential amino acids are called *complete proteins*. They include animal proteins since they can completely transform into the organism`s own proteins. The proteins of eggs, meat, fish, milk have the highest biological value.

The biological value of vegetable proteins is lower. The absence of food proteins leads to inhibition of a child`s growth, weakening of the organism, serious metabolic disorders, low immunity, and other diseases. For example,

valine deficiency results in equilibrium disorders. In mixed feeding, when both animal and vegetable products are available in diet — a set of amino acids necessary for synthesis comes into the body, which is especially important for a growing organism.

The need of the human body in proteins depends on sex, age, climatic region, and nationality. Daily, an adult should take about 0.8-1 g of proteins per 1 kg of body weight, of which 30 % should be of animal nature. In physical exercise an adult should take 100–120 g of proteins, in strenuous physical activity — about 150.

Nitrogen balance

The nitrogen balance is the difference between the amount of nitrogen taken into the body and the amount of nitrogen excreted from the body in final metabolites. Calculations of the nitrogen balance presume that on average proteins contain approximately 16 % nitrogen, i. e. each 16 g nitrogen correspond to 100 g protein (hence, 1 g nitrogen corresponds to 6.25 g protein). The amount of nitrogen ingested with food differs from the amount of acquired nitrogen since some part of nitrogen is lost with feces, urine, and sweat.

If the total nitrogen intake is equal to its total nitrogen loss, this is ***nitrogen equilibrium or zero nitrogen balance*** (is typical of healthy adults).

A condition in which the intake of nitrogen exceeds its excretion is called ***positive nitrogen balance*** (Table 3.1), which is typical of growth periods (i.e., in the young), pregnancy and recovery from illness, intensive physical exercise. ***Negative nitrogen balance***, which occurs when more nitrogen is excreted than is taken in, indicates a state when protein destruction predominates over their synthesis (occurs in ageing, burns, serious injuries, and protein-losing enteropathy).

Table 3.1 — Nitrogen balance

Kind of balance	Characteristics	Example
Nitrogen equilibrium or zero nitrogen balance	The intake of nitrogen is equal to its excretion (the synthesis of proteins is equal to the breakdown of proteins)	It is observed in healthy adults
Positive nitrogen balance	The intake of nitrogen exceeds its excretion (the synthesis of proteins predominates over the breakdown of proteins)	It is observed: • in children; • in recovery; •in pregnancy; •intensive physical exercise
Negative nitrogen balance	The excretion of nitrogen exceeds its intake (the breakdown of proteins predominates over the synthesis of proteins)	It is observed: • in protein starvation; • in aging; • in serious diseases or injuries

Rubner's breaking index

The minimal amount of proteins which is constantly degraded in the body is called the **breaking index.**

When no protein is taken with food, 0.028– 0.065 g of nitrogen per 1 kg of body weight of an adult at rest is lost per day. Thus, the loss of protein in an adult with weight of 70 kg is 23 g/day. An inadequate protein intake results in a negative nitrogen balance, which does not meet the plastic and energy needs of the body.

Regulation of protein exchange

There are data that in the hypothalamus there are special centers regulating protein exchange. The mechanism of the CNS influence is carried out through the endocrine system (Figure 3.3). The hormonal regulation of protein metabolism provides dynamic equilibrium of their synthesis and breakdown.

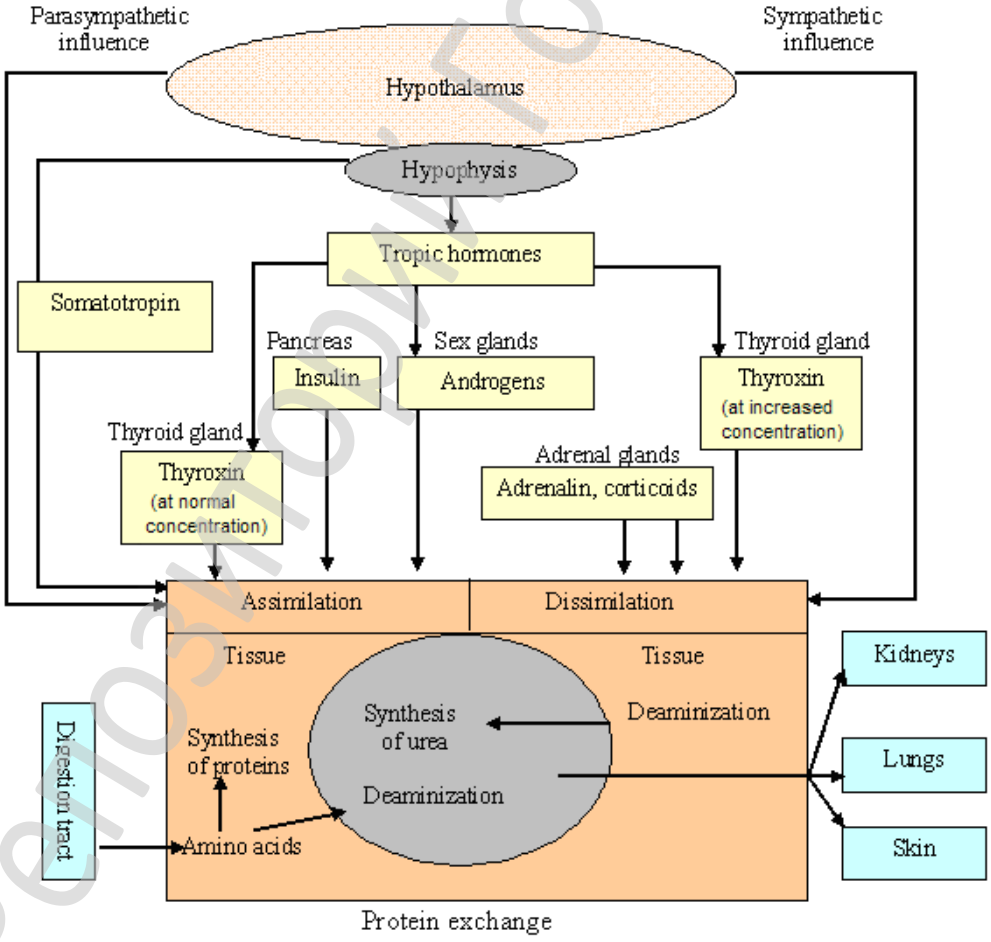


Figure 3.3 — Regulation of protein exchange (by Korobkov A. V., Chesnokova S. A., 1986)

The synthesis of proteins is regulated by the hormone of the adenohypophysis ***somatotropin*** or growth hormone (STH), which stimulates

mass increase of all organs and tissues during body growth. STH in adults promotes the synthesis of proteins due to the high permeability of cellular membranes to amino acids and decreased cathepsine synthesis (intracellular proteolytic enzymes). The similar effect is performed by the hormones of the pancreas (***insulin***) and male sexual glands ***(androgens)***. Intensive protein formation due to the excess of these hormones results in excessive body growth, overweight. In a number of cases, e.g. in puberty, these phenomena have a physiological value. In others (e.g. inpituitary tumor), gigantism and other hyperplastic processes can develop.

Protein dissimilation is regulated by the hormones of the thyroid gland— ***thyroxine*** and ***triiodothyronine*** — and also by the hormones of the cortical (***glucocorticoids***) and medullary (***adrenalin***) layers of the adrenal glands. The excess of these hormones strengthens protein disintegration in tissues, which is accompanied by exhaustion and a negative nitrogen balance.

The hormones of the thyroid gland, in certain concentrations, can stimulate the synthesis of proteins and thus can accelerate growth, development, and differentiation of tissues and organs.

The adrenal hormones — glucocorticoids — induce the breakdown of proteins, especially in muscular and lymphoid tissues. In the liver glucocorticoids can stimulate the synthesis of proteins.

3.1.2. Exchange of fats

Fats are complex chemical structures consisting of triglycerides and lipoid substances (phosphatides, sterols).

The functions of fats:

Fats participate in energy and plastic exchange**.**

1. Structural, or plastic role of fats, is that they are a part of structural components of the cell — nucleus, cytoplasm, membrane, and substantially provide their properties (in nervous tissue they are about 25%, in cellular membranes — up to 40% of fats). They are a source of the synthesis of steroid hormones.

2. Energy function provides 25–30% of all energy necessary for the body. 1g of fats on oxidation provide 39.0 kilojoules (9.0 kilocalories), which is more than double the amount of calories from carbohydrates and proteins.

3. Fats — suppliers of endogenic water; 100 g of fats on oxidation produce 107 mL of H_2O.

4. Reserving of nutrients (fatty depot).

5. Protection of the organs — stored fats surround vital organs and keep them protected from sudden movements or outside impacts (periocular cushion, adipose body of the kidneys).

6. Transport function — transport of liposoluble vitamins.

7. Temperature regulation — fat cells, stored in adipose tissue, insulate the body and help sustain a normal core body temperature as they poorly conduct heat.

Hydrolysis of fats.

Fats which come into the digestive tract are split into monoacylglycerol and fatty acids, which are absorbed into the lymphatic vessels and further from lymph pass into the bloodstream. Then they are delivered to tissues where they are oxidated, i. e. are used as energy materials (Figure 3.4). Fatty acid oxidation is twice more effective than that of amino acids and monosaccharides. The big role in the exchange of fats is played by the liver.

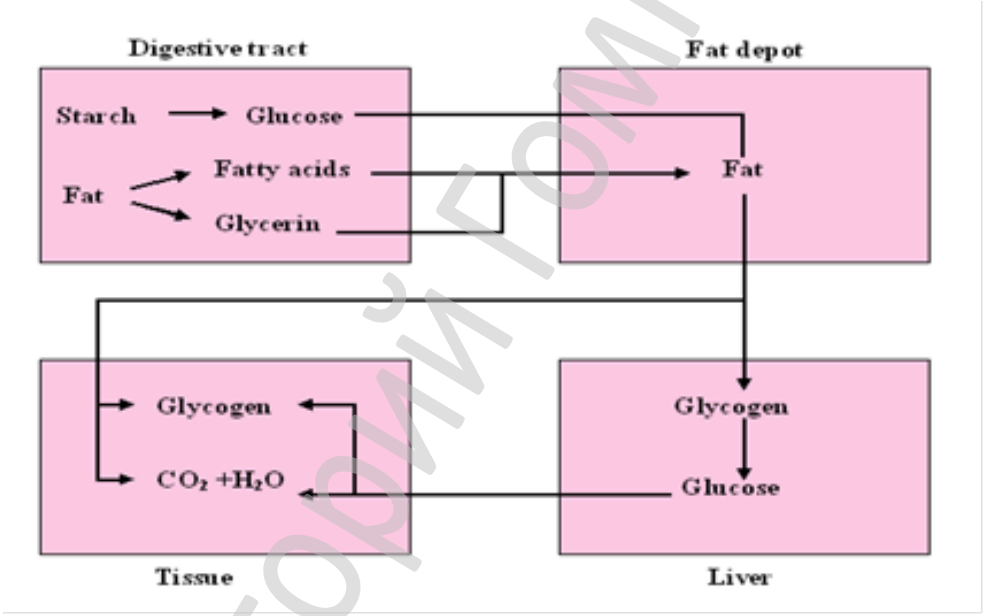


Figure 3.4 — Fat exchange (by A. Ginetsinskiy, 1986)

Neutral fats are the major energy source; due to their oxidation 50 % of the total energy in the body is formed. Physiological deposition of neutral fats is carried out by lipocytes, which accumulate them in subcutaneous fat, epiploon, adipose capsules of various organs enlarging in size. The number of lipoblasts is considered to increase in childhood. Fats deposited in subcutaneous fat protect the body from heat losses, and fats surrounding the internal organs protect them from mechanical damage. Fat can be deposited in the liver, muscles. The amount of fat accumulated in the depot depends on the character of food, constitution, sex, age, occupation, lifestyle, etc.

On average a person needs 70–125 g of fat a day. Excessive fat is accumulated in certain parts of the body as fatty depots.

For normal vital activity the presence of essential fatty acids in diet is necessary. Essential fatty acids are not synthesized in the body. They include linoleic, linolenic (in vegetable fats) and arachidonic (in animal fats) acids.

However, fats can be produced in the body from carbohydrates and proteins due to their excessive consumption with food. People can receive a significant amount of fats with sausages — 20–40 %, bacon — 90 %, butter — 72–82 %, cheese — 15–50 %, sour cream — 20–30 %.

The total amount of fats in the human organism is 10–20 % of body weight. A 20–25 % increase of body weight is an ultimate physiological border. 30 % of the population in economically developed countries has the body weight exceeding the normal parameters.

Regulation of fat exchange

The processes of the formation, deposit, and mobilization of fats from the depot are regulated by the nervous and endocrine systems (Figure 3.5).

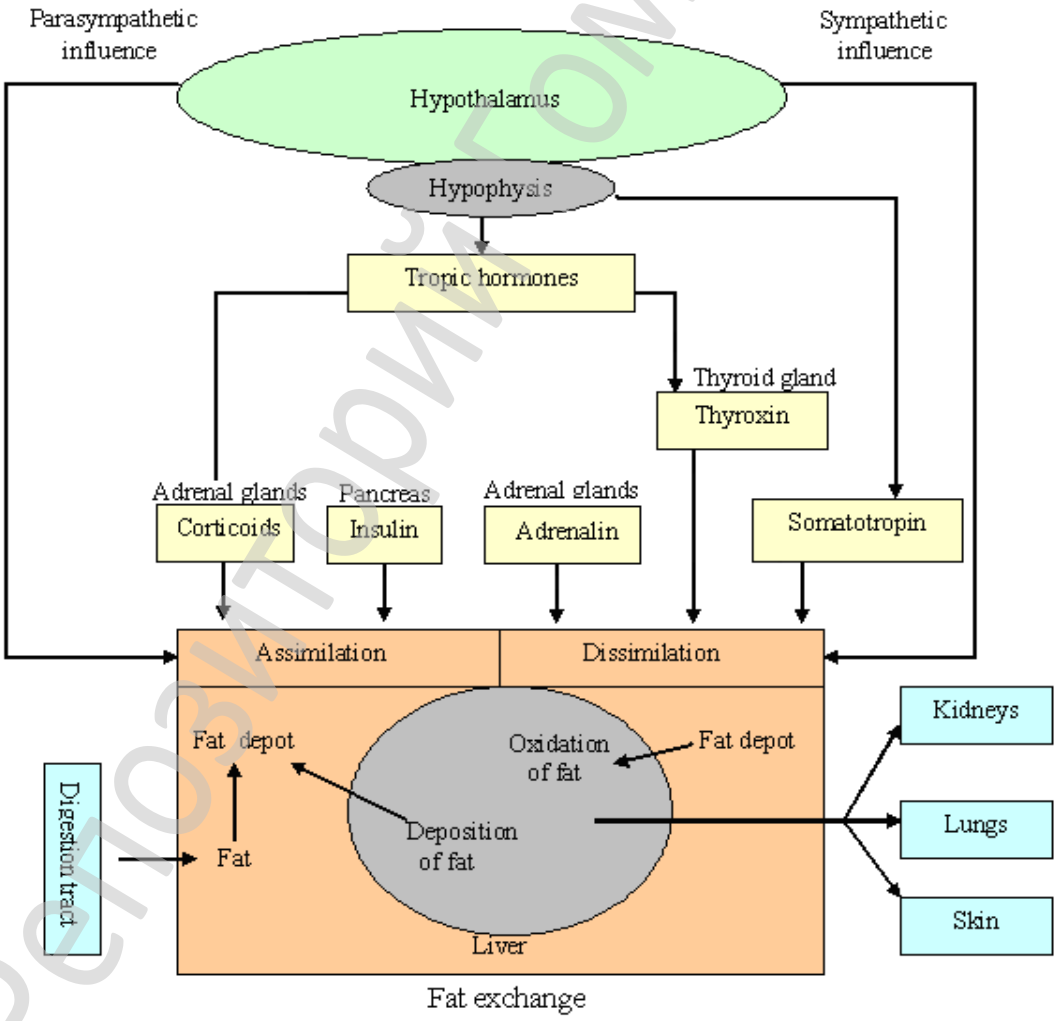


Figure3.5 — Regulation of fat exchange (by Korobkov A. V., Chesnokova S. A., 1986)

The participation of the nervous system in the regulation of lipometabolism was proved by the experiment with the damaged hypothalamus nuclei.

If damaged, the ***ventromedial nucleus*** (the ***satiety center***) in animals causes ***obesity*** due to a continuous rise of appetite (hyperphagia); a damage of the lateral nucleus (the hunger center) inhibits appetite and leads to exhaustion (aphagia).

The sympathetic nervous system inhibits the synthesis of triglycerides, increases their breakdown. The parasympathetic system promotes obesity.

The influence of the nervous system on lipometabolism is carried out by changing endocrine secretion — hypophysis, thyroid, pancreas, and sexual glands.

Adrenalin and noradrenalin, as well as ***growth hormone*** and ***thyroxin*** provoke a fat-mobilizing action (the hyperfunction of the thyroid gland results in body weight loss). Chronic stress accompanied with the strain of the sympaticoadrenal system leads to exhaustion of fatty depots and weight loss. On the contrary, insulin deficiency, e.g. in diabetes, is combined with obesity.

Glucocorticoids inhibit mobilization of fats as they may increase the blood glucose level. Lipometabolism is closely interrelated with carbohydrates — due to the excess of carbohydrates in diet, triglycerides are deposited, their breakdown decreases, their synthesis is activated, and vice versa.

3.1.3. Exchange of carbohydrates

The biological role of carbohydrates for humans is defined first of all by their energetic value: the processes of carbohydrate transformation provide up to 60 % of total energy metabolism. 1 g of carbohydrates on oxidation yields 17.1 kilojoules (4.1 kilocalories) of energy. Carbohydrates are used either as a direct source of chemical energy or as an energy reserve. Basic carbohydrates — sugar, starch, cellulose — are contained in vegetables. The daily need in carbohydrates in an adult is about 500 g a day (the minimal need — 100–150 g/day).

Functions of carbohydrates

1. Structural or plastic — they are a part of the complex structures of cellular membranes (glucoprotein, glycolipid, lipopolisaccharides, and others).

2. Energetic function.

3. Function of nutrient accumulation.

4. Protective function. Carbohydrates (as mucin components) protect the walls of hollow organs (esophagus, intestines, stomach, bronchi) from mechanical damages and penetration of harmful bacteria and viruses.

Carbohydrates come into the digestive tract as poly- and disaccharides and are absorbed into the blood in the form of simple sugars (Figure 3.6). The blood glucose level varies from 3.30 to 5.55 mmol/L.

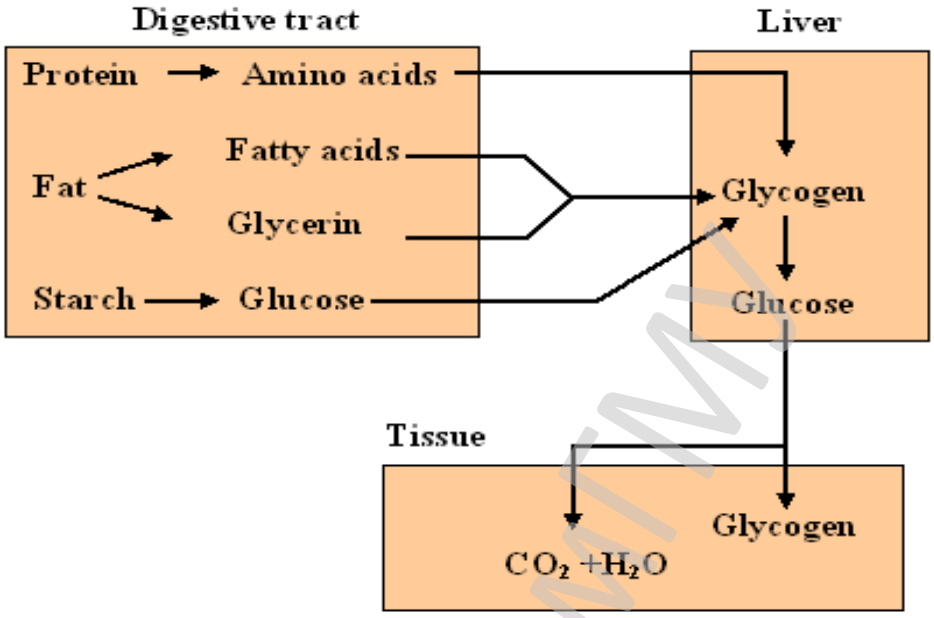


Figure 3.6 — Carbohydrate exchange (by A. Ginetsinskiy, 1986)

In the body carbohydrates are deposited mainly as glycogen — in the liver and partially in muscles (1–2 %).

The brain has no glycogen depot due to which it requires constant glucose supply. Brain has a very high rate of metabolism, using ~5.6 milligram glucose per 100 gram of brain tissue per minute. Carbohydrates are the only nutrients which can match this rate of energy requirement. Cerebral tissue absorbs about 70 % of glucose secreted by the liver.

Hypoglycemia

Hypoglycemia, also called low blood glucose or low blood sugar, occurs when the level of glucose in the blood drops below the normal value. Acute hypoglycemia can lead to death. Carbohydrates are important for the CNS metabolism, and long-term low blood sugar (lower than 3.3 mmole/L) may cause acute CNS disorders. The symptoms of hypoglycemia are cramps, delirium, loss of consciousness, changed position of internals, irregular heart rhythm, visual disturbances, low body temperature.

Hypoglycemia disappears if a person is given a glucose injection into the blood or eats a bit of sugar.

Hyperglycemia

Hyperglycemia is a condition in which an excessive amount of glucose circulates in the blood caused by the excessive intake of carbohydrates with food. Such hyperglycemia is called nutritional, or alimentary. It results in glycosuria, i. e. urinary excretion of sugar if its level in the blood increases above 10.0 mmol/L.

The glucose consumption by various organs from the blood flow is different: the brain holds 12 % of glucose, the intestines — 9 %, the muscles — 7 %, the kidneys — 5 %.

Regulation of carbohydrate exchange

Glycogen mobilization in the liver and high blood sugar occur due to the stimulation of the medulla in the area of the 4th ventricle fundus — called «sugar prick». The stimulation of the hypothalamus results in a similar phenomenon. In the hypothalamus, there are receptors that monitor the blood glucose level. Their stimulation changes the endocrine balance and the balance between the sympathetic and parasympathetic nervous systems (Figure 3.7).

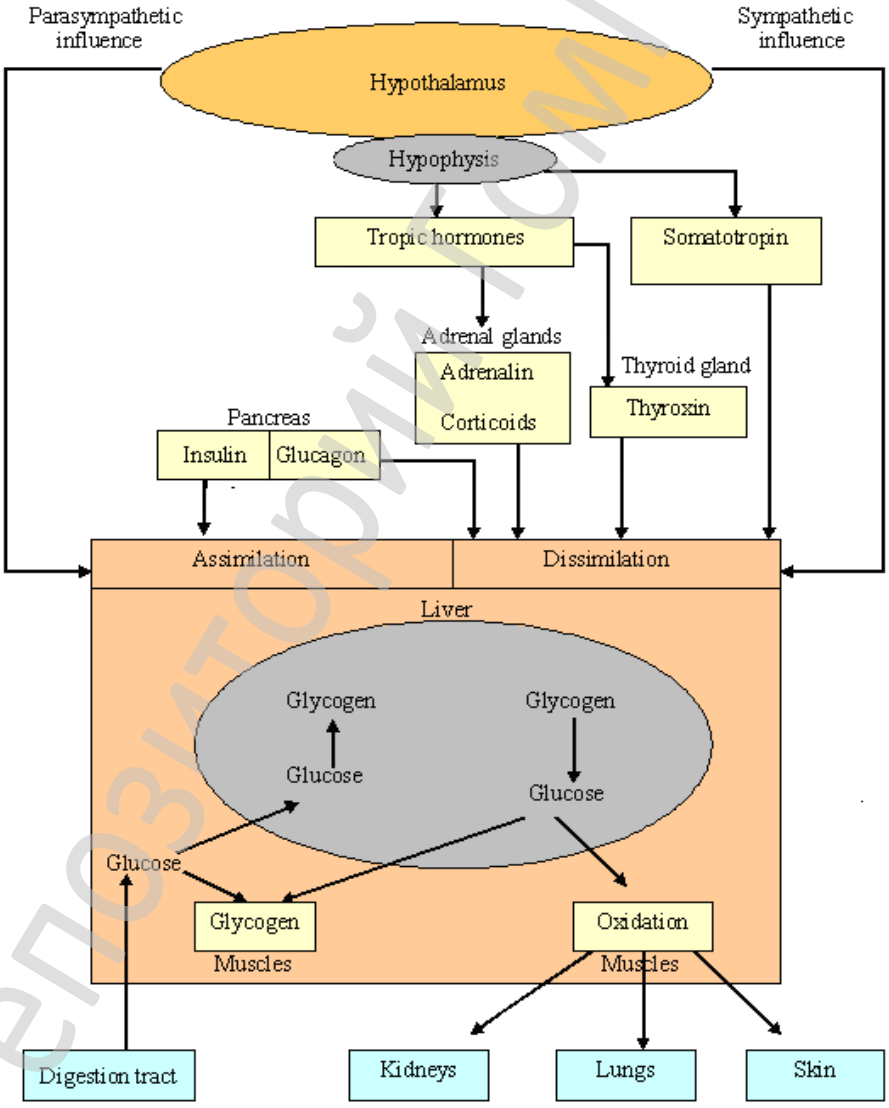


Figure 3.7 — Regulation of carbohydrate exchange (by Korobkov A. V., Chesnokova S. A., 1986)

A high blood glucose level leads to a decrease of the level of catabolic hormones. The release of glucagon is blocked, and insulin secretion into the blood

is activated by the parasympathetic system. A low blood glucose level causes anxiety and stress, which increases the activity of the sympathetic system, i.e. the production of adrenalin, glucagon, adrenocorticotropic and somatotropic hormones increases thus elevating the level of catabolic hormones; the external contour of the regulation boosts the endogenic mechanism — the sensation of hunger arises accompanied by procurement for food.

The participation of the cerebral cortex in the regulation of carbohydrate metabolism is proved by the development of hyperglycemia in students during examinations, in sportsmen before competitions, and in people under hypnosis.

Hormonal regulation

Insulin decreases the blood sugar level since it strengthens glycogen synthesis in the liver and muscles and elevates the glucose consumption by body tissues. Insulin is a unique hormone which decreases the blood glucose level. Low insulin contributes to the development of stable hyperglycemia with consequent glycosuria.

Countra-insular hormones. In low blood sugar ***glucagon, adrenalin, somatotropin,*** and ***hydrocortisol*** «inhibit» the uptake of glucose by cells, stimulate the transformation of glycogen into glucose.

Glucagon promotes the breakdown of glycogen in the liver.

Adrenalin affects the liver and muscles, invokes glycogen mobilization and increases the blood glucose level.

Review questions

1. Give the definition of "metabolism". What is the role of nutrients in the body? What is the difference between the processes of anabolism and catabolism?

2. What are the functions of proteins in the body? What amino acids are called essential? Give the examples. What is the nitrogen balance? Give some examples of positive and negative nitrogen balance. How is the protein exchange regulated? Name the daily consumption of proteins.

3. What are the functions of fats in the body? Where are fats deposed? Name the essential fatty acids. How is the exchange of fats regulated? Name the daily consumption of fats.

4. What are the functions of carbohydrates in the body? What is hyperglycemia? How is the exchange of carbohydrates regulated? What is the role of insulin in the regulation of carbohydrate exchange? Name the daily consumption of carbohydrates.

3.2. Energy metabolism

All the processes happening within the body can be divided into 3 groups: plastic, energetic, and informational.

The use of chemical energy is called energy metabolism.

There is constant transformation of energy during metabolism: the potential energy of complex organic compounds taken in as food is transformed into thermal, mechanical, and electrical energy (Figure 3.8).

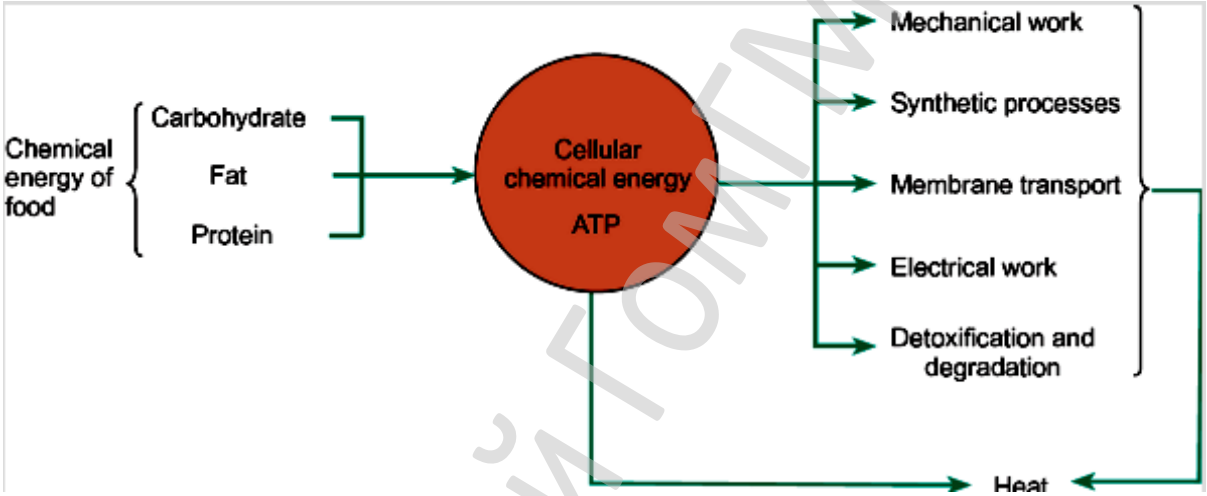


Figure 3.8 — Energy transformation in the human body (from studylib.net)

Due to the release of energy in the body, its constant temperature is maintained and the work of the internal organs is carried out. The largest amount of energy in the body is spent on the processes of movement and cardiac activity, respiration, intestinal peristalsis, etc.

The processes of energy exchange are based on the laws of thermodynamics — mutual transformation of different kinds of energy during its transition from one body to another in the form of heat or work. From this point of view living organisms can be related to open stationary non-equilibrium systems. It means that they exchange their substances and energy with the environment.

Energy expenditure is evaluated by the amount of heat released by the organism per unit of time. The unit of energy measurement in the International system of units (SI) is the **Joule (J)** or **kilojoule (kJ).**

In physiological and medical research, non-SI units are used to determine the amount of energy released by the body— a **calorie (cal)** or a **kilocalorie (kcal)**; **1 cal = 4.19 J.**

The calorie is the unit of energy (heat) required to increase the temperature of 1 g of water by 1°C (in the range from 14.5 to 15.5).

3.2.1. Measurement of body energy consumption

All energy released during the breakdown of nutrients to final products depends only on the state of the initial substance and final products and does not depend on what intermediate stages or pathways their degradation goes through.

Without physical work all chemical energy transforms into heat, which makes it possible to use heat production as a parameter of the intensity of energy metabolism.

The amount of heat released or absorbed during various physical and chemical processes is calculated by means of direct and indirect calorimetry (Figure 3.9).

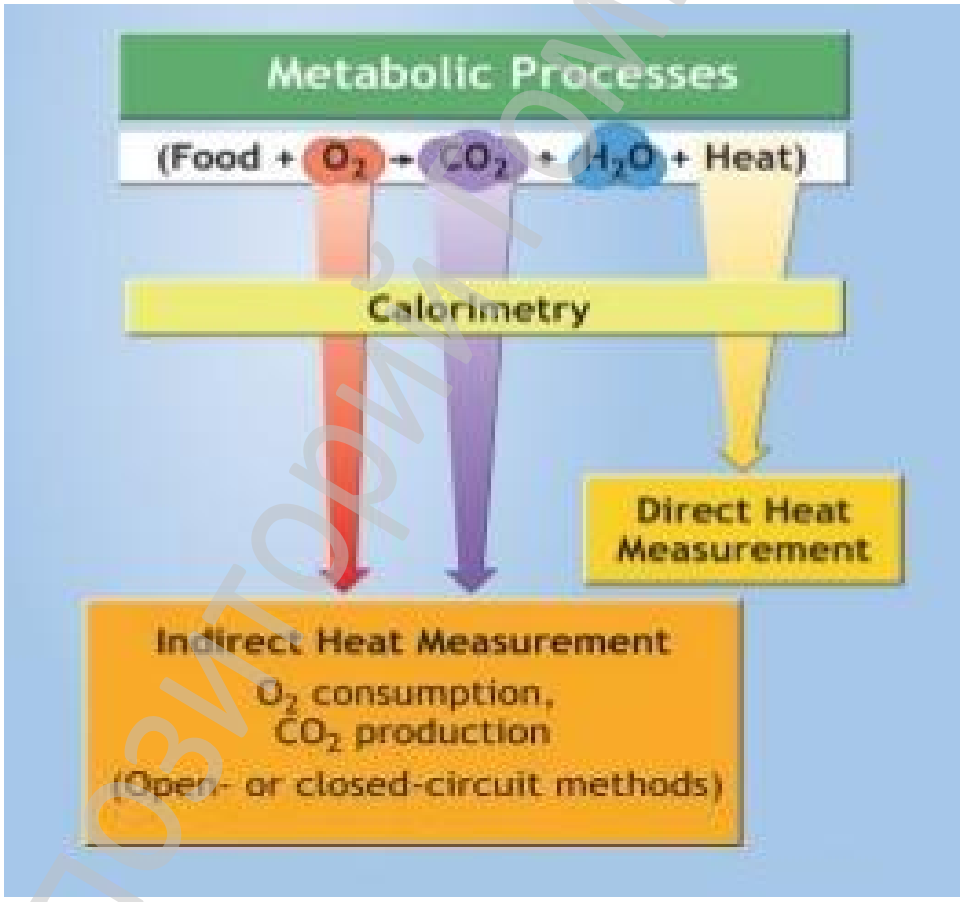


Figure 3.9 — Principles of energy consumption measurement (from slideplayer.com)

In physiology and medicine, calorimetry is used to study thermal effects at rest, in various kinds of activity and diseases.

Direct calorimetry (Figure 3.10a)

Direct calorimetry is based on direct and complete count of the amount of heat released by an organism. The measurements are made in special chambers — biocalorimeters, which are well airproofed and thermoisolated

from the environment. The calculation of the amount of released heat is determined by the difference of the temperature of water coming into the chamber and flowing out from it.

Indirect calorimetry (Figure 3.10b)

The method of indirect calorimetry is based on the measurement of the amount of oxygen intake and the release of carbonic gas during a certain interval of time (complete gas analysis) or in the conditions of relative rest — only the amounts of oxygen intake (incomplete gas analysis) with the subsequent calculation of heat production are determined.

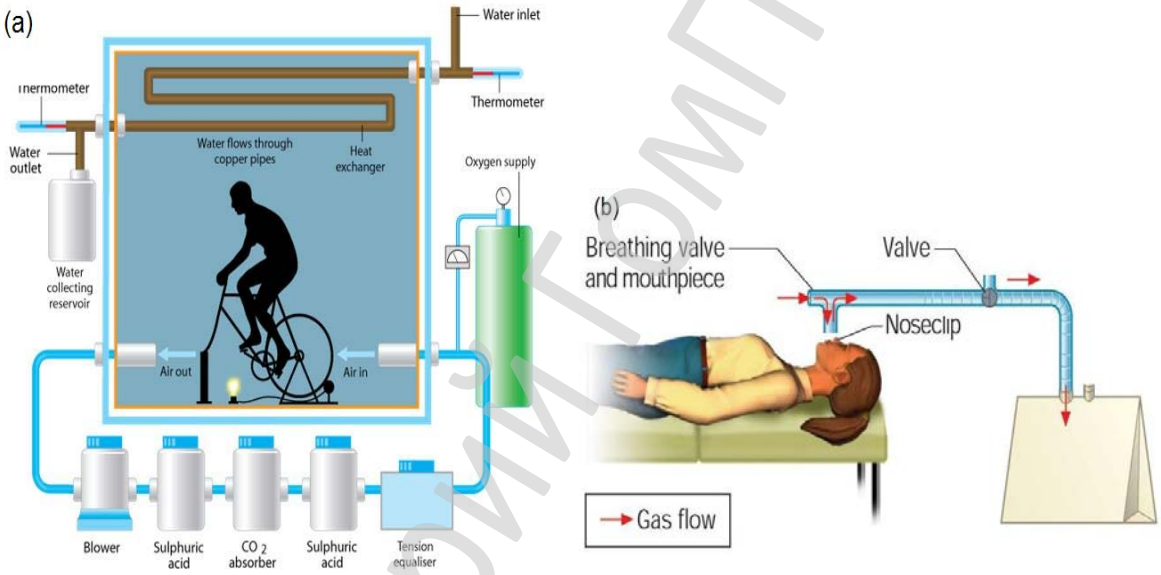


Figure 3.10 — Direct (a) and indirect (b) calorimetry (from studylib.net)

Complete gas analysis

Nowadays, *the complete gas* analysis is performed by the open respiratory method **of Douglas-Choldane**. The method is based on the collection of the expired air into a special reservoir (***airproof sack***) with the consequent determination of its total amount and the amount of oxygen and carbonic gas in it by means of gas analyzers.

The energy consumption measurement routine:

1. According to the amount of gases in the atmospheric air, the amounts of consumed oxygen and excreted CO_2 can be calculated with the following determination of respiratory coefficient.

Respiratory quotient (RQ). The ratio of the volume of released CO_2 to the volume of consumed oxygen is called the respiratory quotient:

$RQ = C0_2$ (L) / 0_2 (L)

The respiratory quotient characterizes the type of nutrients which are mainly oxidized in the body at the time of its determination.

***For carbohydrates: RQ* = 1**
***For fats:* RQ = 0.7**
***For proteins:* RQ = 0.80**
***For mixed food RQ* = 0.8–0.9.**

2. Each respiratory quotient corresponds to the specific ***thermal equivalent of oxygen (TEO)***, i. e. *the amount of heat released during the consumption of 1 L of oxygen.* The TEO is usually determined by tables (for example, the TEO of mixed food for a RQ of 0.85 is 4.8 kilocalories).

3. The determined thermal equivalent of oxygen is multiplied by the amount of consumed oxygen (Table 3.1) and the amount of energy necessary to perform a certain kind of activity per unit of time (t):

$$Q = TEO \cdot VO_2,$$

where Q—amount of energy per unit of time.

Table 3.1 — Oxygen consumption and heat release during oxidation of various substances in the body

The substance oxidized in the body	The amount of heat released during oxidation of 1 g of substance, kJ (kcal)	The amount of consumed O_2, L	The amount of energy released during oxidation of 1 L O_2 , kJ (kcal)
Proteins	17.17 (4,1)	0.966	19.26 (4.60)
Fats	39.94 (9,3)	2.019	19.64 (4.69)
Carbohydrates	17.17 (4,1)	0.830	21.14 (5.05)

4. The energy exchange per day is determined by the formula:

$$Q_{day}=Q \bullet t_{day}$$

Indirect calorimetric calculations

Indirect calorimetric calculations are methods for estimating energy exchange based on calculations by indirect parameters (for example, basal metabolism can be determined using formulas or tables, then the obtained result is multiplied by the activity coefficient). Their accuracy is low, since they have a large error. They are used for approximate estimation of energy consumption.

3.2.2. Basal metabolism

Even in the condition of complete rest people spend some energy. In the body, energy is continuously spent on the maintenance of the physiological processes (Figure 3.11).

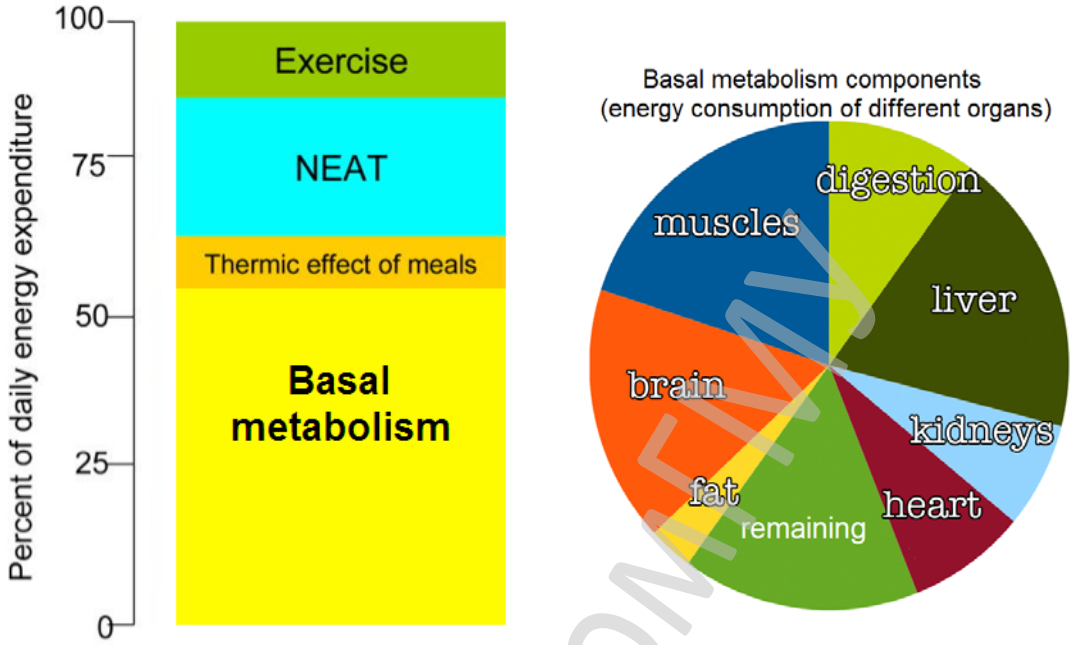


Figure 3.11 — Components of energy expenditure (from studylib.net)

Basal metabolism is the minimum amount of energy necessary for the maintenance of normal vital activity when the person is awake and at complete physical and mental rest, and having normal body temperature. This energy is spent on the processes of cellular metabolism, blood circulation, respiration, excretion, maintenance of body temperature, functioning of the vital nerve centers of the brain, constant secretion of the endocrine glands.

The liver consumes 27 % of basal metabolic energy, the brain — 19 %, the muscles — 18 %, the kidneys — 10 %, the heart — 7 %, all the other organs and tissues — 19 %.

Any work, either physical or mental, and also food intake, the environmental temperature fluctuations and other internal and external factors changing the level of metabolic processes result in increased energy consumption.

Basal metabolism is determined under strictly controlled standard conditions.

Standard conditions for the determination of basal metabolism:

1. In the morning. The intensity of metabolism is exposed to daily fluctuations. It increases in the morning and decreases in the night-time.

2. In the lying position, at a state of complete relaxation. In the conditions of physical and mental strain, the intensity of metabolic processes increases. It is connected with the increased number of muscular cells participating in the work. Brainwork leads to the reflex increase of muscle tone.

3. In the post-absorptive state (12-14 hours after the intake of last meal).

A high metabolic rate after meals may last for 12 hrs, and after the consumption of proteins this period can reach 18 hrs. Energy exchange begins to grow within 1–2 hours reaching its maximum 3 hrs after a meal and lasts for 7–8 hrs after food intake.

4. In a thermally neutral environment (18–20 °C).

The basal metabolic rate for a middle-aged man (aged 35), average body height (1.65 m), average weight (70 kg) is 1 kcal (4.19 kilojoules) per 1 kg of body weight per hour, or **1,700 kcal per day.**

Factors determining basal metabolism

Basal metabolism depends on age, height, body weight, sex. The most intensive basal metabolism (per 1 kg of body weight) is found in children (in newborns — 53 kilocalories/kg a day, in children under 1—42 kilocalories/kg). The average basal metabolic rates in healthy adult males are **1,300–1,700 kilocalorie/day**, or 7,100 kilojoules a day; in females these parameters are 10-15% lower. The male sex hormone testosterone can increase the intensity of metabolism, the female sex hormones usually have a marginal effect on the value of basal metabolism. The significant influence of the male sex hormones is caused by their anabolic effect, which leads to an increase in muscle mass.

With years the rate of basal metabolism gradually reduces.

There are seasonal fluctuations of the basal metabolic rate — it increases in spring and decreases in winter. Besides, the rate of basal metabolism is influenced by muscle work, state of the endocrine glands.

Methods for the determination of basal metabolism

Special tables help to determine the average rates of human basal metabolism by height, age, and body weight.

3.2.3. Working metabolism

Working metabolism is a set of basal metabolism and energy consumption of an organism providing its functioning in conditions of thermoregulational, emotional, food, and working loads.

In cold conditions the thermoregulational increase of metabolism and the intensity of energy exchange develop and a person` metabolism can reach 300 % of basal metabolism.

Positive and negative emotions cause increased energy consumption and in an adult it is usually 40–90 % of the basal metabolic rate, which is mainly

connected with the involvement of muscular reactions. Listening to the radio which causes emotional reactions can raise energy consumption by 50 %, and in crying children the energy expense may increase threefold.

The working metabolic rate exceeds the basal metabolic rate, mainly due to the functions of skeletal muscles. In their intensive contractions the energy consumption in muscles can increase by 100 times, in the participation in this reaction of more than 1/3 skeletal muscles for some seconds the total energy consumption can increase by 50 times. Daily motor activity in the population of industrially developed countries is rather insignificant, therefore their daily energy consumption makes approximately 8,000–10,500 kilojoules, or 2,000–2,250 kcal.

In the sitting position a person spends only by 20 % more energy than in the lying position. In the standing position a person spends 40 % of energy more than in the conditions of basal metabolism. Walking at a speed not less than 5 km/h raises the energy consumption by 3–4 times. A daily two-kilometer walk (without changes in diet) can promote removal of 1 kg of fat within a month. Due to the increased energy consumption in physical dynamic loads (fast walking, running, swimming, skiing) not less than 3 times a week it is possible to raise human health reserves considerably.

The rate of metabolism in a sleeping person is 10–15 % less than in a person who is completely awake. This is caused by relaxation of muscles, also by the low activity of the sympathetic nervous system and low production of adrenal and thyroid hormones, which increases catabolism.

The difference between the energy consumption in physical strain and that of basal metabolism makes ***the working addition,*** which increases once work gets more intensive. The working addition is all the energy which an organism spends on its physical and mental activity during a day.

The factor of physical activity is the ratio of the general energy consumption on all kinds of vital activity to the rate of basal metabolism. This parameter is an objective physical criterion which defines adequate quantity of energy consumption for concrete professional groups of people. The values of the factor of physical activity are identical for men and women, but because of lower body weight in women the energy consumption of basal metabolism in men and women in groups with the same factor of physical activity varies (Table 3.2).

Table 3.2 — The amount of energy consumption depending on the features

The group	Features of the profession	The coefficient of physical activity	Total daily energy expenditure, kcal,	Total daily energy expenditure, kJ
I. *Very low physical activity*.	Predominantly workers of intellectual labor (workers of science, literature and printing, cultural workers, workers of planning and accounting, secretaries, clerks, students of humanitarian specialties, teachers, educators, computer operators, dispatchers and others)	1.4	2100–2450	9799–10265
II. *Low physical activity*.	Workers of simple physical work: tram drivers, trolleybus drivers, conveyor workers, service workers, staff nurses, hospital attendants, veterinary workers, instructors of physical culture and sports, trainers, etc.	1.6	2500–2800	10475–11732
III. *Medium physical activity.*	The workers of average weight work are included into this group (mechanics, bus drivers, surgeons, chemists, textile workers, railwaymen, metallurgists, workers of chemical plants, food industry workers, etc.)	1.9	2950–3300	12360–13827
IV. *High physical activity.*	The workers of heavy physical work: construction workers, most agricultural workers, milkmaids, vegetable growers, metallurgists, workers of oil and gas industry etc.	2.2	3400–3850	14246–16131
V. *Very high physical activity.*	Workers of particularly hard physical work are included into this group, only men (agricultural workers during the sowing and harvest periods, miners, steelworkers, concrete workers, masons, diggers, loaders of non-mechanized work, etc.).	2.5	3850–4200	16131–17598

Energy metabolism in brainwork. The energy consumption in brainwork is considerably less than in physical work.

Difficult mathematical calculations, work with books and other forms of brainwork if they are not accompanied by movement, cause insignificant (2–3 %) increase of energy consumption in comparison with complete rest. However, in most cases various kinds of brainwork are accompanied by muscle activity, especially in emotional excitation of a working person (lecturer, actor, writer, orator, etc.), therefore energy consumption can be rather greater. Emotional excitation can cause a higher metabolic rate (by 11–19 %) within a few days.

3.2.4. Specific dynamic action of food

The specific dynamic action of food is the increased energy expenditure after a meal, caused by the transformation of food substances in the body (mainly during their digestion and absorption from the digestive tract).

Increased metabolism and energy exchange begin after an hour, reach their maximum 3 hours after food intake and are kept within several hours.

Mixed food increases energy expenditure by 5–10 %; carbohydrate and fat food increases it approximately by 14–15 %. Food rich in proteins can increase energy consumption by 30 %. It is caused by the fact that metabolic transformations of proteins in the body are more complex and demand greater expenses of energy in comparison with fats and carbohydrates.

The specific dynamic action of food is one of the mechanisms of self-control of human body weight. Thus, an excessive intake of food especially rich in proteins leads to increased energy expenditure. Limited food intake is accompanied by decreased energy consumption. Therefore, overweight people can correct their body weight not only by limiting the caloric content of food, but also by increasing the energy consumption, e. g., by means of physical exercise or cooling procedures.

3.2.5. Regulation of energy metabolism

The rate of energy metabolism is in close dependence with physical activity, emotional stress, diet, the degree of heat production, and some other factors.

There are conditioned reflexes that are able to influence energy exchange. Any earlier indifferent stimuli being combined over time with muscle activity can serve as a signal for higher metabolic rate and energy exchange.

All this testifies to the fact that the rate of energy metabolism in the body can change under the influence of the cerebral cortex. So, in a racing sportsman

before the start the consumption of oxygen, and, hence, energy exchange sharply increases. The same occurs in a person when they arrive at work under the action of conditional working factors. If a person under hypnosis is impressed that they perform heavy muscle work, their metabolism can rise considerably though actually they do not perform any work.

A special role in the regulation of energy exchange is played by the hypothalamus. Here regulating influences are formed which are realized by the vegetative nerves or humoral part due to increased secretion of some endocrine glands. Energy exchange is especially elevated by thyroxin, triiodothyronine, and adrenaline.

3.3. Physiological bases of nutrition

The science about nutrition is called trophology. It considers all the sets of processes of food intake into the body, transformation of its various components into cell and tissue components, energy transformation of nutrients and ways of excretion of final metabolites.

One of the sections of trophology is the physiology of nutrition. It studies the human needs for nutrients, defines the optimal conditions of food digestion and the following use of nutrients.

Nutrition is a complex process of ingestion, adsorption, and digestion of food substances in the human body. It is a vital physiological need which is necessary for the construction and continuous renewal of cells and tissues, processes of growth and development, maintenance of basal metabolism and vital activity, energy consumption. Correct nutrition increases body resistance to unfavorable environmental conditions and has a great importance in prevention of many diseases.

3.3.1. Theories of nutrition

There are three basal theories of nutrition: antique, which is of interest from the historical point of view; classical (the theory of balanced nutrition); modern (the theory of adequate nutrition).

The antique theory of nutrition was formulated by Aristotel and Halen. According to this theory, the nutrition of an organism occurs due to blood which is formed of food substances as a result of their fermentation in the gastrointestinal tract.

The classical theory, or the theory of balanced nutrition, was formed in the last century and can be reduced to several fundamental postulates:

- Nutrition supports the molecular composition of the body and reimburses its energy and plastic costs.

- Ideal food is the food, in which the intake of nutrients as accurately as possible (by time and composition) corresponds to their expenditure.
- The ratio of proteins, fats and carbohydrates in food makes 1:1:4.
- The equality of intake and consumption of nutrients is reached within a short period of time.
- The process of digestion is reduced to the purification of nutrients useful for the body from ballast and harmful (toxic) substances which should be excreted.
- The supply of nutrients to blood is provided by the hydrolysis of food structures and absorption of nutrients necessary for metabolism through an intestinal barrier.
- The utilization of food is carried out by the body itself.

The theory of adequate nutrition, which is accepted now, most fully reflects all the sides of the problem of adequate nutrition. The basic principles of this theory:

- Nutrition supports molecular composition and reimburses the energy and plastic expenses of the body for basic metabolism, external work, and growth).
- The equality of intake and consumption of nutrients is reached within a rather long period of time.
- The balance of nutrients in the body is achieved by two kinds of nutrients: primary nutrients from food and secondary nutrients, which are formed of its components as a result of enzymatic hydrolysis in the body. Primary and secondary nutrients join in cellular metabolism but their relative role varies widely.
- There is endoecology of the host organism, formed by the intestinal microflora, with which the host organism maintains complex symbiontic relations, as well as intestinal, or enteral, environment.
- Necessary components of food are not only nutrients, but also so-called regulatory, including ballast substances, for example food fibers. It has been found, that they play a huge role in normal digestion and metabolism of nutrients.

Food fibers carry out the following functions:

- they normalize motor activity (motility) of the digestive tract;
- they regulate the speed of nutrient absorption, especially in the small intestine;
- they take part in electrolyte exchange;
- they adsorb (bind) and excrete toxic substances;
- they normalize and provide feeding for bacteria in the large intestine.

The sources of food fibers are rough food, vegetables, bran, groats of coarse grinding, etc. Food fibres are added as a medical component in various culinary products, in bread. They are used in the course of the treatment for pancreatitis, stomach ulcer, colitis.

Review questions

1. What is energy metabolism? What are the reasons and ways of energy transformation in the human body?

2. Name the methods of the measurement of body energy consumption. What is the basis for direct calorimetry? What is indirect calorimetry? What is the respiratory quotient and what factors influence it? What is the calorific equivalent of oxygen? How it is determined?

3. What is basal metabolism? Under what conditions is it determined? What factors influence the rate of basal metabolism? What is the basal metabolic rate?

4. What is working metabolism? What is the working addition? Name and describe the groups of people according to their energy consumption and physical activity.

5. What is the specific dynamic action of food? Which nutrients have the highest specific dynamic action?

6. How is the regulation of energy metabolism carried out?

7. What is trophology? Give the definition of «nutrition». What are the theories of nutrition? What are their peculiarities?

UNIT 4
THERMOREGULATION

4.1. Body temperature and isothermia

The body temperature of humans and higher animals is maintained at a rather constant level despite the fluctuating temperature of the external environment. This constancy of the body temperature is called isothermia. Isothermia is typical only for homoiothermal (warm-blooded) animals.

A decrease of the environmental temperature under 0°C can result in the processes of cellular destruction. A body temperature above 45°C induces protein denaturation. Proteins are responsible for all the regulatory functions of living organisms, therefore their structural and functional integrity is essential.

Human body temperature and its daily variation

The human body temperature depends on the following factors:

1) **processes of thermogenesis and heat loss;**

2) **environmental factors;**

3) **behavioral activity.**

The normal body temperature of a healthy human undergoes periodic fluctuations within 0.5–0.7 °C throughout the day: from its minimum in the morning (3–4 a.m.) and its maximum in the evening (4–6 p.m.).

It is caused by the circadian rhythms of human functional activity because of the change between day and night. The normal daily rhythm of the temperature fluctuations is fixed by genetic and individually acquired biological memory in the central thermoregulatory structures (if a person crosses the time zones, 1–2 weeks are needed for the temperature rhythm to adapt).

The brain and the internal organs of the thoracic and abdominal cavities constitute the body`s central ***«core temperature»*** and provide about 70% of all heat production. The skin, subcutaneous fat, surface muscles compose its peripheral ***«shell temperature»*** (Figure 4.1).

Thermal homeostasis is the ability to maintain the temperature of the internal organs at a constant high level (36–41 °C). The temperature of the body`s «shell» can vary within 10 °C and more. The temperature of the «core» fluctuate no more than within 2 °C.

Thus, thermal homeostasis is regarded only in relation to the body`s «core».

The source of heat production is catabolic processes. Body thermogenesis occurs due to exothermal reactions proceeding continuously. These reactions occur in all the organs and tissues with different intensity. In tissues and organs

producing active work (in muscular tissue, liver, kidneys) more heat is produced than in less active ones (connective tissue, cartilages and bones). In muscle activity thermogenesis increases by 50–80 %, during hard work — by 400–500 %, in cold exposure — by 10 %.

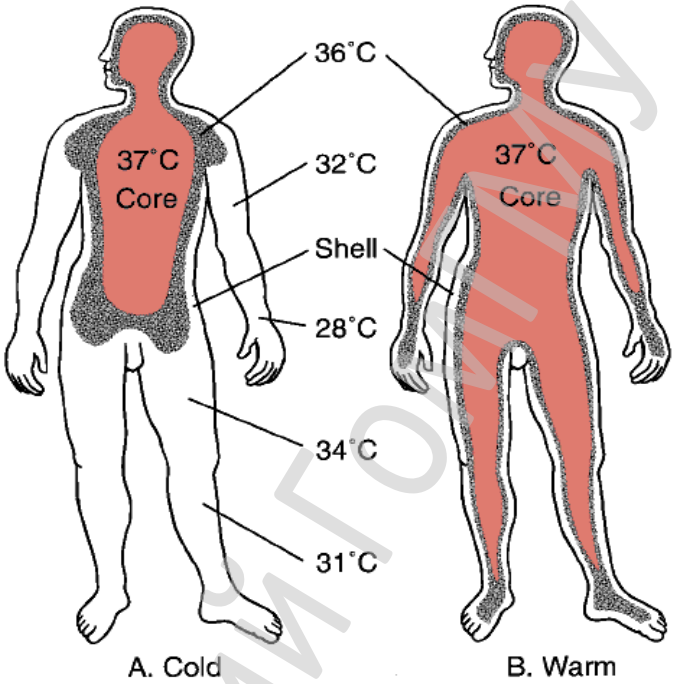


Figure 4.1 — Human body`s core and shell temperatures (from picgalleria.com)

The loss of heat by organs and tissues depends, to a greater extent, on their location; e. g., the surface organs (skin, skeletal muscles) give more heat and get more cold than the internal organs, which are more protected.

The temperature of various organs varies. The liver, located deep in the body and producing a lot of heat, has a constant temperature (37.8–38 °C). The skin temperature (29.5–33.5 °C) depends on the environment. Isothermia is typical for the internal organs and brain (can vary within 1–2 °C).

4.2. Thermoregulation

The constancy of the human body temperature can be stable under the condition of the equality of heat production and heat loss of the whole body. These processes are regulated by the nervous and endocrine systems, which respond to negative feedback. The body temperature is regulated at a set reference temperature, and temperature sensors throughout the body respond to the central controller in the medial preoptic/anterior hypothalamic region of the brainstem, which then adjusts heat production and loss accordingly. Thermoregulation can be divided into chemical and physical (Table 4.1).

Table 4.1 — Mechanisms of thermoregulation

Types of thermoregulation	Name of the mechanism	Description of the mechanism
Chemical thermoregulation (heat production)	Shivering thermogenesis	Irregular involuntary tonic contractions of muscles
	Non- shivering thermogenesis	• Increased metabolic processes in the internal organs. • Increased metabolic processes in brown adipose tissue. • Increased thermogenesis after food intake (due to the digestion process)
Physical thermoregulation (heat loss)	Thermal radiation	Radiation heat transfer occurs via electromagnetic waves
	Convection	If the skin is warmer than the surrounding air, the air layer adjacent to the skin is heated up by conduction from the body, but carries the heat away from the body in the ambient air currents
	Heat conduction	The transfer of heat from one subject to another during an immediate contact with the body surface. Biological tissues serve as isolators (for example, fats)
	Evaporation	The evaporation of fluid (sweat) from the surface of the skin to vapor occurs with energy consumption
	Changing of the lumens of the skin vessels	The dilatation of the skin vessels (peripheral vasodilation) increases heat loss, and constriction of the skin vessels (vasoconstriction) decreases heat loss
	Changing of the respiration rate	The expired air carries heat. Rapid respiration facilitates heat loss.

In addition to these two mechanisms, there is **behavioral thermoregulation** — controlled conscious actions aimed at the maintenance of temperature homeostasis. Changes of behavior along with internal vegetative reactions contribute to the achievement of a body temperature optimal for metabolism. People often tend to increase their muscle work to maintain their temperature. In cold conditions besides muscle reactions (chills, shivering), people make additional energetic movements: fast walking, squats, running, waving, etc. For example, walking increases heat production almost twice, and in running heat production increases by 4-5 times.

4.2.1. Chemical thermoregulation

Heat production

It happens continuously during metabolism and depends on an organism`s individual features (body weight, height, area of body surface, sex, age), the

temperature of the environment, intensity of muscle work, diet, emotional state, oxygen supply, etc. Chemical thermoregulation has an important value for the maintenance of the human body temperature both in normal conditions and if the environmental temperature changes. If the temperature of the environment becomes lower than the optimal comfortable temperature (18–20 °C), metabolic processes strengthen, and thermogenesis increases.

In humans during ontogenesis, isothermia develops gradually. The newborn's ability to maintain the body temperature is imperfect. Newborns are easily exposed both to cold and heat at temperatures which may not affect an adult. Low muscle work caused by long cries can increase the body temperature. During early ontogenesis (about several weeks) in a newborn the constancy of the body temperature is maintained due to the use of brown fat. This tissue is located in the area of the neck, between the scapulae, in the axillae, and provides non-shivering thermogenesis.

Premature children are even less capable to maintain the constant body temperature.

Under the conditions of the sharply decreased environmental temperature, the receptors are excited by cold stimulation resulting in irregular involuntary tonic muscle contractions reflecting as shivering.

The metabolic processes strengthen, the oxygen and carbohydrate consumption by muscle tissue increases.

In chemical thermoregulation, except for muscles, a considerable role is played by the liver and kidneys. The temperature of the blood of the hepatic vein is higher than that of the blood of the hepatic artery.

The acceleration of the metabolic processes which is not caused by muscle contractions is called non-shivering thermogenesis.

The oxidation of proteins, fats, and carbohydrates leads to increased thermogenesis.

4.2.2. Physical thermoregulation

Heat loss. Physical thermoregulation protects the body from overheating and is carried out by changing the organism`s heat radiation (Figures 4.2, 4.3). It becomes vital if the environmental temperature rises.

The means of heat loss are:

1. Radiation
2. Convection.
3. Heat conduction.
4. Evaporation.

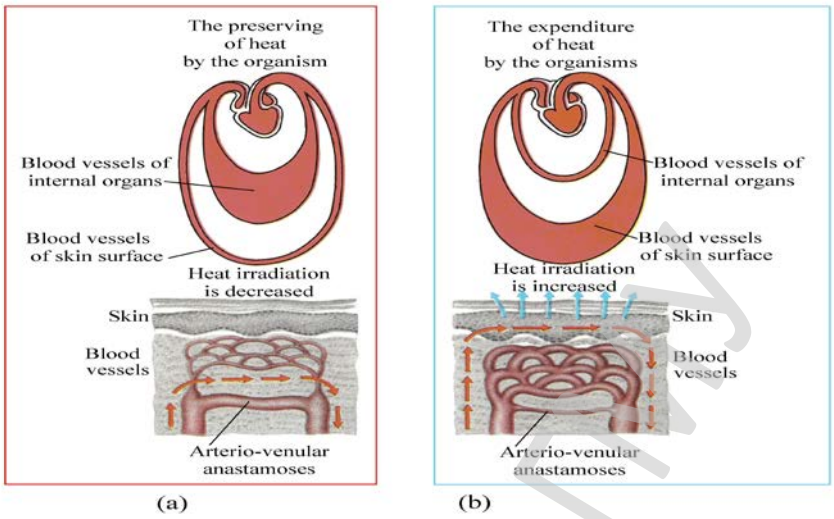


Figure 4.2 — Mechanisms of heat radiation by the organism under the conditions of the cold (a) and heat (b) (by Sherington, 1987)

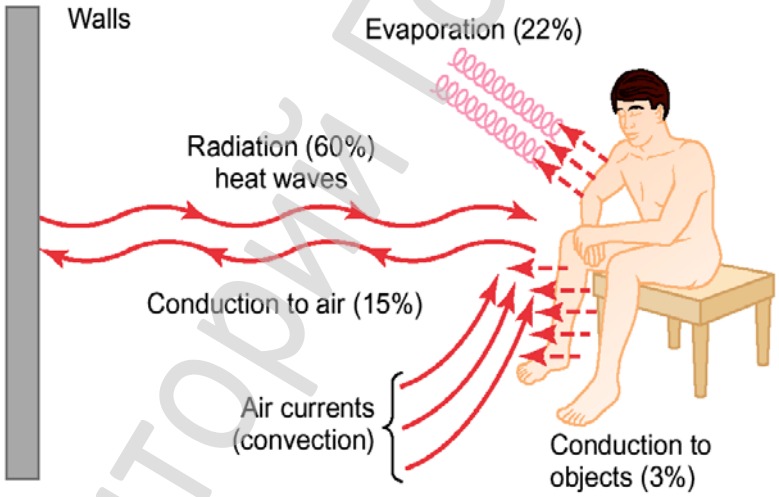


Figure 4.3 — Means of heat loss (by C. Guyton and John E. Hall, 2016)

Thermal radiation

All subjects with a temperature higher than absolute zero give energy via radiation. Radiation heat transfer occurs via electromagnetic waves.

Convection is the process of heat loss which occurs when new unheated air is continually brought in contact with the skin. If the skin is warmer then the surrounding air, the thin air layer adjacent to the skin is heated by conduction from the body, but carries the heat away from the body in the ambient air currents.

Heat conduction

The transfer of heat from one subject to another during an immediate contact with the body surface is called heat conduction (also known as thermal

conduction). Biological tissues serve as isolators, e.g. fats. Heat conduction in mammals is not the basic way of heat loss.

Water evaporation from the skin surface. Thus there are energy expenses for the transition of fluid into vapor. To evaporate 1 ml of water from the body surface, 2.43 kilojoules (0.58 kkal) of energy are used.

The centers of heat production and heat loss are interconnected. **The temperature reflexes can be controlled by the spinal cord.** The separation of the spinal cord from the medulla will result in disrupted physical thermoregulation. The endocrine glands participate in the hypothalamic regulation of the body temperature. In particular, adrenalin increases oxidative processes in muscles, increases heat production and constricts dermal vessels thus reducing heat loss.

Androgens promote the development of pyrogens (substances rising the body temperature).

If the external temperature is equal to the body temperature, heat loss occurs due to the evaporation of sweat, as convection and radiation are impossible. A humid environment reduces evaporation, therefore it is rather hard to tolerate high temperatures in the conditions of high humidity. In a very humid bathhouse, the body keeps pumping out sweat which does not evaporate, so the body temperature does not drop. The human body can badly tolerate a temperature of 32 °C with high humidity. Synthetic clothes interfere with heat loss. The respiratory organs participate in heat loss (expired air carries heat). At a high temperature respiration becomes frequent, and the respiratory center gets exited, and vice versa.

Thus, these mechanisms maintain a thermal balance – a certain ratio between the formation of heat in the body and its release to the external environment.

Equation of heat balance

$M \pm Q_t \pm Q_c \pm Q_r - Q_e = 0$	Normothermia;
$M \pm Q_t \pm Q_c \pm Q_r - Q_e > 0$	Hyperthermia;
$M \pm Q_t \pm Q_c \pm Q_r - Q_e < 0$	Hypothermia,

where: M — heat production; Q_t — heat transfer by thermal conduction; Q_c — heat transfer by convection; Q_r — heat transfer by thermal radiation; Q_e — heat exchange by evaporation

4.3. Regulation of isothermia (nervous and humoral)

The regulation of a constant body temperature is a complex reflex exercised as a result of the irritation of the skin receptors, dermal and hypodermic vessels, and also the CNS (Figure 4.4). Both the peripheral and

central thermoreceptors have two subtypes: those responding to cold and those responding to warmth. Cold receptors raise the pulse rate at a low temperature, and warm receptors do the opposite (Table 4.2).

Table 4.2 — Regulation of constant body temperature

Receptors	Spinal cord	Hypothalamus	Cerebral cortex
Cold and warm thermoreceptors are located in the skin, dermal and hypodermic vessels, and in the CNS.	In the spinal cord there are some centers of thermoregulatory reflexes (it participates in the regulation of shivering thermogenesis and in the regulation of the lumen of the skin vessels)	The centers of heat loss are located in the region of the anterior nuclei of the hypothalamus; the centers of heat production are located in the lateral-dorsal region of the hypothalamus	It is possible to form the conditioned reflex resulting in a body temperature rise. The body temperature can increase under hypnosis, in mental diseases, hysteria.

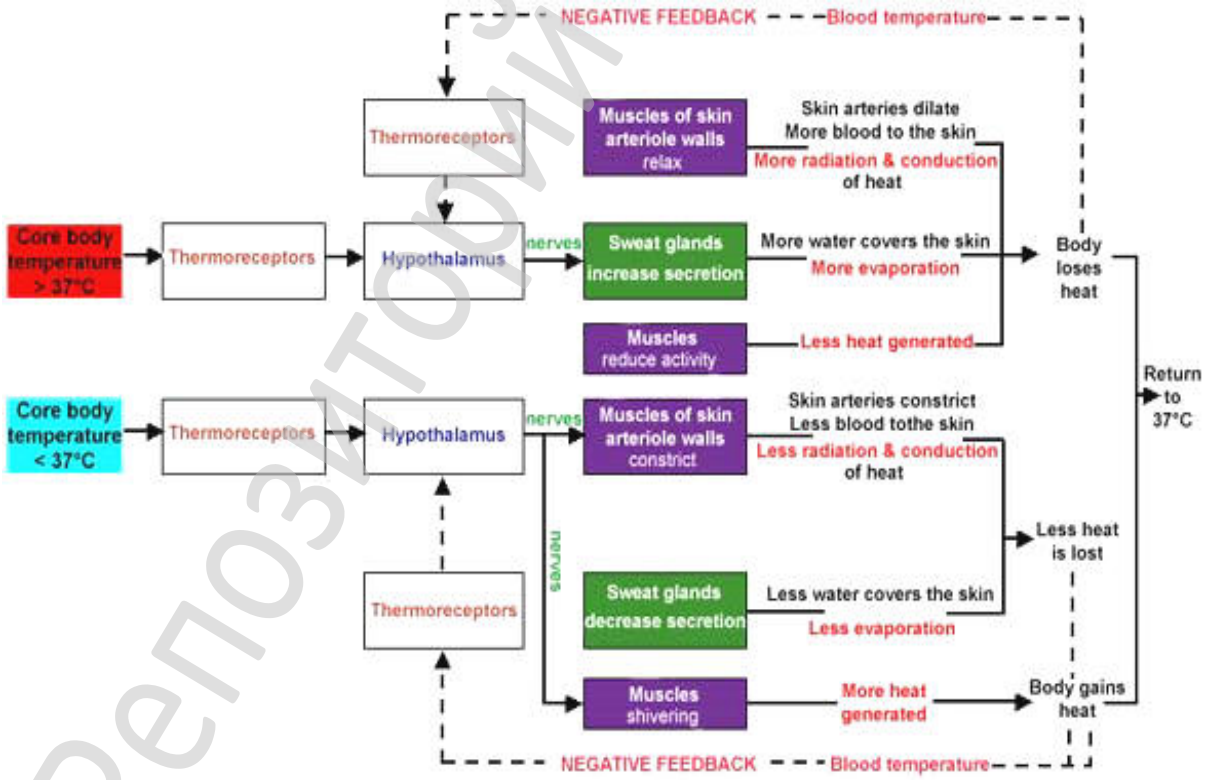


Figure 4.4 — Regulation of body temperature (from studylib.net)

The warm and cold receptors in the CNS react to changes of the temperature of the blood flowing to the nerve centers. The hypothalamus is the coordinating or central integration center for thermoregulation, and its

preoptic anterior part is the most important region for autonomic temperature control. A destructive lesion of the hypothalamus in an animal disrupts the ability to adjust the body temperature and the animal becomes poikilothermal.

Depending on the environmental temperature, clothes and physical activity, the body can set its temperature at different levels upon reaching the equality of heat production and heat loss. However, due to the function of the hypothalamic center of thermoregulation, this level of temperature is quite certain and is called the “set point” of the temperature control mechanism. Its value may vary in different warm-blooded organisms. Thus, in birds it is about 40–41 °C, in rabbits — about 38 °C, in humans — about 37 °C. The formation of a certain level of the body temperature by the neural structures in the hypothalamus is an important function of thermoregulation. All the temperature control mechanisms continually attempt to bring the body temperature back the “set point” level.

The posterior part of the hypothalamus regulates heat production. The stimulation of this part results is intensified metabolism, increased heart rate, shivering, which altogether lead to increased thermogenesis. If the posterior part of the hypothalamus is damaged, the animal cannot stand low temperatures.

The anterior part of the hypothalamus is responsible for heat loss. If this region of the hypothalamus is stimulated, the skin vessels are dilated, and the sweat release increases. If the anterior part of the hypothalamus is damaged, the animal cannot stand hot temperatures.

The cerebral cortex also participates in the regulation of the body temperature. In experimental conditions it is possible to produce the conditioned reflex of changing the body temperature in animals. The human body temperature rises under hypnosis, in mental diseases, hysteria. There is evidence that the body temperature may rise in orators, actors, and in students during examinations.

4.4. Hypothermia and hyperthermia

If a person stays in conditions of low or high environmental temperature for a long time, the mechanisms of isothermia regulation appear insufficient. Low body temperature is called hypothermia, and high — hyperthermia.

Hypothermia is a life-threatening condition which occurs when the body temperature falls below **35 °C.** It classically develops from exposure to extreme cold (e. g. being in cold water). Thus the excitation of the sympathetic nervous system is observed, heat loss slows down, and heat production strengthens. This is promoted by muscular shiver. After a while the body temperature starts to fall. Thus a state similar to narcosis is observed: low sensitivity, weak reflex reactions, low excitability of the nerve centers. The metabolic rate goes down

sharply, the respiration rate and heart rates, and arterial pressure decrease (at a body temperature of 24–25 °C it can make 15 % of the initial rate). Artificially induced hypothermia, when the body is cooled to 24–28 °C, is used in surgical practice (surgery on the heart and CNS). Hypothermia reduces brain metabolism and consequently oxygen consumption. Therefore, a long cease of the blood supply of the brain is possible (instead of 3–5 minutes at a normal body temperature, at a temperature of 25–28 °C it takes 15 minutes). In hypothermia, patients can stand temporary cardiac and respiratory arrest more easily.

Medical preparations which exclude the influence of the sympathetic nervous system can be applied to suppress the adaptive reactions intended for the maintenance of the body temperature. These preparations stop the transfer of pulses from nerves along skeletal muscles (relaxants).

Hyperthermia is a condition when the body temperature rises to levels higher than normal (above 37 °C). It arises under the influence of internal causes, increased thermogenesis (thyroxine, fatty acids) or in hot environmental temperature. An acute hyperthermia state when the body temperature reaches 40–41 °C refers to as ***heatstroke***. It is accompanied by dizziness, vomiting, and sometimes loss of consciousness. It is known, that the body temperature of 42°C is the threshold temperature for survival, a human can sustain a short period with the body temperature of about 43 °C.

Fever

Two basic groups of fever:

1. Infectious (bacteria, viruses).

2. Non-infectious, i. e. non-microbial origin. Fever develops under the influence of exogenous and internal causes, producing tissue damage and aseptic inflammation (combustions, traumas, infarcts, hemorrhages). Non-infectious fever can occur in hormonal distresses, emotional stress, hysteria, under the action of pharmacological preparations.

Fever is an adaptive protective reaction of the body arising under the action of pathogenic factors. In fever the process of thermoregulation is aimed at the maintenance of a higher body temperature.

In the mechanism of the development of fever the leading part belongs to pyrogenic substances: exogenous, endogenous, which influence the hypothalamic centers of thermoregulation (Figure 4.5).

Exogenous pyrogens are mainly released from bacteria (e. g., lipopolysaccharide toxins released from bacterial cell membranes). After phagocytosis of bacteria, leukocytes or tissue macrophages produce cytokines (signaling molecules involved in immune responses). Cytokines which cause fever are called ***endogenous pyrogens***. One of the most important of these cytokines in causing fever is ***interleukin-1 (IL-1).*** Interleukin-1 causes fever by inducing the

formation of mainly ***prostaglandin E_2***, which acts in the hypothalamus to elicit fever reactions. Prostaglandin E_2 is one of the main stimulating factors for the thermoreceptors of the preoptic area of the hypothalamus. When prostaglandin formation is blocked by drugs (e. g., aspirin), fever is either completely abrogated or at least reduced.

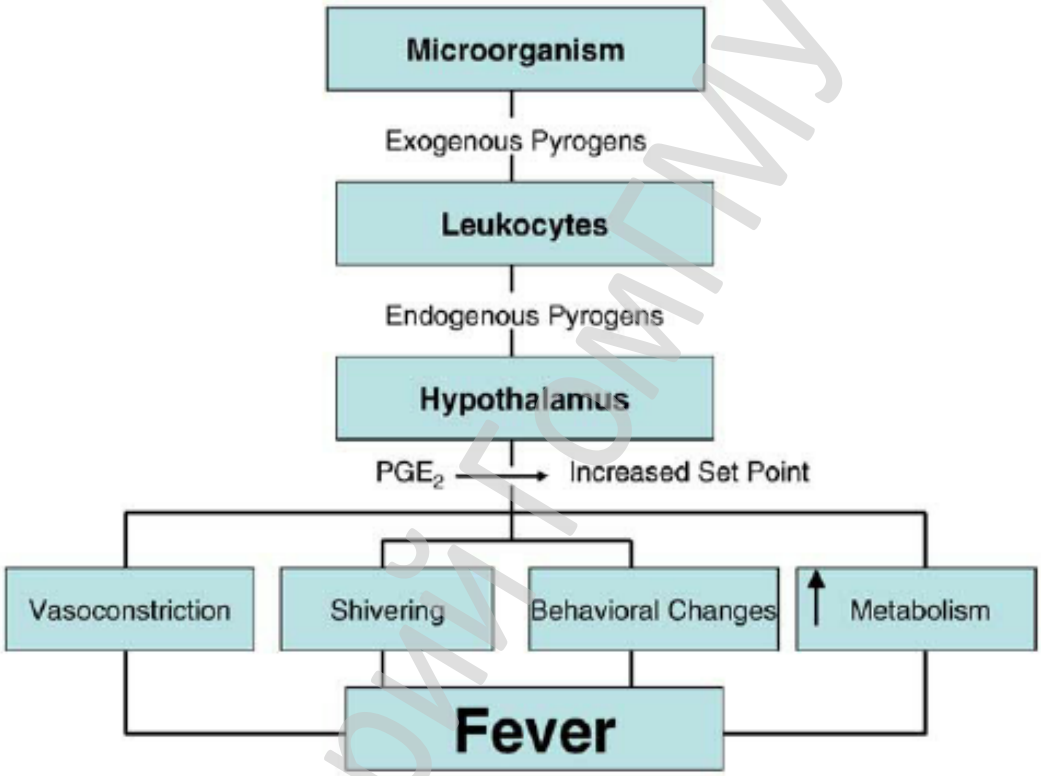


Figure 4.5 —Development of infectious fever

As fever develops, the temperature balance is established at a new higher level and the mechanisms raising the body temperature are activated, including decreased heat loss and increased heat production. During fever, a person feels extremely cold, even though their body temperature may already be above normal. Also, the skin becomes cold because of vasoconstriction, and the person shivers. When the body temperature is stabilized at a new high level, the person no longer experiences chills but instead feels neither cold nor hot. If the factor causing high temperature is removed, the hypothalamus will regulate the temperature according to the normal set-point. This will cause intense sweating and vasodilation of the skin vessels, and the body temperature gets normalized.

Difference of fever from hyperthermia. Hyperthermia is caused mainly by a high environmental temperature, disorders of heat loss and heat production. Fever is caused by pyrogens (without an increase of the environmental temperature). In hyperthermia the body temperature increases passively, and in fever — actively with energy expenditure.

Review questions

1. What is isothermia? What is the value of the constancy of the internal temperature? What factors influence the human body temperature?

2. Name the daily fluctuations of the human body temperature. At what time are the maximal and the minimal body temperatures observed? Give the definitions for the «core temperature» and «shell temperature». On what areas of the body surface is the temperature measured? Give its normal values.

3. What is chemical thermoregulation? Name the mechanisms of heat production. What is physical thermoregulation? Name the mechanisms of heat loss.

4. Where are the thermoreceptors located? Give their classification. Where is the main center of thermoregulation located? Where is the center of heat production located? Where is the center of heat loss located? Name the humeral factors which participate in the regulation of isothermia.

5. What is hypothermia? Name its symptoms. For what purpose is hypothermia used in clinical practice? What is hyperthermia? What is fever? Name the groups of fevers. What is the mechanism of fiver development?

Multiple Choice Questions
METABOLISM AND ENERGY. THERMOREGULATION

1. The breakdown of the body`s own complex organic substances into simple ones with energy release is called …

Variants of answer:

a) assimilation;
b) energy balance;
c) dissimilation;
d) basal metabolism;
e) working exchange.

2. The synthesis of the body`s own complex organic substances from simple substances with energy consumption is called…

Variants of answer:

a) assimilation;
b) working exchange;
c) dissimilation;
d) basal metabolism;
e) energy balance.

3. What transformations of substances give energy to the body?

Variants of answer:

a) synthesis of substances in cells;
b) oxidation of substances in tissues up to end-products;
c) processes of absorption;
d) hydrolysis of substances;
e) the release of substances from the body.

4. How much energy is released during the breakdown of 1 g of proteins in the body?

Variants of answer:

a) 4.0 kcal;
b) 9.3 kcal;
c) 5.1 kcal;
d) 39.3 kcal;
e) 17.1 kcal.

5. The daily protein requirements of a middle-aged person with the body weight of 80 kg are equal to …

Variants of answer:

a) 150–200 g;
b) 400–450 g;
c) 70–80 g;
d) up to 800 g;
e) 15–20 g.

6. The condition, at which the amount of nitrogen excreted from the body is less than that of consumed nitrogen, is named …

Variants of answer:

a) positive nitrogen balance;
b) negative nitrogen balance;
c) nitrogenous equilibrium;
d) nitrogen optimum;
e) nitrogen pessimum.

7. The positive nitrogen balance is typical…

Variants of answer:

a) of senior people;
b) of sportsmen;
c) of starvation;
d) of serious diseases;
e) all the answers are correct.

8. The positive nitrogen balance is observed …

Variants of answer:

a) in adults;
b) in senior people;
c) in starvation;
d) in children and pregnant women;
e) all the answers are correct.

9. The negative nitrogen balance is observed…

Variants of answer:

a) during growth;
b) in long physical exercise;
c) during pregnancy;
d) in senior people;
e) all the answers are correct.

10. How will the nitrogen balance change in a significant decrease of proteins?

Variants of answer:

a) it will become positive;
b) it will become equilibrium;
c) it will become negative;
d) it will not change;
e) it will become optimal.

11. What will be observed if there are no essential amino acids in diet?

Variants of answer:

a) positive nitrogen balance;
b) negative nitrogen balance;
c) nitrogen equilibrium;
d) no changes will be observed;
e) optimal nitrogen balance.

12. The minimum amount of proteins which is constantly breaking up in an organism at rest, counted per 1 kg of body weight is named…

Variants of answer:

a) the efficiency coefficient;
b) the respiratory factor;
c) the breaking coefficient;
d) the ventilation-perfusion coefficient;
e) the coefficient of O_2 consumption.

13. The daily carbohydrate requirements of a middle-aged person are equal to …

Variants of answer:

a) 150–200 g;
b) 400–450 g;
c) 80–100 g;
d) up to 800 g;
e) 15–20 g.

14. The daily balance of water for an adult makes ….

Variants of answer:

a) 150–200 mL;
b) 4,000–4,500 mL;
c) about 2,500 mL;
d) more than 10 liters;
e) about 5 liters.

15. What is the principle of direct calorimetry?

Variants of answer:

a) calculation of the amount of consumed oxygen;

b) direct measurement of heat irradiated by the body;

c) determination of the respiratory factor;

d) principle of isodynamia;

e) calculation of the amount of exhaled carbon dioxide.

16. The thermal equivalent of oxygen is…

Variants of answer:

a) the ratio of exhaled CO_2 to inhaled O_2;

b) the amount of heat released during the consumption of 1 liter of oxygen;

c) the ratio of inhaled O_2 to exhaled CO_2;

d) the amount of energy necessary for life in usual conditions;

e) the maximum amount of energy necessary for life.

17. Basal metabolism of an organism is …

Variants of answer:

a) the amount of energy necessary for life in usual conditions;

b) the minimum amount of energy necessary for the maintenance of the ability to live;

c) the maximum amount of energy necessary for life;

d) the ratio of exhaled CO_2 to inhaled O_2;

e) the amount of heat released during the consumption of 1 liter of oxygen.

18. The average rate of daily basal metabolism in men makes …

Variants of answer:

a) 3,000 kcal;

b) 1,000 kcal;

c) 2,500 kcal;

d) 1,700 kcal;

e) 4,100 kcal.

19. In women the basal metabolic rate in comparison to men…

Variants of answer:

a) is identical;

b) is 10–15 % less;

c) is 10–15 % more;

d) is 30–40 % less;

e) is 30–40 % more.

20. How does the rate of basal metabolism change in people over 40–45?

a) it increases;
b) it decreases;
c) it does not change;
d) it disappears;
e) it changes in different ways.

21 The total energy consumption is the sum of …

Variants of answer:

a) the specific dynamic action of food and the working addition;
b) basal metabolism and the specific dynamic action of food;
c) basal metabolism and the working addition;
d) basal metabolism and the thermal equivalent of oxygen;
e) the thermal equivalent of oxygen and the working addition.

22. The effect of increased metabolism and energy consumption after meals is named…

Variants of answer:

a) isodynamia of nutrients;
b) specific dynamic action of food;
c) digestibility of food;
d) basal metabolism;
e) digestive metabolism.

23. Which food has the highest specific dynamic action?

Variants of answer:

a) protein;
b) mixed;
c) fat;
d) carbohydrate;
e) all the substances have the same specific dynamic action.

24. Which ratio of proteins, fats, and carbohydrates is optimal in diet?

Variants of answer:

a) 1 : 4 : 1;
b) 4 : 1 : 1;
c) 1 : 1 : 4;
d) 1 : 2 : 4 ;
e) 1 : 1 : 1.

25. What is the feature of homoiothermal animals?

Variants of answer:

a) their body temperature depends on the temperature of the environment;

b) they have a constant metabolic rate;

c) their body temperature is constant and does not depend on the temperature of the environment;

d) their body temperature is constantly less than the temperature of the environment;

e) there is no correct answer.

26. Which part of the human body has the highest temperature?

Variants of answer:

a) the liver;

b) the rectum;

c) the axillary area;

d) under the tongue;

e) the brain.

27. The highest body temperature of a healthy person is observed …

Variants of answer:

a) at about 7 a.m.;

b) at about 6 p.m.;

c) at about 4 a.m.;

d) at about 10 a.m.;

e) at about 11 p.m..

28. The lowest body temperature of a healthy person is observed …

Variants of answer:

a) at about 7 a.m.;

b) at about 1 p.m.;

c) at about 4 a.m.;

d) at about 7 p.m.;

e) at about 4 p.m..

29. The thermal balance is…

Variants of answer:

a) all the answers are correct;

b) the balance between heat production and heat loss;

c) the balance between shivering and non-shivering thermogenesis;

d) the balance between the temperatures of the body and environment;

e) the balance between heat production and the temperature of the environment.

30. Which organ mainly provides heat production in an organism at rest?

Variants of answer:

a) skin and subcutaneous fat tissue;
b) skeletal muscles;
c) the organs of the thoracic cavity;
d) the liver;
e) the stomach.

31. How does heat production change under the action of cold?

Variants of answer:

a) it decreases;
b) it increases;
c) it does not change;
d) it disappears;
e) it changes in different ways.

32. How does the state of skeletal muscles change under the action of cold?

Variants of answer:

a) there is relaxation of skeletal muscles;
b) it does not change;
c) all the answers are correct;
d) there is muscle shivering;
e) there is muscle tremor.

33. Cold shivering is an example of …

Variants of answer:

a) physical thermoregulation;
b) heat conduction;
c) chemical thermoregulation;
d) muscle disease;
e) all the answers are correct.

34. Brown fat in the body provides…

Variants of answer:

a) increased heat loss;
b) ATP synthesis;
c) increased heat production;
d) mobilization of glycogen;
e) cold shivering.

35. The comfortable temperature is the air temperature (in Celsius degrees) of…

Variants of answer:

a) 16–18;
b) 22–24;
c) 26–28;
d) 18–20;
e) 30–35.

36. In usual conditions the release of heat by the body is carried out by …

Variants of answer:

a) heat radiation;
b) convection;
c) heat conduction;
d) evaporation;
e) all the answers are correct.

37. Which means of heat loss is the main for a person if the surrounding temperature is 40 °C and humidity is normal?

Variants of answer:

a) heat conduction;
b) heat radiation;
c) convection;
d) evaporation;
e) all the answers are correct.

38. Which means of heat loss will the body use in a sauna?

Variants of answer:

a) convection;
b) heat conduction;
c) heat radiation;
d) evaporation;
e) all the answers are correct.

39. In a person who is in cold water heat is released mainly by …

Variants of answer:

a) evaporation;
b) heat radiation;
c) heat conduction;
d) convection;
e) all answers are correct.

40. Why does a person feel colder in wet weather than in dry weather at the same low temperature of the air?

Variants of answer:

a) the evaporation of liquids decreases;
b) the heat conductivity of the air increases;
c) the evaporation of liquids increases;
d) the heat radiation of the body increases;
e) the heat radiation of the body decreases.

41. Under which condition increased sweat production will not lead to increased heat loss?

Variants of answer:

a) if very concentrated sweat is produced;
b) if the air humidity is low;
c) if the air humidity is high;
d) in skin diseases;
e) all the answers are correct.

42. Why does a person wearing synthetic (nylon) clothes tolerate hot weather worse, than a person wearing cotton clothes?

Variants of answer:

a) heat production is decreased;
b) heat irradiation is decreased;
c) the evaporation of sweat is decreased;
d) convection is decreased;
e) all the answers are correct.

43. How does the tone of the skin vessels change under the influence of the cold?

Variants of answer:

a) it decreases;
b) it increases;
c) it does not change;
d) it disappears;
e) it changes in different ways.

44. Subcutaneous fatty tissue with low heat conduction of fat …

Variants of answer:

a) increases heat loss;
b) decreases heat loss;
c) has no influence on heat loss;

d) decreases heat production;
e) increases heat production.

45. Low body temperature in a cool environment occurs because…
Variants of answer:
a) shivering thermogenesis is more than non-shivering thermogenesis;
b) heat loss is more than heat production;
c) chemical thermoregulation increases;
d) physical thermoregulation increases;
e) all the answers are correct.

46. Where is the center of thermoregulation situated?
Variants of answer:
a) in the medulla;
b) in the midbrain;
c) in the hypothalamus;
d) in the cerebellum;
e) in the pons varolii.

47. A surgical operation has led to the decreased ability of an animal to maintain its normal body temperature in low environmental temperatures because…
Variants of answer:
a) the hypophysis is damaged;
b) the nuclei of the anterior group of the hypothalamus are damaged;
c) the epiphysis is damaged;
d) the nuclei of the posterior group of the hypothalamus are damaged;
e) the adenohypophysis is damaged.

48. Which hormone increases heat production most strongly?
Variants of answer:
a) insulin;
b) aldosteron;
c) oxythocin;
d) thyroxin;
e) antidiuretic hormone.

49. Under the influence of adrenaline excess, the body temperature …
Variants of answer:
a) goes down;
b) does not change;

c) increases;
d) disappears;
e) changes in different ways.

50. In clinical practice hypothermia is applied…

Variants of answer:

a) to increase the metabolism of the brain and increase its oxygen requirements;
b) to promote the oxidizing processes of the body;
c) to decrease the metabolism of the brain and its oxygen needs;
d) to increase the consumption of oxygen by an organism;
e) all the answers are correct.

51. A diet poor in carbohydrates causes…

Variants of answer:

a) obesity;
b) hypercapnia;
c) has no effect;
d) hyperglycemia;
e) ketosis.

***52.* Hyperthermia is a state when the body temperature increases above …**

Variants of answer:

a) 36 °C ;
b) 37°C;
c) 38 °C;
d) 39 °C;
e) 40 °C.

53. Sweating is stimulated by...

Variants of answer:

a) adrenal hormones;
b) sympathetic cholinergic nerve fibers;
c) sympathetic adrenergic nerve fibers;
d) parasympathetic cholinergic nerve fibers;
e) all the answers are correct.

54. In humans, the least useful physiological response to low environmental temperatures is...

Variants of answer:

a) shivering;

b) vasoconstriction;
c) release of thyroxine;
d) erection of the hair of the skin;
e) increased metabolic processes in the internal organs.

55. The first physiological response to high environmental temperatures is…
Variants of answer:
a) sweating;
b) vasodilatation;
c) decreased heat production;
d) non-shivering thermogenesis;
e) shivering thermogenesis.

CORRECT ANSWERS
METABOLISM AND ENERGY. THERMOREGULATION

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	15	b	29	b	43	b
2	a	16	b	30	d	44	b
3	b	17	b	31	b	45	b
4	a	18	d	32	d	46	c
5	c	19	b	33	c	47	d
6	a	20	b	34	c	48	d
7	b	21	c	35	d	49	c
8	d	22	b	36	e	50	c
9	d	23	a	37	d	51	e
10	c	24	c	38	d	52	b
11	b	25	c	39	c	53	b
12	c	26	a	40	b	54	d
13	b	27	b	41	c	55	b
14	c	28	c	42	c		

UNIT 5
PHYSIOLOGY OF EXCRETION

5.1. Organs of excretion and their participation in the maintenance of homeostasis

Excretion is an important process of homeostasis, as it provides elimination of no longer useful products of exchange from the organism, i. e. metabolic waste — CO_2 and H_2O, alien, toxic and other substances.

The human organs of excretion are the kidneys, lungs, gastrointestinal tract (salivary and stomach glands, pancreas and intestinal glands), skin glands (sweat glands, sebaceous and mammary glands) (Figure 5.1).

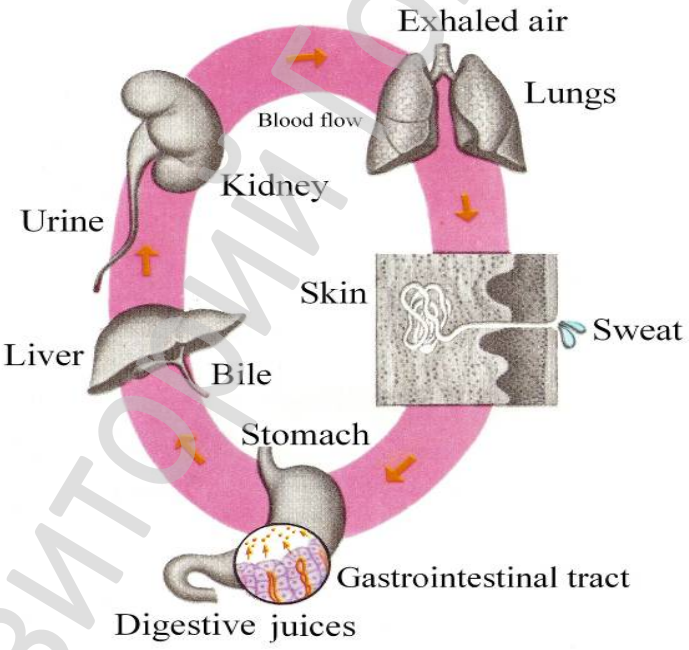


Figure 5.1 — Organs which participate in excretory processes (by Korobkov A. V., Chesnokova S. A., 1986)

The basic purpose of the organs of excretion is to sustain the constancy of the composition and volume of the fluids of the organism`s internal environment, first of all, blood, plasma, and lymph.

The excretory function of the **kidneys** is dominant. The kidneys delete excess of water, inorganic and organic substances, end products of exchange and alien substances.

The lungs are also organs of excretion as through them CO_2 and H_2O and some volatile matters, for example vapors of ether and chloroform in narcosis, intoxication, are eliminated from the organism

The salivary and stomach glands excrete water, salts, Ca^{2+}, Mg^{2+}, and other ions, some heavy metals, series of medicinal substances (morphie, quinine, salicylates).

The pancreas and intestinal glands excrete heavy metals, medicinal substances.

The important excretory function which **the liver** carries out is the excretion of hormones (thyroxin, folliculin), products of hemoglobin exchange, nitrous metabolism and many other substances from the blood.

The skin carries out diverse functions. The skin glands are: sweat glands, sebaceous, and mammary glands. There are about 2–2.5 million *sweat glands*. They are located in subcutaneous cellular tissue (more on palms, soles, in axillae, there are 400–500 sweat glands per 1 cm^2). 98 % of sweat consists of water and 2% is organic and inorganic substances (mineral salts, urea, uric acid). The amount of sweat in comfortable temperature conditions is up to 500 mL/day, thus 2 g of NaCl and 1g of nitrogen are eliminated. However, in hot climate hidrosis can reach 4 liters a day, in intensive physical activity — up to 10 liters.

A special place among the organs of excretion is occupied by the sebaceous and mammary glands.

Sebaceous glands. On the skin surface some oil excreted by the sebaceous glands is admixed to sweat. Dermal oil softens the skin and greases hair. At the moment of its secretion dermal oil is fluid, but quickly gets denser. Under the influence of acids dermal oil cankers, forming fat acids with their characteristic scent.

Mammary glands. Substances secreted by the mammary glands are the end products of metabolism and have an independent physiological value, for example, milk as food for newborns. Mother's milk contains bactericidal substances, antibodies promoting seroimmunity. Mineral substances: Ca, Mg, P, Fe, proteins of 1.5 %, fats of 4.5 %, carbohydrates, vitamins A, B, C, D.

5.2. Kidneys and their functions

The basic function of the kidneys consists *in the regulation of the volume of fluids*, *mineral* composition, *and acid-base state of the organism* due to excretion of water and inorganic electrolytes in amounts necessary for the maintenance of their balance in the body and normal concentration of these substances in extracellular fluid. The concentrations of sodium, potassium, chlorine, calcium, magnesium, and other ions are regulated in this way.

The important function of the kidneys *is the excretion of the end products* of metabolism, which are called so because they have no functional value. Urea, uric acid, creatinine, end products of hemoglobin disintegration, metabolites of various hormones are related to these substances. Besides, the

kidneys excrete many alien substances — medicines, pesticides, various alimentary additives etc. — with urine.

Hence, the main objective of the kidneys consists of the selective excretion of various substances with the purpose of the maintenance of the relative constancy of the chemical compounds of blood plasma and extracellular fluid.

Besides, the kidneys *participate in the metabolism* of proteins, lipids, and carbohydrates, for example, during long starvation the kidneys synthesize glucose from amino acids. The kidneys release approximately 20 % of the amount of glucose which the liver synthesizes in this situation.

Also, the kidneys develop several biologically active substances excreted into the blood (renin, erythropoietin, urokinase), which can act as enzymes, which allows to survey the kidneys as incretory organs. Renin participates in the maintenance of arterial pressure and volume of circulating blood. The substance termed erythropoietin stimulates erythrocyte formation.

5.3. Nephrons as morpho-functional units of the kidneys. Types of nephrons. Features of renal blood flow

In humans each kidney consists approximately of one million structural units termed nephrons (Figure 5.2). The nephron is a structural and functional unit of the kidneys because it carries out all the processes which lead to urine formation.

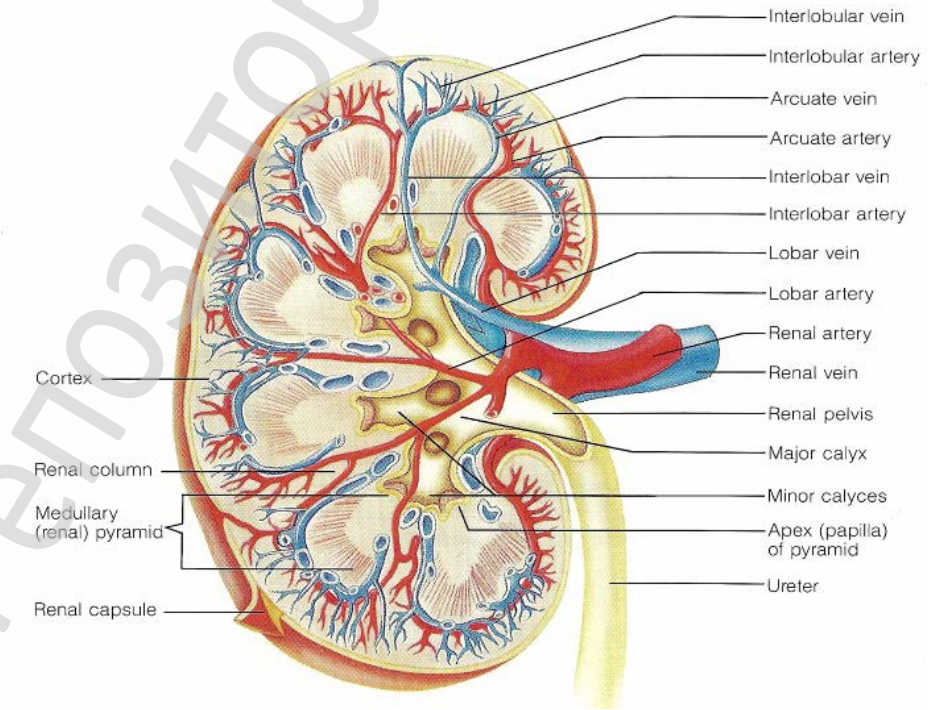


Figure 5.2 — Internal anatomy of the kidney (diagrammatic view of a coronally sectioned kidney illustrating the major blood vessels) (by Elaine N. Marieb, 1989)

Each nephron is composed of a renal corpuscle (also called malpighian body), the initial filtering device consisting of a knot of capillaries (***capsule of glomerulus***) surrounded by a double-walled capsule (***Bowman's capsule***) that opens into a tubule (Figure 5.3).

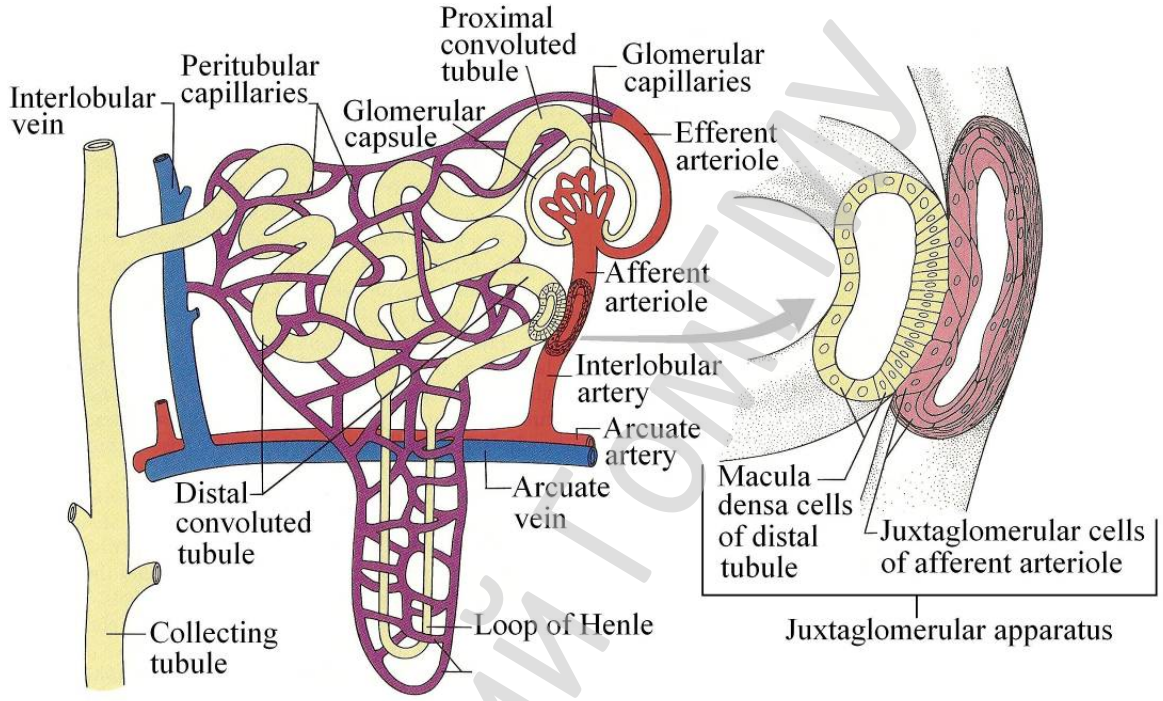


Figure 5.3 — Structure of the nephron and its associated capillaries (by Elaine N. Marieb, 1989)

The renal corpuscle is formed by the glomerulus of capillaries, which is the branching of *afferent arterioles* — afferent vessels; these capillaries are collected in *efferent vessels*. Between the walls of the capsule there is a cavity from which the proximal convoluted renal tubule begins.

The renal tubule begins with the convoluted parts which pass in a short direct tubule. *The proximal part of the nephron* consists of the convoluted and direct tubules; the distinctive feature is the presence of a striated border (a great number of microvilli inverted in the tubule lumen). Between the proximal and distal parts, a thin segment is located — the *descending limb of Henle's loop*. It comes to an end with a stemnode of the loop, and the tubule rises further in parallel with the descending part. *The ascending part of Henle's loop* can include thin and thick parts which rise up to the level of the nephron glomerulus where the *distal convoluted tubule* begins. The cells of the ascending part of Henle's loop of the nephron and the distal convoluted tubule have no striated border. The big value has the fact, that this part of the nephron tubule necessarily touches the glomerule between the afferent and efferent arterioles within the range of the macula densa. The range of the

contact of these structures is called the *juxteglomerular complex*. In the cortical substance the distal convoluted tubule opens in the *collecting tubule*. The branches of these tubules settle down in the cortical substance and intrinsic layers of the medullary substance, the collecting tubules open within the range of the papillas of the cups of renal pelvis.

Every renal pelvis is connected with the lumen of the ureter, which is connected with the urinary bladder, where urine temporarily stays and is periodically removed from it.

Types of nephrons

In various segments of the nephron tubules, there are essential differences which depend on the localization of the nephron in the kidneys, size of the glomeruli, depth of their location and depth of the proximal tubule, length of the separate parts of the nephron, especially the loops.

There are three types of nephrons in the kidneys: ***superficial*** (short loop); ***intracortical*** (inside the cortical layer) and ***juxtemedular*** (at the border of the cortical and medullary layers). One of the important differences of the above three types of nephrons is the length of Henle's loop (Figure 5.4).

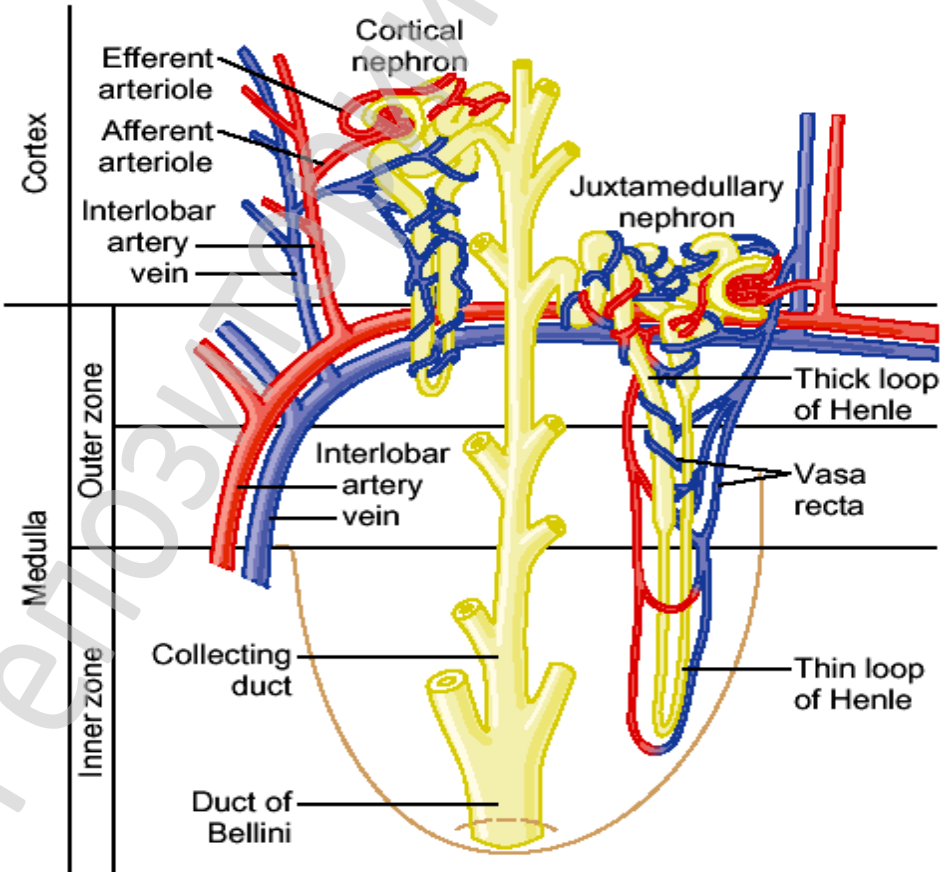


Figure 5.4 — Types of nephrons and their localization in the kidney (by C. Guyton and John E. Hall, 2016)

Features of renal blood flow

About 1,200 mL of blood passes through the vessels of both the kidneys per minute, i.e. about 20 % of the blood which the heart outputs into the aorta. The weight of the kidney compounds 0.43 % of the body weight of a healthy human. About 91–93 % of blood flows through the vessels of the cortical substance of the kidneys, and the other part supplies the medullary layer of the kidneys. Normally, the blood flow in the cortical substance of the kidney compounds 4–5 mL / minute per 1 g tissue. It is the highest level of organic blood flow. The feature of renal blood flow is that if arterial pressure (from 90 up to 190 mm. Hg) changes, renal blood flow remains constant. **The Ostroumov-Beilis phenomenon** is a mechanism of myogenic autoregulation that ensures the constancy of renal blood flow regardless of systemic blood pressure changes. Thanks to it the value of renal blood flow is maintained at a constant level despite some fluctuations in systemic pressure. It is caused by the high level of self-regulation of renal blood circulation. Most of the blood in the kidneys passes twice through the capillaries — first in the glomerulus, then around the tubules.

High renal blood flow is necessary to ensure a sufficiently large volume of glomerular filtration and is not associated with the metabolic needs of the kidneys.

The determination of renal blood flow and plasma flow is carried out using a substance introduced into the blood and completely removed from the plasma into the urine along a single passage of blood through the kidneys.

This property is most pronounced *in paraaminohippuric acid (PAH)*, which is used for this purpose.

The amount of a substance (for example, PAH) coming from the blood, is equal to its concentration in the blood (C_{bl}, milligrams or mole per milliliter), multiplied by the volume of plasma flow (V_{pl}, mL) per minute.

The amount of PAH excreted from the kidneys is equal to its concentration in the urine (C_u, milligrams or mole per milliliter), multiplied by the volume of diuresis per minute (Vu, ml).

$$C_{bl} \bullet V_{pl} = C_u \bullet Vu, \text{ so}$$
$$V_{pl} = (C_u \bullet V_u)/C_{bl}$$

To determine renal blood flow (V_{bl}, mL/min), some adjustments must be made taking into account the hematocrit (Hct).

$$V_{bl} = V_{pl}/\ 1 - Hct$$

5.4. Uropoietic process

Urine is formed in three consecutive processes (Figures 5.4, 5.5):

I. The initial stage of uropoiesis occurs in the renal glomerulus — **glomerular ultrafiltration** of protein-free fluid from blood plasma into the capsule of the renal glomerulus therefore primary urine is formed.

II. Tubular reabsorption — the process of anatropic adsorption of filtered substances and water.

III. Secretion. The cells of some tubule parts transfer some organic and inorganic substances from extracellular fluid to the lumen of the nephron (secretion) or excrete the molecules synthesized in the cell tubule into the lumen tubule.

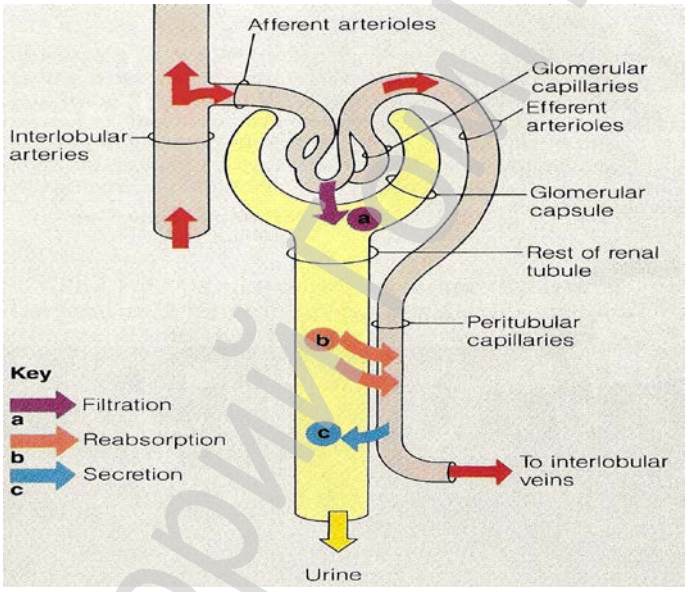


Figure 5.4 — Processes which take place in the nephron (by Elaine N. Marieb, 1989)

Note: The three major mechanisms by means of which the kidney adjusts the composition of plasma are: (a) glomerular filtration, (b) tubular reabsorption, (c) tubular secretion.

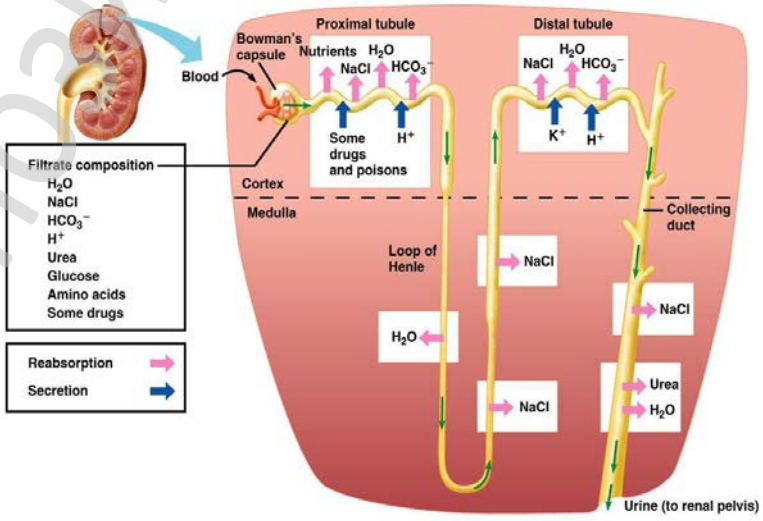


Figure 5.5 — Role of different parts of the nephron in urine formation (from studylib.net)

5.4.1. Glomerular filtration

Urine formation begins with glomerular filtration, i. e. the transmission of fluid from the glomerular capillary into the Bowman's capsule, thus the fluid passes through the glomerular filter.

The filtrating membrane in the renal corpuscle consists of three layers (Figure 5.6): *endothelium of the glomerular capillary, basal membrane* and one-row layer of *epithelial cells covering the Bowman's capsule*. The first layer — the endothelial cells of the capillaries — is perforated by a set of foramens («windows» or «fenestrae»). The basal membrane is a gel structure, acellular, honeycomb formation. The cells of the capsule epithelium which are based upon the basal membrane are named podocytes. Like an octopus, the podocyte cell body emits thick extensions – finger-shaped processes pressed into the basal membrane. The gap junctions between the processes represent passages along which the filtrate, passing the endothelial cells and basal membrane, penetrates into the Bowman's space.

In the basal membrane, there are pores which limit the transit of the formed elements of blood, and also large molecules more than 5–6 microns. Therefore, large proteins do not get into the filtrate. The albumins of blood plasma pass into the filtrate in insignificant amounts. Into the lumen of the capsule of the nephron inulin, about 22 % of egg albumin, 3 % of hemoglobin and less than 0.01 % of seralbumin are transited. Negatively charged molecules in the basal membrane interfere free protein transit through the glomerular filter.

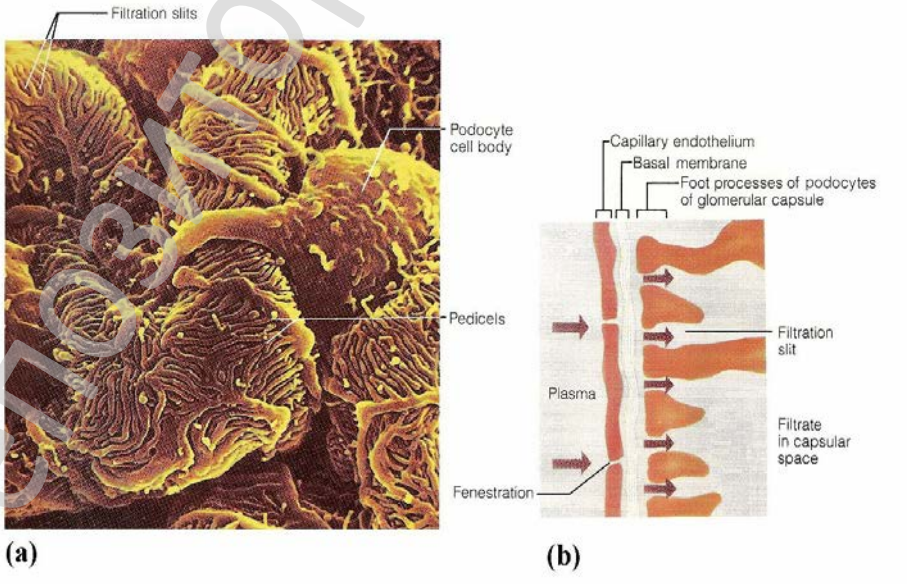


Figure 5.6 — Filtration membrane (by Elaine N. Marieb, 1989)

Notes: **(a)** Scanning electron micrograph of the layer of podocytes. Filtration slits between the podocyte foot processes are evident (39.000 X); **(b)** Diagrammatic view of a section taken through the filtration membrane showing all the three structural elements

Inorganic salts and low-molecular organic compounds (urea, uric acid, glucose, amino acids, creatinine) freely pass through the glomerular filter and get into the lumen of the Bowman's capsule. The resistance of the efferent arterioles causes sufficient hydrostatic pressure within the renal glomerulus to provide the force for ultrafiltration. This high hydrostatic pressure is created in the glomerulus by having a wide afferent arteriole and a narrow efferent arteriole.

The effective filtration pressure (EFP) on which the glomerular filtration rate depends, is defined by the difference between the *hydrostatic pressure of the blood in the capillaries of the glomeruli* (in humans from 60–90 mm Hg) and counteracting to its factors — *oncotic pressure of blood plasma proteins* (it is equal to 30 mm Hg) and *hydrostatic pressure of the fluid in the Bowman's capsule* (about 20 mm Hg) (Figure 5.7).

EFP= 70 mm Hg – (30 mm Hg + 20 mm Hg) = 20 mm Hg.

Filtration takes place only if the glomerular blood pressure exceeds the value of oncotic pressure of the proteins in blood plasma and the pressure of the fluid in the glomerular capsule. If the filtration pressure rises, diuresis is increased, if it goes down — diuresis is decreased.

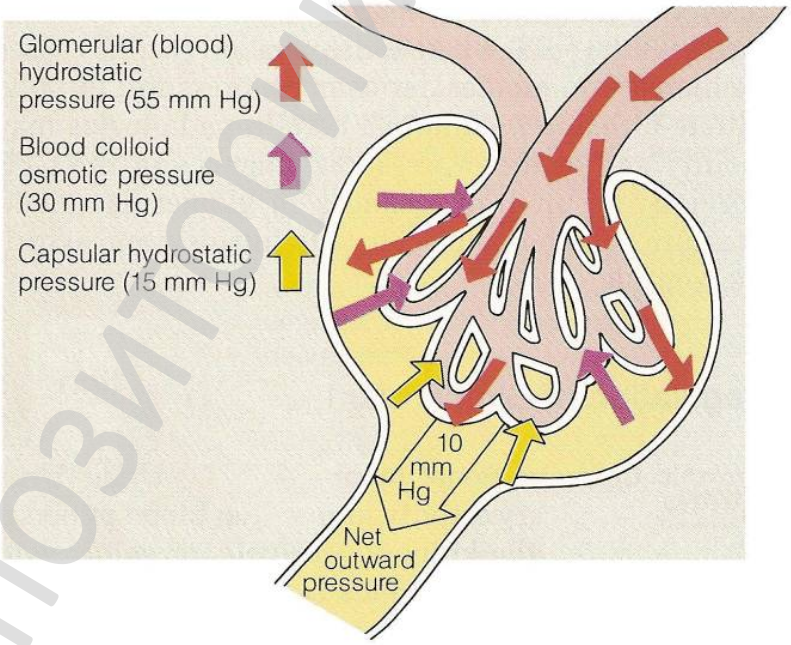


Figure 5.7 — Forces that determine glomerular filtration and the effective filtration pressure (by Elaine N. Marieb, 1989)

The amount of primary urine is 150–180 L/day. The kidneys filter about 1,700 liters of blood per day.

The general surface of the walls of the glomerular capillaries through which filtration passes is peer 1.5–2 m 2/100 g kidney, i.e. peer to the body surface.

The average total amount of plasma in the human organism compounds approximately 3 liters, it means, that all plasma is filtrated in the kidneys about 60 times per day. The ability of the kidneys to filtrate such a huge volume of plasma enables them to excrete significant amounts of the end products of metabolism and to regulate the element composition of the fluids of the internal environment.

5.4.2. Tubular reabsorption

In the human kidneys up to 170 liters of filtrate is formed per day, and 1–1.5 liters of final urine is excreted, the rest of the fluid is absorbed in the tubule. Primary urine is isotonic to blood plasma. Tubular reabsorption is the movement of vital water and solutes in necessary amounts from primary urine back into the plasma (Table 5.1).

Table 5.1 — Reabsorption capabilities of different segments of the renal tubules and collecting tubules

Proximal convoluted tubule	Sodium ions (Na^+) Virtually all nutrients (glucose, amino acids, vitamins) Cations (K^+, Mg^{2+}, Ca^{2+}, and others) Anions (Cl^-, HCO_3^-) Water Urea and lipid — soluble solutes Small proteins
Loop of Henle: Descending loop Ascending loop	 Water Na^+, K^+ and Cl^-
Distal convoluted tubule	Na^+ Anions
Collecting tubule	Water Urea

The molecular mechanisms participating in the processes of reabsorption, are the same as the mechanisms reacting during the transmission of molecules through the plasma membranes in other parts of the body (Figure 5.8). These mechanisms include diffusion, active and passive transport, endocytosis etc. There are two ways of the transport of reabsorbed substances from the lumen into the interstitial space. The former is the transfer of substances across an epithelium between cells, i.e. through an intercellular space between two adjacent cells — **para-cellular way**. The latter way of reabsorption — **trans-**

cellular («through» cell), where the substances travel through the cell passing through both the membranes on the way from the tubular lumen to interstitial fluid. In the apical membrane the excreting fluid in the lumen tubule is separated from the cell cytoplasm, and in the basolateral membrane the cytoplasm is separated from the interstitial fluid.

If substances are reabsorbed against the electrochemical and concentration gradients, this process is called active transport. There are two types of transport — **primary-active** and **secondary-active**. Primary-active transport occurs when substances are transmitted against the electrochemical gradient due to the energy of cellular metabolism. This transport is provided with energy received immediately after the breakdown of ATP molecules. The example is the transport of Na^+ ions, which happens with the participation of Na^+, K^+-ATPase, using ATP energy.

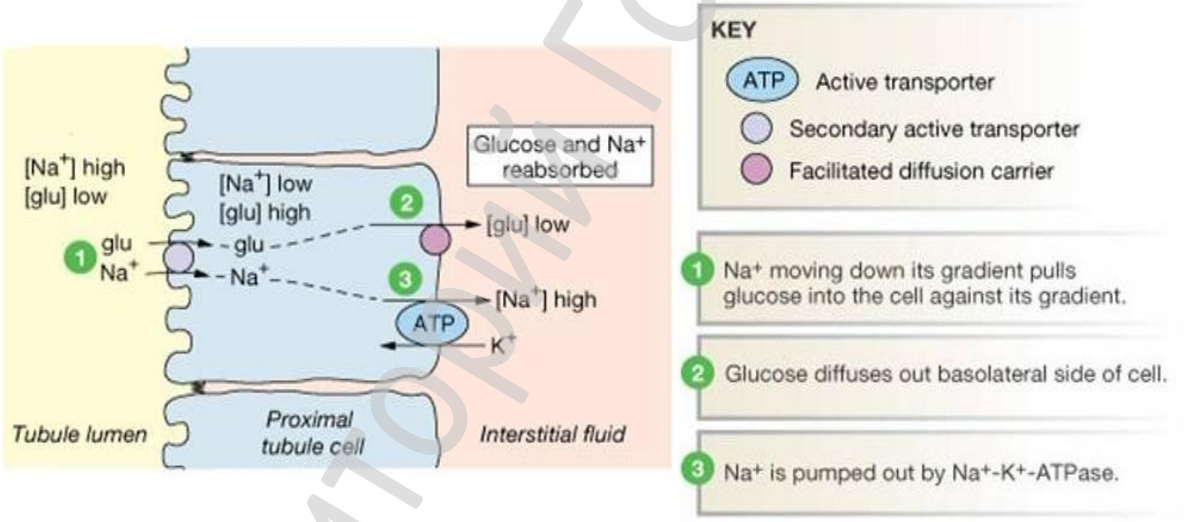


Figure 5.8 — Glucose reabsorption by secondary-active transport (from studylib.net)

In secondary-active transport a molecule is moved down its electrochemical gradient as another is moved up its concentration gradient. This energy comes from the electrochemical gradient created by pumping ions out of the cell. That is the way how glucose, amino acids are reabsorbed. From the tubule lumen these organic substances get into the cells of the proximal tubule with the help of special transporter molecules which necessarily should attach Na^+ ions. This complex (transporter molecule + organic substance + Na^+) promotes the moving of the substances through the membrane of the striated border and its entering inside the cell.

For water reabsorption, there are special water channels called the **aquaporins** – special proteins of the cell membrane that provide water

transport. Until now 10 varieties of aquaporins have been identified in humans. The kidneys contain eight of their isoforms (AQP_{1-4}, AQP_{6-8}, and AQP_{11}). In 2003 Peter Agre of Johns Hopkins University (USA), received the Nobel Prize in Chemistry for his discovery of the aquaporins.

Various parts of the renal tubules differ in terms of their ability to absorb substances. The analysis of fluids from various parts of the nephron made it possible to determine the composition of the fluids and features of the work of all the parts of the nephron.

Proximal tubule. Most of the components of primary urine are reabsorbed in the proximal convoluted renal tubule (the volume of primary urine decreases approximately by 2/3). In the proximal part of the nephron amino acids, glucose, vitamins, necessary amount of protein, trace substances, significant amounts of Na^+, K^+, Ca^+, Mg^+, Cl^- are completely reabsorbed. The proximal tubule plays the leading role in the returning of all these filtered substances into the blood with the help of effective reabsorption. Filtrated glucose is almost completely reabsorbed by the cells of the proximal tubule, and its insignificant amount can be excreted with urine. Glucose goes against the gradient: from the tubule lumen through the apical membrane to the cytoplasm with sodium. This transport of glucose with the participation of a transporter molecule is secondary-active transport, as the energy necessary for the transport of glucose through the apical membrane is developed due to sodium transport down its electrochemical gradient. Having penetrated into the cell, glucose should go across the baselateral membrane, which happens by means of facilitated diffusion independent from sodium participation, this transport down the gradient is sustained due to the high concentration of glucose in the cell.

Amino acids, inorganic phosphates, sulfates, and some organic substances are reabsorbed in the same way as glucose. The reabsorption of proteins begins with endocytosis (pinocytosis) on the apical membrane (Figure 5.9). The detached endocellular vesicle, appearing in the course of endocytosis, inside the cell merge with lysosomes, whose enzymes split up proteins to low-molecular fragments — dipeptides and amino acids which go from the cell into the blood through the baselateral membrane (Figure 5.9). Normally, urinary excretion of proteins makes no more than 20–75 mg per day, and in kidney disorders it can increase up to 50 g per day. The increased urinary excretion of proteins (proteinuria) can also be caused by disorders of their reabsorption or filtration.

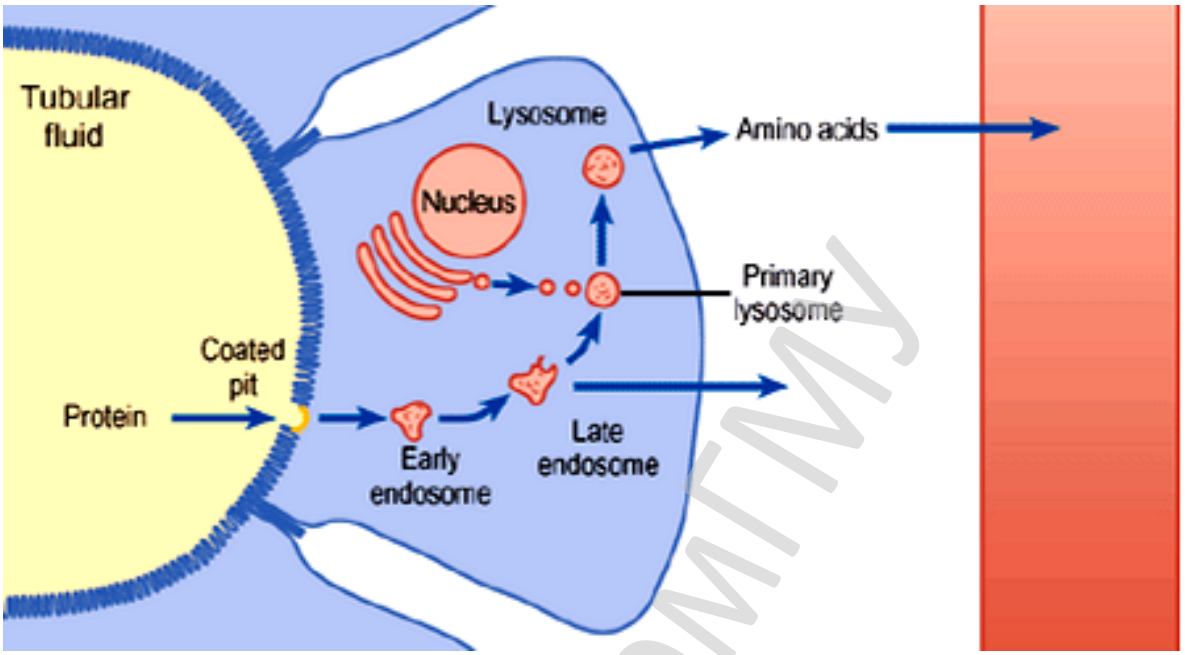


Figure 5.9 — Mechanism of protein reabsorption (from slideplayer.com)

In Henle's loop more sodium and chlorine (about % of the filtrated amount) are reabsorbed, than water (10 % of volume of filtered water). It is the important difference of Henle's loop from the proximal tubule, where water and sodium are reabsorbed practically in equal proportions. *The descending part of the loop* does not reabsorb sodium and chlorine, but it has rather high permeability to water and reabsorbs it. *The ascending part* (thick part) reabsorbs sodium and chlorine and practically does not reabsorb water, as it is impermeable to it. The transition of sodium chloride from the ascending part of the loop in the interstitial fluid increases the osmolarity of this fluid, and it entails high reabsorption of water by means of diffusion from the water-permeable descending part of the loop. Consequently, the fluid being already hypotonic in the ascending thick part of Henle's loop owing to the output of sodium gets into the distal convoluted renal tubule, where the process of delution proceeds and it becomes even more hypotonic as in the subsequent parts of the nephron organic substances are not absorbed (only ions and H_2O are reabsorbed there) (Figure 5.10).

The distal convoluted renal tubule and the ascending part of Henle's loop function as segments where there is urinary dilution. During the progression of medullary substance along the collecting tubule the tubular fluid becomes more and more hypertonic since the reabsorption of sodium and water proceeds in the collecting tubules also; the formation of final urine takes place. The ratio of water reabsorption can widely vary depending on the body water balance (Figure 5.10).

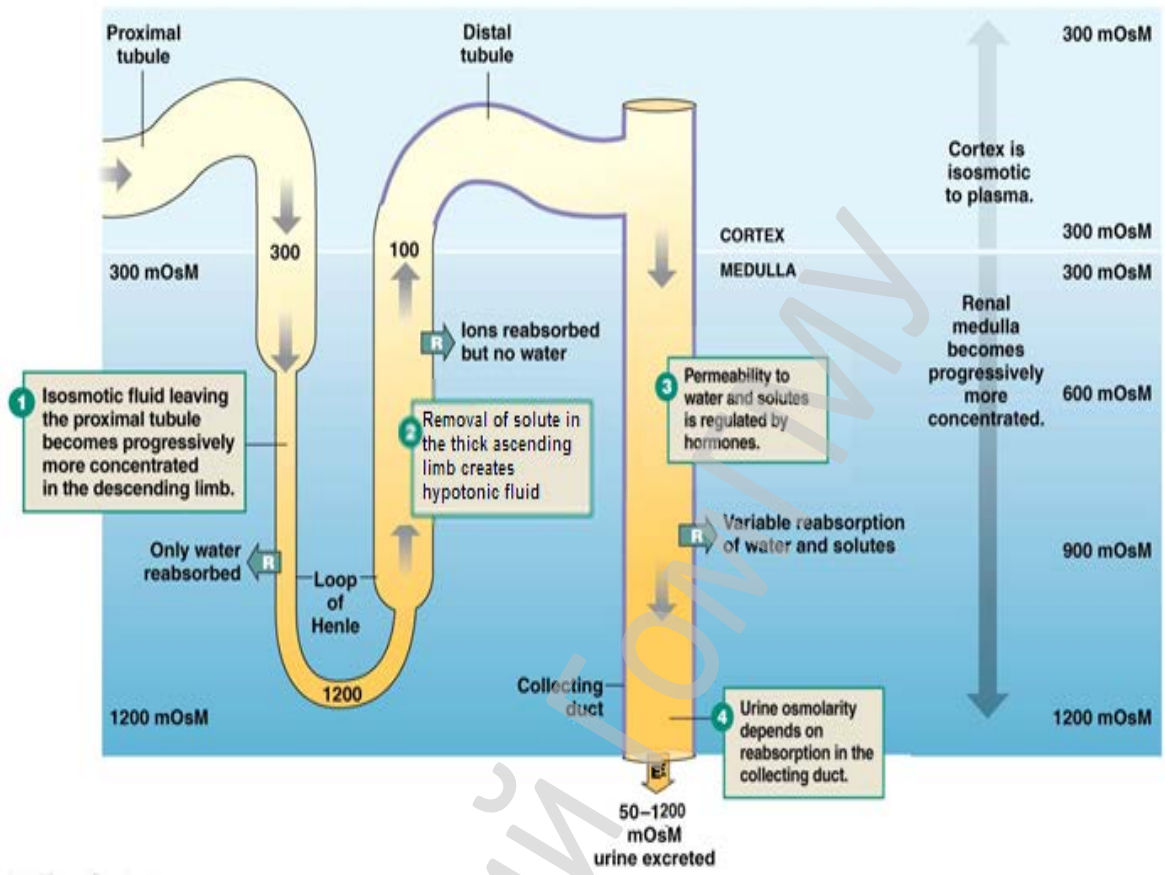


Figure 5.10 —Mechanism of urine concentration (from slideplayer.com)

Threshold and non-threshold substances

The reabsorption of substances depends on their concentration in the blood. The threshold of excretion is the concentration of substances in the blood at which it cannot be completely reabsorbed in the tubule and gets into final urine. The threshold values of excretion of different substances varies.

The threshold substances are substances which are completely reabsorbed in the renal tubule and appear in final urine, only if their concentration in the blood exceeds the defined level. Thus, if the blood glucose level exceeds 5 up to 10 millimole/L — glucose appears in urine.

The non-threshold substances are excreted with urine at their any concentration in the blood. These are the end products of exchange subjected to excretion from the organism (for example, inulin, creatinine, diodrast, urea).

5.4.3. Osmotic dilution and the concentration of urine. Countercurrent multiplier system. Urea recycling.

The regulation of osmotic homeostasis is based on the ability of the kidneys to concentrate or dilute urine, depending on the body's need for water

and osmotically active substances. With an excess of water in the human body (hyperhydration) hypotonic urine (in relation to plasma) is excreted with a low concentration of osmotically active substances. In dehydration hypertonic urine is excreted in small amounts, with a high concentration of osmotically active substances (4-5 times higher than in blood plasma). Only the kidneys of warm-blooded animals have the ability to produce urine with a higher concentration of osmotically active substances than in the blood (hypertonic urine).

The formation of osmotically concentrated urine is caused by the activity of the countercurrent multiplier system.

Components of the countercurrent multiplier system:

— thin segments of the ascending and descending parts of Henle's loops,

— departments of the collecting tubules of the renal medulla,

— ascending and descending vasa recta of the kidney,

— interstitial tissue.

The principle of counter-current exchange. Since the streams of fluid in the descending and ascending parts of Henle`s loop moves towards each other, small transverse gradients (200 mosmol/L) on each section are added together, and a large longitudinal gradient is formed. If to imagine, that secondary urine does not move — only a single transverse osmolality gradient is created in the loop along its entire length (Figure 5.11 (1)). As soon as secondary urine begins to move, the summation of single transverse gradients begins in the lower part, which extends over the entire length of Henle's loop (Figure 5.11 (2-7)). The difference of osmotic pressure between two adjacent sections of the descending and ascending parts is small, but Henle's loop works as a concentration mechanism: it multiplies the "single" effect, which leads to the concentration of liquid in one part of Henle's loop due to its dilution in the other.

Mechanism of the action of the countercurrent multiplier system. The descending and ascending parts of Henle's loop, which are closely in contact with each other, are associated in functions. The descending part of Henle's loop receives isoosmotic urine (the concentration of osmotically active substances is the same as in the plasma ultrafiltrate, although the composition of the liquid is different).

The epithelial cells of the descending part of Henle's loop are permeable to **water**, but are not permeable to Na+. Water passes from the tubule to the interstitial tissue passively down the osmotic gradient, since an increased osmolar concentration is created in the interstitial tissue. Therefore, passing through the descending part, the urine concentrates and at the top of Henle's loop, the tubular fluid becomes hypertonic.

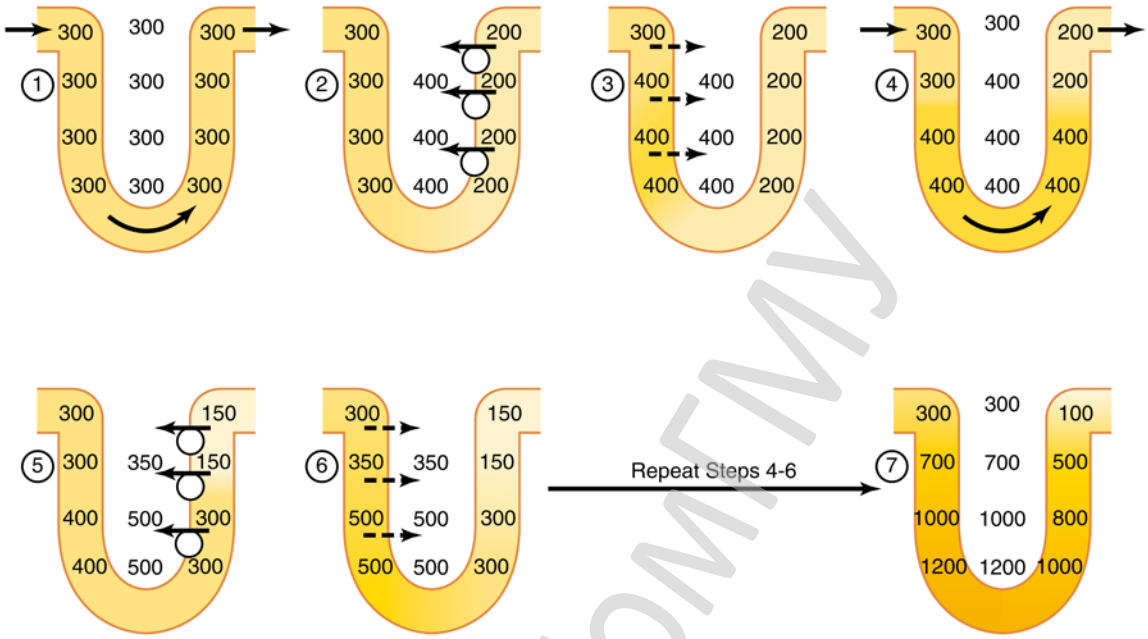


Figure 5.11 — Figure Countercurrent multiplier system in the loop of Henle (by C. Guyton and John E. Hall, 2016)

Notes: Step 1 – the loop of Henle is filled with fluid with a concentration of 300 mOsm/L; Step 2 – the active ion pump of the ascending part of Henle's loop reduces the concentration inside the tubule and raises the interstitial concentration; Step 3 – the tubular fluid in the descending part of Henle's loop and the interstitial fluid reach osmotic equilibrium because of water osmosis out of the descending part; Step 4 – the flow of fluid into the Henle's loop from the proximal tubule causes the hyperosmotic fluid in the descending limb to flow into the ascending limb: Step 5 – once this fluid is in the ascending limb, additional ions are pumped into the interstitium with the interstitial fluid osmolarity rising to 500 mOsm/L: Step 6 – the fluid in the descending limb again reaches equilibrium with the hyperosmotic medullary interstitial fluid; Step 7 – the steps are repeated and this process gradually multiplies the concentration gradient raising the interstitial fluid osmolarity to 1200 to 1400 mOsm/L.

The epithelial cells of the ascending part of Henle's loop actively reabsorb Na+ (against the concentration gradient with the expenditure of ATP energy), but do not reabsorb water. The transition of Na+ from the ascending part increases the osmolarity of the interstitial fluid, which leads to greater reabsorption of water by diffusion from the descending part of the loop. Intensive reabsorption of Na+ in the complete absence of water reabsorption in the ascending part of the loop leads to the fact that at the end of the ascending part of the loop, the urine becomes hypotonic, i.e. its osmotic pressure becomes lower than that of the plasma (Figure 5.12). Hypotonic fluid gets into the initial parts of the distal convoluted tubules (both in water diuresis and antidiuresis).

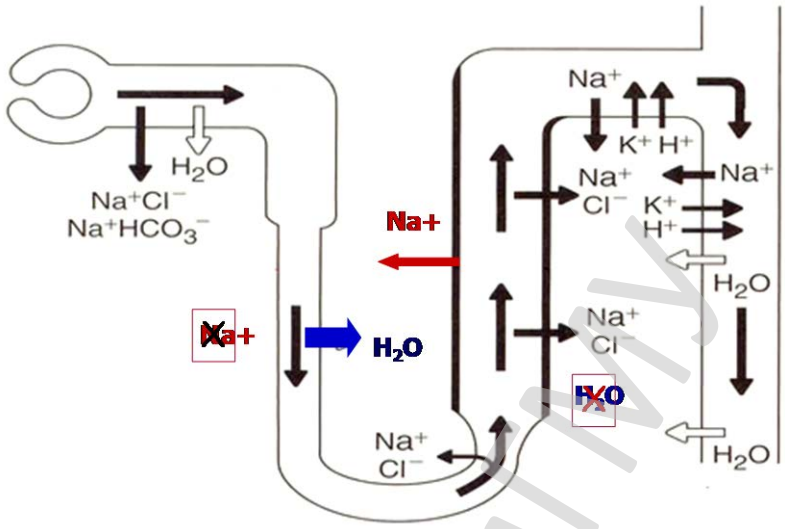


Figure 5.12 — Kidney function in the osmotic concentration of urine (from biology.reachingfordreams.com)

The vasa recta of the renal medulla, like the tubules of Henle's loop, form a countercurrent system (Figure 5.13). They are located in parallel to the tubules of Henle's loop and are organized, like the loop: the descending vasa recta descend into the renal medulla, and the ascending vasa recta rise into the cortical layer. When the blood moves towards the top of the medullary layer, the concentration of osmotically active substances there increases, and during the reverse movement of the blood to the cortical layer, salts and other substances diffuse through the vascular wall and pass into the interstitial tissue.

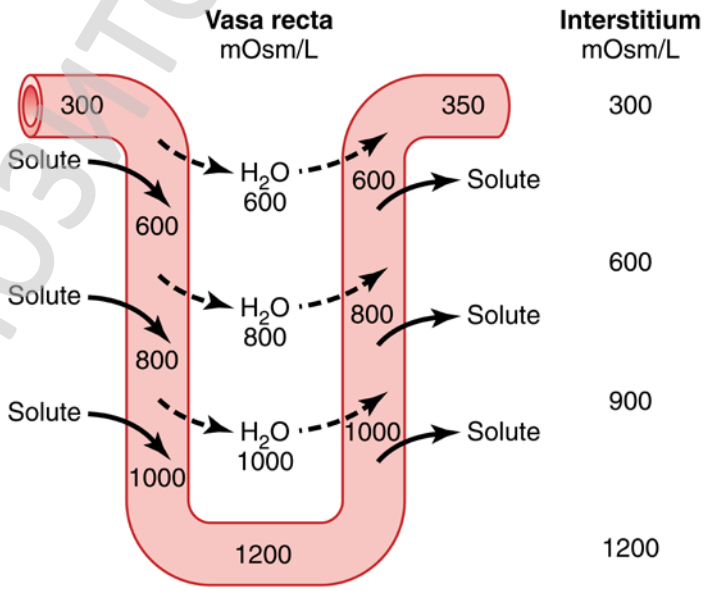


Figure 5.13 — Countercurrent exchange in the vasa recta (by C. Guyton and John E. Hall, 2016)

This preserves the concentration gradient of osmotically active substances inside the kidney, and the vasa recta are functioning as a countercurrent system. The speed of blood flow through the vasa recta determines the amounts of salts and urea removed from the medullar layer and the outflow of reabsorbed water.

The regulation of osmotic homeostasis depends on the organism's need for water.

When the amount of water in the organism is reduced (blood volume decreases), the secretion of antidiuretic hormone (ADH, vasopressin) by the neurohypophysis is elevated. ADH increases the permeability of the end parts of the distal segment and collecting tubules to water. Therefore, more water is reabsorbed from the tubules to the interstitium, water is stored in the body, diuresis is decreased and the osmolality and density of formed urine is increased (a small amount of osmotically concentrated urine is excreted).

Also, if there is a lack of water in the organism, the secretion of aldosterone in the adrenal cortex increases. Under the action of aldosterone, the reabsorption of Na^+ increases (together with Cl^- and water) in the cells of the tubular epithelium, which also leads to a decrease in urine formation.

Urea recycling. Urea reabsorption plays an important role in creating high osmotic pressure in the medullar layer of the kidney, necessary for the concentration of urine. In antidiuresis, ADH increases the permeability of the collecting tubes of the medullar layer not only to water, but also to urea. Urea is a non-polar low-molecular compound and can relatively easily pass through the cell membranes. It is freely filtered in the glomeruli. In the proximal tubule, up to 50 % of the filtered urea is reabsorbed. However, at the beginning of the distal tubule, the amount of urea is slightly more than the amount of urea which is received with the filtrate. Almost all non-reabsorbed urea is retained in the tubule as the fluid flows through Henle`s loop, the distal convoluted tubule, and the collecting tube of the medulla, since all these segments are relatively impermeable to urea. Water reabsorption in these segments causes a progressive increase in the concentration of urea in the lumen of the tubule. Then, in the internal parts of the renal medulla, a high concentration of urea in the tubule creates conditions for reabsorption of urea from the lumen of the collecting tubule into the interstitial fluid of the medulla. This reabsorption occurs with the help of transporters which facilitate the diffusion of urea through both the apical and basolateral membranes (Figure 5.14).

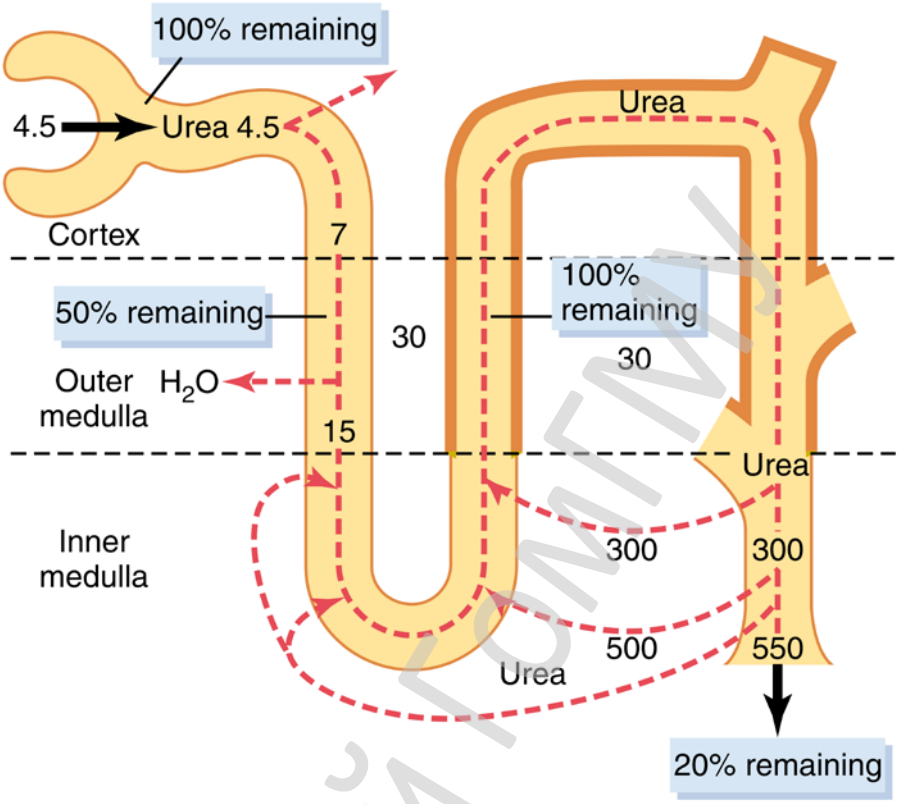


Figure 5.14 —Urea recycling (by C. Guyton and John E. Hall,2016)

Notes: Recirculation of urea absorbed from the medullary collecting duct into the interstitial fluid. This urea diffuses into the thin loop of Henle and then passes through the distal tubules, and it finally returns back into the collecting duct.

Osmotic pressure in the interstitial fluid practically does not change due to the transition of water and urea to the interstitial fluid in proportional quantities, i.e. with an unchanged concentration. This means that the transition of water with urea does not reduce or increase the osmotic pressure in the interstitium. Since the concentration of the urea in the interstitium of the medullar layer of the kidney is higher than in the ascending part of Henle's loop, the urea from the interstitium enters the lumen of Henle's loop down to the concentration gradient.

Then the urea with the flow of secondary urine goes from the ascending part of Henle's loop to the distal convoluted tubule, and from it - to the collecting tubule, then to the interstitium, and again this process repeats. This urea circulation occurs mainly in juxtaglomerular nephrons that have a long nephron loop. The amount of urea leaving the collecting tubes is determined by the amount of water reabsorbed into the interstitium and the state of permeability of the walls of the collecting tubes. Normally, from 20 to 50 % of the urea of the primary urine is excreted in the final urine.

If there is an increase in blood volume (water excess in the organism), the production of ADH, aldosterone and the permeability of the collecting tubes to urea are decreased, which leads to the release of a large volume of diluted (hypotonic) urine.

5.4.4. Tubular secretion

Canalicular secretion represents the result of the activity of the canalicular epithelial cells participating in the transfer of substances from the blood into the tubule lumen, i.e. in the direction inverse to the process of canalicular reabsorption. Secretion is similar to filtration, however filtration occurs only in the glomerulus, and secretion in all parts of the nephron.

In the proximal part of the nephron three transport systems which actively secrete various (mainly foreign) substances are found. One of them is mainly responsible for the secretion of organic acids (phenolic red, para-aminohippuric acid (PAH), iodine-content substances like-diodrast, penicillin, sulfanilamids, and other antibiotics), the second — for secretion concerning strong organic bases (choline, guanine, etc.), the third — for secretion of ethylene diamine tetraacetate (EDTA). These three systems react independently from one another.

The process of the secretion of organic acids can be best described on the example of PAH. After PAH introduction into the blood, its secretion by the kidneys increases. It means, that PAH is not only filtrated in the glomeruli, but also besides the glomeruli its appreciable amounts get into the nephron lumen. In the cell membrane of the proximal part of the tubules, inverted to interstitial fluid, there is a carrier having high affinity to PAH. In the presence of PAH, a complex of the carrier with PAH is formed, which moves to the membrane and to its surfaces and breaks up, liberating PAH into the cytoplasm, and the carrier gets again the ability to move to the outside surface of the membrane and to be connected with a new molecule of PAH. This process takes place with an expense of energy (active transport).

In the final parts of the distal segment and collecting tubules, K^+, H^+, NH ions can be secreted. Potassium excess in the body is secreted into the tubule lumen. In the regulation of K+ secretion the hormone of the cortical substance of the adrenal gland — aldosterone — has the most important value, as it increases sodium reabsorption and simultaneously strengthens potassium secretion.

5.4.5. Evaluation of the excretory functions of the kidneys. Renal clearance

For clinical evaluation of the excretory functions of the kidneys formed by glomerular filtration, tubular reabsorption, and tubular secretion, both methods of visualization and measurement of renal clearance are applied.

The clearance rate of the substance of interest X (Cx) is the parameter describing excretion of the substance of interest X from an organism by the kidneys. The clearance rate is expressed in volumetric units per unit of time (for example, mL/minute). In other words, the clearance rate of the substance of interest X is the speed of its excretion related to the virtual volume of the blood completely cleared of the substance X.

For instance, normally the clearance rate of Na^+ makes 1 mL/minute. This value is determined from the following calculations. Every minute about 1000 ml of blood (700 mL of plasma) flows through the kidney. These 700 mL of blood plasma contain about 100 millimoles of Na^+ (the concentration of Na^+ in blood plasma is practically equal to 140 millimole/L). Only 0.14 millimoles of Na^+ is excreted from them with urine, i. e. one hundredth part of the Na^+ concentration in blood plasma. In other words, the clearance rate of Na^+ — the speed of its excretion related to the virtual volume of the blood completely cleared from Na^+, makes 1 mL/minute.

A general expression for assessing the clearance of any substance of interest is given by the following equation (Cx, expressed in milliliters per minute):

$$Cx = \frac{Ux \times V}{Px};$$

where Ux is the concentration of the substance X in urine (milligrams or mole per milliliter); Px — the concentration of the substance X in the blood (milligrams or mole per milliliter); V— the volume of urine per minute; the product «UxV» — the speed of the excretion of the substance X with urine.

The value of clearance (Cx) for different substances varies. Thus, for glucose, which in norm is not excreted, Cx is equal to 0. At the same time, for para-aminohippuric acid, which is completely eliminated from the blood, the value of Cx makes 700 ml/minutes, i.e. it is equal to the plasma flow through the kidney.

5.5. Homeostatic functions of the kidneys

The kidneys participate in the regulation of:

1. Volume of blood and other body fluids.

2. Constancy of the osmotic pressure of blood, plasma, lymph, and other body fluids.

3. Ionic composition of body fluids and their ionic balance (Na^+, K^+, Cl^-, P, Ca^+) (Figure 5.15).

4. Maintenance of acid-base equilibrium (Figure 5.16).

5. Excretion of excessive organic substances ingested with food, or formed during metabolism (glucose, amino acids).

6. Excretion of the end products of nitrogen metabolism and alien substances.

7. Maintenance of arterial pressure (renin-angiotensin-aldosterone system) (Figure 5.15).

8. Secretion of enzymes and physiologically active substances (renin, bradykinin, prostaglandins, urokinase, vitamin D_3).

9. Erythrogenesis (the kidneys synthesize erythropoietin).

10. Fibrinolysis (the kidneys synthesize urokinase, which participates in fibrinolysis).

Consequently, the kidneys are organs participating in the maintenance of the constancy of the basic physical and chemical constants of blood and other body fluids, regulation of exchange of various organic substances.

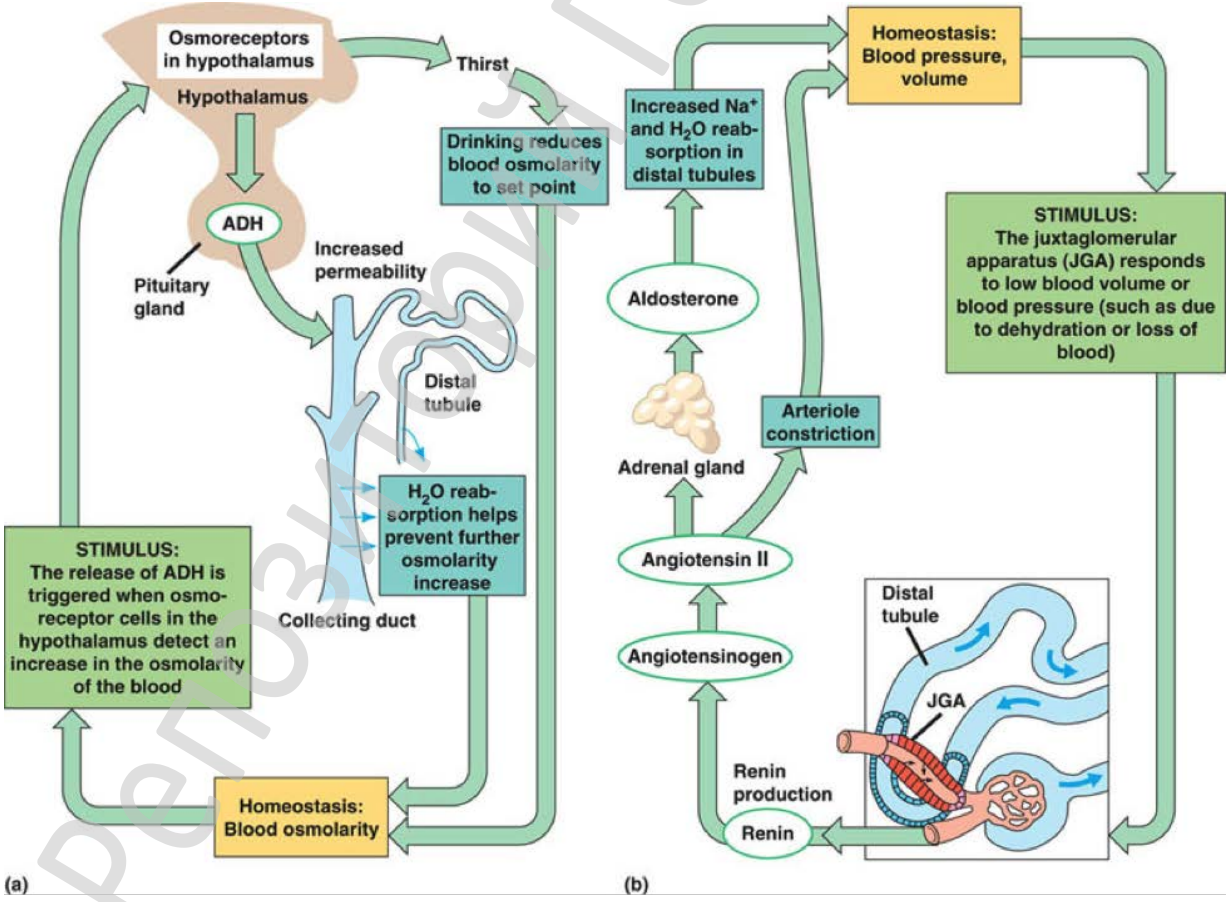


Figure 5.15 — Role of the kidneys in the regulation of blood osmolarity (a) and arterial pressure (b) (from studylib.net)

Note: (a) Hypothalamus antidiuretic hormone (ADH) kidneys loop; (b) the renin-angiotensin-aldosterone system.

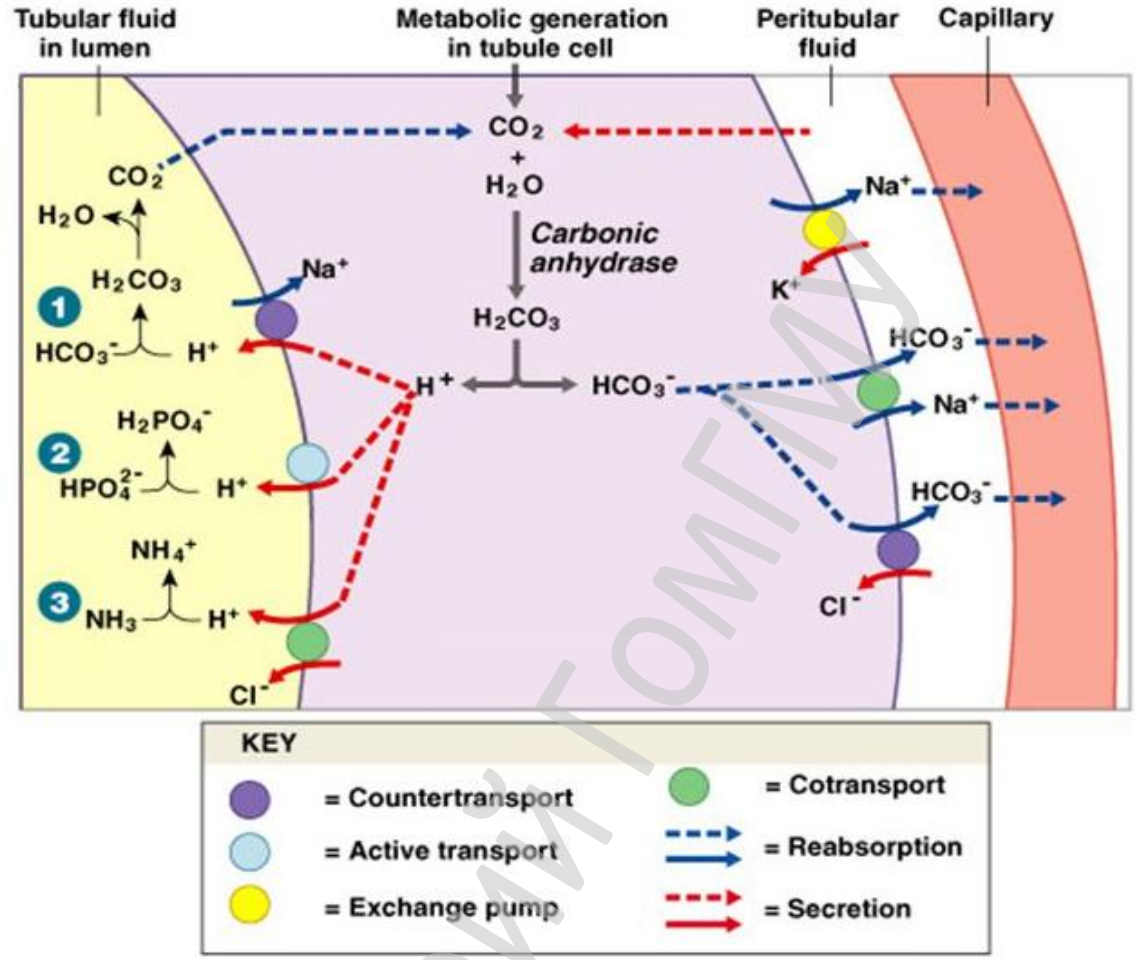


Figure 5.16 — Role of the kidney in the regulation of acid-base balance (from biology.reachingfordreams.com)

5.6. Amount, composition and properties of urine

Diuresis is the amount of urine excreted by an individual over a certain time. This value varies widely in a healthy person depending on the state of water metabolism. In normal water balance 1-1. 5 liters of urine is excreted per day. A decrease in the daily volume of urine (less than 400 mL) is called *oliguria*, increased urine output (more than 2 liters) per day in normal water intake is called *polyuria.* The concentration of osmotically active substances in the urine depends on the state of water metabolism. In the functional test with a water load (when an individual drinks water in the amount of 20 mL per 1 kg of body weight), the rate of uropoiesis reaches 15-20 mL/min. In conditions of high environmental temperature, due to increased sweating, the amount of excreted urine decreases. At night, during sleep, diuresis is less than during the day-time.

Composition and properties of urine. Most of substances present in blood plasma, as well as some compounds synthesized in the kidney, can be excreted with urine.

With the help of the kidneys, almost all nitrogen-containing products of protein metabolism are excreted from the organism. Their amount in the urine, as well as some other substances, such as glucose, not only indicates the state of kidney function, but also the functions of some other organs. Per day with urine 25-35 g of urea, 0.5–1 g of uric acid, 0.4–1.2 g of nitrogen, which is part of ammonia (it is released as ammonium salts), about 0.5 g of amino acids, 1.5 g of creatinine, (which is formed from muscle creatine phosphate), 1.5–3 g of potassium, 3-6 g of sodium are excreted.

The examination of the composition, physical and chemical properties of urine and, if necessary, the volume of final urine (general urine analysis and daily diuresis according to Zimnitsky test) provides important information about the state and functions of the kidneys and urinary system, as well as makes it possible to judge about the processes (normal and pathological) occurring in a number of other organs (liver, heart, etc.). As u rule, fresh urine from the morning portion is used for the examination of its composition and physical and chemical properties. General urine analysis includes the determination of the general physical and chemical properties of urine (color, transparency, smell, volume, pH, density, qualitative reactions to protein, glucose and ketone bodies) and microscopy of urine sediment (red blood cells, white blood cells, epithelial cells, cylinders, bacteria, salts).

The color of urine depends on the amount of diuresis and the level of excretion of pigments that are formed from bilirubin (mainly urochrome and urobilin). The color varies from *light yellow to orange*.

The reaction of urine (pH) is determined by the concentration of free H^+. Under physiological conditions, the pH of urine can range widely from *4.5 to 8.0,* which is due to the ability of the kidneys to maintain a constant concentration of H^+ ions in the blood. In normal diet with a predominant consumption of animal proteins (meats), the reaction of urine is usually acidic. In an individual keeping a vegetarian diet, the urine usually has an alkaline reaction.

The relative density of urine during the day can vary widely from 1.003-1.005 kg/L to 1.020-1.030 kg/L, which depends on the amount of fluid intake, diuresis, and the concentration ability of the kidneys. The density of morning urine ≥1.018 kg/L indicates the preserved concentration capacity of the kidneys and eliminates the need for its study with special tests.

Various biologically active substances and products of their transformation are released with urine, which allows evaluating about the function of certain endocrine glands. Urine contains derivatives of *adrenal cortical hormones, estrogens, ADH, vitamins (ascorbic acid, thiamine), enzymes (amylase, lipase, transaminase, etc.).*

In various pathological conditions some substances may appear in the urine, such as *glucose (glycosuria* in diabetes), *protein (proteinuria)* in kidney diseases, *acetone* in diabetes, *stercobilin, bilirubin and bile acids* (beer-colored urine) in hepatitis and hepatocyte cytolysis. In diseases of the kidneys or urinary tract, the numbers of *white blood cells (pyuria)* and *red blood cells (hematuria)* increase in the urine.

Almost always, epithelial cells from various parts of the urinary tract are detected in the urine sediment. The urine of a healthy person is sterile. The detection of *bacteria* in the urine (*bacteriuria*) may be due to its external contamination, or infectious diseases of the kidneys and urinary tract.

5.7. Urination and its regulation

Formed in the renal tubule urine is excreted into the renal cup. The muscle contractions of the renal pelvis provide the progression of urine to the ureter, which further drain it to the urinary bladder. The urinary bladder represents a hollow organ formed by a network of smooth muscle fibers. Within the floor of the bladder there is a triangular area, called the trigone, formed by thin smooth muscle fibers. In the angles of the base of this triangle the ostia of the ureters are located. The ureters open into the bladder in a slanting direction and small flaps of mucosa cover the openings and act as valves that allow urine to enter the bladder but prevent it from backing up from the bladder into the ureters. At the apex of the trigone, is the opening into the urethra. A band of the detrusor muscle encircles this opening to form the functional internal urethral sphincter (contracted involuntary). The urethra ends with the external sphincter (contracted voluntary), formed by transversal striated muscle fibers.

Uropoiesis is constant in the kidneys; urine is collected in the urinary bladder, which is periodically completely evacuated. This function, which has a huge value for humans, happens due to the activity of the smooth muscles of the urinary bladder and the influences of the vegetative and somatic nerves. There are special systems of the reflex regulation of the kidneys. Urination can be changed by reflexes caused by the irritation of the internal organs.

The neural regulation of the urinary bladder function consists in alternating the long filling and short emptying phases. The filling phase is characterized by voluntary contractions of the external urethral sphincter, with

sympathetic contractions of the internal urethral sphincter. The stimulation of the mechanoreceptors of the urinary bladder pulses on the centripetal nerves get into the sacral parts of the spinal cord, in II–IV segments of which there is the reflex center of urination. The spinal center of urination is under the influence of the overlying parts of the brain. Inhibiting influences on this urination reflex proceed from the cerebral cortex, excitation influences — from the posterior hypothalamus and the anterior part of the pons varolii. Excitation of the urination center produces contractions of the urinary bladder muscles, the pressure in it increases up to 20–60 cm of water, and the internal sphincter of urethra gets relaxed. The stream of pulses to the external sphincter of the urethra decreases, its muscles are relaxed and urination begins (Figure 5.17). Thus the micturition or emptying phase displays a coordinated relaxation of the internal and external urethral sphincters, under sympathetic and somatic regulation respectively, with strong contractions of the detrusor muscle due to parasympathetic impulses.

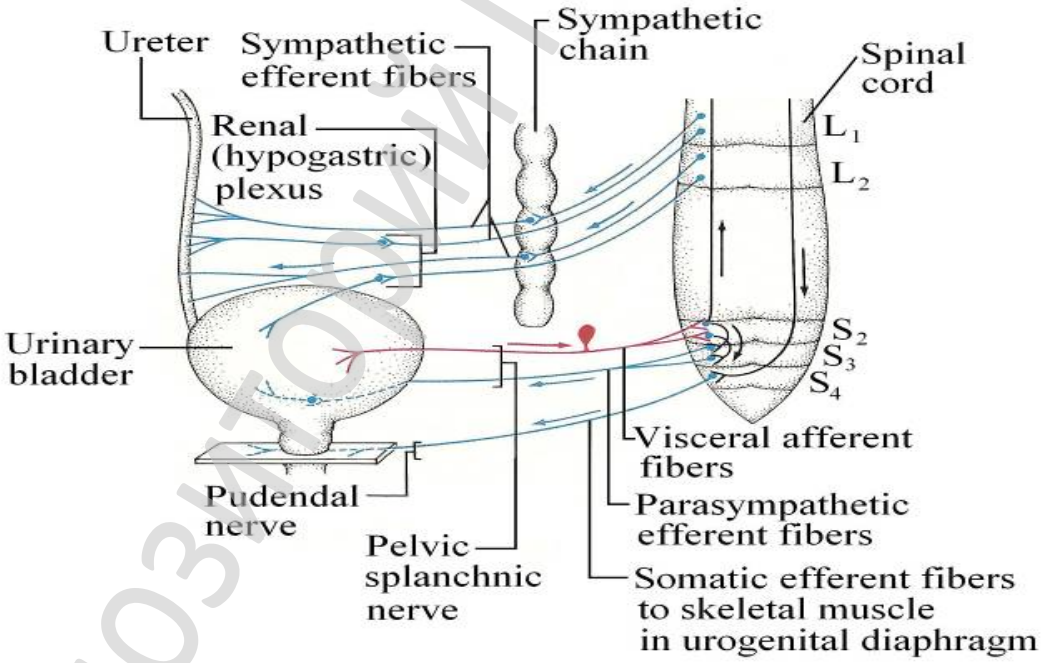


Figure 5.17 — Micturition (urination) reflex arc pathway (by Elaine N. Marieb, 1989)

The filling rate of the urinary bladder makes about 50 mL per hour. Owing to the plasticity of the smooth muscles of the bladder, the pressure in it only insignificantly rises if its volume increases. Accumulation of approximately 150–250 mL of urine in the bladder causes the first short desires to urinate, caused by short-term rising of intravesical pressure. The micturition phase usually begins, when about 250–500 mL of urine is collected in the urinary bladder.

5.8. Complications of kidney removal and artificial kidney

After the removal of one kidney (nephrectomy) in humans and animals within several weeks the mass of the other kidney is enlarged — there comes its compensatory hypertrophy. Glomerular filtration in the remaining kidney increases almost 1–1/2 times in comparison with an initial level, reabsorption and secretory ability of the kidney increase. Although the overall kidney function decreases after a nephrectomy, a single kidney can successfully provide the fastness of the organism.

For temporary replacement of some renal functions during acute and chronic kidney diseases, and also constantly in patients after nephrectomy a device called «artificial kidney» is used. It represents a dialyzer where through the pores of the semipermeable membrane the blood is cleared of metabolic waste and its composition is normalized. The dialyzer, or filter, has two parts, one for human blood (the patient`s blood flows from the artery and after transit through the machine is poured in into the vein) and the other for a washing fluid called dialysate. This solution by its ionic composition and osmotic concentration is similar to blood plasma, but does not contain urea and other end products of nitrogen metabolism. A thin membrane separates these two parts. The sieving properties of the membrane exclude all solutes above a certain threshold from crossing the membrane. Solutes within the permeability range of the membrane pass it while diffusing along existing concentration gradients. Blood cells, protein, and other important things remain in the blood because they are too big to pass through the membrane. Low-molecular components of blood plasma, such as urea, creatinine, urinary acid, polypeptides, potassium and extra fluid pass through the membrane and are washed away. The patient has to be connected to the «artificial kidney» 2–3 times a week and with the help of this method it is possible to sustain the patient`s life for many years. One session of hemodialysis lasts 4 hours.

Review questions

1. What is the physiological role of excretion? Name the organs of excretion. What is the function of these organs in the maintenance of homeostasis?

2. What are the excretory and non-excretory functions of the kidneys?

3. Name the structural elements of the nephron being a morpho-functional unit of the kidneys. What are the types of nephrons and what are their characteristics? What are the features of renal blood supply?

4. Name the processes of uropoiesis according to the filtration-reabsorption theory of urine formation. What are the functions of the main parts of the nephron?

5. Name the structural features of the filtrating membrane of the nephron. How is the effective filtrational pressure calculated? What is the amount of primary urine? What is its composition?

6. What are the mechanisms of tubular reabsorption in different parts of the nephron? What are the features of reabsorption in the loop of Henle? What is clearance? How is it calculated? What substances are called the threshold substances? Give examples. What substances are called non threshold substances? Give examples.

7. What is tubular secretion? Give the example of the mechanism of tubular secretion.

8. Name the homeostatic functions of the kidneys. What is the role of the kidneys in the maintenance of the acid-base state, osmotic pressure, ionic composition of the blood, water and electrolytic balance? What is the role of the kidneys in the regulation of arterial pressure?

9. What amount of final urine is formed per day? What is its composition? What substances can be present in final urine and what substances are absent in final urine in norm?

10. What is urination? How is this process regulated?

11. What are the complications of kidney removal? What is the artificial kidney? What is the mechanism of hemodialysis?

Multiple Choice Questions
PHYSIOLOGY OF EXCRETION

1. The excretory function of the glands of the gastrointestinal tract mainly consists in…

Variants of answer:

a) excretion of heavy metals, some medicines, alien organic substances;

b) excretion of water and CO_2;

c) excretion of inorganic and organic substances, water;

d) excretion of the end-products of metabolism;

e) all the answers are correct.

2. The basic homeostatic function of the kidneys is the maintenance of the constancy of …

Variants of answer:

a) body temperature;

b) blood plasma proteins;

c) counts of leukocytes, thrombocytes, pressure of the ultrafiltrate;

d) oncotic pressure, the level of nutrients in the blood;

e) oncotic pressure, acid-alkaline balance, arterial pressure.

3. The kidneys participate in the regulation of blood coagulation due to the production of the activator of plasminogen, which is named …

Variants of answer:

a) phosphatase;

b) renin;

c) urokinase;

d) angiotensin;

e) erythropoietin.

4. The kidneys participate in the regulation of haemopoiesis due to the production of…

Variants of answer:

a) renin;

b) urokinase;

c) angiotensin;

d) erythropoietin;

e) phosphatase.

5. Renin is formed in …

Variants of answer:

a) the adrenal glands;

b) the juxtaglomerular apparatus of the kidneys;

c) the superficial nephron;

d) the anterior lobe of the hypophysis;

e) the right atrium.

6. The formation of final urine is the result of …

Variants of answer:

a) filtration, reabsorption, active transport;

b) filtration, reabsorption, pinocytosis;

c) filtrations, reabsorption, tubular secretion;

d) filtration, adsorption;

e) active transport, pinocytosis, tubular secretion.

7. The process of primary urine formation in the capsule of Shymlanski-Bowman is named…

Variants of answer:

a) tubular excretion;

b) tubular reabsorption;

c) tubular secretion;

d) glomerular filtration;

e) adsorption.

8. The process of reabsorption in urine formation is:

Variants of answer:

a) active absorption of some substances from the blood into the renal tubules;

b) the process of absorption of substances from the renal tubules in the blood;

c) passive absorption of some substances from the blood into the renal tubules;

d) active filtration of glucose into the renal tubules;

e) passive excretion of exchange products from an organism.

9. The process of secretion in urine formation is …

Variants of answer:

a) passive excretion of exchange products from an organism;

b) active excretion of substances from blood into the renal tubules;

c) filtration of blood plasma into the renal tubules;

d) active filtration of glucose into the renal tubules;

e) reverse absorption of substances from the renal tubules into the blood.

10. The formation of primary urine from blood plasma is the function of …

Variants of answer:

a) the proximal tubules of the nephron;

b) the capillaries of the renal glomerulus;

c) the distal tubules of the nephron;

d) the collective tubules of the nephron;

e) Henle's loop

11. How is the formed glomerular filtrate named?

Variants of answer:

a) final urine;

b) secondary urine;

c) clearance;

d) primary urine;

e) serum.

12. Which parameter depends on the size of the lumens of the afferent and efferent arterioles and on the permeability of the capillary membranes of the renal glomerulus?

Variants of answer:

a) oncotic pressure;

b) secretion;

c) filtration;

d) reabsorption;

e) absorption.

13. How will the rate of glomerular filtration change in the narrowing of efferent arteriole?

Variants of answer:

a) it will increase;

b) it will decrease;

c) it will not change;

d) the filtration will stop

e) at first it will decrease, then it will increase.

14. How much primary urine is formed per day?

Variants of answer:

a) 15–20 L/day;

b) 150–180 L/ day;

c) 1.5–2 L/ day;
d) 30–40 mL/ day;
e) 150–180 mL/ day.

15. The composition of the glomerular ultrafiltrate is similar to that of …

Variants of answer:

a) final urine;
b) arterial blood;
c) venous blood;
d) blood plasma;
e) blood serum.

16. The hydrostatic pressure of blood in the glomerular capillaries is equal to…

Variants of answer:

a) 11 mm Hg;
b) 70 mmHg;
c) 120 mmHg;
d) 50mmHg;
e) 30 mmHg.

17. How effective will the filtration pressure in the kidney change if the oncotic pressure of blood increases?

Variants of answer:

a) it will decrease;
b) it will increase;
c) it will not change;
d) it will disappear;
e) at first it will decrease, then it will increase.

18. How is the increased amount of excreted urine called?

Variants of answer:

a) proteinuria;
b) glucoseuria;
c) polyuria;
d) anuria;
e) oliguria.

19. How will the daily amount of urine change if the oncotic pressure of plasma decreases?

Variants of answer:

a) it will decrease;

b) it will increase;

c) it will not change

d) urine will not be formed;

e) at first it will decrease, then it will increase.

20. How does the amount of excreted urine change under the action of vasopressin?

Variants of answer:

a) it increases;

b) it decreases;

c) it does not change;

d) urine will not be excreted;

e) at first it will decrease, then it will increase.

21. Which proteins of blood plasma can appear in the urine in kidney pathology?

Variants of answer:

a) globulins;

b) fibrinogen;

c) gamma-globulins;

d) albumins;

e) angiotensinogen.

22. The process of the return of some filtered substances from primary urine into the blood is named…

Variants of answer:

a) tubular secretion;

b) tubular reabsorption;

c) glomerular filtration;

d) adsorption;

e) synthesis.

23. In which part of the nephron is glucose basically reabsorbed?

Variants of answer:

a) Henle`s loop;

b) distal tubules;

c) collective tubules;
d) proximal tubules;
e) capillaries of the renal glomerulus.

24. Proteins are reabsorbed in …
Variants of answer:
a) the descending part of Henle`s loop;
b) the ascending part of Henle`s loop;
c) the proximal tubules of the nephron;
d) the distal tubules of the nephron;
e) the capillaries of the renal glomerulus.

25. What is passively reabsorbed in the proximal part of the nephron?
Variants of answer:
a) glucose;
b) sodium;
c) aminoacids;
d) water;
e) lipids.

26. What is reabsorbed along the whole nephron except for the ascending part of Henle`s loop?
Variants of answer:
a) glucose;
b) protein;
c) sodium and potassium ions;
d) water;
e) chlorine ions.

27. Water reabsorption in the kidneys is carried out by …
Variants of answer:
a) active transport;
b) secretion;
c) all the answers are correct;
d) passive transport;
e) pinocytosis.

28. The formation of primary urine is the result of …
Variants of answer:
a) filtration, reabsorption;

b) filtration, reabsorption, secretion;
c) filtration;
d) reabsorption;
e) secretion.

29. The kidneys participate in the regulation of arterial pressure due to the production of…

Variants of answer:
a) renin;
b) urokinase;
c) angiotensin;
d) erythropoietin;
e) phosphatase.

30. Which part of the nephron is almost completely impermeable to water?

Variants of answer:
a) proximal convoluted tubule;
b) descending part of Henle`s loop;
c) ascending part of Henle`s loop;
d) collective tubules;
e) distal tubules of the nephron.

31. Which substance is a threshold substance?

Variants of answer:
a) protein;
b) glucose;
c) creatinine;
d) inulin;
e) diodrast.

32. Which substance is non-threshold during the excretion by the kidneys?

Variants of answer:
a) amino acids;
b) glucose;
c) ions of potassium;
d) inulin;
e) vitamins.

33. Para-aminohippuric acid is used to determine renal blood flow because …

Variants of answer:

a) the walls of the renal tubules are impenetrable to it;
b) it is fully reabsorbed and does not pass into secondary urine;
c) it is filtered, completely secreted and not reabsorbed into the blood;
d) it is filtered and reabsorbed into the blood;
e) it is filtered, completely secreted and reabsorbed into the blood.

34. Normal daily amount of final urine is equal to …

Variants of answer:

a) 15–20 L/day;
b) 150–180 L/day;
c) 1.5–2 L/day;
d) 3–5 L/day;
e) 300–500 mL/day.

35. What reaction (pH) does the urine in a healthy person have?

Variants of answer:

a) acid;
b) neutral;
c) all the answers are correct;
d) alkaline;
e) 4.5.

36. Which volume of urine in the urine bladder causes the first desires to urinate?

Variants of answer:

a) 300 mL;
b) 150 mL;
c) 500 mL;
d) 1000 mL;
e) 750 mL.

37. How is the termination of urine formation named?

Variants of answer:

a) proteinuria;
b) glucoseuria;
c) polyuria;
d) anuria;
e) oliguria.

38. What urine is formed in the conditions of decreased water amount in an organism?

Variants of answer:

a) hypotonic urine;
b) normotonic urine;
c) hypertonic urine;
d) isoosmolar urine;
e) urine with glucose.

39. What urine is formed in the conditions of increased water amount in an organism?

Variants of answer:

a) hypotonic urine;
b) normotonic urine;
c) hypertonic urine;
d) isoosmolar urine;
e) urine with glucose.

40. What substances are not normally revealed in final urine?

Variants of answer:

a) urea, creatinine;
b) glucose, acethone;
c) sodium, potassium;
d) hormones, vitamins;
e) all the answers are correct.

41.Specific cells-osmoreceptors are located in …

Variants of answer:

a) the hypophysis;
b) the hypothalamus;
c) the cerebral cortex;
d) the thalamus;
e) the spinal cord.

42. Where is antidiuretic hormone secreted?

Variants of answer:

a) in the thalamus;
b) in the hypophysis;
c) in the frontal lobe of the cerebral cortex;
d) in the thyroid glands
e) in the adrenal glands.

43. The antidiuretic mechanism activates in …

Variants of answer:

a) excessive water intake;
b) intake of salty food, loss of water;
c) intake of sour food;
d) intake of spicy food;
e) all the answers are correct.

44.Which hormone increases sodium reabsorption?

Variants of answer:

a) antidiuretic hormone;
b) natriuretic hormone;
c) parathyroid hormone;
d) aldosterone;
e) adrenaline.

45. Aldosteron causes …

Variants of answer:

a) decreased sodium reabsorption, potassium and hydrogen secretion;
b) increased sodium reabsorption, potassium and hydrogen secretion;
c) increased potassium reabsorption, sodium and hydrogen secretion;
d) decreased potassium reabsorption, sodium and hydrogen secretion;
e) increased hydrogen reabsorption, sodium and potassium secretion.

46. Which hormone causes increased water reabsorption in the kidneys?

Variants of answer:

a) insulin;
b) natriuretic hormone;
c) adrenaline;
d) antidiuretic hormone;
e) parathyroid.

47. The physiological role of renin consists in …

Variants of answer:

a) the maintenance of normal count of blood cells;
b) the regulation of arterial pressure;
c) blood coagulation;
d) the regulation of vitamin D;
e) all the answers are correct.

48. What changes of the hydrostatic pressure in the afferent arteriole of the renal glomerulus will increase renin production?

Variants of answer:

a) if the hydrostatic pressure sharply increases and then sharply decreases;

b) if the hydrostatic pressure increases;

c) if the hydrostatic pressure decreases;

d) the hydrostatic pressure in the afferent arteriole does not influence renin production;

e) if there is no hydrostatic pressure.

49. Angiotensin II causes …

Variants of answer:

a) decreased production of aldosteron, vascular dilatation;

b) activation of renin formation;

c) increased production of aldosteron, vascular constriction;

d) decreased blood pressure;

e) activation of gastric secretion.

50. The work of an artificial kidney is based on …

Variants of answer:

a) the reflex mechanism of regulation;

b) the endocrine mechanism of regulation;

c) the process of hemodialysis through the partially permeable membrane;

d) the mechanism of secretion;

e) the mechanism of reabsorption.

51. Renin is secreted by...

Variants of answer:

a) the proximal convoluted tubules;

b) the urinary bladder;

c) the collecting duct;

d) the juxatglomerular apparatus;

e) the loop of Henle.

52. Which of the following biological active substances is not secreted by the kidney...

Variants of answer:

a) renin;

b) angiotensin I;
c) erythropoietin;
d) vitamin D_3;
e) urokinase.

53. Which of the following does not form a filtration barrier in nephrons?
Variants of answer:
a) podocytes;
b) mesangium;
c) endothelial cell;
d) basement membrane;
e) all the answers are correct.

54. Hypertonic urine is excreted due to water absorption in...
Variants of answer:
a) the collecting ducts;
b) the distal convoluted tubules;
c) the ascending part of the loop of Henle;
d) the descending part of the loop of Henle;
e) all the answers are correct.

55. The main site of bicarbonate reabsorption is…
Variants of answer:
a) the proximal convoluted tubule;
b) the distal convoluted tubule;
c) the cortical collecting duct**;**
d) the medullary collecting duct;
e) the thick ascending loop of Henle.

56. Normal urinary excretion of proteins per day is...
Variants of answer:
a) 100 mg;
b) 250 mg;
c) 400 mg;
d) 600 mg;
e) 1000 mg.

57. What is assumed by the fact that a drug has higher renal clearance rate than the glomerular filtration rate?
Variants of answer:
a) the drug is reabsorbed in the tubules;
b) the drug is secreted in the tubules;

c) the drug is excreted in bile;
d) the drug is neither secreted, nor resorbed;
e) the drug is only filtrated in the glomerulus.

58. Which statement is true about a substance which is present in the concentration of 2 mg % in the afferent arteriole and zero mg% in the efferent?

Variants of answer:
a) it is not filtrated in the glomerulus;
b) it is secreted in the cortical nephron;
c) it is absorbed in the proximal convoluted tubules;
d) it is impermeable in the loop of Henle;
e) it is freely filtered in the glomerulus.

59. The best test for the glomerular filtration rate is done with...

Variants of answer:
a) inulin;
b) hippuric acid;
c) creatinine;
d) PAH;
e) insulin.

60. All of these statements about renal physiology are correct except...

Variants of answer:
a) sodium absorption occurs in the distal convoluted tubules;
b) potassium is both secreted and absorbed in the renal tubules;
c) glucose is reabsorbed in the distal convoluted tubules;
d) Hb is not excreted as it is a large molecule;
e) amino acids are reabsorbed in the proximal convoluted tubules**.**

CORRECT ANSWERS
PHYSIOLOGY OF EXCRETION

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	a	16	b	31	b	46	d
2	e	17	a	32	d	47	b
3	c	18	c	33	c	48	c
4	d	19	b	34	c	49	c
5	b	20	b	35	c	50	c
6	c	21	d	36	b	51	d
7	d	22	b	37	d	52	b
8	b	23	d	38	c	53	b
9	b	24	c	39	a	54	a
10	b	25	d	40	b	55	a
11	d	26	d	41	b	56	a
12	c	27	d	42	b	57	b
13	a	28	c	43	b	58	e
14	b	29	a	44	d	59	a
15	d	30	c	45	b	60	c

UNIT 6
PHYSIOLOGY OF THE SENSORY SYSTEMS

6.1. General physiology of the sensory systems

6.1.1. General principles of the constitution of the sensory systems

The sensory system (the analyzer by I. P. Pavlov) is a part of the nervous system consisting of perceiving elements —***sensory receptors*** (the peripheral part of the analyzer), receiving signals from the external or internal environment, ***nerve pathways*** (the conductive part), transmitting information from receptors to the brain, and ***parts of the brain*** (the central part of the analyzer), which process the obtained information (Figure 6.1).

A sense organ is a peripheral part that perceives and partially analyzes changes in the external environment of the body, and excitation of this part leads to the formation of sensations. There are 5 senses: *vision, hearing, smell, touch, and taste.*

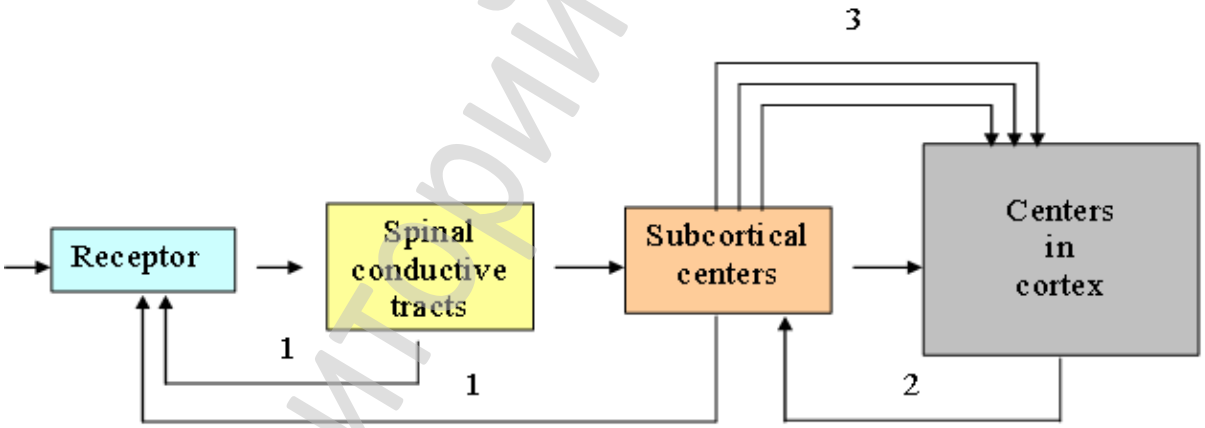


Figure 6.1 — General principle of the structure and functioning of the sensory system (by Korobkov A. V., Chesnokova S. A., 1986)

Notes: 1 — The sympathetic system regulating the level of the receptor excitation;
2 — «Cortex»; 3— Reticular formation

The main principles of the structure of the sensory system in higher vertebral animals and humans are:

1. Multilevel structure, i. e. the presence of several levels of nervous cells, the first of which is connected with the receptors, and the last one — with the neurons of the sensory regions of the cerebral cortex. This feature gives an opportunity to differentiate the neuron levels during the processing of different kinds of sensory information.

2. Multichanneling of the sensory system, i.e. presence in each layer of a multitude (from dozens of thousands to millions) of nervous cells connected with the multitude of the next layer cells. The availability of the multitude of these parallel channels of information transmission provides the sensory system with accurate and detailed analysis of signals, and high reliability.

3. Different number of elements in the neighboring layers, which forms **«sensory funnels»** (Figure 6.2). Thus, the retina of the human eye counts 130 million photoreceptors, in the layer of the ganglionic cells of the retina the number of neurons is 100 times less («narrowed funnel»). The following levels of the visual system form an «extending funnel»: the number of neurons in the initial projective part of the visual region of the cerebral cortex is thousand times higher than that of the ganglionic cells of the retina. In the acoustical and some other sensory systems, the «extending funnel» goes from the receptors to the cerebral cortex. The physiological sense of the «narrowing funnel» is in decrease of the redundancy of information, and that of the «extending funnel» — ensuring of the fractional and complex analysis of different indicators of signals. The presence of lateral inhibition between the neurons of the sensory system provides the choice of the most significant data about signals.

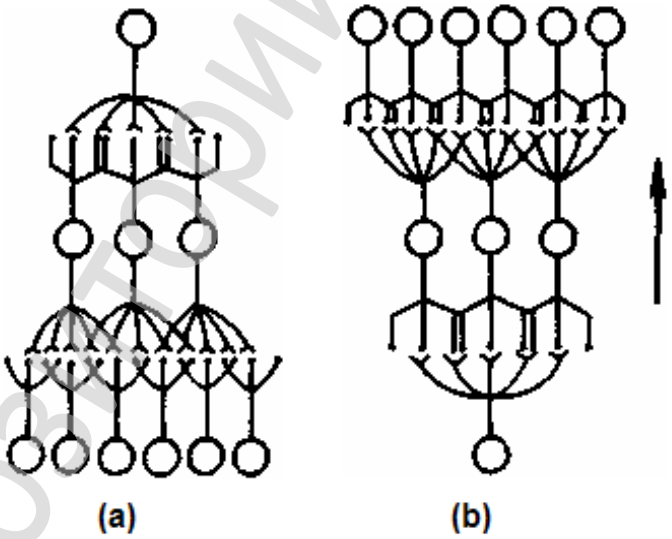


Figure 6.2 —«Narrowed» (a) and «extending» (b) sensory funnels (by Pokrovskiy V. M., Korotko G. F., 2000)

4. Differentiation of the sensory systems by the vertical and horizontal axes. Differentiation by the vertical axe means formation of parts each of which has several neuron layers. Thus, any of the above parts represents a bigger morpho-physiological formation than a neuron layer. Each part (for example, olfactory bulbs, cochlear nuclei or geniculate bodies) performs a specific function.

Differentiation by the horizontal axe means different properties of receptors, neurons, and connections between them within each layer. Thus, vision involves the work of two parallel canals of neurons going from the photoreceptors to the cortex of cerebrum and processing the information coming from the center and from the periphery of the eye retina in its own way.

6.1.2. Properties of the analyzers

The analyzers have several properties:

1. High excitability of receptors. For example, one quantum of light is enough to excite the retinal photoreceptor, one molecule of odorous substance — to excite the olfactory receptor; the hair receptors of the inner ear are able to detect the movement of the membrane equal to the diameter of a hydrogen atom. The excitability of different receptors varies and depends on their sensitivity and specificity.

The quantitative measure of the sensitivity of the sensory receptors is the **absolute threshold of sensitivity** — the minimum force of a stimulus that can cause excitation of a receptor.

The threshold of a sensation is the minimal force of an adequate stimulus causing the excitation of receptors, which is perceived subjectively in the form of a sensation.

Between the absolute sensitivity and its threshold there are the following relations: **the higher the threshold is, the higher the sensitivity is; and vice versa, the lower the sensitivity is, the higher the threshold is.**

2. **Inertia.** Inertia is a relatively slow rise of sensations after the stimulus is turned on and the slow disappearance of sensations after the stimulus is turned off (for example: the continuation of the light sensation after the light is turned off).

3. Induction interaction. Induction interaction is the change in the excitability of one analyzer during the excitation of another analyzer, accompanied by a change in the degree of sensations (for example: light affects music perception; taste sensations are increased if they are accompanied by pleasant smells; noise impairs visual perception; listening to music during dental procedures decreases pain).

4. **Adaptation.** Sensory adaptation is a common property of the sensory systems consisting in their adaptation to long-acting stimuli. Adaptation is the phenomenon of decreased excitation in receptors under the action of a long-term (background) stimulus of constant force, i. e. the response (frequency of the action potential generation) to a stimulus after constant exposure to it decreases over time.

Adaptation is manifested in **decreased absolute sensitivity and increased differential sensitivity**. When the action of a constant stimulus stops, the sensitivity of the analyzers increases (adaptation to light, darkness, sound, smell, effects on the tactile receptors). Adaptation begins at the receptor level and covers all the levels of the sensory system.

Depending on the rate of adaptation, all receptors are divided into tonic, intermediate, and phasic receptors (Figure 6.3).

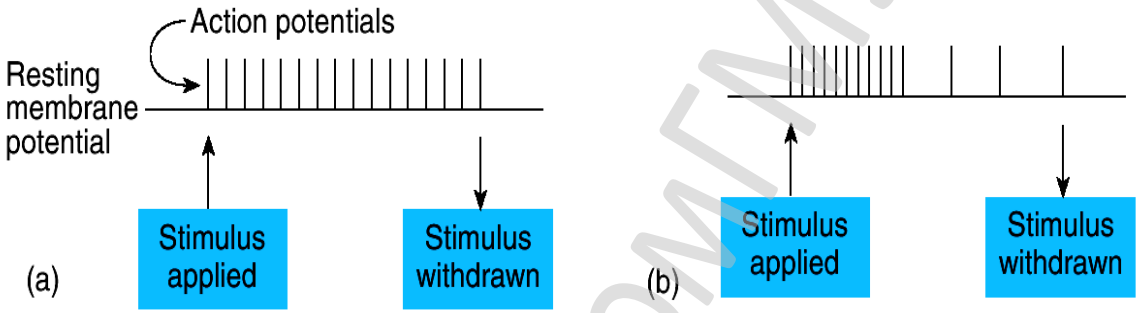


Figure 6.3—Slowly adapting (a) and rapidly adapting (b) receptors (from biology.reachingfordreams.com)

The tonic receptors are *slowly adapting receptors* which constantly send information to the brain about the position of the body, its individual parts and the state of the internal environment. These receptors generate nerve impulses at a constant level throughout the duration of the action of a stimulus.

These receptors include: *muscle spindles, Golgi tendon receptors, vascular baroreceptors, some pain receptors.*

The intermediate (phase-tonic) receptors adapt *at an average rate*, they generate nerve impulses during the entire time of the action of a stimulus, but their frequency is significantly reduced. The receptors with the average rate of adaptation include the *photoreceptors of the retina, the thermoreceptors of the skin.*

The phasic receptors are rapidly *adapting* receptors. These receptors are stimulated only when the strength of a stimulus changes. They generate nerve impulses in the initial (ON-response) and final (OFF-response) periods of the action of a stimulus. Thus, the Pacinian corpuscles adapt extremely quickly, within a fraction of a second (for example, over time we do not notice the continuous pressure of clothes or rings on the skin, the action of odorous substances).

6.1.3. Basic functions of the sensory system

The sensory system performs the following basic functions, or operations, with signals: 1) detection; 2) differentiation; 3) transmission and transformation; 4) encoding; 5) detection of signs; 6) identification of images. The detection and

primary differentiation of signals are done by receptors, and the detection and identification of signals — by the neurons of the cerebral cortex. The transmission, transformation and encoding of signals are performed by the neurons of all the layers of the sensory systems (Figure 6.4).

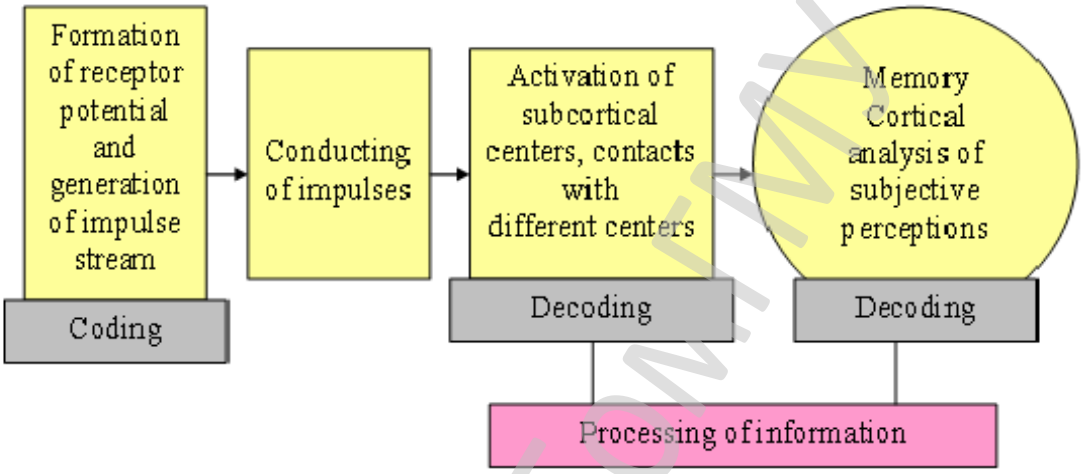


Figure6.4 — Stages of analyzer functioning (by Korobkov A. V., Chesnokova S. A., 1986)

The detection of signals starts in receptors — special cells adapted to perceive stimuli from the external or internal environments and transform them from their physical or chemical form into the form of nervous excitation.

Classification of receptors. There are several classifications of receptors.

1. Psychophysiological classification of receptors (it is the most important). According to this classification, humans have visual, acoustic, olfactory, gustatory, tactile, termo-, proprio- and vestibular receptors, and pain receptors.

2. By localization:

• external receptors (exteroreceptors); they include acoustic, visual, olfactory, gustatory, tactile receptors;

• internal (interoreceptors) receptors; they include vestibular- and proprioreceptors (receptors of movements), and also visceroreceptors (interpret stimuli from the internal organs and tissues, such as the receptors that sense the increase in blood pressure in the aorta or carotid sinus);

• proprioceptors are receptors located near a moving part of the body, such as a muscle or joint capsule, that interpret the positions of tissues as they move.

3*. By the character of their contact with the environment:* receptors are divided into:

• distant receptors — receive information from distant sources of stimulation (visual, acoustic and olfactory);

• contact — are exited during an immediate contact with stimuli (gustatory, tactile).

4. By the nature of stimuli to which they can respond:

• photoreceptors;

• mechanoreceptors (acoustic, vestibular receptors, tactile receptors of the skin, receptors of movement, baroreceptors of the cardiovascular system);

• chemoreceptors (gustatory and olfactory receptors, vascular and tissue receptors);

• thermoreceptors;

• pain (nociceptive) receptors.

5. By their structural features (Figure 6.5) all the receptors are divided into:

• primary-sensitive (olfactory, tactile and proprioreceptors) — they are endings of the dendrites of sensory neurons;

• secondary-sensitive (taste, vision, auditory, vestibular receptors) — they have the specialized receptor cell between the stimulus and the first neuron.

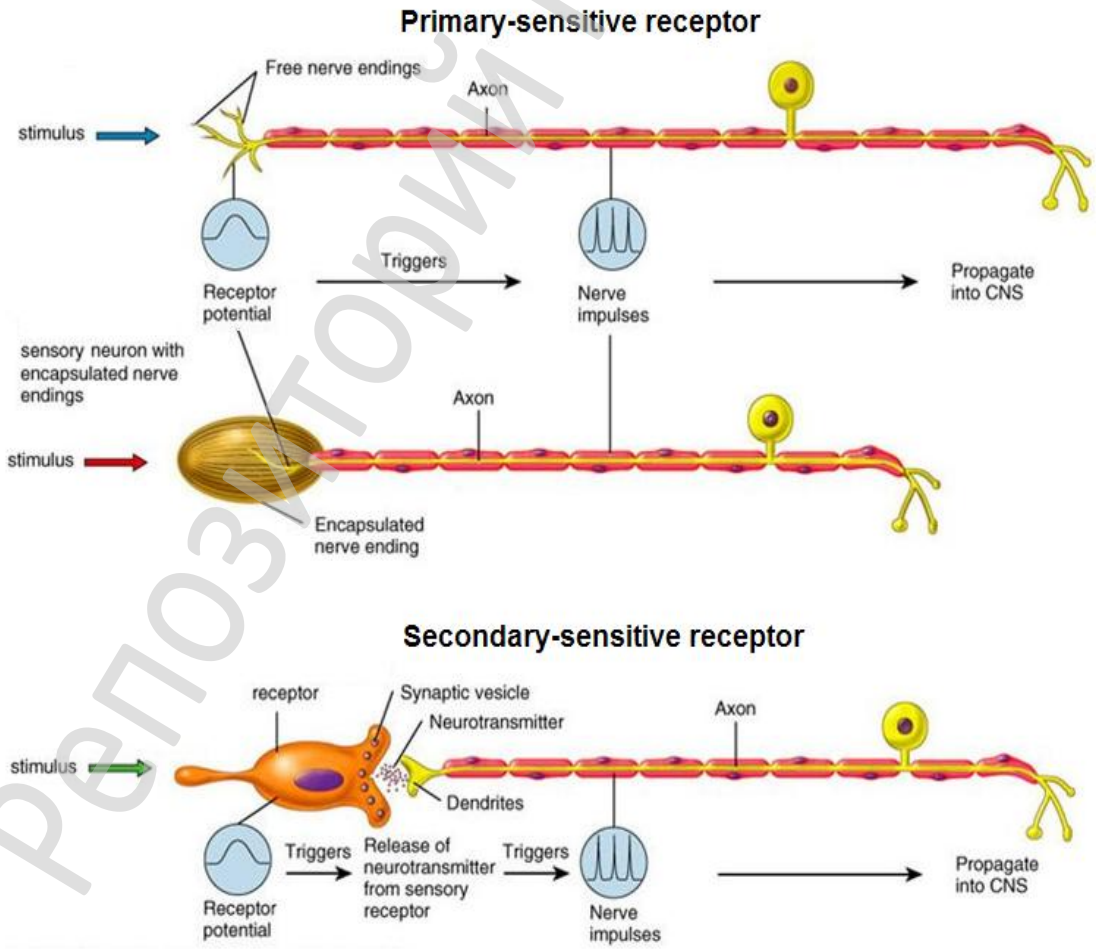


Figure 6.5— Primary-sensitive and secondary-sensitive receptors (from bianoti.com)

Transformation of the stimulus energy

The contact of a stimulus with the membrane of a receptor causes the increased the *membrane permeability to ions (in most receptors – to sodium ions)***.** These ions diffuse into the sensory terminal, which is depolarized, and *a receptor potential* (RP) arises.

The primary transformation of a stimulus into the receptor potential is called ***transformation.*** RP excites the initial segment of the sensory nerve and in the primary-sensitive receptors *the nerve impulse (action potential, AP)* arises, the frequency of which depends on the force of RP.

In the secondary-sensitive receptors during the RP formation the receptor cell *secretes the mediator*, which causes the formation of a *generator potential (GP)* on the postsynaptic membrane of the neuron, followed by the appearance of *a nerve impulse (AP).*

The sequence of events from the beginning of the action of a stimulus to the formation of AP:

In the primary-sensitive receptors:

Stimulus → depolarization of the membrane of the nerve terminal → RP → AP

In the secondary- sensitive receptors:

Stimulus → depolarization of the membrane of the nerve terminal → RP → secretion of the mediator → generator potential (GP) → AP

Differentiation of signals. The important feature of the sensory system is its ability to distinguish the difference in the properties of simultaneously or consistently acting stimuli. The difference begins in receptors but this process involves the neurons of the whole sensory system.

The differential threshold of the stimulus intensity is practically always higher than the previous stimulation which influenced a certain zone (Weber's law). Thus, a person can feel increased pressure on the skin of a hand if the load increases by 3 % (3 g weight is added to 100 g weigh, and 6 g — to 200 g).

There are two kinds of signal differentiation: **spatial and temporal**. Spatial differentiation means that if two stimuli excite two adjacent receptors, the differentiation of these stimuli is impossible and they are accepted as one stimulus. For spatial differentiation there should be at least one unexcited receptor between the two excited ones.

For temporal differentiation of the two stimuli it is necessary that induced nerve processes should not synchronize in time and the signal induced by the second impulse should not coincide with the refractory period of the first signal.

Transmission and transformation of signals. The processes of the signal transformation and transmission in the sensory system provide the higher centers of the brain with the most important information about the stimulus for its reliable and fast analysis.

The encoding of information is the transformation of information into its conditional form — code. In the sensory system signals are encoded by the binary code, i. e. the presence or absence of electrical impulses. This method of encoding is quite simple and resistant to any interference. The information about stimulation and its size is transferred as separate impulses, and also groups, or «packs» of impulses. The amplitude, duration, and form of each impulse are similar, but the number of impulses in a pack, their frequency, duration of packs and intervals between them are various and depend on the features of the stimulus.

The following characteristics of the stimulus are coded: quality (type), quantity (strength), localization (area of action), the time of its action.

1. The quality (type) of the stimulus is encoded by the presence of different types of receptors that have the greatest sensitivity to a certain (adequate) type of stimuli (except for pain).

2. The strength of the stimulus is encoded by changing the number of excited receptors and changing the frequency of impulses.

3. The time of the action is encoded by the excitation of receptors, the stimulus is turned on and the cessation of excitation after it is switched off, and also due to the presence of on, off, and on-off receptors.

There are neurons that respond to stimuli only when they are turned on ("on"-neurons), turned off ("off"-neurons), turned on and off ("on-off" neurons) — i. e., neurons that mark the most informative time intervals.

The principal feature of neural coding is the ***multiplicity and overlapping of codes.***

Signal detection is the selective isolation by a sensory neuron of this or that sign of a stimulus having a behavioral value. Such analysis is performed by feature detectors, individual neurons or groups of neurons which selectively react only to certain parameters of a stimulus. A typical neuron of the visual region of the cerebral cortex responds only to one certain orientation of a dark or light strip located in the certain region of the field of vision. If the position changes, other neurons will respond to the same strip (e.g. the detectors of the face).

Image identification is the final and the most complex operation of the sensory system. It presumes the identification of images with this or that class of objects which an organism has previously encountered, i. e. the classification of images. Synthesizing signals from the feature detectors, the higher part of

the sensory system forms an image of the stimulus and compares it with the set of images kept in memory. The image identification ends with a resolution, consequently, we realize whose face we see, whose voice we hear, etc.

6.2. Particular physiology of the sensory systems

6.2.1. Visual system

Vision evolutionary adapts to the perception of electromagnetic radiation in a separate, narrowed part of their diapason (visible light). The visual system provides the brain with more than 90 % of sensory information.

Structure and functions of the optical device of the eye

The eyeball has a spherical shape which ensures its rotations for the focusing on objects a person is looking at. On the way to the photosensitive layer of the eye (retina) light rays pass through some translucent mediums — cornea, lens, and vitreous body (Figure 6.6).

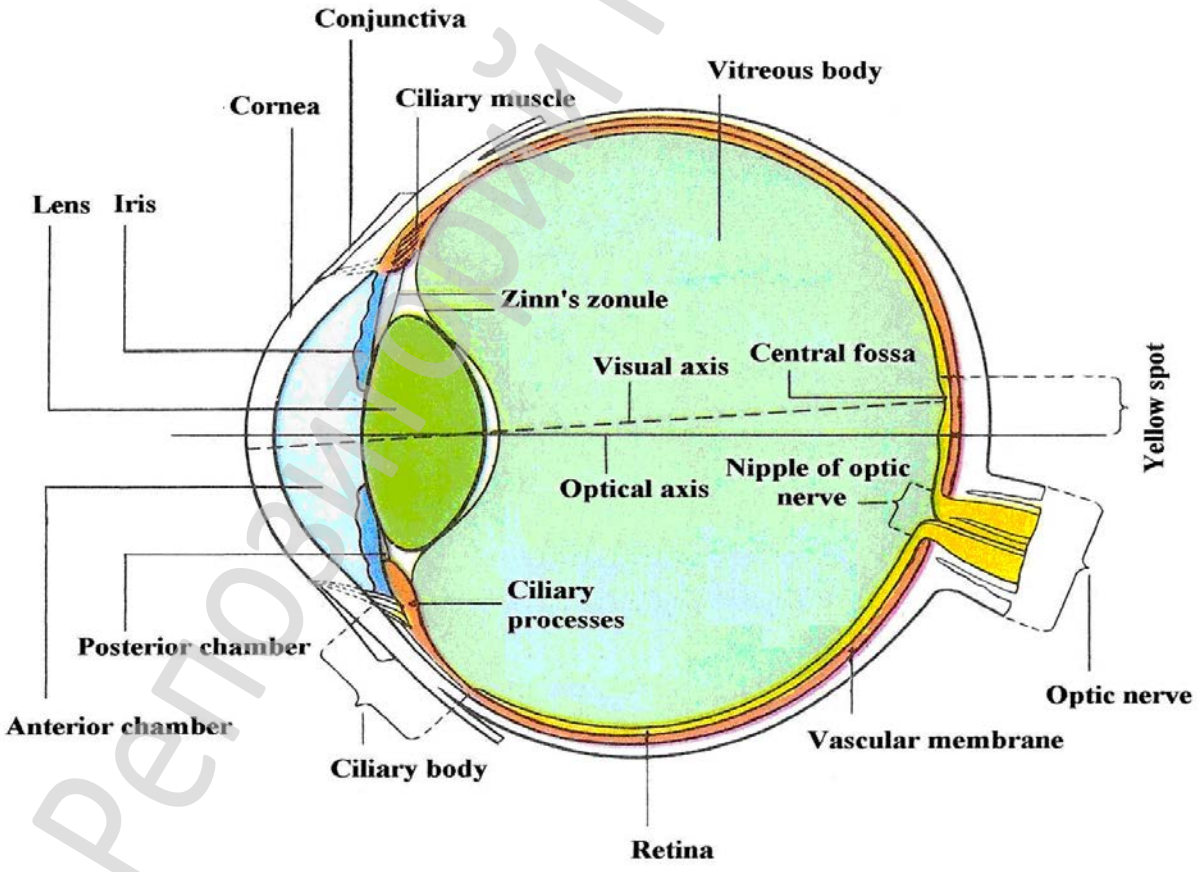


Figure 6.6 — Structure of the human eye (by Korobkov A. V., Chesnokova S. A., 1986)

The refracting power of any optical system is measured in dioptres (D). One dioptre is equal to the refracting power of lens with a focal length of 100 cm. The

refracting power of a healthy eye is 59D when a person is looking at remote objects, and 70.5D when they are looking at close objects (Figure 6.7). The retina gets an image sharply reduced in size and turned upside down and from right to left.

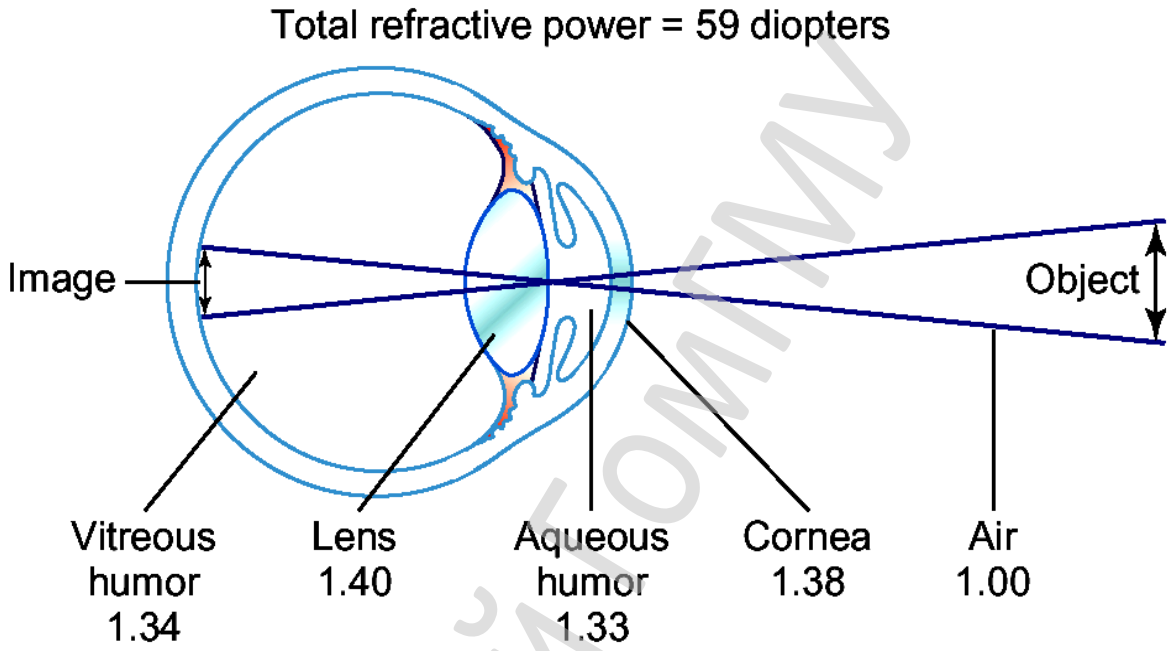


Figure 6.7 —Optical system of the eye (from studylib.net)

Accommodation is the adjustment of the eye to get clear vision of objects located at different distances, i.e. the ability of the eye to change its focus from near to distant objects. (Figure 6.8). In order to get clear vision of an object, it should be focused on the retina, i.e. the rays from all the spots of its surface should be projected on the retina. When we look at distant subjects, their image is focused on the retina and they are seen clearly. But the image of close subjects is foggy because the rays from them are collected behind the retina. The leading role in the accommodation is played by the eye lens which changes its curvature and, therefore, refractivity. When we look at close subjects, the lens becomes more convex. The mechanism of accommodation is the contraction of ciliary muscles which change the curvature of the lens. The lens is located in a thin clear capsule which is always stretched, or flattened, by the fibers of the ciliary (Zinn's) zonule. The contractions of the smooth muscular cells of the ciliary body decreases the traction force of the ciliary zonule, which increases the convexity of the lens due to its elasticity.

For the normal eye of a young person the distant point of clear vision lays in infinity. Distant subjects can be seen without stress of accommodation, i. e. without contraction of the ciliary muscle. The nearest point of clear vision is at a distance of 10 cm from the eye.

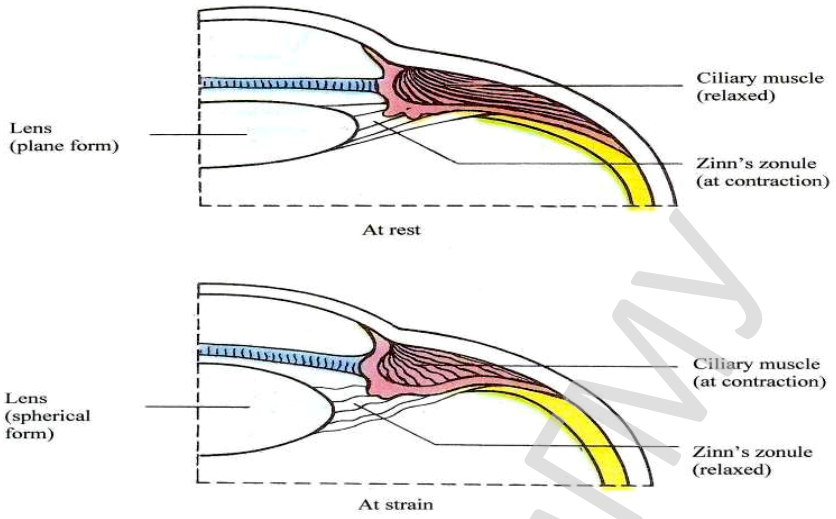


Figure 6.8 — Mechanism of eye accommodation (by Korobkov A. V., Chesnokova S. A., 1986)

Presbyopia. In the eye, the crystalline lens is located just behind the iris and the pupil. Tiny ciliary muscles pull and push the lens, adjusting its curvature, and thereby adjusting the eye's focal power to bring objects into focus. As individuals age, the lens becomes less flexible and elastic, and the muscles become less powerful. Because these changes result in inadequate adjustment of the lens of the eye for various distances, objects that are close appear blurry. That is why the closest point of clear vision is now not at the distance of 10 cm from the eye, but farther. This phenomenon is called *presbyopia.* That is why elderly people have to wear glasses with the biconvex lens.

Anomalies of eye refraction

The two main anomalies of eye refraction — myopia and hypermetropia — are determined by the change of the length of the eyeball (Figure 6.9).

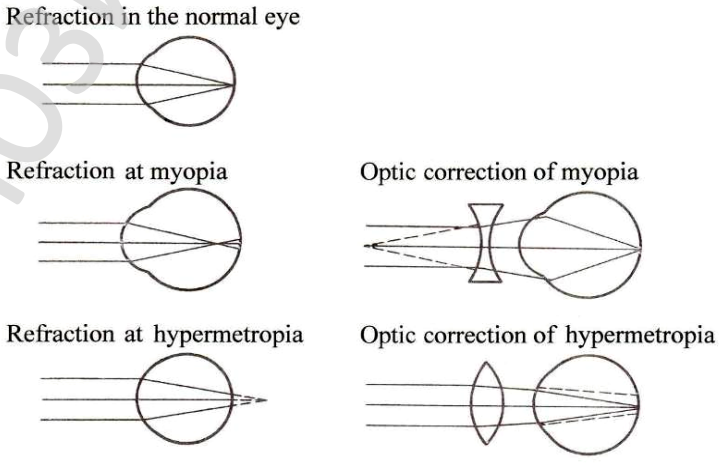


Figure 6.9 — Refraction in a normal eye in myopia and hypermetropia.
Optic correction of myopia and hypermetropia (by Pokrovskiy V. M., Korotko G. F., 2000)

Myopia. In people with normal vision, parallel light rays enter the eye and are bent by the cornea and lens (refraction) to focus precisely on the retina, providing a clear image. In the myopic eye, the focusing power of the cornea (the major refracting structure of the eye) and the lens is too great with respect to the length of the eyeball. If the longitudinal axis of the eye is too long, light rays from distant objects are bent too much, and they converge in front of the retina, in the vitreous body. For clear vision of a distant object, it is necessary to place concave glasses before the eye which will move the focused image on the retina.

Hyperopia. Hyperopia, or hypermetropia is opposite to myopia. In the hypermetropic eye the longitudinal axis of the eye is shortened, and rays from a distant object are focused not on the retina but behind it. This condition exists when the combined curvature of the lens and cornea is insufficient. This defect of refraction can be compensated by the accommodation effort, i.e. increased convexity of the lens. For reading people with hyperopia have to wear glasses with the biconcave lens intensifying light diffraction.

Astigmatism is unequal refraction of rays in different directions (for example, by the horizontal and vertical meridian). Astigmatism is the result of the inability of the cornea to properly focus an image onto the retina. In severe astigmatism this surface may be close to cylindrical, which is corrected by cylindrical glasses.

Eye pupil and pupillary reflex

The pupil is the perforation in the center of the iris through which light rays enter the eye. The pupil increases image sharpness on the retina and improves images on the retina due to the removal of spherical aberration because it lets only the central rays to pass through. If we close one eye and then open it, the pupil quickly narrows («iris contraction reflex»). The muscles of the iris change the size of the pupil, regulating the amount of light entering the eye. The pupil is constricted and has the minimal diameter (1.8 mm) when exposed to strong light and when the focus is on a near object; in average daylight it extends (2.4 mm) and is dilated in the dark (maximum 7.5 mm) and when the focus is on a distant object. (Figure 6.10).

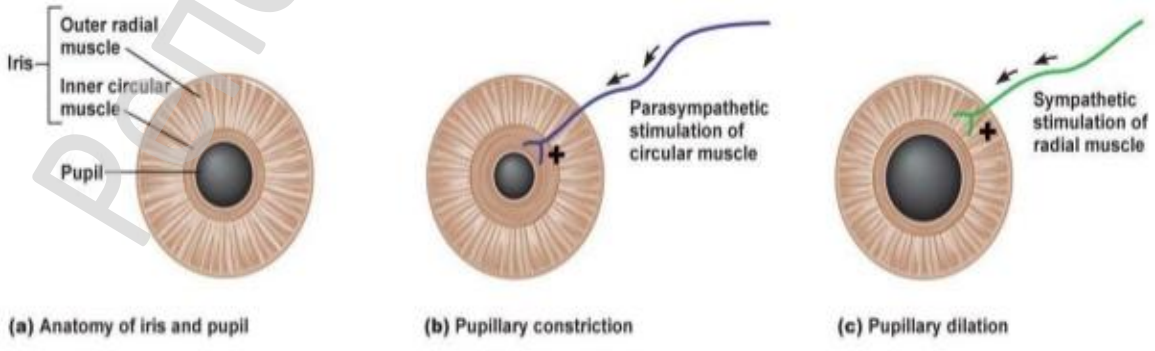


Figure 6.10 — Pupillary reflex (from bianoti.com)

The iris of the eye has two kinds of muscle fibers surrounding the pupil: circular innervated by the parasympathetic fibers of the 3rd cranial nerve, and radial, innervated by sympathetic nerves. The contractions of the former produce narrowing, contraction of the latter — dilation. Acetylcholine and eserine produce narrowing (miosis), and adrenaline — dilation (mydriasis). Dilation of the pupil is most often observed under the effect of pain, strong emotions (fear, fury) or after treatment with mydriatic drugs (such as atropine, scopolamine, or homatropine). Pupillary dilation may be an important sign of some pathological states, for example, pain shock, hypoxia, etc.

Structure and functions of the retina (Figure 6.11).

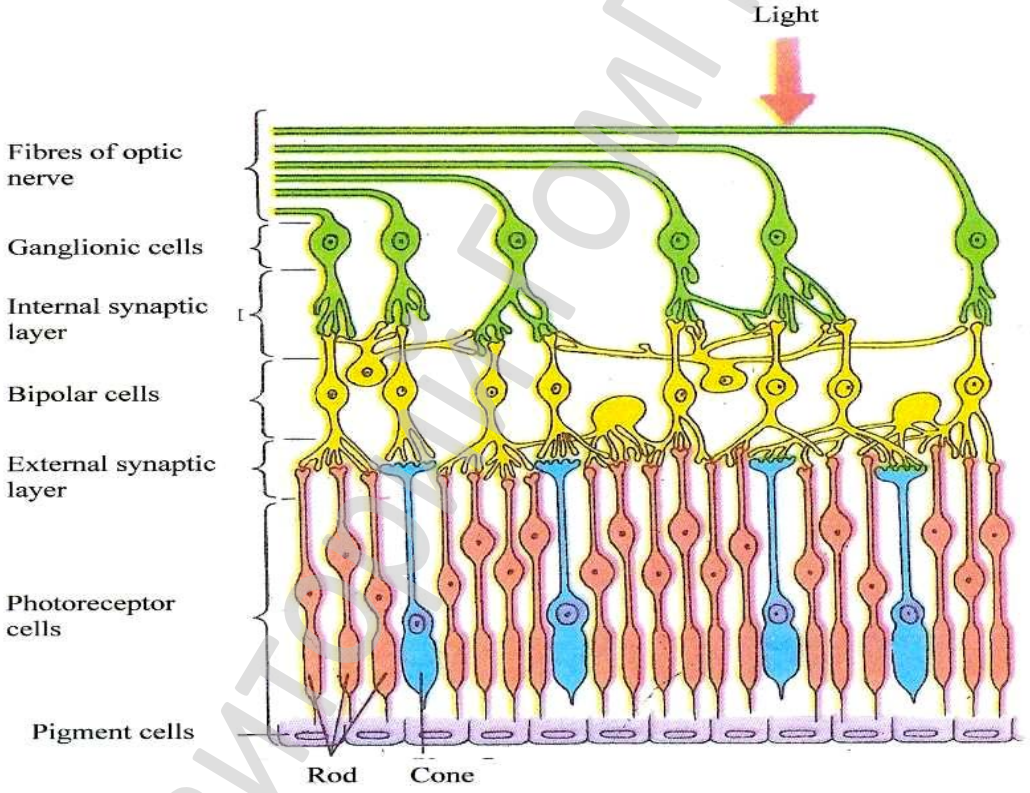


Figure 6.11 — Structure of the retina (by Korobkov A. V., Chesnokova S. A., 1986)

The retina represents the internal photosensitive layer of the eye. It has the complex multilayer structure. The retina is composed of light-sensitive neurons arranged in three layers; the first layer is made up of the photoreceptors (rods and cones) and the other two transmit impulses from the rods and cones to the optic nerve. The activation of the photoreceptors stimulates the first nervous cell of the retina (*bipolar neuron*). The excitation of bipolar neurons activates the *ganglionic cells* of the retina, which transmit signals to the subcortical visual centers. All the listed neurons of the retina with their processes not only transfer the information to the visual centers of the brain, but also participates in its analysis and processing.

The exit point of the optic nerve from the eyeball, or optic disk, is called the blind spot. It has no photoreceptors and therefore is not sensitive to light.

Pigment layer. This layer is formed by one set of epithelial cells which have a large number of various intracellular organelles including melanosoma giving the black color to this layer. This pigment absorbs the light which comes to it and prevents light reflection and dispersion thus promoting image sharpness. The cells of the pigment epithelium have numerous processes which densely surround the photosensitive external segments of the rods and cones. The pigment epithelium plays the main role in the re-synthesis of rhodopsin after its decolorization; in phagocytosis and digestion of the fragments of the external segments of the rods and cones; in the mechanism of constant regenerating of the external segments of visual cells; in protection of the visual cells against the danger of light damage, and also in the transmission of oxygen and other necessary substances to photoreceptors. The contact between the cells of the pigment epithelium and photoreceptors is very weak. In this place the detachment of the retina (dangerous disease of the eye) occurs.

Photoreceptors. The photoreceptors (rods and cones) are found on the outermost layer of the retina.

The retina of each person has 6–7 million cones and 110–123 million rods. They are irregularly distributed in the retina. The central fossa of the retina (*fovea centralis*) contains only cones (up to 140 thousand per 1 mm^2). Along their direction to the periphery of the retina their number decreases, and the number of the rods increases, so at the distant periphery there are only rods. The cone function in the conditions at big amount of light, they provide day and color vision; the rods being much more photosensitive are responsible for twilight vision.

The structure of the photoreceptor cell. The photoreceptor cell — either the rod or the cone — consists of the external (outer) segment sensitive to light and having a visual pigment, internal (inner) segment, connecting the crus, a nuclear part with a large nucleus, and the presynaptic terminal (Figure 6.12). The rods and cones of the retina are directed by their photosensitive external segments to the pigment epithelium, i. e. to the side opposite to light. In the human the external segment of the photoreceptor (rod or cone) contains about one thousand photoreceptor disks. The external segment of the rod is much longer than that of the cone and contains more visual pigment.

The internal segment has a large nucleus and all organelles include mitochondria which ensure the energy needs of the photoreceptor, and a system of the protein synthesis provides the renewal of the membranes of the external segment.

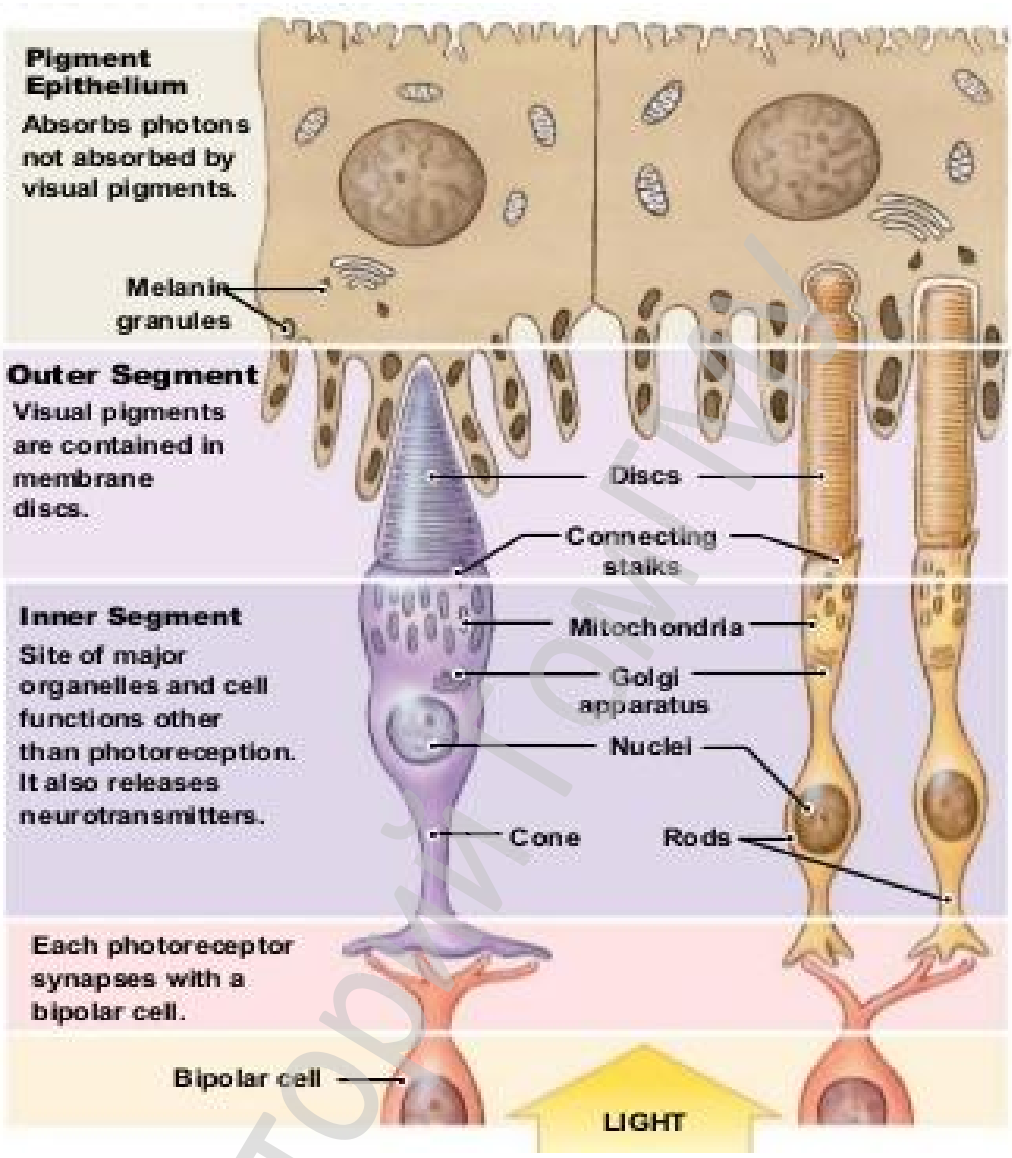


Figure 6.12 — Structure of the rods and cones (from bianoti.com)

Visual pigments. The rods of the human retina contain the pigment of rhodopsin. In the external segments of three types of the cones (blue-, green- and red-sensitive) there are three types of visual pigment.

Neurons of retina. The photoreceptors of the retina are connected with bipolar neurons. From them a nerve signal is transferred to the ganglionic cells whose axons are the fibers of the optic nerve. Per 130 million photoreceptor cells there are only 1 million 22 thousand ganglionic cells. It means that signals from many photoreceptors converge through the bipolar neurons to one ganglionic cell.

Nerve pathways and connections in the visual system (Figure 6.13). Visual information from the retina goes to the brain along the fibers of the optic nerve (2nd cranial). The optic nerves from each eye meet at the basis of the

brain where the optic chiasm is formed. Here some part of the fibers of each optic nerve comes over to the opposite side. The optic nerve fibers from *the nasal (medial)* halves of the retina cross to the opposite sides, where they join the fibers from the *temporal (lateral)* halves of the opposite retinas. Partial crossing of the fibers provides each hemisphere of the cerebrum with the information from both the eyes.

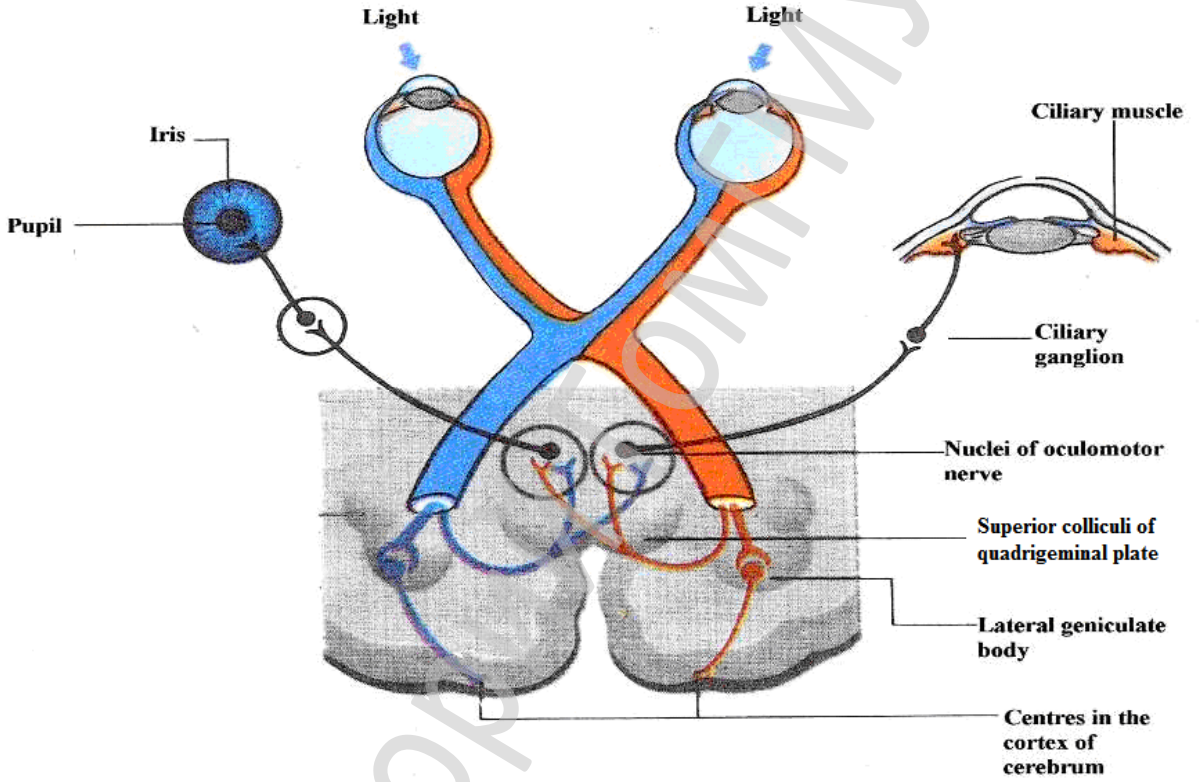


Figure 6.13 — Relations of the optic ways with the process controlling the pupil's diameter and accommodation (by Korobkov A. V., Chesnokova S. A., 1986)

The optic pathways after the visual chiasm are called visual tracts. They are projected into a series of the cerebral structure but the main number of fibers comes to the thalamic subcortical visual center — lateral, or external, geniculate body. From here signals come to the initial projective region of the visual zone of the cortex of cerebrum (field 17).

Electrical activity of the centers of the visual system

Under the action of light electrical potentials are generated in receptors, and then and in the neurons of the retina.

The summary electrical response of the retina of the eye to the action of light is called the electroretinogram (ERG). It can be registered from the whole eye or only from the retina. For this, one electrode is applied on the surface of the cornea, and the other one — on the skin of the face near the eye or the ear

lobe. The ERG distinguishes several typical waves. The wave *a* reflects the excitation of the internal segments of the photoreceptors and horizontal cells. The wave *b* appears from the activation of the glial cells of the retina by potassium ions released during the excitation of bipolar and amacrine neurons. The wave *c* reflects the activation of the cells of the pigment epithelium, and wave *d* — that of horizontal cells (Figure 6.14).

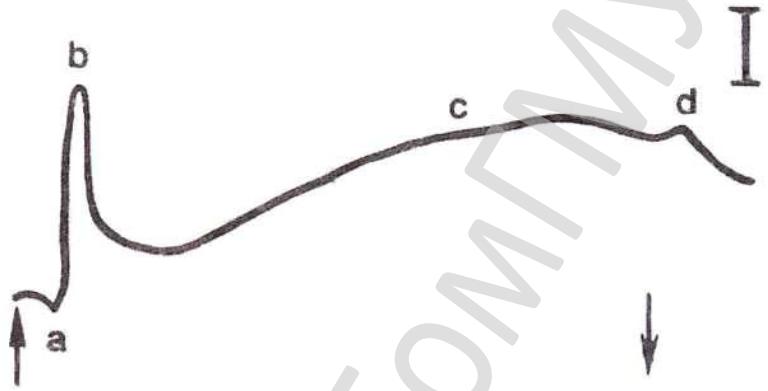


Figure 6.14 — Electroretinogram (by Pokrovskiy V. M., Korotko G. F., 2000)

Color vision

Theories of chromatic sensitivity

M. V. Lomonosov was the first who wrote about the existence of the three-component mechanism of color perception. Then this theory was formulated in 1801 by T. Jung and was finished G. Helmgolts. According to the three-component theory (G. Helmholtz), color perception is provided by three types of the cones with various color sensitivity. One of them is sensitive to the red color, the second — to the green color, and the third — to the blue color. Any color affects all the three color-perceptive elements, but in a different degree. These excitations are summarized by the visual neurons and they give the sensation of this or that color to the cortex of the cerebrum.

According to the other theory (E. Goering, the theory of opponent colors), the cones have substances sensitive to white-black, red-green and yellow-blue radiances.

Experimentally, signals from the ganglionic cells were registered by means of microelectrodes under monochrome light and revealed that the signals from the majority of neurons (dominators) arise under the action of any color. In other ganglionic cells (modulators) impulses arise under the influence of one color only. There are 7 types of modulators with an optimal response to light with different wave-length (from 400 to 600 nanometers).

Color blindness. Partial colorblindness was described by D. Dalton, who suffered from it himself (that is why this color perception abnormality is called

daltonism). Daltonism is present in 8 % of men and 0.5 % of women. Its appearance is connected with the absence of certain genes in sex unpaired X-chromosome in men.

There are three types of particulate colorblindness: protanopia, deuteranopia, and tritanopia. Each of them is characterized by the absence of perception of one of the three main colors.

People with *protanopia* do not perceive the red color and consider blue rays as colorless. People with *deuteranopia* do not distinguish green colors from dark red and blue. A person with *tritanopia* — rare abnormality of color vision — does not perceive blue and violet color rays.

There is also complete colorblindness — *achromasia* causing a person perceive all subjects only in different shades of the grey color.

Visual acuity. The acuity of vision is characterized by the smallest visual angle at which the eye can see two separate points. Normal visual acuity is the ability of the eye to distinguish between the details of the surrounding environment seen at the visual angle of 1 minute. The visual angle of 1 minute is traditionally accepted in practice as a norm of visual acuity. Macula lutea has the typical maximal acuity of vision.

Visual acuity is determined with the help of special tables in which parallel lines of letters or open-ended rings are located in a decreasing order downwards. Each line is marked with a distance in meters from which a person should distinguish the letters of the line.

Visual field. The visual field is the area simultaneously visible to one eye without movement and it is often measured by means of a bowl perimeter located 330 mm from the eye. It depends on the functional state of the retina, anatomical features of the face (depth of the eye location, form of the eyeball, superciliary arch, nose), and also on the color of subjects. The visual field for black-and-white subjects (achromatic) is larger than that for color ones (chromatic), which is caused by the unequal location of the rods and cones in the center and on periphery of the retina. The chromatic visual field also depends on the color (for green it is the smallest, for yellow it is the largest). The borders of the achromatic visual field are: external — 90°, upward and internal — 60°; downward — 65°. The determination of the visual field has an important diagnostic value in the detection of the abnormalities of the eye retina.

Review questions

1. Give the definition of the sensory system by I.P. Pavlov. What parts does the sensory system have? What is the sense organ? How many senses do humans have? Name the basic principles of the structure and properties of the sensory systems.

2. What are the main functions of the sensory systems? How does signal detection occur? How are receptors classified? What is the mechanism of the transformation of stimuli in receptors (primary-sensitive and secondary-sensitive)?

3. How does signal differentiation occur? Name the types of signal differentiation. What are the features of information coding? How does the detection of signals take place? What processes occur in the central part of the analyzer during the analysis of afferent signals?

4. What are the structure and functions of the optical system of the eye? What is accommodation? Explain its mechanisms? Name the anomalies of the eye refraction. What are myopia and hyperopia? How can they be corrected?

5. What is the eye pupil? What is the pupillary reflex? How is the diameter of the pupil regulated?

6. What are the structure and functions of the retina? Describe the receptor device of the retina.

7. Name the conductive and central parts of the visual analyzer. What is the electroretinogram? Describe it.

8. What are the theories of chromatic sensitivity? What is color blindness? Name the kinds of color blindness.

9. What is visual acuity? What is the visual field? What does it depend on?

6.2.2. Auditory system

The auditory system is one of the major distant human sensory systems for the sense of hearing. Acoustic signals represent air vibrations of different frequency and force. They excite the auditory receptors located in the cochlea of the internal ear. The receptors activate the first auditory neurons, then sensory information is transmitted to the auditory region of the cortex of the cerebrum.

Structure and functions of the external and middle ear (Figure 6.15).

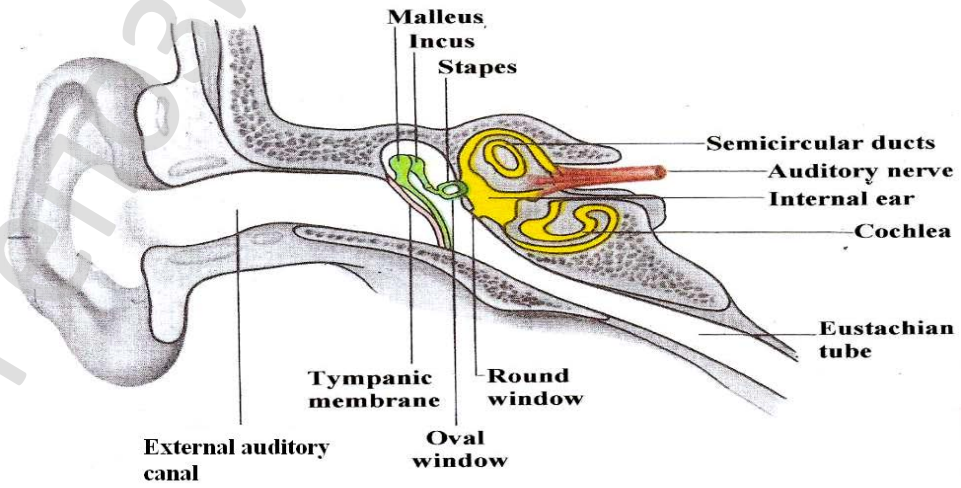


Figure 6.15 — Structure of the external and middle ear (by Korobkov A. V., Chesnokova S. A., 1986)

External ear. The external auditory canal conducts sound vibrations to the tympanic membrane. The membrane separates the external ear from the middle ear and represents a thin (0.1 mm) inside-directed shaped septum. The membrane vibrates under the influence of sound vibrations coming to it through the external auditory canal.

Middle ear (Figure 6.16). In the middle ear filled with air there are three auditory ossicles: malleus, incus, and stapes, which consistently transmit the vibrations of the tympanic membrane into the internal ear. Malleus'es handle is interlaced into the tympanic membrane, its other side is connected with the incus transmitting the vibrations to the stapes. The vibrations from the tympanic membrane to the stapes are transferred at a decreased amplitude but with increased force. The surface of the stapes is 22 times less than that of the tympanic membrane, which by 22 times intensifies its pressure on the membrane of the oval window. Consequently, weak sound waves influencing the tympanic membrane can overcome the resistance of the oval window membrane of the vestibulum and reveal in the vibrations of the fluid in the cochlea. Favorable conditions for the vibrations of the tympanic membrane are also produced by the auditory (Eustachian) tube, connecting the middle ear with the nasopharynx, which ensures equal pressure on both the sides of the tympanic membrane. The vibrations of the fluid of the cochlea which arise at the oval window of the vestibule in the ducts of the cochlea, reach the round window of the cochlea and do not fade. With the absence of the round window the vibrations of the fluid would be impossible due to its incompressibility.

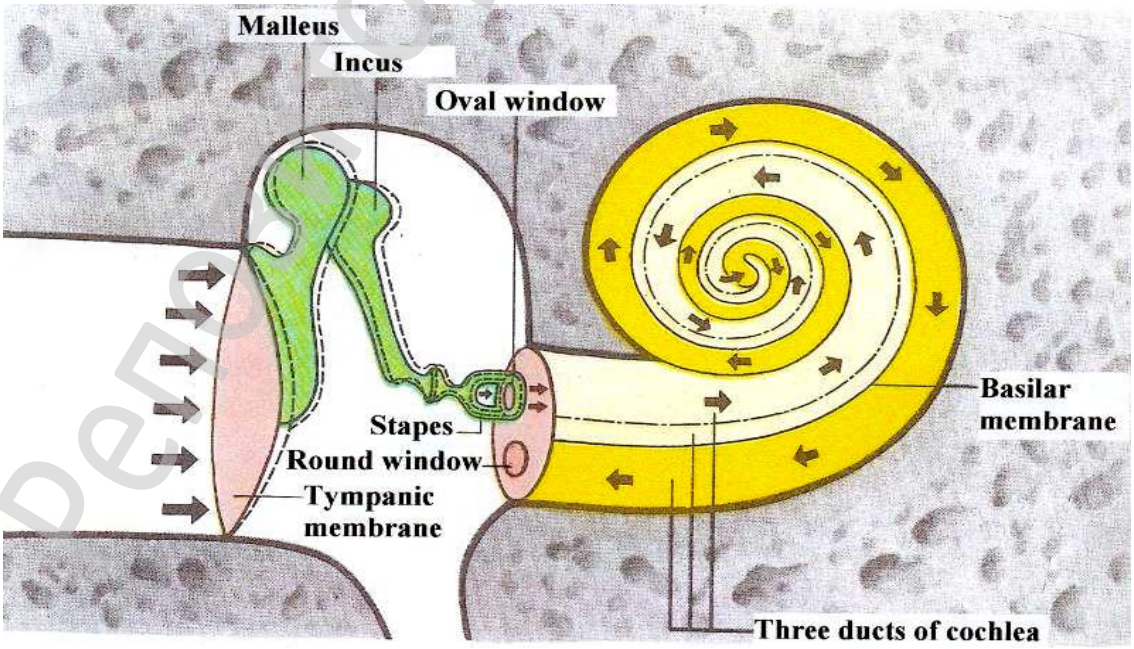


Figure 6.16 — Structure of the middle and internal ear (by Korobkov A. V., Chesnokova S. A., 1986)

The middle ear has two muscles: tensor tympani muscle and stapedius muscle. The contractions of the former intensifies the tension of the tympanic membrane and limits the amplitude of its vibrations in strong sounds; the latter fixes the stapes and limits its movements. The reflex contractions of these muscles occur within 40–80 ms after the beginning of a strong sound and depends on its amplitude. This automatically protects the internal ear from overloads.

Structure and functions of the internal ear

Structure of the cochlea. The internal ear contains the cochlea, which has auditory receptors. The cochlea represents an osteal spiral duct forming 2.5 coils. Along the whole length of the cochlea the osteal duct is divided into two membranes: the thin vestibular membrane (Reissner's membrane) and the denser and more elastic basilar membrane. At the apex of the cochlea both the membranes join. The width of the basilar membrane at the base of the cochlea is 0.04 mm, and at the apex — 0.5 mm. The vestibular and basilar membrane divide the osteal duct of the cochlea into three ducts: superior, middle and inferior (Figure 6.17).

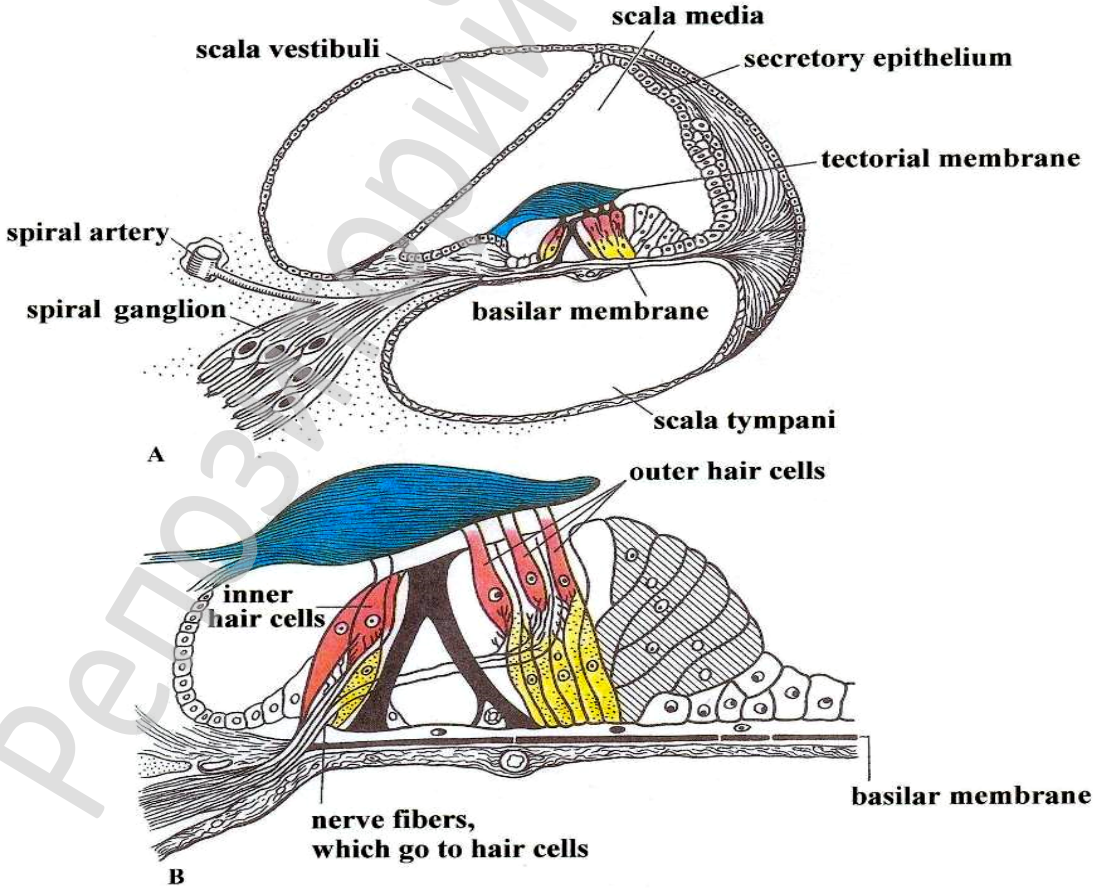


Figure 6.17 — Cross-section of the cochlea (A) and the structure of the spiral (Corti's) organ (B) (by Pokrovskiy V. M., Korotko G. F., 2000)

The superior duct of the cochlea, or vestibular duct (scalavestibuli) communicates with the inferior duct of the cochlea (scala tympani) through the opening at the apex of the cochlea (helicotrema). Both the superior and inferior ducts of the cochlea are filled with perilymph, which is similar to the cerebrospinal fluid by its content.

Between the ducts there is a medium duct — scala media. The cavity of this duct does not communicate with those of the other ducts and is filled with endolymph.

Inside the middle duct of the cochlea on the basilar membrane a sound-receiving apparatus is located — the organ of Corti, a spiral organ which has receptor hair cells. These cells transform mechanical vibrations into electrical potentials.

Conduction of sound vibrations along the cochlear ducts. The vibrations of the membrane of the oval window of the vestibule invoke the vibrations of the perilymph in the superior and inferior ducts of the cochlea which come up to the round window of the cochlea. The vestibular membrane is very thin, therefore the fluid in the superior and middle ducts vibrates as if both the ducts were uniform. The sound vibrations extending along the perilymph and endolymph of the superior and middle ducts as the traveling wave set in motion the basilar membrane and are transferred to the perilymph of the inferior duct (Figure 6.18).

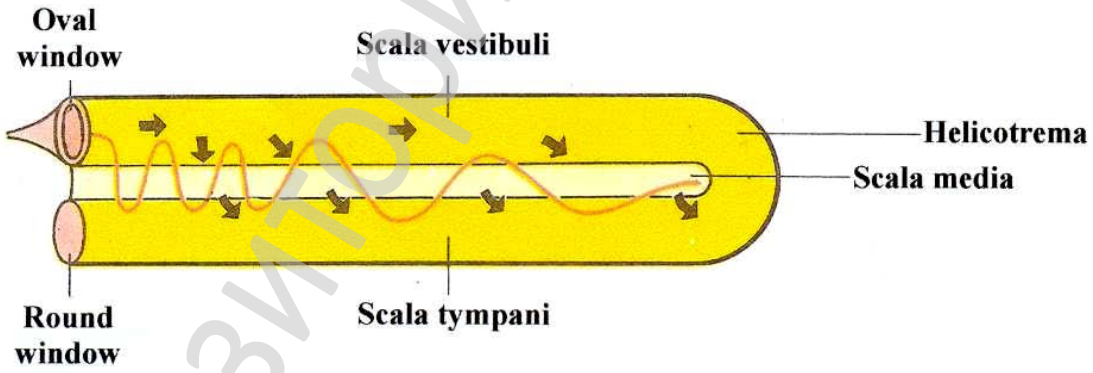


Figure 6.18 — Sound vibrations in the cochlea (by Korobkov A. V., Chesnokova S. A., 1986)

Location and structure of the receptor cells of the spiral organ. The basilar membrane has two kinds of receptor hair cells: inner and outer separated by the Corti's arches. The inner hair cells organize one row; their total number is 320. The outer hair cells are organized in 3–4 rows; their total number is 12,000–20,000. Each hair cell has the prolate form, one of its poles is fixed on the basilar membrane, the other is located in the scala media of the cochlea. At the end of this pole there is hair, or stereocilia. The hair of the receptor cells is washed by endolymph and contacts with the tectorial membrane, which is located above the hair cells. The bases of the hair cells form synapses with nerve endings.

Mechanisms of auditory reception. Under the action of a sound the basilar membrane starts to vibrate, the steriocilia touch the tectorial membrane and deflect a little. The hair deflection to some extent induces the stretching of the thinnest vertical filaments (microfilaments). This strain opens from 1 to 5 ion channels in the membrane. Through the opened channels *potassium ions* come into the hair.

The depolarization of the presynaptic end of the hair cells results in the exit of the neuromediator (*glutamate or aspartate*) into the synaptic gap. Influencing the synaptic membrane of afferent fiber, the mediator generates an excitant postsynaptic potential.

Theories of sound perception

In 1863 H. Helmholtz formulated the *resonance theory* of hearing. According to this theory, the membrane can act as a set of cross-stretched elastic resonant filaments, similar to piano strings which are not connected among themselves, i. e. the vibration of one part of the membrane is not conducted to the next fields. The shortest filaments in the narrow part at the base of the cochlea resonate in response to high frequency. Other filaments located closer to the apex of the cochlea resonate at a low frequency.

In 1950-1960s G.Bekeshi disproved this theory. He demonstrated that the basilar membrane is not stretched in the cross direction and has a mechanical connection along the whole length. He thus proposed *the theory of a traveling wave* (Figure 6.19). According to the theory, the basilar membrane is mostly rigid at the base of the cochlea, i.e. at its narrowest point. Its rigidity decreases towards the apex. During the vibration of the membrane the wave «runs» from its base to the apex. High-frequency vibrations pass along the basilar membrane at a short distance, and long low-frequency waves pass more distantly.

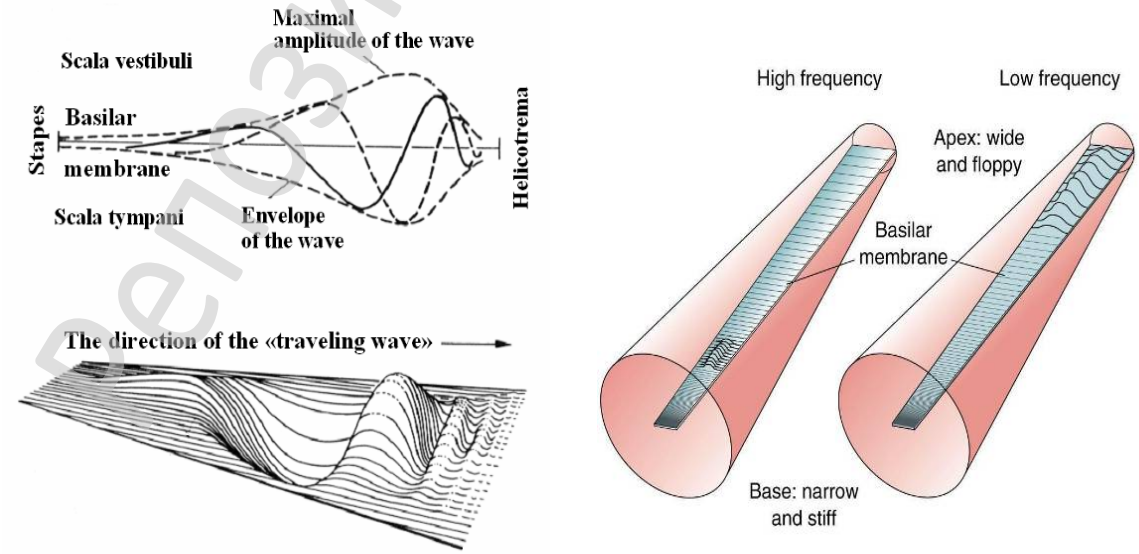


Figure 6.19 — Theory of a traveling wave (from studylib.net)

Electrical phenomena in the cochlea

The registration of electrical potentials from different parts of the cochlea detects five various phenomena: two of them — the membrane potential of the auditory receptor cell and endolymph potential — are not induced by the action of a sound; three electrical phenomena — the microphone potential of the cochlea, summation potential and potentials of the auditory nerve — arise under the influence of sound stimulations. If to place electrodes into the cochlea, connect them with a speaker through an amplifier, and expose the ear to a sound, the speaker will reproduce this sound. Such a phenomenon is called the *microphone effect of the cochlea,* and the registered electrical potential is called *the cochlear microphone potential.* It is proved to be generated on the membrane hair cells as a result of the deflection of the stereocilia.

In response to high-frequency sounds (high tones) there appears a steady shift of the initial potential difference. This phenomenon is called the *summation potential.* There are positive and negative summation potentials. Their sizes are proportional to the intensity of the sound pressure and force of the hair receptor cells pressing to the tectorial membrane.

The negative summation potential is generated by the inner hair cells, and the microphone and positive summation potentials — by the outer hair cells.

As a result of the receptor excitation there occurs generation of a signal in the fibers of the auditory nerve.

Conducting pathways of the auditory analyzer (Figure 6.20).

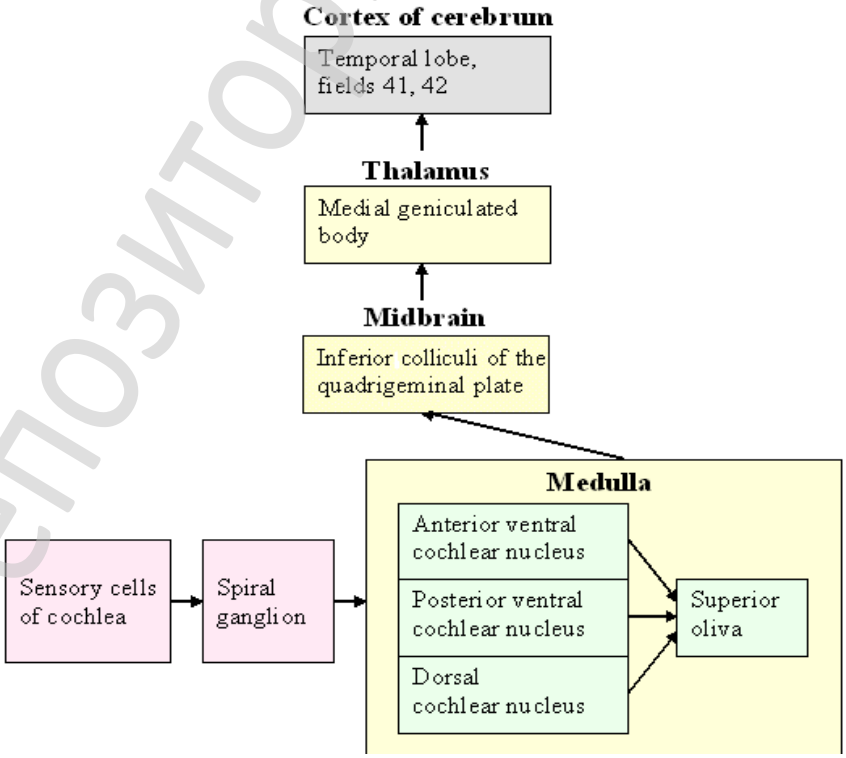


Figure6.20 — Scheme of the conduction pathways of the auditory analyzer (by Vlasova A., 1980)

Signals from the hair cells come to the spiral ganglion, where the bodies of the first neurons are located from which information goes further to the cochlear nuclei of the medulla. From the medulla the signals go to the inferior colliculi of the quadrigeminal plate of the midbrain and to the medial geniculate body. These structures contain the third neurons from which information goes to the superior temporal gyrus, where the highest analysis of auditory information is performed.

Auditory functions

Analysis of sound frequency. Sound vibrations of different frequency involve unequally the basilar membrane into the vibrational process along the whole length. Thus, the action of sounds of different frequency induces the excitation process which involves different receptor cells of the spiral organ. Each neuron responds only to a very narrow field of the frequency diapason.

Auditory sensations. *Sound tonality.* Humans perceive sound vibrations with the frequency of 16–20,000 Hz. At low and average sound frequencies a human can distinguish the differences of 1–2 Hz. There are people with absolute hearing who can recognize and reproduce any sound even in the absence of a comparison sound. The upper limit of the perceived frequency depends on the person`s age: the older the person is, the lower the upper limit is; that is why elderly people often cannot hear high tones.

Auditory sensitivity. The hearing thresholds depend on the frequency of sounds. Within 1,000–4,000 Hz the human hearing is maximally sensitive. The sensitivity sharply decreases for sounds lower than 1,000 and higher than 4,000 Hz: for example, at 20 and 20,000 Hz the threshold energy of a sound is million times higher.

Intense sounds may produce unpleasant sensation of pressure and even pain in the ear. Sounds of such a force characterize the upper limit of auditory perception. Inside this region there are so called speech fields in which speech sounds are distributed.

Sound loudness. It is necessary to distinguish the subjective sound loudness from its physical force. The sensation of a loud sound is not necessarily related to the increased intensity of the sound. The unit of sound loudness is «bel». In practice as a unit of sound measurement the decibel is used. Depending on the frequency of a sound the increased sensation of loudness in its strengthening is not identical. Within the average range of audibility frequencies (1,000 Hz) the person notices changes of intensity within 0.59 decibel (dB), and the differential loudness threshold of the range reaches up to 3 dB. The maximum level of sound loudness, when the sound causes painful sensations, is equal to 130–140 dB above the threshold of human audibility. Thus, sound loudness depends on the interaction of these parameters as intensity (force) and height of tone (frequency).

Binaural hearing. Humans and animals possess the ability of space hearing, i.e. they can identify location of a sound source in space. This property is ensured by binaural hearing, or hearing with two ears. The acuity of binaural hearing is very high: the accuracy angle of the sound source detection is up to 1°. If the sound source is shifted from the middle line of the body, the sound wave comes to one ear earlier and has a bigger force than in the other ear.

6.2.3. Vestibular system

The vestibular system plays the leading role in spatial orientation of humans along with the visual and somatosensory systems. It receives, transfers and analyzes information about accelerations or decelerations which arise in the process of linear or rotary motion, and also if the spatial position of the head is changed. During uniform motions or at rest the receptors of the vestibular sensory system are not excited. Signals from the vestibular receptors produce redistribution of the tone of skeletal muscles that provides the maintenance of equilibrium.

Structure and functions of the receptors of the vestibular system

The peripheral part of the vestibular system is the vestibular apparatus located in the labyrinth of the pyramid of the temporal bone. The vestibular apparatus consists of *vestibule (vestibulum)* and *three semicircular ducts*. Apart from the vestibular apparatus, the labyrinth has the cochlea having auditory receptors. The semicircular ducts are located in three inter-perpendicular planes: superior — in the frontal, posterior — in the sagittal, and lateral — in the horizontal. One end of each duct is dilated (ampula) (Figure 6.21).

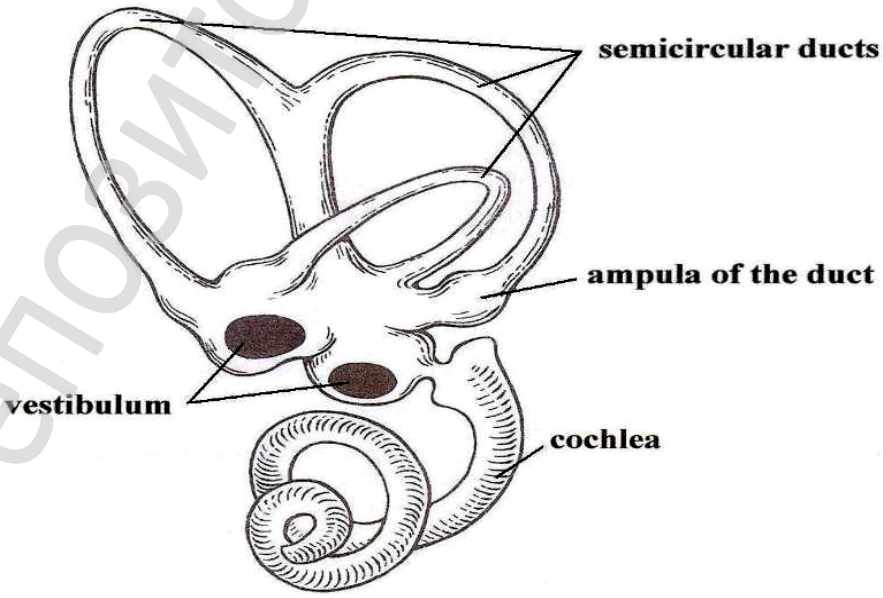


Figure 6.21 — Structure of the labyrinth of the temporal bone (by Pokrovskiy V. M., Korotko G. F., 2000)

The vestibular apparatus also includes two sacculi: orbicular (sacculus) and elliptic, or utricle (utriculus). The first one is located closer to the cochlea, the second one — to the semicircular ducts. The sacculi of the vestibule have *the otolithic apparatus:* accumulation of receptor cells in eminences (macula sacculi, macula utriculi). The part of receptor cell located in the lumen of the saccule have one longer mobile hair (kinocilium) and 60–80 immobile hairs (strereocilia) agglutinated together. The thinnest filamentous attachments connect the tip of each stereocilium to the next stereocilium and, finally, to the kinocilium.

The hairs of the receptors cells penetrate the jelly-like membrane which contains the crystals of calcium carbonate —otoliths. The excitation of the hair cells of the vestibule arises due to the sliding of the otolithic membranes on the hair, i. e. their flexions (Figure 6.22). The bases of the hair cells form synapses with the sensory endings of the vestibular nerve.

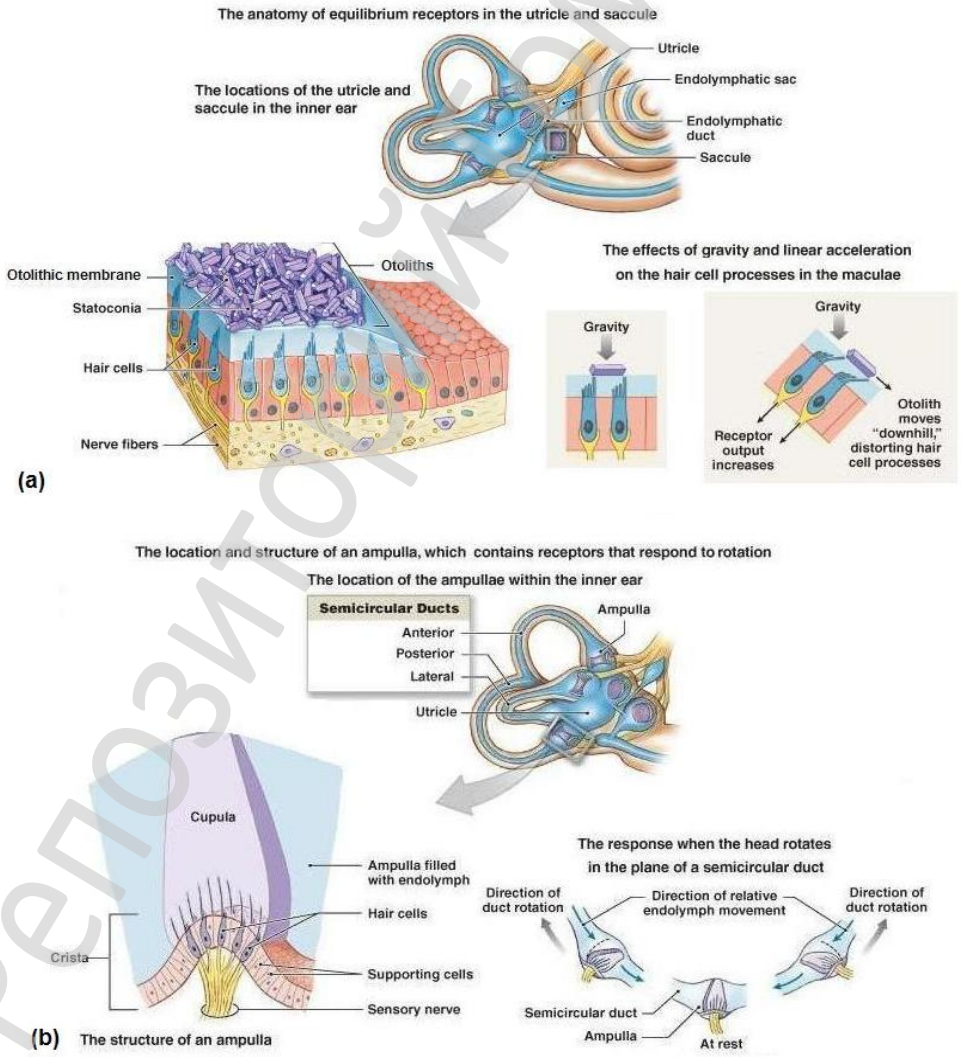


Figure 6.22 — Structure of the vestibular apparatus (from bianoti.com)

Notes: (a) —otolithic apparatus (in the vestibulum); (b) —-receptors in the semicircular ducts (cristae ampularis).

In the semicircular ducts filled with endolymph (its viscosity is 2–3 times as high as that of water) the receptor hair cells are concentrated only in the ampulas at the crista (cristae ampularis). They also have hairs. During motions of the endolymph (during angle accelerations) when the hairs bend to one side, the hair cells become excited, during their inverse movement they become inhibited.

When the receptor potential is generated in the hairs, the flexion in the hair cells of the vestibule and ampula, this intensifies the secretion of acetylcholine in synapses and activates the terminals of the fibers of the vestibular nerve (Figure 6.23).

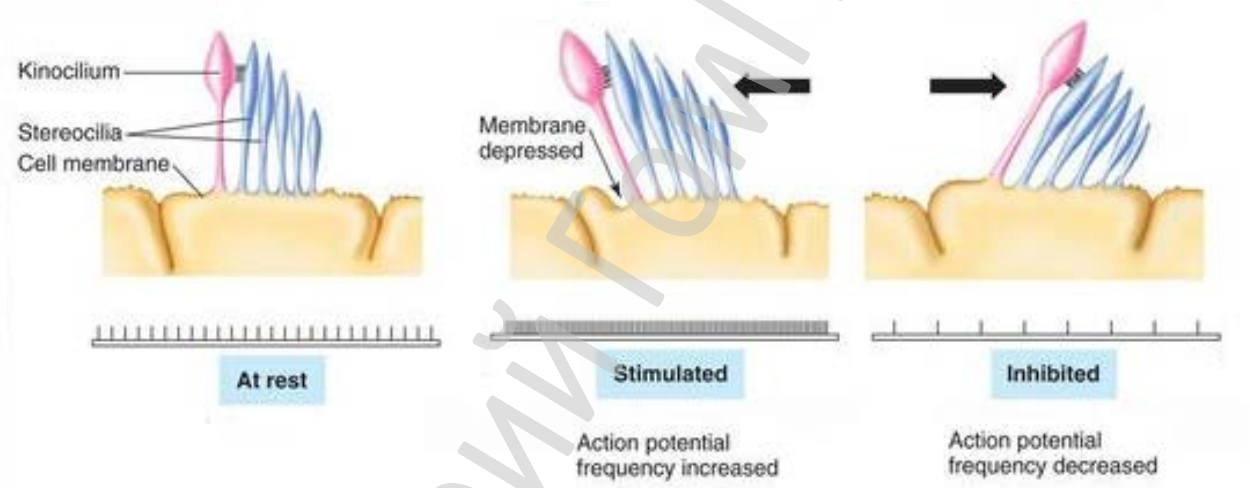


Figure 6.23 — Sensory hair cells in the vestibular apparatus (from bianoti.com)

The fibers of the vestibular nerve (processes of bipolar neurons) go to the medulla. The signals which come along these fibers activate the neurons of the bulbar vestibular complex. From here the signals go to many regions of the CNS: the spinal cord, cerebellum, oculomotor nuclei, cortex of cerebrum, reticular formation and ganglia of the vegetative nervous system.

Complex reflexes connected with vestibular stimulation

The neurons of the vestibular nuclei regulate various motor reactions. The main reactions are as follows: vestibulospinal, vestibulovegetative and vestibulo-oculomotor. The v*estibulospinal influences* through the vestibulo-, reticulo- and rubrospinal tracts change the impulses of the neurons of the spinal cord. This is the way how dynamic redistribution of the tone of skeletal musculation is performed and reflex reactions necessary for the maintenance of equilibrium are switched on.

The vestibulovegetative reactions involve the cardiovascular system, digestive system and other internal organs. Strong and long-term loads on the

vestibular apparatus cause a set of pathological symptoms called naupathia, for example sea-sickness. It is revealed in the change of cardiac rhythm (acceleration and then retardation), vasoconstriction and then vasodilatation, intensified contractions of the stomach, giddiness, nausea and vomiting. Increased predisposition to naupathia can be decreased by special training (rotation, swing) and some medicaments.

The vestibulo-oculomotor reflexes (ocular nystagmus) are slow movements of the eye in the direction opposite to their rotation, and then jumping motions of the eye back to the previous position. The appearance and characteristics of rotary ocular nystagmus are the important parameters of the state of the vestibular system widely used in naval, air and space medicine, and also in experiments and clinical practice.

Conduction and the cortical region of the vestibular analyzer (Figure 6.24).

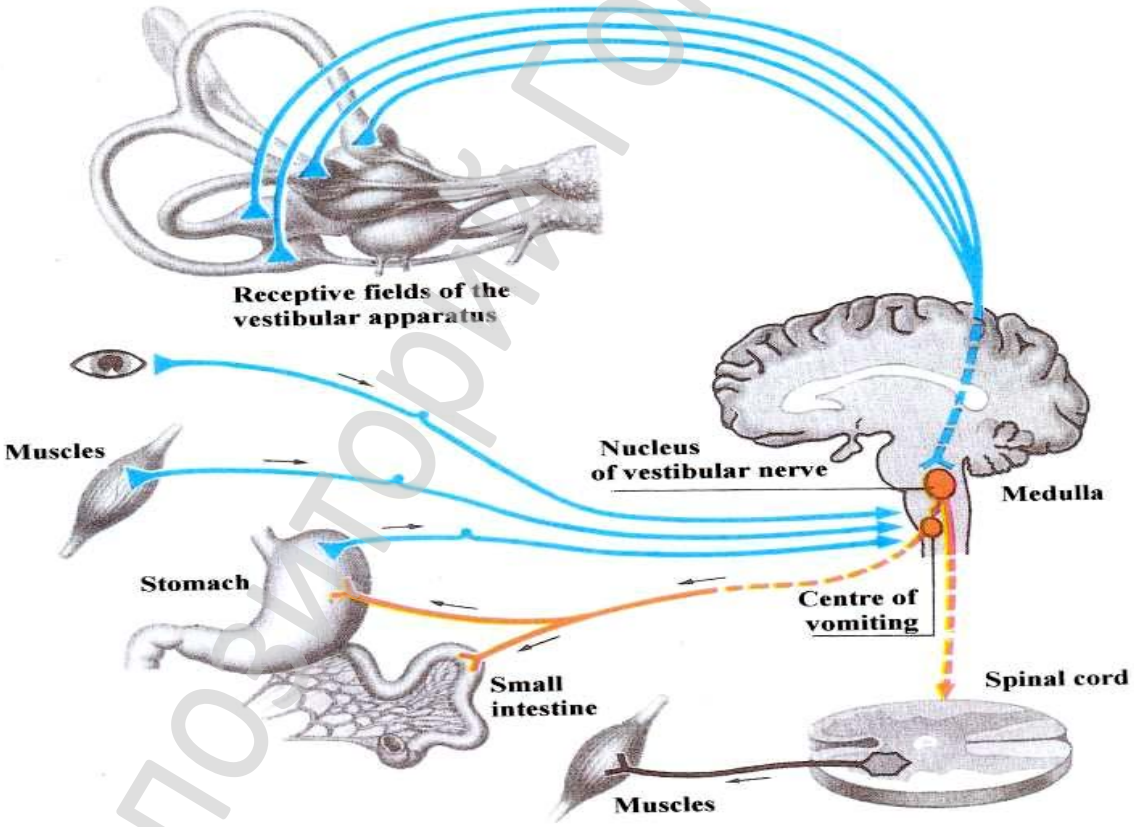


Figure 6.24 — Afferent and efferent connections of the vestibular apparatus (by Korobkov A. V., Chesnokova S. A., 1986)

From the vestibular ganglion (first neurons) signals pass to the medulla, then to the thalamus where the bodies of the third neurons which transfer information are located. The basic afferent projections of the vestibular apparatus are localized in posterior part of the postcentral gyrus of the cortex of the cerebrum.

Review questions

1. What are the structure and functions of the external ear? What are the structure and functions of the middle ear?

2. What are the structure and functions of the internal ear? What is the structure of the receptor cells of internal rear? Where are they located in the spiral organ? What is the mechanism of sound reception?

3. What are the theories of sound perception? Explain them.

4. What are the potentials in the cochlea? Describe them.

5. Name the conductive and central parts of the auditory analyzer.

6. What are the auditory functions? Describe them. What is binaural hearing? What is the role of binaural hearing in the perception of sound signals?

7. What are the structure and functions of the vestibular receptors?

8. What complex reflexes are associated with the stimulation of the vestibular system?

9. Name the conductive and central parts of the vestibular system.

6.2.4. Somatosensory system

The somatosensory system includes dermal sensitivity and sensitivity of the musculoskeletal apparatus; its leading role belongs to the proprioceptive system.

6.2.4.1. Dermal reception

The receptor surface of the skin is great (1.4–2.1 m^2). It contains many receptors sensitive to touch, pressure, vibration, heat and cold, and also to pain stimulations (Figure 6.25). Their structure is very different. They are localized at different depth of the skin and irregularly distributed on its surface. The majority of these receptors are in the skin of the fingers, palms, soles, lips and genitals. The basic type of receptors of the human skin is free terminals of nerves going along the small vessels, and also deeper localized *branchings of thin nerves braiding the hair bulb.* These terminals provide high sensitivity of hair to touch.

Touch receptors are also *tactile disks* (Merkel's discs) formed in the inferior part of the epidermis by a contact of free nerve terminations with epidermal structures. They are especially numerous in the skin of the fingers.

In bare skin (i. e. hairless) there are many *touch corpuscles* (Meissner's corpuscles). They are located in the papillary layer of the derma of the fingers and toes, palms, soles, lips, tongue, genitals and nipples. These corpuscles are

cone-shaped, have the complex internal structure and are coated with a capsule. Other encapsulated nerve terminations are *laminar corpuscles,* or Vater-Pacini corpuscles (receptors of pressure and vibration) located more deeply. They also present in the tendons, ligaments, mesentery. In the connective tissue of the mucous membranes, under the epidermis and among the muscular fibers of the tongue there are encapsulated nervous corpuscles (Krause's end-bulb).

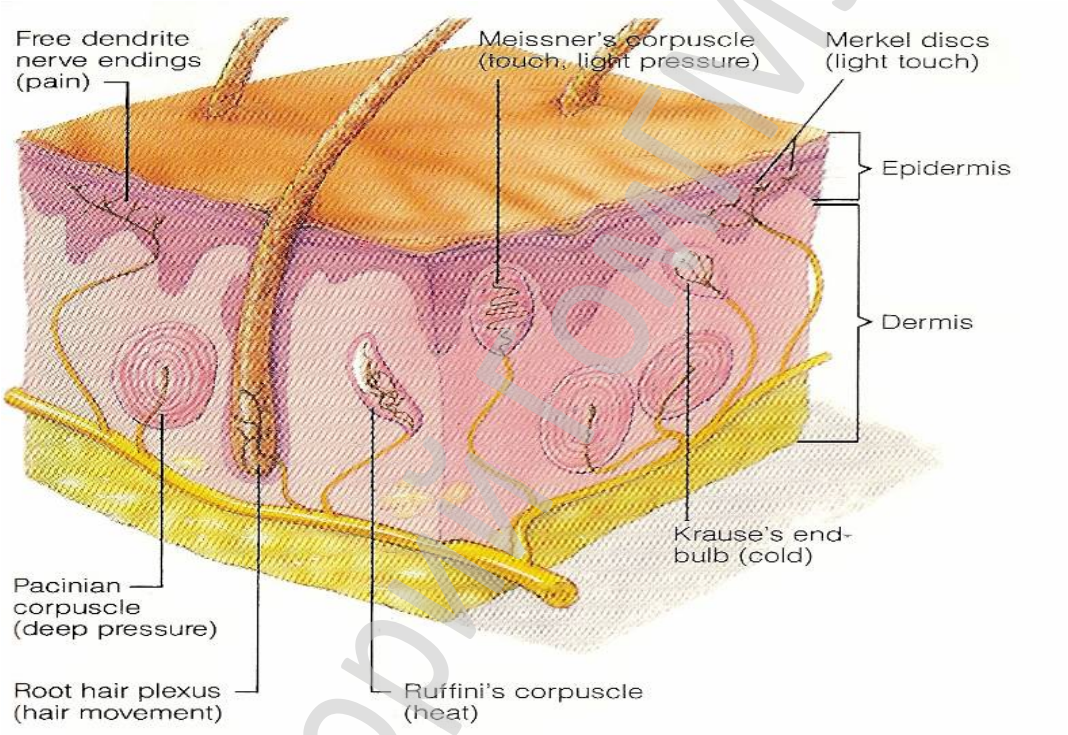


Figure 6.25 — Skin receptors (by Elaine N. Marieb, 1989)

Theories of dermal sensitivity. One of the most common theories is the one about the presence of specific receptors for 4 basic kinds of dermal sensitivity: tactile, thermal, cold and pain. According to this theory, the different character of dermal sensations is based on the differences in spatial and temporal distribution of signals in afferent fibers induced by different kinds of dermal stimulations.

Mechanisms of the excitation of dermal receptors. A mechanical stimulus results in the deformation of the membrane of a receptor. As a result of this, the electric resistance of the membrane decreases, its permeability to Na+ increases. Through the receptor membrane the ions enter inside the cell, which generates a receptor potential. As the receptor potential rises up to the critical level of depolarization, signals are generated in the receptor and come into the CNS.

Adaptation of dermal receptors. By the speed of their adaptation the majority of dermal receptors are divided into rapidly- and slowly-adapted. The

tactile receptors are most quickly adapted. They are located in the hair follicles. As a result of the adaptation of the dermal mechanoreceptors we do not feel constant pressure of clothes on our body or watches on our hands.

Properties of tactile perception. The sensation of touch and pressure upon the skin is localized rather precisely. This localization is developed and fixed in ontogenesis with the participation of vision and the proprioceptive system. The absolute tactile sensitivity essentially differs in different areas of the skin: from 2 mg to 10 g. The ability of a person to separately percept touch to two adjacent points of the skin also strongly differs in its different regions. In the mucous membrane of the tongue the threshold of space difference is 0.5 mm, and that of the skin of the spine — more than 60 mm. These differences are caused mainly by various dimensions of dermal receptive fields (from 0.5 mm^2 up to 3 cm^2) and the degree of their overlap.

Temperature reception. The human body temperature varies within rather narrow limits, therefore the information about the environmental temperature necessary for the activity of thermoregulation mechanisms has an important value. Thermoreceptors are located in the skin, cornea of the eye, in the mucous membranes, and also in the CNS (in the hypothalamus). They are divided into two kinds: cold and warm receptors (the latter are much fewer and in the skin they are located more deeply than the cold receptors). Most of the thermoreceptors are in the skin of the face and neck.

The thermoreceptors react to temperature changes by rising the frequency of generated signals. Increased frequency of the signals is proportional to temperature changes, and constant pulses in the warm receptors are observed within the temperature ranges of 20 to 2 °C, and in the cold receptors — from 10 to 41 °C.

Under certain conditions the cold receptors can be excited by heat (more than 4 °C). Therefore, the sensation of cold appears in a person rapidly immersing into a hot bath. The initial intensity of temperature sensations depends on the difference of the temperature of the skin and the temperature of an acting stimulus. For example, if we place a hand which has been in 27 °C water into 25 °C water, at first the temperature of the water seems to be cold but in some seconds the true sensation of actual temperature of the water is possible.

The conductive tracts of tactile, temperature and pain sensitivity are shown in the figures 6.26, 6.27.

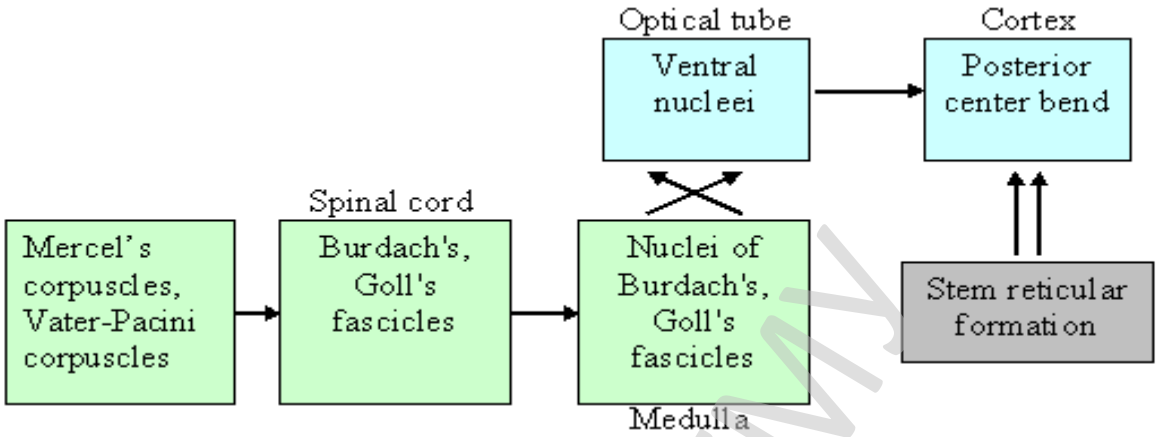


Figure6.26 — Conductive tracts of tactile sensitivity (by Vlasova A., 1980)

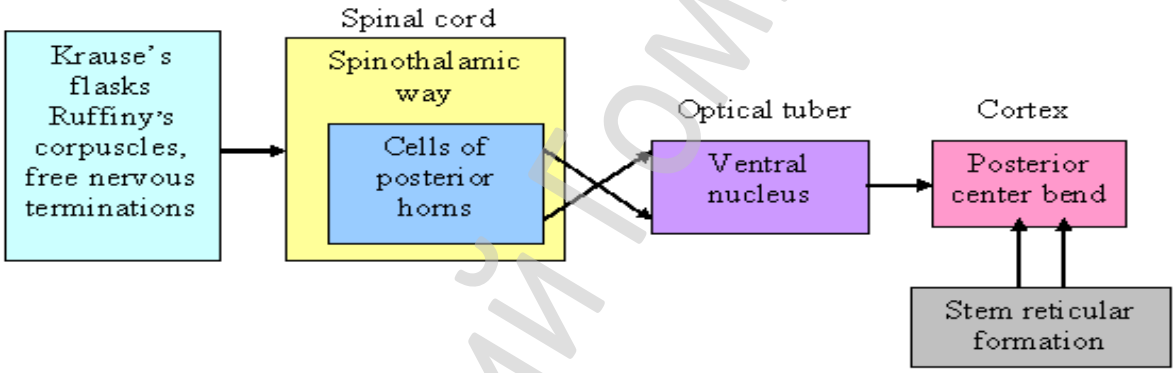


Figure 6.27 — Conductive tracts of temperature and pain sensitivity (by Vlasova A., 1980)

6.2.4.2. Muscular and articular reception (proprioception)

The muscles of mammals and humans have three types of specialized receptors: primary endings of muscle spindles, secondary endings of muscle spindles and Golgi tendon receptors. These receptors react to mechanical stimulations and participate in movement coordination. They are a source of information about the state of the motor apparatus of the organism.

Muscle spindles (Figure 6.28). The muscle spindle represents a small oblong formation some millimeters long and tenth portions of the millimeter wide and is found in skeletal muscles. In different skeletal muscles the number of spindles per 1 g of tissue varies from several units to hundreds.

Each spindle is coated with a capsule. Inside the capsule there is a bundle of striated muscle fibers called ***intrafusal muscle fibers***. All the other muscle fibers are called extrafusal muscle fibers. The spindles are located in parallel to extrafusal fibers, therefore, if the muscle extends, the load on the spindles increases and if contracts — it decreases.

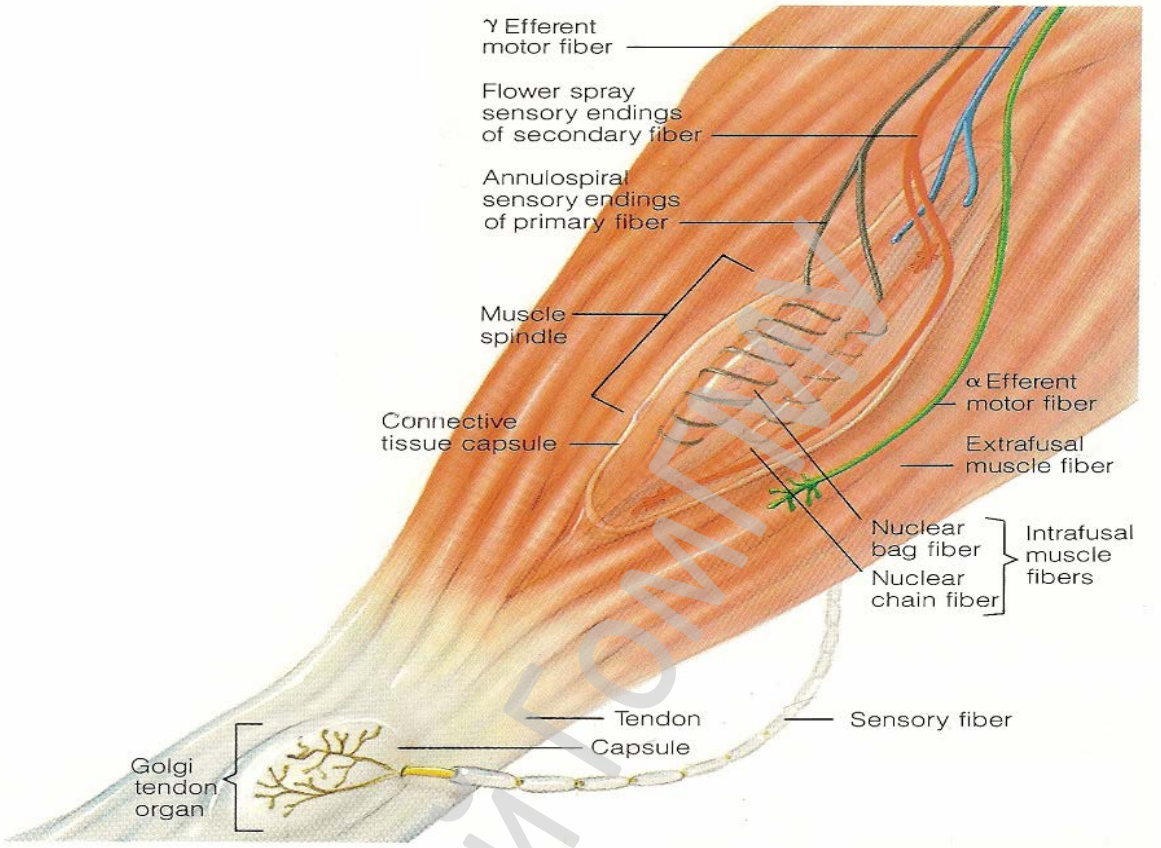


Figure 6.28 — Muscle spindle and Golgi tendon receptor (by Elaine N. Marieb, 1989)

There are two types of intrafusal fibers: 1) thick and long fibers with the nuclei concentrated in medium thickened part of the fiber and 2) short and thin fibers with the nucleus located in chain. The intrafusal fibers have spirally located sensory terminals of afferent fibers of group 1a — so-called ***primary endings***, and sensory terminals of afferent fibers of group II — so-called ***secondary endings***. Signals coming from the spindles along the afferent fibers of group 1a, excite the motoneurons of their own muscle in the spinal cord and through the inhibiting interneuron inhibit the motoneurons of the muscle-antagonist (reciprocal inhibition). The afferent fibers of group II excite the motoneurons of muscles-flexors and inhibit the motoneurons of muscles-extensors.

The spindles have efferent innervation: intrafusal muscle fibers are innervated by the axons coming to them from gamma motoneurons. This is the so-called ***gamma-efferent fiber***. In relaxed muscle impulses which go from the spindles are insignificant. The spindles react with impulses to elongation (extension) of the muscle. The activation of the gamma efferents results in high sensitivity of spindles.

The excitation of α-motoneurons is accompanied with the excitation of gamma motoneurons (α–γ co-activation). The level of the excitation of the gamma system is higher with more intensive excitation of the α-motoneurons

of the given muscle, i.e. with the bigger force of its contraction. In active muscle contractions the decrease of the muscle length renders a deactivating action on the receptors of the spindle, and the excitation of the gamma motoneurons along with the excitation of the α-motoneurons, induces the activation of receptors. That is why impulses from the receptors of the spindles during movements depend on several factors: interrelations of the muscle length, rate and force of its contraction.

Thus, the spindles give information about the length of the muscle and its changes only if the muscle is not excited. In the active state of the muscle it is necessary to consider the influence of the gamma-system. During active movements the gamma motoneurons maintain impulses of the spindles of a contracted muscle, which gives the receptors the opportunity to respond to irregular movements both by increased and decreased frequency of impulses, thus participating in the correction of movements.

Golgi tendon receptors. They are located in the region of the connection of muscle fibers with tendons. The tendon receptors weakly react to the extension of muscles but excite in its contraction. The intensity of their impulses is approximately proportional to the force of muscle contractions, and therefore the tendon receptors are the source of information about the contractile force of muscles. The afferent fibers going from these receptors are related to group 1b. At the spinal level they through interneurons induce inhibition of motoneurons of the own muscle and excitation of motoneurons of the muscle-antagonist.

6.2.5. Pain reception

Pain, or nociceptive sensitivity has a special value for the survival of the organism as it signals about the danger under the action of any excessively powerful and harmful agents. Pain is one of the first symptoms of many diseases, and sometimes it is the only manifestation of a pathology and an important diagnostic indicator. However, the correlation between the degree of pain sensations and the severity of a pathological process is not always marked.

There are two hypotheses about the organization of pain perception: 1) there are specific pain receptors (free nerve terminals with a high threshold of reaction); 2) specific pain receptors do not exist and pain arises under superstrong stimulation of any receptors.

Electrophysiological experiments with the single nerve fibers of type *C* reveal that some of them respond mainly to excessive mechanical, and others — to excessive thermal influences. Under pain stimulations small-amplitude signals also arise in the nerve fibers of type *A.* According to the speed of the signal conduction in the nerve fibers of type C and A, the double sensation of pain is marked: first,

clear by localization and short, then — continuous, extended and strong (burning) sensation of pain.

The mechanism of the excitation of receptors under pain influences is not clear. It is assumed that pH changes in tissues in the region of nerve termination are particularly significant since this factor possesses the pain effect.

The reason for continuous burning pain may be the release of histamine and proteolytic enzymes due to the cell damage. These substances stimulate the formation of some polypeptides (e. g., bradykinin), which excite the terminals of the nerve fibers of type C.

The adaptation of pain receptors is possible: during injections the sensation of pain quickly disappears when a needle is already inside the skin. However, in numerous cases pain receptors do not adapt thus making a patient suffer from continuous and exhausting pain and demand anesthesia.

Pain stimulations cause a number of reflex somatic and vegetative reactions. These reactions have an adaptive value but can result in serious pathological effects, for example, shock. Among these reactions there are increased muscle tone, frequency of heart rate (HR) and respiratory rate (RR), increased blood pressure, dilatation of pupils, increased glucose level in the blood, and a number of other effects.

Nociceptive impacts on the human skin are localized rather precisely but in diseases of the internal organs the referred pain is projected into the certain parts of dermal surface (Zaharen-Gead's zones). Thus, in stenocardia, apart from heart pain, the pain in the left hand and scapula can also be felt (Figure 6.29).

Kinds of pain.There are several classifications of pain. Firstly, it is divided into two types: *primary (early, epicritic)* and secondary *(late, protopathic)*. Primary pain is sharply localized. The person can precisely specify the site of a painful sensation. The pain appears quickly, often has the pricking character, quickly disappears after the removal of the stimulus. Primary pain causes rapid protective reflexes — the motion reactions directed on the removal of the stimuli. Primary pain arises under the influence on mechanoreceptors and the pain impulses from them are conducted to the posterior horns of the spinal cord, from which the impulses go into the thalamus and then to the projective zone of the somatosensory cortex of the cerebrum where the precisely localized pain sensation is formed.

Secondary (late, protopathic) pain arises after 1 second after the primary pain, slowly increases and has no precise localization. It is dull and is accompanied by general indisposition and disappears gradually after the removal of the action of the damaging factor.

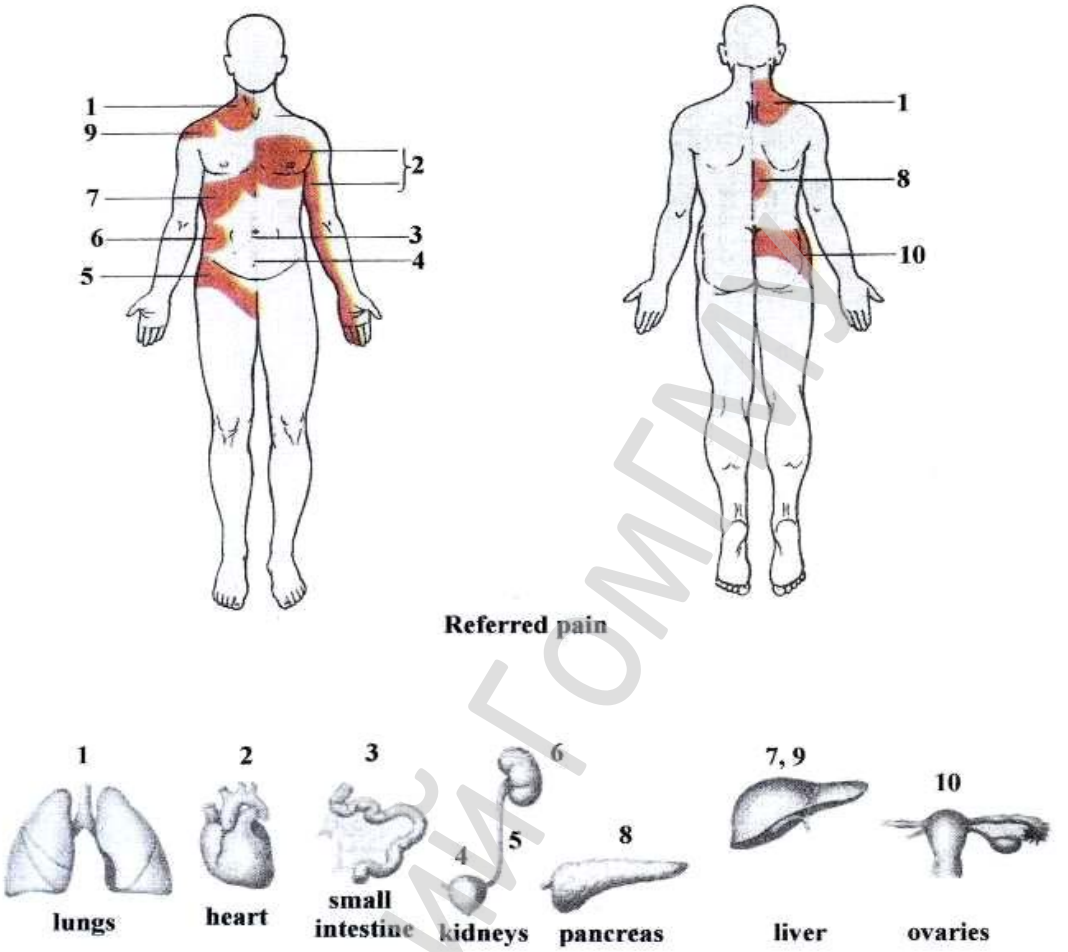


Figure 6.29 — Pain zones on the skin surface, which appear in injuries of the internal organs (by Korobkov A. V., Chesnokova S. A., 1986)

In medical practice the following kinds of pain can be distinguished: local, projective, referred, phantom, somatic, and visceral pain.

Local pain is perceived in the same site where the center of damage or nociceptive influences is localized.

Projective pain is perceived in the damage or direct stimulation of the nerve trunk along the course of a nerve in the site of the body innervated by this nerve. The place of the damage does not coincide with the place of the sensation of pain.

Referred pain is perceived not in the affected organ, but in other areas (Figure 6.30).

Phantom pain is perceived in a removed or denervated organ, for example in an amputated leg.

S*omatic* pain arises at the localization of a source of painful sensations in the skin, muscles or joints. It is divided into superficial and deep pain.

Visceral pain arises at localization of the source of pain in the internal organs.

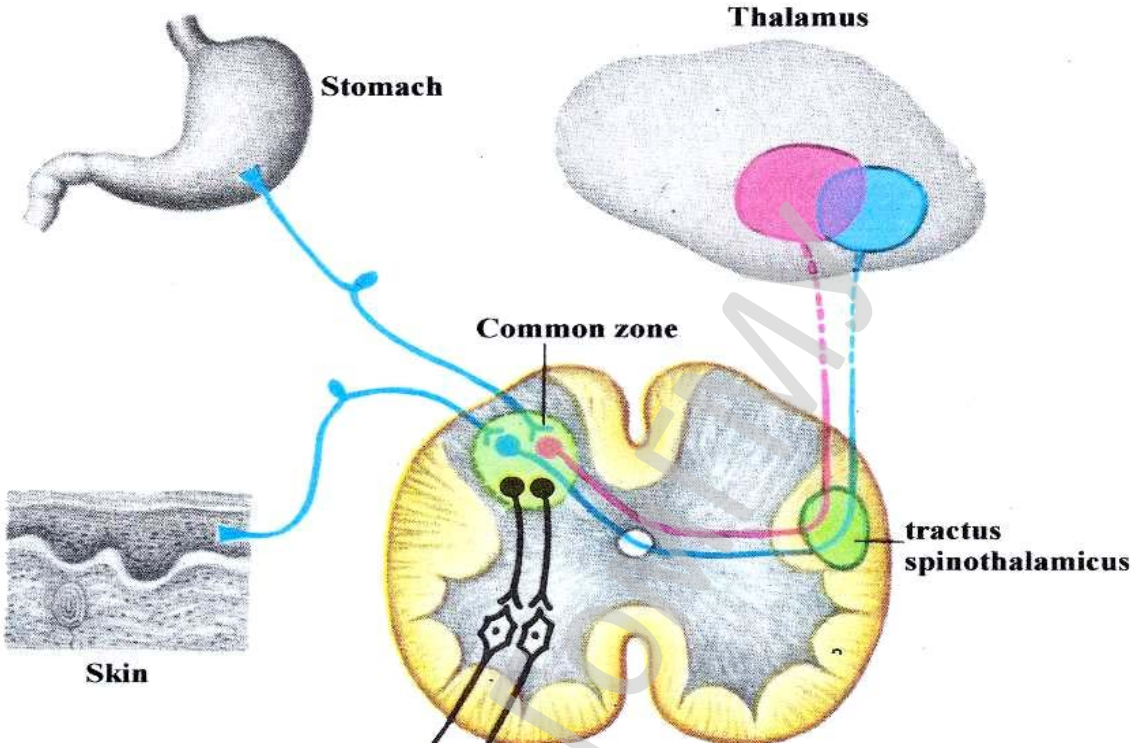


Figure 6.30 — Supposed mechanism of the origin of referred pain (by Korobkov A. V., Chesnokova S. A., 1986)

Antinociceptive system. A set of nervous structures and humoral factors counteracting the development of painful sensations is called the antinociceptive system. The antinociceptive nervous centers are located in the grey matter around the sylvian aqueduct, nuclei of the anterior hypothalamus, frontal and somatosensory zones of the cortex of the cerebrum, reticular formation. Any of these centers uses its own mediators: serotonin, noradrenaline, gamma aminobutyric acid. According to this principle there are serotonergic, adrenergic and other antinociceptive systems.

A medical procedure causing the absence of all sensation, especially sensitivity to pain, as induced by an anesthetic substance (analgetic and narcotic) is called *anesthesia*. Anesthesia induced for medical or surgical purposes may be topical, local, regional, or general *(narcosis)*.

By the localization of their action, anesthetics are divided into substances of local and general action. The anesthetic substances of local action (for example, novocain) block generation and conduction of pain signals from receptors to the spinal cord or parts of the brain stem. The anesthetic substances of general action (for example, ether) remove sensation of pain by blocking the conduction of signals between the neurons of the cortex of cerebrum and reticular formation of the brain (state of narcotic sleep).

6.2.6. Olfactory system

The receptors of the olfactory system are located in the region of the superior nasal ducts (Figure 6.31). The olfactory epithelium is located aside the main respiratory way, it has a depth of 100–150 micrometers and contains receptor cells having the diameter of 5–10 micrometers located between the sustentacular cells. The total number of the olfactory receptors in humans is about 10 million. On the surface of each olfactory cell there is a spherical thickening — the olfactory bulb from which 6–12 thinnest (0.3 micrometer) cilia overhang with a length up to 10 micrometers. The olfactory cilia are located in a fluid medium, excreted by the olfactory (Bowman's) glands. The presence of the cilia by ten times increases the area of the contact of the receptor with the molecules of odorants.

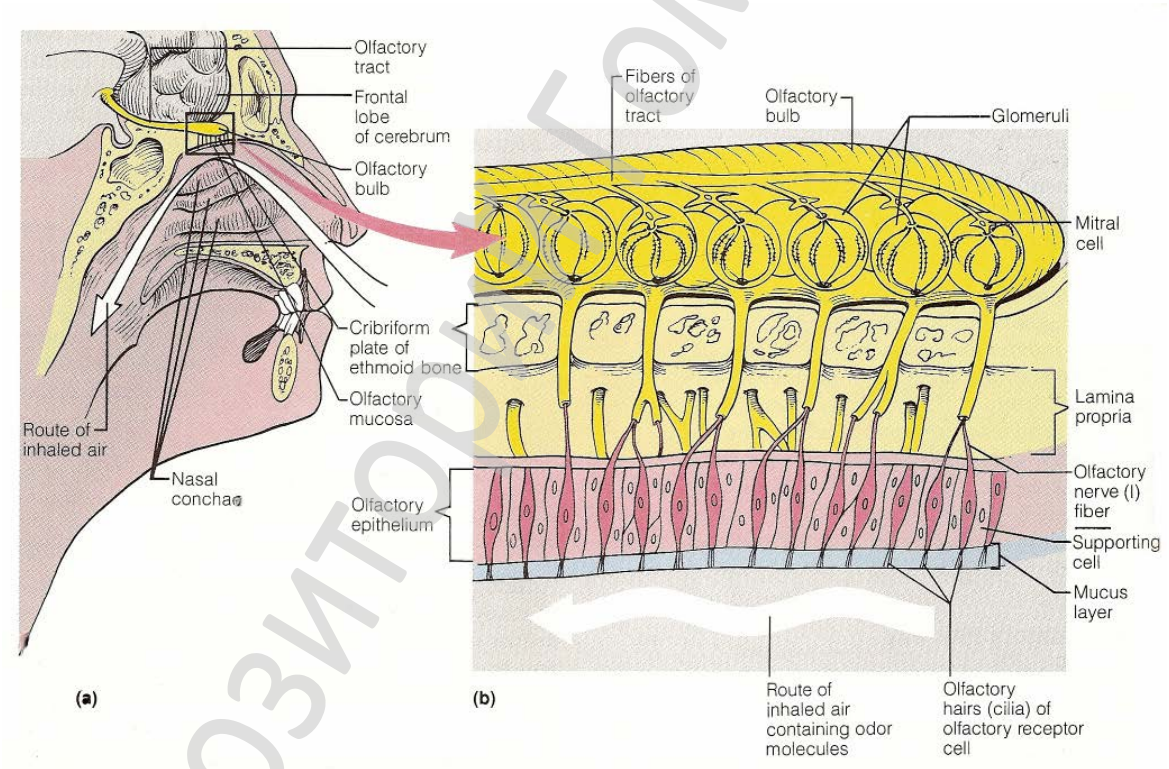


Figure 6.31 — Olfactory receptors (by Elaine N. Marieb, 1989)

Notes: (a) Site of the olfactory epithelium in the superior aspects of the nasal cavity; (b) Enlarged view illustrating the cellular composition of the olfactory epithelium and the course of the fibers of the olfactory nerve (I) through the ethmoid bone to the synapse in the overlying olfactory bulb. The glomeruli and mitral cells (output cells) within the olfactory bulb are also shown.

The olfactory receptor cell is a bipolar cell, on the apical pole of which there are the cilia, and from its basal part starts an unmyelinated axon. The

axons of the receptors form the olfactory nerve, which penetrates into the skull base and enters the olfactory bulb. The olfactory cells are constantly renewed. The lifetime of the olfactory cell is about 2 months.

Odorant molecules get into the mucus where they bind with the olfactory proteins, which activate G-protein, which, in its turn, activates enzyme adenylatecyclase, synthesizing cyclic adenosine monophosphate (CAMP). High CAMP concentration in the cytoplasma invokes opening of natrium channels in the plasma membrane of the receptor cell and generation of the receptor potential.

The olfactory cells are capable to react to millions of various spatial configurations of odorant molecules. However, each receptor cell is capable to respond to the physiological excitation to a spectrum of odorants typical for it. More than 2 % of odorants appear to be general for any two olfactory cells.

Central projections of the olfactory system. The olfactory path coming from the olfactory bulb consists of several fascicles which go to different parts of the forebrain: anterior olfactory nucleus, olfactory tubercle, prepyriform cortex, periamygdallary cortex and part of nuclei of amygdaloid complex. It is known that the presence of a significant number of the centers of rhinencephalons is not necessary for odour identification; therefore, the majority of the nerve centers into which the olfactory path is projected, are possible to regard as associative centers providing the connection of the olfactory sensory system with other sensory systems and the organization on this basis of some complex forms of behaviour— alimentary, defensive, sexual, etc.

The sensitivity of the human olfactory system is extremely great: one olfactory receptor can be excited by one odorant molecule, and the excitation of a small number of receptors results in originating of sensation. Changed intensity of the action of substances (differential threshold) is roughly estimated by people (the least percepted difference in the force of the odour is 30–60 % of its initial concentration). In dogs these parameters are as 3–6 times as high.

6.2.7. Gustatory system

In the process of evolution taste has been formed as the mechanism of selection or rejection of food. In natural conditions gustatory sensations are combined with olfactory, tactile, and thermal ones.

Taste is based on chemoreception. The gustatory receptors carry information about the character and concentration of substances coming in the mouth.

Taste receptors. The gustatory buds — taste receptors — are located in the tongue, back wall of the pharynx, soft palate, tonsils and epiglottis. Most of

them are on the tip of the human tongue, its edges and back part. Each of approximately 10,000 human gustatory buds consists of several (2–6) receptor cells and sustentacular cells. The gustatory bud has the cone-shaped form; its length and width are about 70 micrometers. The gustatory bud does not reach the mucous membrane of the tongue and is connected with the oral cavity through the gustatory pore.

The taste cells are the most short-living epithelial cells of an organism: on average, each 22 hours an old cell is renewed with a young one. Each of the receptor taste cells being 10–20 microns long and 3–4 microns wide has an ending with the lumen of the pore having 30–40 thinnest microvilli of 0.1–0.2 microns thick and 1–2 microns long (Figure 6.32). The miccrovilli play an important role in the excitation of receptor cells percepting these or those chemical substances adsorbed in the canal of the bud.

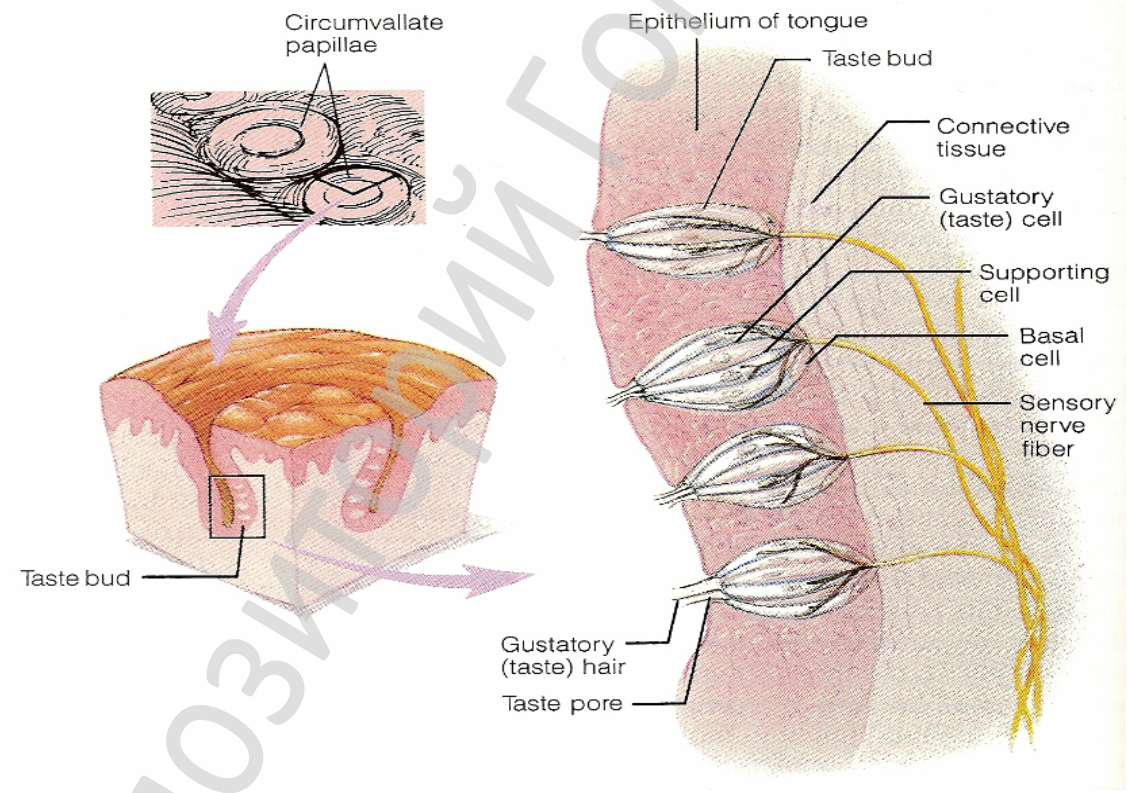


Figure 6.32 — Structure of the taste buds (by Elaine N. Marieb, 1989)

Conduction paths and taste centers. Conductors of all kinds of gustatory sensitivity are the tympanichord and glossopharyngeal nerves whose nuclei in the medulla contain the first neurons of the gustatory system. Many fibers differ in certain specificity as during the acceleration of signals they respond only to the action of salt, acids, and quinine. Other fibers react to sugar.

Gustatory afferent signals come into the nucleus of the tractus solitarius of the brainstem. From the nucleus of the single fascicle axons of the second

neurons within the structure of the medial loop reach the thalamus, where the third neurons are located whose axons are directed to the cortex of the cerebellum.

Gustatory sensations and perception

Humans distinguish four primary tastes (sweet, sour, bitter, and salty), as well as "umami" (from the Japanese "delicious", taste of sodium glutamate).

The sour taste is caused by acids, i.e., by the hydrogen ion concentration. *The salty taste* is elicited by ionized salts. The cations of salts, especially sodium cations, are mainly responsible for the salty taste, but anions also contribute to a lesser extent. *The sweet taste* is caused sugars, glycols, alcohols, aldehydes, ketones, amides, esters, some amino acids, some small proteins, sulfonic acids, halogenated acids, and others. Most of the substances that cause the sweet taste are organic chemicals.

The bitter taste is also caused mainly by organic substances, mainly by long-chain organic substances that contain nitrogen and alkaloids. The alkaloids include many of drugs used in medicines, such as quinine, caffeine, strychnine, and nicotine. The bitter taste, when it occurs in high intensity, usually causes humans or animals to reject the food. This is an important function of the bitter taste sensation because many deadly toxins found in poisonous plants are alkaloids.

In different people the absolute thresholds of gustatory sensitivity to different substances differ up to «gustatory blindness» for separate agents (for example, to creatine). The absolute thresholds of gustatory sensitivity to a great extent depend on the state of the organism (they change in starvation, pregnancy, etc.). The differential thresholds are minimal in the range of the average concentrations of substances but in high concentrations they sharply rise. Therefore, 20 % solution of sugar is accepted as maximum sweet, 10 % solution of sodium chloride — as maximum salty, 0.2 % solution of hydrochloric acid — as maximum sour, and 0.1% solution of quinine — as maximum bitter (Figure 6.33).

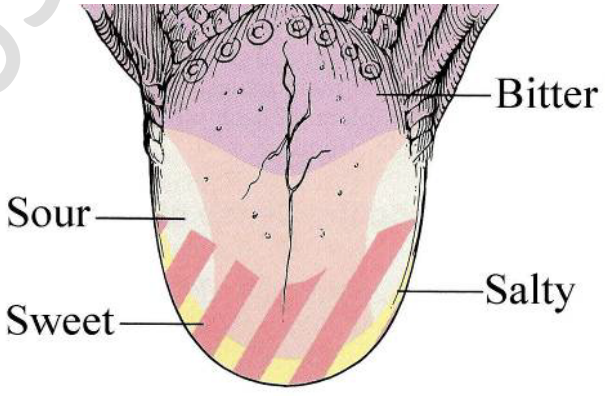


Figure 6.33 — Relative patterns of taste sensitivity on the tongue dorsum (by Elaine N. Marieb, 1989)

Gustatory adaptation. The long action of gustatory substances leads to the adaptation to them (the intensity of gustatory sensation is reduced). The duration of the adaptation is proportional to the concentration of solution. The adaptation to sweet and salty substances develops faster than to bitter and sour ones. The application of several gustatory stimuli simultaneously or at a time gives effects of a gustatory contrast or mixture of tastes. For example, the adaptation to bitter substances raises the sensitivity to sour and salty ones; the adaptation to sweet substances intensifies the perception of all other gustatory stimulants.

Review questions

1. What does the somatosensory system include? What are the structure and functions of the skin receptors?

2. What are the proprioceptors? How are they classified? Describe them.

3. What are the causes of pain? Name the theories of pain perception. What are the nociceptors? Name the conductive and central parts of the nociceptors. What are the classifications of pain?

4. What is the antinoceptive system? What levels does it have in the CNS? List the methods of anesthesia. Describe them.

5. What are the functions and structure of the olfactory system? Where are the olfactory receptors localized and what is their structure? What is the mechanism of the perception of odorous substances? Name the conductive and the central parts of the olfactory system. What factors influence the perception of olfactory signals?

6. What receptors are located in the oral cavity? What is the mechanism of taste perception? What are the main taste sensations in humans? What factors influence the perception of taste? How does the taste adaptation occur? Name the conductive and central parts of the taste analyzer.

Multiple Choice Questions
PHYSIOLOGY OF SENSORY SYSTEMS

1. The physiological sense of the «narrowing funnel» consists …

Variants of answer:

a) in increased divergence of signals at the subcortical level;

b) in increased speed of the conduction of afferent signals;

c) in decreased redundancy of information and increased sensitivity of the sensory channel;

d) it gives an opportunity to differentiate the neuron layers during the processing of different kinds of sensory information;

e) all the answers are correct.

2. The physiological sense of the «extending funnel» consists …

Variants of answer:

a) in the limited amount of incoming information;

b) in fractional and complex analysis of different signal indicators;

c) in the detachment of the most important signal indicators;

d) it gives an opportunity to differentiate the neuron layers during the processing of different kinds of sensory information;

e) all the answers are correct.

3. What does lateral inhibition provide in the sensory systems?

Variants of answer:

a) it provides decreased redundancy of information and chooses the most significant data about signals;

b) it provides increased redundancy of information and gives detailed description of signal properties;

c) it provides increased speed of the conduction of afferent signals;

d) it gives an opportunity of the processing of different kinds of sensory information;

e) it provides increased divergence of signals at the subcortical level.

4. The receptor field of neurons is…

Variants of answer:

a) the sum of receptors, signals from which come to a single neuron;

b) the sum of brain neurons, signals from which converge on given neuron;

c) the sum of receptors which receive information from a distant source of stimulation;

d) the sum of receptors which are excited during direct contact with a stimulus;

e) the sum of receptors which have specialized receptor cells between the stimulus and the first neuron.

5. The projective field of the analyzer is…

Variants of answer:

a) the sum of neurons which get signals from a given neuron;

b) the sum of stimulating and inhibiting neurons of the cortical department of the analyzer;

c) the sum of the brain neurons, signals from which converge on a given neuron;

d) the sum of receptors, signals from which come on a given neuron;

e) a special cell adapted to the perception of a stimulus from the external or internal environment.

6. By the nature of stimuli, all receptors are divided into…

Variants of answer:

a) vestibule-, proprio-, viscero-;

b) mechano-, thermo-, photo, chemo-;

c) vibrations, pressure, pain;

d) tactile, gustatory, viscero;

e) all the answers are correct.

7. Interoreceptors can be …

Variants of answer:

a) vestibulo-, proprio-, viscero-;

b) viscero-, photo-;

c) vestibule-, olfactory;

d) tactile, gustatory;

e) all the answers are correct.

8. Which receptors are absent in the human organism?

Variants of answer:

a) chemoreceptor;

b) nociceptor;

c) thermoreceptor;

d) electroreceptors;

e) mechanoreceptors.

9. Stimuli to which the action of the receptor is adapted during evolution, is called…

Variants of answer:

a) biological;
b) physical;
c) adequate;
d) physiological
e) chemical.

10. The presence of the mediator is necessary for the excitation of…

Variants of answer:

a) primary- and secondary-sensitive receptors;
b) secondary-sensitive receptors;
c) primary-sensitive receptors;
d) proprioreceptors;
e) tactile receptors.

11. The olfactory receptors, tactile receptors, and proprioreceptors are…

Variants of answer:

a) secondary-sensitive;
b) primary-sensitive;
c) mechanoreceptors;
d) chemoreceptors;
e) nociceptors.

12. The olfactory, visual, auditory receptors, and those of the vestibular apparatus are…

Variants of answer:

a) secondary-sensitive;
b) primary-sensitive;
c) mechanoreceptors;
d) chemoreceptors;
e) nociceptors.

13. The detection and identification of signals is provided by neurons which are located in…

Variants of answer:

a) the spinal cord;
b) the cerebral cortex;
c) the thalamus;
d) the reticular formation;
e) the cerebellum.

14. At what levels of the CNS the interaction of the sensory systems is performed?

Variants of answer:

a) reticular;

b) cortical;

c) all the answers are correct;

d) thalamic;

e) midbrain.

15. Decreased sensitivity under the long action of a constant stimulus is called…

Variants of answer:

a) accommodation;

b) adaptation;

c) depolarization;

d) repolarization;

e) dominant.

16. Adaptation in the sensory systems results in…

Variants of answer:

a) all the answers are correct;

b) increased activity of the processes of excitation and inhibition;

c) decreased activity of the processes of excitation and inhibition;

d) changed sensitivity to long acting stimuli;

e) increased divergence of signals at the subcortical level.

17. During the long action of stimuli the adaptation of a receptor results in…

Variants of answer:

a) its constant excitability;

b) its changing conductivity;

c) its changing excitability;

d) its inconstant structure;

e) its changing structure.

18. The intermediate (phase-tonic) receptors are…

Variants of answer:

a) photo- and thermo receptors;

b) Pacinian corpuscles ;

c) muscle spindles, Golgi tendon receptors;

d) vascular barorecepotors;
e) all the answers are correct.

19. The slowly adapting (tonic) receptors are…
Variants of answer:
a) thermoreceptors;
b) Pacinian corpuscles;
c) muscle spindles, Golgi tendon receptors;
d) photoreceptors ;
e) all the answers are correct.

20. The rapidly adapting (phasic) receptors are…
Variants of answer:
a) photoreceptors;
b) pain (nociceptor);
c) Pacinian corpuscles;
d) muscle spindles, Golgi tendon receptors;
e) all the answers are correct.

21. The eye adjustment to clear vision of subjects located at different distances is called…
Variants of answer:
a) accommodation;
b) hypermetropia;
c) myopia;
d) astigmatism;
e) presbyopia.

22. Which element of the refractive systems of the eye has the greatest refracting force?
Variants of answer:
a) the aqueous humor of the anterior chamber;
b) the lens;
c) the vitreous body;
d) the cornea;
e) all the elements of the refractive system have the same refracting force.

23. Which factor plays an important role in the evaluation of distances up to the object of interest?
Variants of answer:
a) the size of the image on the retina;

b) the degree of accommodation;
c) bipolar vision;
d) the state of the retina;
e) all the answers are correct.

24. Vision abnormalities caused by the loss of the lens at the middle age are called…

Variants of answer:
a) astigmatism;
b) myopia;
c) hypermetropia;
d) presbyopia;
e) accommodation.

25. Vision abnormalities caused by the increased length of the eyeball are called…

Variants of answer:
a) astigmatism;
b) myopia;
c) hypermetropia;
d) presbyopia;
e) accommodation.

26. In myopia images are focused …

Variants of answer:
a) on the anterior chamber of the eye;
b) on the retina;
c) behind the retina;
d) before the retina;
e) on the cornea.

27. In hypermetropia images are focused …

Variants of answer:
a) on the posterior chamber of the eye;
b) on the retina;
c) behind the retina;
d) before the retina;
e) on the cornea.

8. Unequal refraction of light rays in different planes of the optical system of the eye is called…

Variants of answer:

a) accommodation;
b) hypermetropia;
c) myopia;
d) astigmatism;
e) presbyopia.

29. Mydriasis is …

Variants of answer:

a) pupillary narrowing;
b) narrowing of palpebral fissure;
c) dilation of the pupil;
d) tremor of the eye muscles;
e) loss of vision.

30. The stimulation of sympathetic fibers which innervate the iris of the eye causes …

Variants of answer:

a) pupillary narrowing;
b) pupillary dilatation;
c) narrowing of palpebral fissure;
d) tremor of the eye muscles;
e) loss of vision.

31. The stimulation of the parasympathetic fibers of the oculomotor nerve causes…

Variants of answer:

a) pupillary narrowing;
b) pupillary dilatation;
c) dilatation of palpebral fissure;
d) tremor of the eye muscles;
e) loss of vision.

32. The primary subcortical visual centers are located…

Variants of answer:

a) in the superior colliculi of the quadrigeminal plate;
b) in the inferior colliculi of the quadrigeminal plate.

c) in the spinal cord;
d) in the cerebral cortex;
e) in the reticular formation.

33. Into which cerebral hemisphere does information come from the right and left halves of the eye retina?

Variants of answer:

a) from the right half into the left, from the left – into the right;
b) from the right half into the right, from the left – into the left;
c) from the right and left into the right;
d) from the right and left into the left.
e) information does not go into the cerebral hemisphere.

34. The projective zone of the visual analyzer is located in …

Variants of answer:

a) the parietal area of the cerebral cortex;
b) the temporal area of the cerebral cortex;
c) the occipital area of the cerebral cortex;
d) the frontal area of the cerebral cortex;
e) the motor zone of the cortex.

35. If there is any damage to the nerve pathways of the visual system, and the receptor and cortical parts are normal, will a person be able to see and how will they see the surrounding objects?

Variants of answer:

a) they will see only black-and-white objects;
b) they will see them normally;
c) they will see only color objects;
d) they will not see anything;
e) they will see only closely located objects.

36. In color perception the basic role is played by …

Variants of answer:

a) the rods;
b) the cones;
c) the pigment cells;
d) the bipolar cells;
e) ganglionic cells.

37. What neurons of the retina and visual centers are called color-opponent?

Variants of answer:

a) all the answers are correct;

b) stimulated by one color and inhibited by the other;

c) stimulated by one color if light is switched on and inhibited if light is switched off;

d) neurons transferring information from different cones;

e) neurons non-sensing colors.

38. The absence of the ability to distinguish certain colors is called…

Variants of answer:

a) hypermetropia;

b) myopia;

c) astigmatism;

d) daltonism;

e) presbyopia.

39. The absence of the ability of the perception of the red color is called…

Variants of answer:

a) protanopia;

b) deuternopia;

c) tritanopia;

d) achromasia;

e) presbyopia.

40. The absence of the ability of the perception of the blue and violet colors is called…

Variants of answer:

a) protanopia;

b) deuternopia;

c) tritanopia;

d) achromasia;

e) presbyopia.

41. Which property of the visual analyzer is estimated with the help of the Golovin–Sivtsev Table?

Variants of answer:

a) field of vision;

b) color sensation;
c) acuity of vision;
d) bipolar vision;
e) degree of accommodation.

42. Visual acuity in light increase and physical contrast will be…

Variants of answer:

a) decreased;
b) increased;
c) does not change;
d) disappeared;
e) firstly increased, then decreased.

43. The space which can be seen by the eye if it is fixed on one point is called…

Variants of answer:

a) field of vision;
b) acuity of vision;
c) accommodation;
d) myopia;
e) bipolar vision.

44. The sound-conducting structures of the acoustic analyzer are…

Variants of answer:

a) the tympanic membrane, auditory ossicles;
b) the Eustachian tube;
c) the spiral ganglion of cochlea, semicircular channels;
d) the vestibulum and semicircular channels;
e) the cochlea.

45. Air pressure in the cavity of the middle ear is approximately …

Variants of answer:

a) higher than atmospheric air by 75 mm of Hg;
b) it is equal to atmospheric air;
c) it is lower than atmospheric air by 75 mm of Hg;
d) it is higher than atmospheric air by 35 mm of Hg;
e) it is lower than atmospheric air by 35 mm of Hg.

46. The spiral (Corti's) organ of the cochlea is located on …

Variants of answer:

a) the Reissner's (vestibular) membrane;
b) the basilar membrane;
c) the membrane of the round window;
d) the membrane of the oval window;
e) the tympanic membrane.

47. The receptors of the acoustic analyzer are …

Variants of answer:

a) the cells of the spiral ganglion of the cochlea;
b) the formations of the internal ear;
c) the hair cells;
d) the auditoryossicles;
e) the neurons of the superior temporal gyrus.

48. The excitation of the receptors of the spiral organ in the cochlea is caused by the…

Variants of answer:

a) bending of the cilia of the hair cells;
b) deformation of the tympanic membrane;
c) deformation of the auditory ossicles;
d) deformation of the membrane of the oval window;
e) deformation of the membrane of the round window.

49. The area of sound perception by the acoustic analyzer of humans has the borders of …

Variants of answer:

a) 6–2,000 Hz;
b) 16–20,000 Hz;
c) 10 –2,000 Hz;
d) 6–10,000 Hz;
e) 16–16,000 Hz.

50. Which theory of sound perception is considered to be main now?

Variants of answer:

a) telephone theory of Rutherford;
b) resonance theory of Helmholtz;
c) the theory of the «traveling wave» of Bekeshi;
d) three-component theory;
e) the theory of opposing pairs.

51. The projective zone of the acoustic analyzer is located in …

Variants of answer:

a) the inferior frontal gyrus;
b) the precentral gyrus;
c) the postcentral gyrus;
d) the superior temporal gyrus;
e) all the answers are correct.

52. Which kind of «funnel» is situated in the central acoustical system?

Variants of answer:

a) narrowing «funnel»;
b) extending «funnel»;
c) twisted «funnel»;
d) straight «funnel»;
e) all the answers are correct.

53. Thanks to binaural hearing humans can …

Variants of answer:

a) hear low tones;
b) hear high tones;
c) locate the source of sounds;
d) perceive sounds of any frequency;
e) all the answers are correct.

54. Adequate stimuli of the receptors of the utricle and saccule of the vestibular analyzer are…

Variants of answer:

a) linear and angular acceleration;
b) only linear acceleration;
c) only angular acceleration;
d) sounds;
e) chemical substances.

55. For the full characteristic of body positions in space except for vestibular impulses, it is necessary to get additional information from …

Variants of answer:

a) the proprioreceptors of the neck muscles;
b) the proprioreceptors of the muscles of extremities;
c) the proprioreceptors of the muscles of the trunk;
d) the proprioreceptors of the respiratory muscles;
e) all the answers are correct.

56. The minimal spatial threshold of tactile sensitivity is on the surface of…

Variants of answer:

a) feet soles;
b) back;
c) fingers;
d) forearms;
e) upper arm.

57. Minimal tactile sensitivity is on the surface of…

Variants of answer:

a) the backside of the palm;
b) back;
c) fingers;
d) forearms;
e) upper arm.

58. In conditions of muscle contractions the frequency of impulses from the Golgi tendinous receptors…

Variants of answer:

a) does not change;
b) changes are inverse to the force of contractions;
c) increases proportionally to the force of contractions;
d) disappears;
e) decreases proportionally to the force of contractions.

59. Pain receptors are called…

Variants of answer:

a) osmoreceptors;
b) nociceptor;
c) proprioreceptors;
d) distant receptors;
e) photoreceptors.

60. The minimal force of stimuli capable to cause painful sensations is called…

Variants of answer:

a) subthreshold;
b) pain barrier;
c) indifferent;
d) the threshold of tactile sensitivity;
e) superthreshold.

61. The objective signs of pain are changes of …

Variants of answer:

a) blood pressure;

b) all the answers are correct;

c) rhythm of heart activity;

d) rhythm of respiration;

e) leukocytic formula and amount of hormones in blood plasma.

62. Which kind of pain appears in damages to connective tissue, joints, muscles?

Variants of answer:

a) visceral pain;

b) somatic, superficial pain;

c) somatic, deep pain;

d) projective pain;

e) phantom pain.

63. The greatest number of the nociceptors per unit of area are situated …

Variants of answer:

a) in tendons;

b) in skin;

c) in internal organs;

d) in muscles;

e) in bones.

64. The antinociceptive system is the system of the CNS structures which can…

Variants of answer:

a) reduce pain sensations;

b) activate pain sensations;

c) both reduce and activate pain sensitivity;

d) increase the speed of the conduction of pain impulses;

e) excite the pain receptors.

65. The sensitivity in the excitation of the structures of the antinociceptive systems of the brain will …

Variants of answer:

a) increase;

b) will not change;
c) decrease;
d) disappear;
e) change in different ways.

66. The sensitivity during the blocking of the structures of the antinociceptive systems of the brain will …

Variants of answer:
a) sharply decrease;
b) will not change;
c) sharply increase;
d) disappear;
e) change in different ways.

67. What substances produced by the antinociceptive system of the brain suppress painful sensitivity?

Variants of answer:
a) acetylcholine, histamine;
b) prostaglandins, potassium ions;
c) endorphines, enkephalins.
d) oxytocin, vasopressin;
e) all the answers are correct.

68. Sensitivity under the long action of a painful stimulus …

Variants of answer:
a) decreases;
b) increases;
c) does not change;
d) disappears;
e) changes in different ways.

69. The receptors of which part of the tongue perceive the sweet taste best?

Variants of answer:
a) the base of the tongue;
b) the edges of the tongue;
c) the lateral surface of the tongue;
d) the apex of the tongue;
e) all the answers are correct.

70. The receptors of the tongue which perceive the bitter taste best are located …

Variants of answer:

a) along the edges of the tongue;
b) in the apex of the tongue;
c) in the base of the tongue;
d) the lateral surface of the tongue;
e) all the answers are correct.

71. The visible range of the electromagnetic spectrum of the human eye is ...

Variants of answer:

a) 370-740 nm;
b) 740-1,140 nm;
c) 200-340 nm;
d) 200-370 nm;
e) less than 370 nm.

72. The function of the stapedius muscle is...

Variants of answer:

a) to protect the ear from loud sounds;
b) to help people hear sounds of low frequency;
c) to help people hear sounds of high frequency;
d) to help people hear whisper;
e) all the answers are correct.

73. Which muscle is the smallest in the human body?

Variants of answer:

a) interarytenoid;
b) stapedius;
c) corrugator supercilli;
d) superior oblique;
e) tensor tympani.

74. Which of the following statements describes the Pacinian corpuscles best…

Variants of answer:

a) they are pain receptors;
b) they are slowly adapting touch receptors;

c) they are rapidly adapting touch receptors;
d) they are located in the joints**;**
e) they are thermal receptors.

75. The intrafusal fibers of the striated skeletal muscles are innervated by one of the following types of motor neurons. Choose the correct answer.

Variants of answer:
a) alpha;
b) beta;
c) gamma;
d) delta;
e) sigma.

CORRECT ANSWERS
PHYSIOLOGY OF SENSORY SYSTEMS

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	20	c	39	a	58	c
2	b	21	a	40	c	59	b
3	a	22	d	41	c	60	b
4	a	23	e	42	b	61	b
5	b	24	d	43	a	62	c
6	b	25	b	44	a	63	b
7	a	26	d	45	b	64	a
8	d	27	c	46	b	65	c
9	c	28	d	47	c	66	c
10	b	29	c	48	a	67	c
11	b	30	b	49	b	68	c
12	a	31	a	50	c	69	d
13	b	32	a	51	d	70	c
14	c	33	b	52	b	71	a
15	b	34	c	53	c	72	a
16	d	35	d	54	b	73	b
17	c	36	b	55	a	74	c
18	a	37	b	56	c	75	c
19	c	38	d	57	b		

UNIT 7
INTEGRATIVE ACTIVITY OF THE ORGANISM

7.1. Biological bases of behavior

The **integrative activity of the brain** is understood as the interaction of neurons and other brain structures that provide performing of complex behavioral reactions of the organism, which form the basis of higher nervous activity.

The term **"higher nervous activity" (HNA)** was proposed by I. P. Pavlov for designation of neurophysiological processes that ensure the formation of acquired behavioral responses and learning. Later, this term was used in a broader sense, in some cases including all the integrative functions of the higher parts of the brain: *the formation of sensations about the action of stimuli on the organism and providing consciousness, congenital and acquired forms of behavior, learning and memory processes, speech and thinking, motivation and emotions, wakefulness and sleep*. These functions provide the integrity of the organism, the coordination of the work of its organs and systems, adaptation to the environment, behavioral responses directed on the life saving of the individual and the survival of the species.

Another series of nervous processes, including the realization of *unconditioned reflexes and instincts*, is called **lower nervous activity**. These reflexes and instincts not only provide congenital responses, but are often the basis for the formation of motives and emotions that determine the choice of direction of acquired behavioral responses.

Behavior is a set of actions performed by an individual during their vital activity. Congenital forms of behavior are manifested by a number of *unconditioned reflexes and instincts.*

Unconditioned reflexes are congenital, inherited stereotypical responses of the organism to external or internal stimuli with the participation of the central nervous system

The examples of behavioral reflexes that last a lifetime are the *orientation reflex and defensive responses to pain stimuli*.

Instinct is a set of complex unconditioned reflexes that depend on metabolic hormonal factors and have a chain character, in which the completion of one reflex serves as a signal for the beginning of the next reflex. Instincts maintain the homeostasis and survival of species regardless of random changes in the environment.

Classification of instincts and unconditioned reflexes (according to P. V. Simonov):

1. **Vital** – eating, drinking, defense, regulation of "sleep-awake state" (their implementation does not require the participation of another individual, inhibition of these instincts leads to death).

2. **Role-playing (zoosocial) -** occur only during interaction of individuals of the same species. These include sexual, parental, territorial and hierarchical instincts, the effect of emotional resonance (empathy) (these instincts are aimed at the survival of the species, the effective existence of the group — "what is good for the species, is good for you").

3. **Self-development**. These instincts and reflexes are focused on the future, are not absolutely necessary for survival, and are directed on improvement of mental activity and satisfaction of the ideal needs. This includes research, simulation, and game reflexes, as well as the overcoming reflex (resistance, freedom).

7.2. Conditioned reflexes

The bases of HNA were created by I.P. Pavlov. The basic instrument which helped him to study many issues was the **conditioned reflex**.

The conditioned reflex is a form of the organism`s adaptation to environmental changes. There are some differences between unconditioned and conditioned reflexes (Table 7.1)

Table 7.1 — Differences between unconditioned and conditioned reflexes:

Unconditioned reflex	Conditioned reflex
They are congenital, inherited	They are acquired, not inherited
They appear at the first presentation of a certain stimulus	They are produced on the basis of several repetitions of a combination of actions of conditional and unconditional stimuli
They exist in every member of a species	They are individual (depend on individual experience)
They are Relatively constant, most of them are present during lifetime	They are not constant (i.e. they can appear and disappear or change)
Occur in response to adequate stimulation of a certain receptive field	Can be developed from most of the receptive fields
They are formed with the participation of the spinal cord and brain structures	In higher animals and humans they are formed with the participation of the cerebral cortex

The requirements for the formation of conditioned reflexes:

1. Presence of not less than two stimuli: conditioned (for example, light) and unconditioned (for example, food) (Figure 7.1).

2. Sequence of the action of the stimuli: the conditioned stimulus should act first, followed by the unconditioned one.

3. Multiple action of the stimuli (not less than 10 times).

4. Normal state of the CC.

5. Absence of side stimuli.

The extent of the conditioned reflex depends on the force of conditioned and unconditioned stimuli.

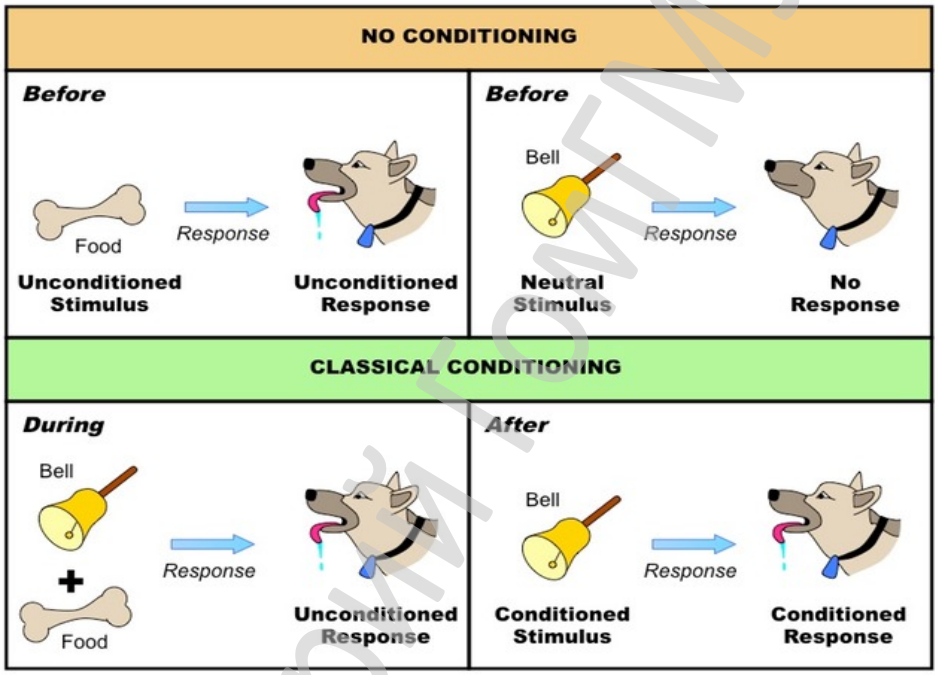


Figure 7.1 —Development of the conditioned reflex of salivation due to the action of sounds (from studylib.net)

7.2.1. Classification of conditioned reflexes

1) By the character of reflexes:

• Sensory conditioned reflexes. For example, images of food make people salivate.

• Operant, or instrumental conditioned reflexes. For example, to get a banana, a monkey should press a button.

2) By the nature of conditioned signals:

• Natural (a conditioned signal is a natural combination for an unconditioned signal, for example, image and smell of food cause salivation).

• Artificial (a conditioned signal is not a natural combination for an unconditioned signal, for example, salivation under the action of light or sound).

3) By the coordinated action of conditioned and unconditioned signals:

• Available conditioned reflexes (conditioned and unconditioned stimuli act simultaneously).

• Trace (conditioned and unconditioned stimuli do not act simultaneously).

4) By the character of unconditioned reactions:

• Conditioned — secretory.

• Conditioned — motor, etc.

5) By the character of their formation:

According to this classification, there are conditioned reflexes of the higher order. If conditioned reflexes are formed in the combination of a conditioned stimulus with an unconditioned one, they are called first-order reflexes. On the basis of a strictly learnt conditioned reflex of the first order it is possible to develop secondary-order reflexes. These reflexes are formed due to the combination of a new conditioned stimulus with the conditioned signal of the prior first-order reflex, etc. In animals it is possible to develop third-order reflexes, in children — sixth-order ones, and in adults even higher.

7.2.2. Mechanisms of the formation of conditioned reflexes

The basis for the formation of a conditioned reflex is the **time connection,** which is formed in the CC between the center of a conditioned stimulus and an unconditioned reflex (Figure 7.2).

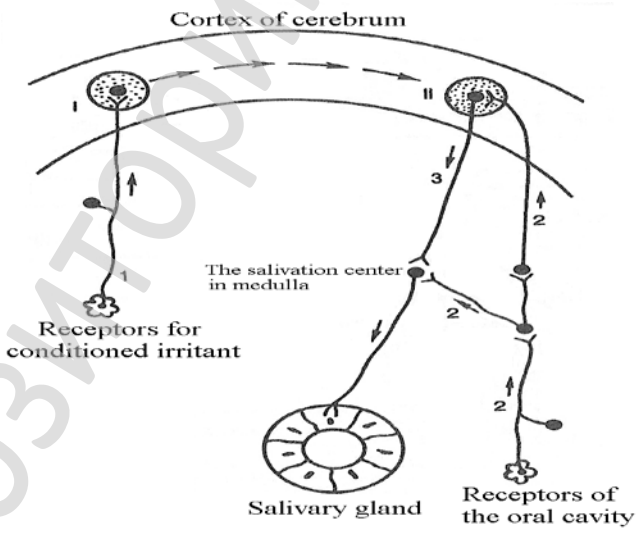


Figure 7.2 — Formation of a conditioned reflex (by Pokrovskiy V. M., Korotko G. F., 2000)

Notes: I — the focus of excitation in the cortex of the cerebrum which is formed under the action of a conditioned stimulus; II — the focus of excitation in the cortex of the cerebrum which is formed under the action of an unconditioned stimulus; 1 — afferent nerve pathways of a conditioned signal; 2 — afferent nerve pathways of an unconditioned signal; 3 — efferent nerve pathways.

In Pavlov's opinion, under the action of a light stimulus in the CC there appears a focus of excitation (in the visual region of the CC). Under the action of an

unconditioned stimulus (for example, food), a second focus of excitation appears first in the subcortical structures, then in the CC. Under the multiple repetitive action of these two stimuli, the time connection between the focuses of excitation in the CC is formed. An important role in the formation of this connection is played by the dominant whose property is the summation of excitation, i. e. the unconditioned stimulus is the dominant and attracts signals from the focus of excitation arisen under the influence of the conditioned stimulus.

From the morphological point of view, during the formation of a conditioned reflex the neuron processes are growing, and on their dendrites small dendritic spines appear, which increases the contact area with other cells. It is assumed that glia cells may participate in the formation of a conditioned reflex, which can provide axon myelination, which increases the velocity of the signal conduction.

7.2.3. Inhibition of conditioned reflexes

Extinction of conditioned reflexes is caused by the presence of an inhibiting process in the CC, which can be caused by the action of side stimuli or other factors.

There are two kinds of inhibition (Figure 7.3):

1. External (unconditioned) inhibition.

2. Internal (conditioned) inhibition.

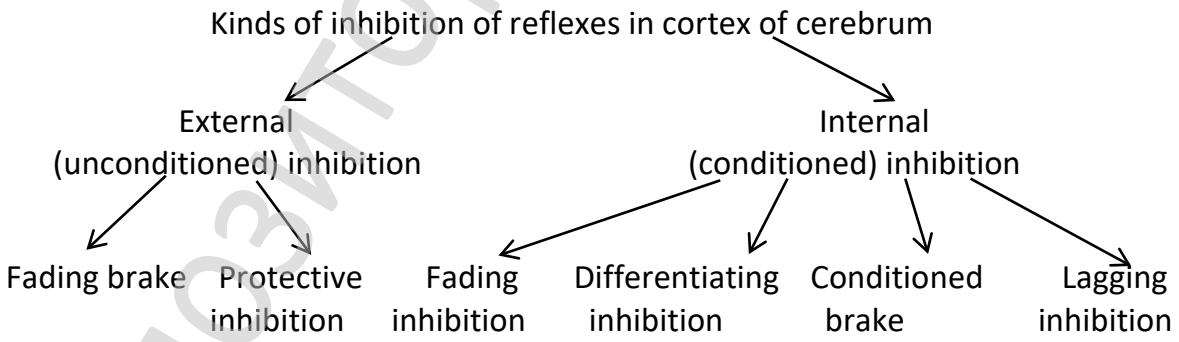


Figure 7.3 — Kinds of the inhibition of the reflexes in the cortex of cerebrum

External (unconditioned) inhibition is a congenital kind which is typical for all the CNS parts. With the help of inhibition, both conditioned and unconditioned reflexes may disappear. External inhibition arises without preliminary development and is based on the influence of a superthreshold stimulus on the center of a conditioned reflex. For example, a dog has the

conditioned salivary reflex to light. If to create a noise at the moment when the lights are being turned on, salivary secretion in the dog does not appear. It is connected with the fact that the sound becomes a new dominating focus of excitation in the CC, which by the mechanism of negative induction inhibits the conditioned reflex. This kind of inhibition is called ***the fading brake*****.** If to perform this experience several times, the action of the side stimulus becomes weaker and does not produce any reaction at all. For example, a cat hears some rustle and reacts to it, but when the rustle repeats several times, its value weakens.

A second kind of external inhibition is ***exorbitant (protective) inhibition,*** which appears if a conditioned stimulus reaches a superthreshold force or reacts for a very long time.

Internal (conditioned) inhibition arises in the nerve centers of conditioned reflexes and certain conditions are necessary for its formation.

The kinds of internal (conditioned) inhibition are as follows:

1. Fading inhibition. If a conditioned signal in response to which a reflex develops, is not supported with the action of an unconditioned signal, the given conditioned reflex disappears. For example, if a circus animal does not get any reward after performing a trick, it stops performing it.

However, conditioned reflexes can be renewed (disinhibition).

2. Differentiating inhibition. If an animal has the conditioned reflex to a sound of 1000 Hz, a positive response can arise to sounds of any frequency (900 Hz and 1100 Hz). This phenomenon is called generalization. To develop conditioned inhibition, it is necessary to support 1000 Hz sounds with an unconditioned stimulus and stop supporting 900 Hz and 1100 Hz sounds. The phenomenon when a significant signal is distinguished among similar stimuli is called differentiation.

3. Conditioned brake. If a dog secretes saliva under the action of light (A), this reaction will be also observed under the combined action of light (A) and sound (B), since this combination of the stimuli produces a similar response to that produced only by stimulus A (the phenomenon of generalization). It is possible to develop conditioned inhibition, if to support the signal A with an unconditioned stimulus and not to support the combination A+B. In this case the combination A+B loses its positive value and the signal B will be the conditioned brake for the signal A. An additional signal B acquires independent negative values. This signal inhibits responses to any conditioned stimuli which it has not experienced earlier. For example, while going along a street a person encounters their friend walking next to an unpleasant person, so they would prefer to avoid meeting the friend. In this situation the unpleasant person is the conditioned brake.

4. Lagging inhibition. If the support of a conditioned signal with an unconditioned one is constantly delayed for some time from the beginning of the action of the conditioned signal, the beginning of the action of the conditioned reflex will be postponed and, as result, the reflex will only appear by the end of the action of the conditioned signal. The cause of the delay of the conditioned reflex is that the conditioned signal during the first moments of its action is not supported with the unconditioned one. For example, a reaction to a flying ball during the game of cricket develops during the last moment when the ball can be hit.

Interactions between the processes of excitation and inhibition in the CC are an important condition for the analysis and synthesis of stimuli.

Review questions

1. What scientists studied the biological bases of behavior? What are their merits? Name the two basic forms of behavior. What are the features of unconditioned reflexes? How are unconditioned reflexes classified? How are motives formed? How are they classified?

2. What is higher nervous activity? What are the features of conditioned reflexes? What are the requirements for the formation of conditioned reflexes? How are conditioned reflexes classified?

3. What are the mechanisms of the formation of conditioned reflexes?

4. What is inhibition in the cortex of the cerebrum? What are the kinds of conditioned inhibition? What is external (unconditioned) inhibition? What are the kinds of unconditioned inhibition? Give some examples. What is internal (conditioned) inhibition? What are the kinds of conditioned inhibition? Give some examples.

7.2.4. Analysis and synthesis of stimuli in the cortex of the cerebrum. Dynamic stereotyping

Analysis and synthesis are important functions of the CC.

Analysis consists in the separation of signals, differentiation of influences on the organism. The analysis of influences begins in receptors, proceeds in the lower parts of the CNS and finishes in the CC.

Synthesis consists in the integration of signals, generalization of excitation of different portions of the CC. As a result of the synthesis, a temporary connection which is the basis of a reflex, is formed.

The example of the synthetic activity of the cortex is dynamic stereotyping. A **dynamic stereotype** is a fixed succession of a certain group of

conditioned reflexes which is produced as a result of repeated exposure to a set of conditional stimuli coming in a certain order, and united by the performance of a specific task and allow to perform various automated actions.

Each peripheral stimulus corresponds to its space-time area of excitation in the CC — a dynamically structural complex. Internal inhibition plays an important role during the analysis and synthesis. A complex of stimuli leads to more complex analysis and synthesis. For example, several signals follow each other in the certain order: A+B+C+D supported with an unconditioned stimulus. In the reverse order this combination is not supported. If differentiation appears, the CC accepts signals not only as a set but also in the certain sequence. The CC forms a certain dynamic stereotype to a set of signals. Even if only one signal is used in an experience (for example, B or C) from the complex, the CC responds to this signal accepting it as a component of the certain system of signals. In the basis of dynamic stereotyping, or system in the work of the CC there is a certain state of the focuses of excitation and inhibition which arise and are replaced in a certain order.

Dynamic stereotyping is the integral activity performed by the cerebrum of humans and higher animals and manifested by a fixed succession of conditioned reflexes. The dynamic stereotype is related to processes of education, skill formation, and behavior. The dynamic stereotype is the product of very complex interactions between the areas of the cortex and is the physiological basis for automation of skills, as it aids in the efficient performance of tasks and in rapid adaptation to the conditions of existence. The biological value of dynamic stereotyping consists in saving of an organism`s energy, as the CC does not have to repeat the same actions again and again. For example, when going outdoors people automatically lock the door or turn on the light entering the room not even thinking about this.

Dynamic stereotypes (habits) can be positive (morning exercises) and negative (smoking). For the nervous system generation of a positive or negative stereotype is an equally difficult problem. A developed dynamic stereotype is hard to reconstruct. Especially strong are those stereotypes which develop during childhood. 25 repetitions are enough to establish a dynamic stereotype, and approximately 3 times as more to alter or break it. Breaking of a dynamic stereotype places a great strain on the neural elements of the cerebral cortex thus leading to disturbances in higher nervous activity and to the development of neurotic states. Changes of a familiar way of life, for example, forced moving from a habitual place of residence or death of a close person, cause mental crises and emotional turmoil. The degree of difficulty in reconstructing a

dynamic stereotype depends on the nature of the stimuli and the specific characteristics of the nervous system, as well as on the age and condition of the organism.

7.2.5. Specific features of human higher nervous activity. Signal systems

A **signal system** is a set of mechanisms that provide perception, processing, and exchange of information between an organism and the environment.

The first signal system is a set of all analyzers that provide perception of sensory information (the main feature is the concrete character of perception, i.e. the obligatory presence of the displayed object).

The second signal system is a set of analyzers that are responsible for speech and abstract thinking (in this case, the word is a universal substitute for all other signals).

There are some differences between conditioned reflexes that are formed on the basis of the first and second signal systems (Table 7.2)

Table 7.2 — The difference between conditioned reflexes that are formed on the basis of the first and second signal systems

The first signal system	**The second signal system**
Conditioned reflex:	Conditioned reflex:
– is supported by an unconditional stimulus;	– is supported by any stimulus
– has a concrete character;	– has an abstract character;
– has a physiological orientation;	– has a social character;
– develops slowly, but persists for a long time;	– develops quickly and is quickly canceled;
– is less susceptible to fatigue	– is more susceptible to fatigue

The human first-signal system functions separately only for the first 6 months of life and its signals are concrete. Information about the environment includes sounds, smells, etc. but words contain more information, since they bear information not about only one person but the whole mankind.

The word is an independent stimulus. This is proved with the fact that the activity of the CC increases not only during communication but even thinking. Words give information about a subject or an action without any contact with them. However, this has the risk of detachment from reality, i. e. there can be a lie. In this respect it is very important to have a connection between the first and second signal systems.

I. P. Pavlov called a language ‘the signal of signals’. The second signal system makes the basis of abstract spoken thinking which is typical only for humans.

The second signal system develops with age. Newborns can pronounce only sounds. By the end of the first year of life, words acquire their independent meaning. At the end of the second year of life, the second signal system is developed and becomes dominant at the age of 6–7. It means that at this age it is very important to encourage and praise children verbally.

How is the second signal system formed?

The second signal system is formed by the rules of conditioned reflexes. One word is constantly combined with the varying structure of stimuli, which intensifies excitation caused by the repetition of the word. The changing components are influenced by negative inductive inhibition and the word turns into an independent conditioned signal. It happens due to the formation of a large amount of conditioned connections for a verbal stimulus.

For example, a child says the word «mother» for the first time. Soon they learn that other people also have a mother, then discover that cats and dogs have their mothers, too. Thus, the word «mother» combines with a changing amount of stimuli, which is the basic principle upon which the second signal system is formed.

To form the second signal system quickly, babies should hear speaking since birth, otherwise this process will be prolonged or will not start at all.

In 1920s in India two girls (4 and 7 years old) were found who were alleged to have been raised by a wolf family. All their habits were wolf-like. They would not allow themselves to be dressed, scratched and bit people who tried to feed them, rejected cooked food and walked on all fours. At night they would howl like wolves and were not able to speak. After rescuing the girls from the wolves' den the people started to teach them to speak. At the age of 7, the younger girl could remember only 45 words, the older one even less. This example proves the necessity of talking to a child soon after birth.

For a doctor the word has a very important value. Words can both treat and hurt and even kill a patient.

Speech is one of the most important functions of the human brain. The processing of a speech signal has the specific features determined by the complex structure of speech. Speech as a signal has actually physical signs (sounds and words) and information contents.

There are several areas of the brain that play a critical role in speech and language (Figure 7.4, Table 7.3). In 95 % people the centers of speech are located in the left hemisphere of the brain.

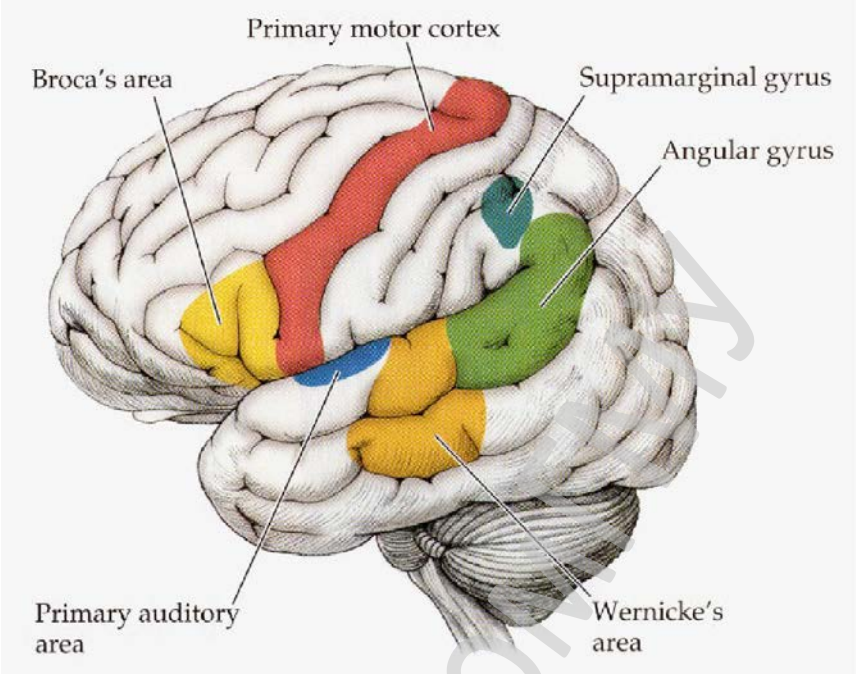


Figure 7.4 — Critical areas of the brain involved in speech and language (from bianoti.com)

Table 7.3 — The centers of the second signal system (speech centers)

Name of center	Localization	Functions
The sensory (auditory) center of speech *Wernicke's area*	In the posterior part of the superior temporal gyrus	Provides speech comprehension and intelligence
The motor center of spoken speech *Broca's area*	In the posterior part of the inferior frontal gyrus	Provides the formation of words, phrases and sentences
The visual center of speech	Angular gyrus of the occipital lobe	Provides recognition and understanding of the text
The articulation centers	The parts of the precentral gyrus that provide innervation of articulation muscles	Provides playback of generated phrases and sentences

7.2.6. Types of higher nervous activity

Hippocrates was the first to study the types of temperament. Later this issue was studied by many scientists, that is why there are several classifications of HNA types.

The type of HNA is a set of individual properties of the nervous system that defines features of the psychophysiological mechanisms of interrelations between an organism and an environment. The synonyms to the term «type of HNA» are words «character, temperament».

To define the type of HNA, it is necessary to take into account:

1. Quickness of the formation of a conditioned reflex.
2. Volume of a conditioned reflex (effect).
3. Stability of a conditioned reflex i.e. how long it is preserved.
4. Intensity of external and internal inhibition.
5. Speed of irradiation and concentration of excitation and inhibition.
6. Exposure to impacts which may cause a pathological state of HNA.

I. P. Pavlov classified HNA types according to several attributes considered as the most reliable parameters of higher nervous activity (Figures 7.5, 7.6). These are intensity, lability of the processes of excitation and inhibition, and the ratio of these processes in the central nervous system and their mobility, i. e. how quickly they are substituted. In experimental practice the following four principle types of higher nervous activity were discovered:

1. Strong, unbalanced, labile characterized by predominance of excitation over inhibition. According to Hippocrates, the choleric temperament corresponds to this type of HNA. Choleric individuals are impatient, straightforward, stubborn, short-tempered, intolerant, moody, vengeful. They are described as independent, decisive, goal-oriented, and ambitious. These combined with their dominant, result-oriented outlook make them natural leaders. The representatives of the choleric type were I. P. Pavlov, Bonaparte Napoleon, Alexander Pushkin, Peter-the-Great, Julius Caesar, Adolph Hilter, Winston Churchill.

2. Strong, well-balanced, labile characterized by high mobility of nerve processes. According to Hippocrates, the sanguine temperament corresponds to this type of HNA. Individuals with this type are energetic, talkative, enthusiastic, active, easy-going and social people. They quickly get used to a new environment and have a flexible mind, constantly seek variety and entertainment, tend to overestimate themselves, easily overcome misfortunes, but at times are not self-organized. Elvis Presley, Pablo Picasso, Alexander Suvorov were people with the sanguine temperament.

3. Strong, well-balanced, inert characterized by low mobility of nerve processes. According to Hippocrates, the phlegmatic temperament corresponds to this type of HNA. Phlegmatic individuals are even-tempered, reliable, patient, inoffensive, and are good at generalizing ideas. They do not like to be in an unfamiliar environment, strictly follow their daily schedule, tend to be diplomatic to avoid conflicts, and always try to make compromises to restore peace and harmony. Ivan Krylov, Alexander Kutuzov, Bill Gates, Albert Einstein, Walt Disney, Margaret Thatcher were representatives of the phlegmatic personality type.

4. Weak type of HNA characterized by extremely weak development of both excitation and inhibition, which cause fatigue and low workability according to I. P. Pavlov, or melancholic temperament according to Hippocrates. Melancholic individuals are shy people who easily get confused in a new situation, have low self-esteem, involuntarily adapt to the character of a person they talk to, sensitive to encouragements and reproaches, are hypochondriac and very sentimental. Melancholic people are very social and seek to contribute to the community. Being extremely thorough and accurate, they are fantastic managers with good personalities. Melancholic people were Michelangelo, Vladimir Lenin, Pyotr Tchaikovsky, Leonid Brezhnev, Leo Tolstoy, Chopin.

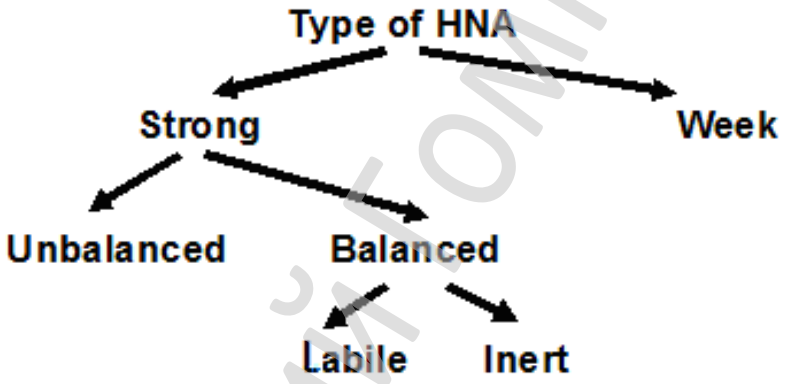


Figure 7.5 — Classification of HNA types by I. P. Pavlov

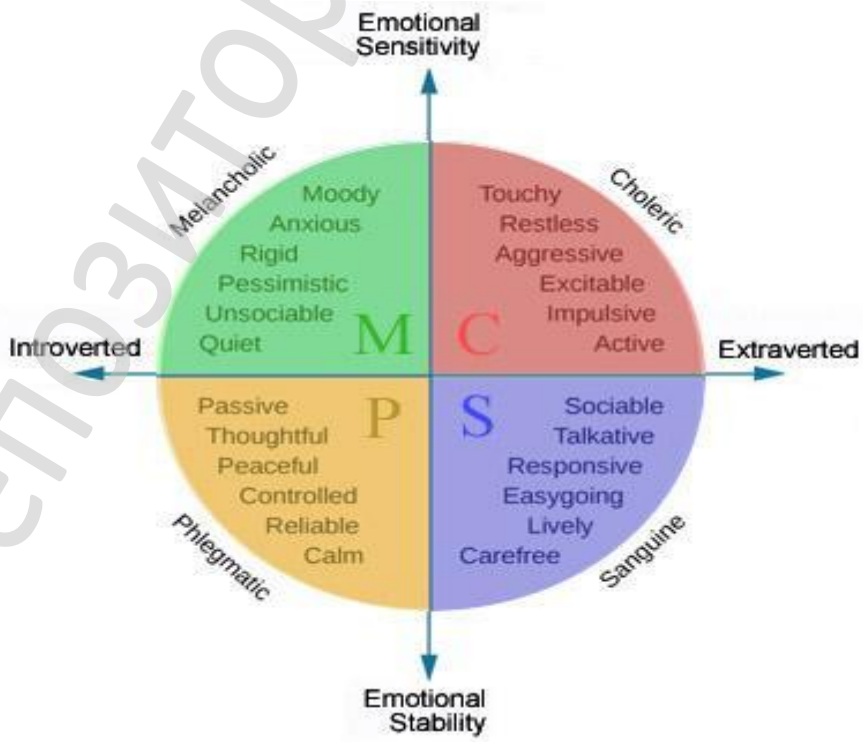


Figure 7.6 — Characteristics of personality types (from slideplayer.com)

These types of HNA are extreme, but the majority of people and animals have mixed types of HNA. An individual is already born with an inborn type of HNA and, influenced by education it can be changed, since the nervous system is very flexible, especially in childhood. It means that people restrain some of their actions.

The types of HNA discovered by I. P. Pavlov are also found in animals.

Between the activities of the first and the second signal systems there are different interrelations. By this feature I. P. Pavlov revealed 3 types of HNA which are typical of all people:

1. Artistic type. The first signal system dominates. People with this type of HNA have creative thinking. For example, Raphael, who would say that he painted pictures better when he was not thinking about his painting.

2. Intellectual type. The second signal system dominates and these people have abstract thinking and are good inventors.

3. Average type of HNA (mixed). In these people both the signal systems are similarly active (Leonardo da Vinci).

Practical medicine discovered that people with the predominant first signal system tend to develop hysteria, frequent changes of mood. If the second system predominates, psychasthenia can be observed (diffidence, timidity, increased vulnerability).

There are also other types of HNA. E. Krechmer defined the types of psychics depending on the body types:

1. Picnics — are characterized with plump forms of the body, rich hair. These people often suffer from kidney or gastrointestinal diseases.

2. Athletic — have wide shoulders and narrow pelvis, developed musculation, they more frequently suffer from musculoskeletal diseases.

3. Asthenic — are characterized with elongated and thin parts of the body; more often suffer from pulmonary diseases.

Krechmer united the revealed types of body constitution into two kinds of psychics:

I. Schizoids (athletic and asthenic). These people have difficulties when communicating with other people.

II. Cycloids (picnics). For these people cyclic changes of psychics are typical but they get on well with other people.

Exact determination of a HNA type is a complex process and requires, according to some methods, up to 2 years.

7.2.7. Disorders of higher nervous activity

Experimental neuroses. Functional disorders of nervous processes and HNA lead to nervous diseases whose cause was identified after the experimental study of experimental neuroses.

I. P. Pavlov defined that neuroses could develop in overstrain of processes of excitation or inhibition, and also in their interference.

Medical practice has revealed that neuroses appear as a result of strong shock. Neuroses are observed:

1. Under overstrain of the excitation process by superstrong stimuli.

2. Under overstrain of an inhibiting process that can be induced due to very delicate differentiations of close stimuli (for example, solution of a difficult problem), interference with constant prohibition, deceit, disappointment.

3*. Under overstrain of the mobility of nervous processes*, i. e. when a dynamic stereotype is broken. Frequently, neurotic states can be caused by unexpected events, which leads to reevaluation of life priorities.

4. HNA disorders arise *due to the interference of excitation and inhibition processes*, i. e. under the simultaneous action of positive and negative stimuli. Using this technique in his laboratory, I. P. Pavlov managed to develop neurosis in a dog which was given food in an iron bowl attached to an electric current.

Neurotic conditions are manifested in various forms. Two extreme types of HNA (choleric and melancholic people) are exposed to neuroses.

The following three phases are typical of the initial stages of the development of neurosis:

1. Equaling of responses. During this phase, both strong and weak stimuli produce identical responses.

2. Paradoxic — a strong conditioned stimulus produces a less strong response than a weak one.

3. Ultraparadoxic. During this phase, neither strong positive nor weak stimuli produce responses.

Neuroses result in changes of vegetative functions (increased pH of gastric juice, high blood pressure, etc.).

Sometimes continuous rest, good sleep, and change of an environment are sufficient to normalize HNA after neurosis. However, depending on the state of the CNS and form of neurosis medication is also used which can either inhibit or intensify the activity of the nervous system.

7.3. Physiology of sleep

Sleep is both a physiological and social issue. William Shakespeare called sleep a «miracle of the mother nature».

The average human life expectancy is 79 years. If the average night's sleep is eight hours, one sleeps for one third of one's life, i. e. the average person spends about 26 years sleeping. A healthy man can fall asleep in any situation (for example, soldiers can sleep while marching), however if the

mechanisms of sleep are affected, falling asleep can be disturbed (for example, striking of a clock). There are several *kinds of sleep* (Table 7.4)

Table 7.4 — Kinds of sleep

Kinds of sleep	
Normal	**Pathological**
• periodic seasonal sleep (hibernation) • periodic daily sleep: – monophase (1 time per day); – diphase (2 times a day); – polyphase (more than twice a day)	• narcotic sleep; • lethargic sleep; • sleep with special lesions of the CNS; • hypnotic sleep (intermediate abnormal forms)

With aging, sleep duration and sleep patterns tend to change:

- newborns spend from 16 to 20 hours asleep each day;
- babies aged 6 months to 1 year sleep about 14 hours a day;
- between the ages of one and four, total daily sleep time decreases to about 11 or 12 hours;
- a 10-year old child sleeps 10 hours;
- an adult requires 7–8 hours;
- although the elderly may still require up to 8 hours, they sleep less (6-7 hours) and have some trouble falling asleep or struggle to obtain those hours in one block due to the prevailing processes of excitation in their nervous system.

Sleep deprivation for 60–80 hours causes a number of effects: the speed of psychological reactions decreases, the body temperature lowers, high fatigability appears, and the heart rate decreases.

Depth of sleep is maximal the first 2–3 hours. Then it decreases and by the 6^{th}–7^{th} hour of sleep it raises again; therefore, if to go to bed at 10 p.m., to wake up at 4 a.m. will be the easiest.

During night the depth of sleep also varies, which is reflected on the EEG.

Phases of sleep:

1. Non-rapid eye movement sleep or orthodox (quiescent) sleep consists of several phases.

A — phase (wake), is marked by state of relaxation, mild sleepiness, the alpha rhythm is registered on the EEG.

B — phase (falling asleep) with slow eye movement, the alpha rhythm disappears on the EEG, low theta-waves appear. This state is sometimes referred to as relaxed wakefulness.

C — phase (superficial sleep) with no eye movement, and dreaming is very rare, the delta-rhythm and "sleep spindles", which are short bursts of high frequency brain activity, and K-complexes appear on the EEG.

D — phase (mild deep sleep), delta waves dominate on the EEG.

E — phase (also referred to as slow wave sleep (SWS), delta sleep, or deep sleep), during which heart rate and breathing slow to their lowest levels, high slow delta waves dominate on the EEG.

2. Paradoxical (fast, REM) sleep. During this sleep, fast eye movement and slow movements of hands and legs, arrhythmia can be observed. It seems like the person is waking up but he is sleeping even more deeply than before. Paradoxical sleep appears within 1.5 hours after falling asleep. On average, out of 8 hours of sleep humans spend about 2.5 hours in the phase of paradoxical sleep. In the beginning this phase is short, and in the morning its duration can be 35 minutes. During night orthodox sleep is replaced by paradoxical, then this cycle repeats. During paradoxical sleep daily processing of information takes place.

Sleep which develops under the influence of background monotonous stimuli is called *active sleep*. For example, students can fall asleep during monotonous reading of a lecture, or passengers on the train tend to fall asleep under hammering of wheels, or we may fall asleep listening to the rain outside.

If to immobilize a person and to limit inflow of stimuli, he falls asleep. This kind of sleep is called *passive sleep*.

People react to sleep deprivation differently. Commonly, adults need 7 to 9 hours sleep per night, but some people can survive on 4–5 hours.

Hypotheses of sleep appearance

1. Hemodynamic hypothesis. According to this hypothesis, sleep arises because of redistribution of the volume of circulating blood between the head and body.

2. Histologic hypothesis. Sleep arises because of impaired contacts between neurons.

3. Humoral hypothesis. Sleep arises due to hypnotoxin accumulation in the awake organism.

4. *Neurogenic hypothesis*. I. P. Pavlov considered the CC to be the initiator of sleep.

5. *Anokhin's cortical-subcortical theory of sleep*. In his opinion, the frontal parts of the CC constantly inhibit the hypothalamus. In the CC fatigue the inhibiting influence of its neurons decreases. This activates the nuclei of the hypothalamus, which can inhibit the activity of the reticular formation. The reticular formation usually exerts constant active influence on the CC, which now disappears, therefore the activity of the CC reduces and sleep develops.

During the day the CC accumulates a large amount of information, whose perception is difficult, therefore during sleep the processing of information and its encoding in memory proceed.

Sleep is accompanied by dreams. During night the average person may have 4–6 dreams during the paradoxical phase. If to wake a person immediately after the paradoxical phase, they will remember the dream, if 10 minutes later — they will have only vague memories, if even more time passes after he had a dream, the person will not remember it. About 70 % of people have color dreams, about 13 % — semi-color, and 17 % have achromatic dreams.

The role of dreams:

1. They protect sleep, i.e. interfere with waking up.

2. They protect the human psychics from overstrain since our desires are realized in our night dreams.

Review questions

1. What is the process of analysis in the cortex of the cerebrum? What is the process of synthesis in the cortex of the cerebrum? What is dynamic stereotyping? What is its physiological role and significance for training and acquisition of new skills?

2. What is the first signaling system according to I. P. Pavlov? What is the second signaling system according to I.P. Pavlov? What is the value of words for humans? What is speech? Where are the speech centers localized? What is their role in the formation of speech?

3. What is the type of higher nervous activity? What are the classifications of the higher nervous activity types? Give their characteristics. Who studied neuroses in experiments? In what situations can neuroses be observed? What three phases are typical for the initial stages of the development of neurosis?

4. What is sleep? What are the kinds of sleep? What are the phases of sleep? Give their characteristics. What are the hypotheses of sleep appearance? What are dreams? What is the role of dreams?

7.4. Motives and emotions

Motives are subjectively realized and emotionally painted states of an organism, which induce it to make the action, directed on the satisfaction of the needs (Figure 7.7).

Motives are subdivided into:

1. Biological (inferior, primary, unconditional).

2. Social (the highest, secondary, complex).

3. Pathologic.

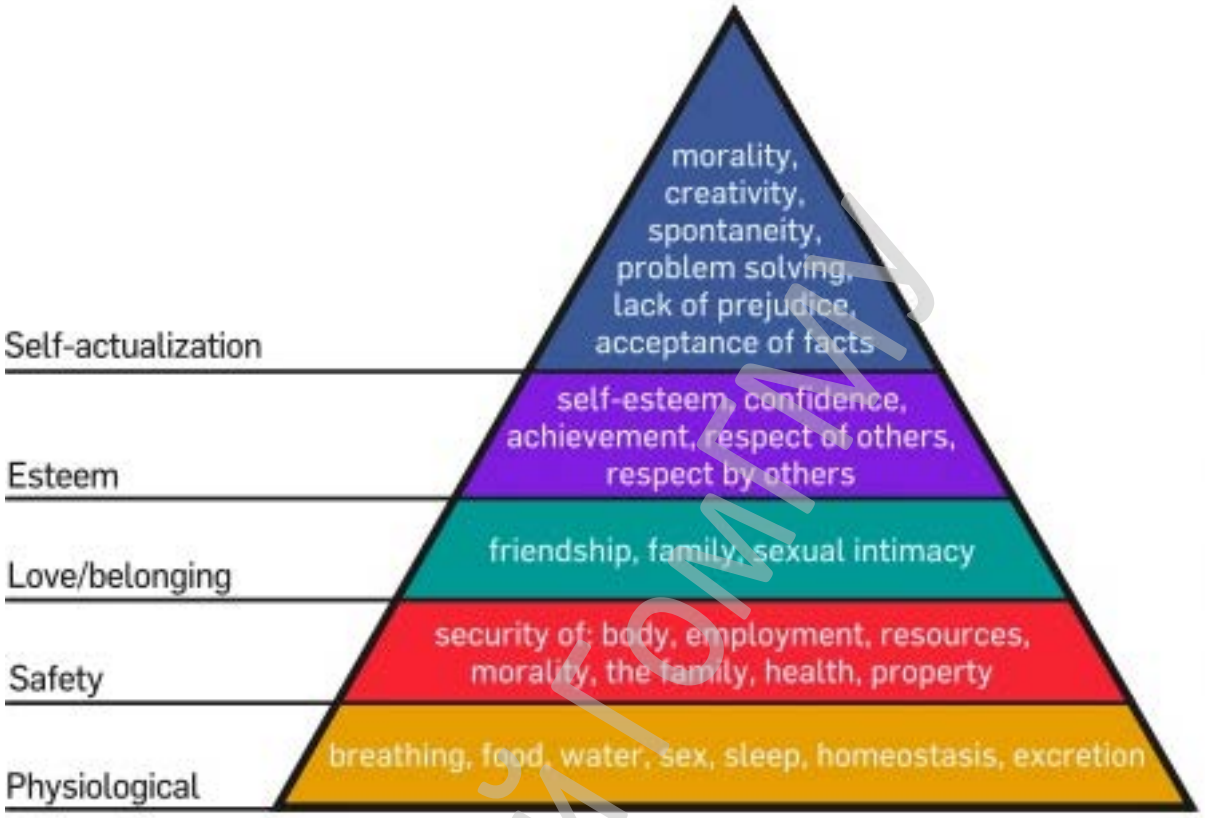


Figure 7.7 — Human motives (from slideplayer.com)

Biological motives are also called physiological motives, as they are essential for the survival of the organism and pertain to both humans and animals. Such motives are triggered when there is imbalance in the body as it always tends to maintain a state of equilibrium — homeostasis — in many of its internal physiological processes. Biological motives include*:* hunger, thirst, sleep, avoidance of pain, sex motive, maternal drive. Excitation for realization of parental, defensive, research instincts, reflexes of freedom etc.

Social motives are specific only to human beings. These are called social motives, because they are learnt in social groups as a result of interaction with the family and society. That is why their strength differs from one individual to another. Some of common social motives are: achievement motive, aggressive motive, power motive, friendship, patriotism.

Pathologic motives can appear due to diseases, bad habits, drug abuse. For example, diabetes can cause excessive thirst, frequent consumption of alcohol — alcohol addiction. Even single consumption of some narcotic drugs may create conditions for the development of related pathologic motives.

One of the main theories offered for the explanation of the mechanisms of the development of motives is the pacemaker theory by P. K. Anokhin. According to this theory, in the hypothalamus there are centers which are selectively sensitive to certain chemical substances and complexes of impulses from sensory receptors. Excitation from these hypothalamic centers is transferred to the reticular structures which selectively activate certain zones of the limbic systems and cerebral cortex. As a result, subjective realization and evaluation of needs aimed at purpose-directing actions are formed. According to Anokhin`s theory, motivation is an integrative state of the brain providing an adequate choice of orientation of an organism towards a behavioral reaction. The presence of the motivational centers in the hypothalamus was proved by an experience of stimulation of these centers through the implanted electrodes. For example, stimulation of the lateral nucleus of the hypothalamus results in food-procuring behavior and excessive eating of food by an animal. Stimulation of the ventromedial nucleus causes aphagia. The centers whose stimulation causes sexual behavior and aggression are located in the hypothalamus. Undoubtedly, the level of hormones in the blood plays a pivotal role in activation of the hypothalamic centers and formation of motives. For example, the hormone glucagon inhibits the motive of hunger, introduction of some sexual hormones (androgens) contribute to sexual arousal in females.

Motives are the leading factor in the formation of emotions.

Emotions

Emotions appear as a result of a specific state of the mental sphere and are forms of a complete behavioral reaction, involving many physiological systems and caused by certain motives, needs of an organism, and level of their possible satisfaction. Subjectivity of emotions is shown in experience by the person of its attitude to the surrounding reality.

Emotions are reflex reactions of an organism to external and internal stimulations which are characterized by strongly expressed subjectivity and include almost all kinds of sensitivity.

Emotions have no biological and physiological value if the organism has sufficient information to satisfy its desires and basic needs. Needs and situations causing an individual emotional reaction considerably vary (Figure 7.8). A person with limited needs gives emotional reactions more rarely in comparison with people with more sophisticated and diverse needs, for example, needs associated with their social status in the society.

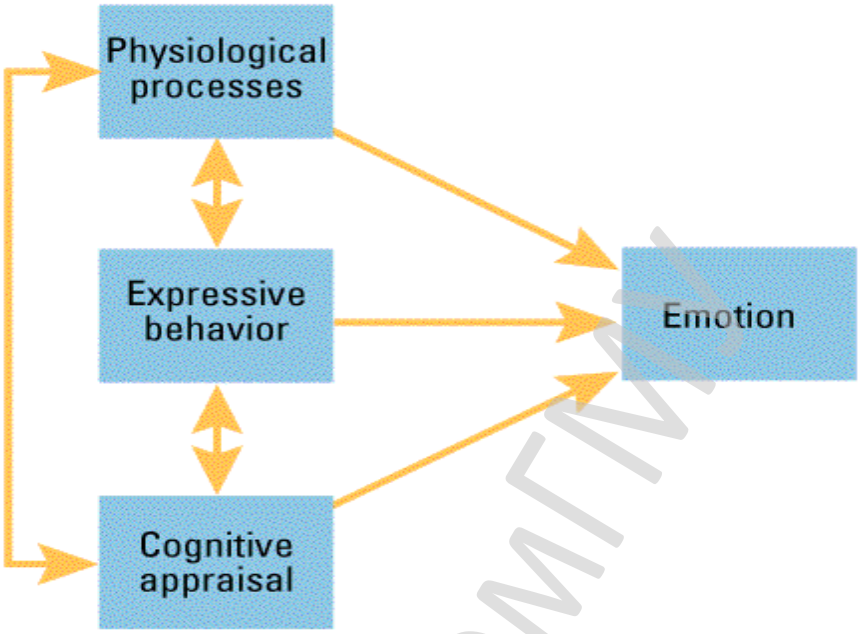


Figure 7.8 — Components of emotions (from studylib.net)

Classification of emotions

1) By the direction of the reactions, emotions are subdivided into:

- positive;
- negative.

Positive subjective experience and emotions (joy, pleasure) are shown in the form of subjectively pleasant sensations due to satisfaction of needs; negative — in the form of unpleasant experience caused by dissatisfaction of needs. The examples of such emotions are: melancholy, anger, disgust, fault, fear, shame.

2) By the character of manifestation, emotions can be:

- sthenic;
- asthenic.

Sthenic emotions are characterized by the improvement of the state of health, vitality, mental activity and self-esteem. All positive and some negative emotions (fury, anger) are related to this type of emotions. Somatovegetative displays of sthenic emotions are mostly often connected with the excitation of the sympathetic department of the vegetative nervous system. Adrenaline is released into the blood, the pulse becomes frequent, the blood pressure and gas exchange increase, bronchi are extended. Emotional excitation can instantly mobilize body reserves and thus provide the actions directed on overcoming of difficulties. It is one of the displays of the biological importance of emotions. In some conditions, for example, preceding stroke, strong emotions (even pleasure) can be dangerous.

Asthenic emotions are accompanied by depression, low mental activity, vitality and poor health state. They arise, in particular, when even at the maximal mobilization of forces there is an insufficiency of resources or time for the decision of behavioral problems. Asthenic emotions contribute to the development of diseases and lead to decrease of protective forces and functional reserves of an organism.

Structures which participate in the formation of emotions are the limbic system, reticular formation, amygdaloidal complex, hypothalamus and cerebral cortex. An important role in the formation of positive emotions belongs to *biologically active substances* similar to morphine: enkephalines and endorphins. The neuropeptide substance P participates in the formation of negative emotions, and it is the same mediator which is involved in transmitting pain impulses. The roles of the right and left hemispheres in the formation of emotions are different. The left hemisphere primarily processes positive emotions and the right hemisphere primarily processes negative emotions, take control over their recognition and external expression in mimicry.

7.5. Functional systems of behavior

Academician P. K. Anokhin developed the theory of functional systems (1935), which in many aspects anticipated a number of principles of cybernetics — the study of communication and control processes in living organisms and machines.

The structure of the functional systems of behavioral acts (Figure 7.9) consists of such components as: afferent synthesis, decision-making, formation of action result acceptor (creation of the ideal image), efferent synthesis (integration of somatic and autonomic excitations in a single behavioral act manifested externally), and program of action occurring in parallel, then action, evaluation of the result of the action, parameters of the result. The formation of functional systems goes along with the construction of the closed contours of regulation of vital processes and use of feedback providing control over the volume of the regulated parameter.

Afferent synthesis precedes each behavioral action and is the result of the integration of numerous neural ensembles of the CC and limbic system, and also their interaction with all the structures of the CNS. Afferent synthesis includes: dominant motivation (e. g., hunger), memory (including evolved biological knowledge and individual experience), situational afferention, and starting stimulus. The organizational beginning of afferent synthesis is dominating motivation. It suppresses the activity of other nervous centers and activates the neural structures obtaining information which is necessary for realization of adaptive behavior from memory. On the basis of afferent

synthesis the purpose of an outstanding behavioral act is defined and a decision leading to its performance is formed.

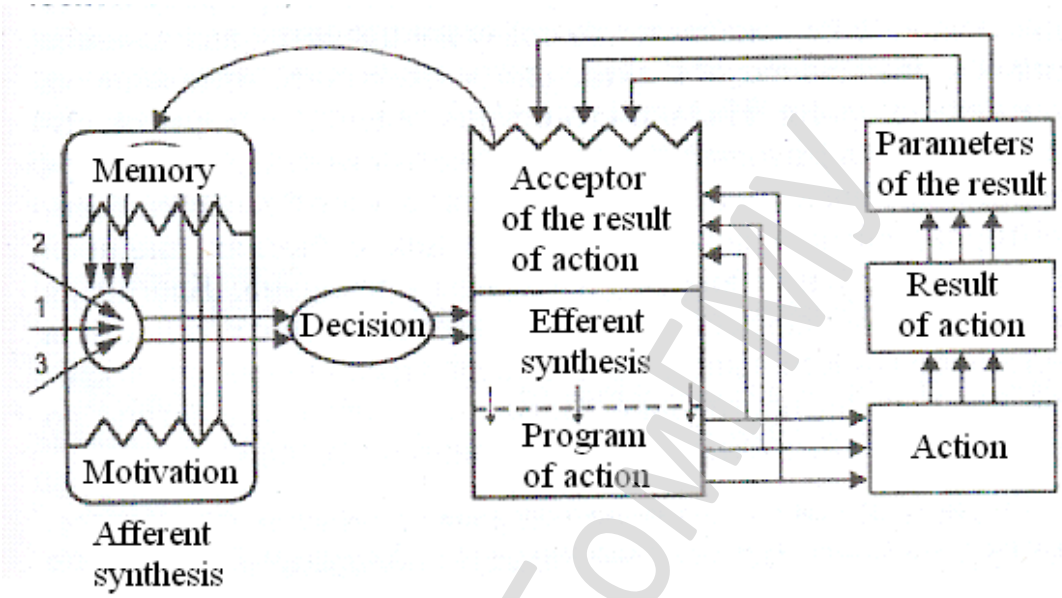


Figure 7.9 — Scheme of the functional system of a behavioral act (by Pokrovskiy V. M., Korotko G. F., 2000)

Notes: 1–3 impulse from extero-, intero- and proprioreceptors.

Decision-making directs activity of an organism towards the achievement of a concrete useful result and removes uncertainty in the choice of one of numerous possible variants of behavior. The major role in decision-making belongs to the frontal lobe.

A necessity to make a decision calls forth efferent synthesis, which mobilizes available memory resources and already formed motor programs. On the basis of efferent synthesis, a concrete program of actions aimed at achievement of a useful adaptive result is formed. In parallel with the program of actions, the acceptor of result of action, which represents a device of prognostication of parameters of a future result is formed. Representation is created about what sensations should be if a desirable result of action is achieved.

However, formation of the program and acceptor of result of action yet do not mean, that performance of the given behavioral act will begin at once, and it can be postponed for a long time. The beginning of its realization depends on situational afferention and starting stimulus. Situational afferention is impulses from the sensory receptors signaling about current events of an environment and the condition of the internal environment of an organism. Owing to situational afferention, an opportunity and expediency of a behavioral reaction in the given concrete conditions are defined. The signal to begin action aimed at realization of a behavioral act is the starting stimulus.

Example of formation of a behavioral act. The student on the basis of dominating motivation and afferent synthesis has a decision to purchase a new suit. This decision mobilizes extraction of information about the ways of achievement of the purpose and forms the concrete program of actions: getting of money, trip to concrete shops and etc. In parallel with the program of actions the acceptor of result of action — representation is formed about what should be a suit, its color, style, the sizes, sensations from a fabric. At presence of favorable situation afferention the beginning of performance of the behavioral act is initiated by starting stimulus, for example, data of delivery of good suits into the shop. The starting stimulus starts action. The student arrives to the shop and discovers that the suit by the price, style and other qualities corresponds to the parameters predicted by an acceptor of result of action.

If the programmed behavioral act is made and parameters of result of action coincide with predicted in an acceptor, the person has a positive emotion. The more difficult and less probable achievement of predicted result was, the stronger positive emotion arises at its achievement. If in the result of the behavioral act a positive result was not reached, there is a negative emotion. Thus, presence of functional system with its feedback, allowing to control the results of action, provides realization of the certain behavioral reactions and achievement of results useful for an organism. Emotions participate in an estimation of importance of achievement of results. At impossibility of achievement of predicted result arising negative emotion can cause long stress-reaction of an organism. In many people it can provoke development of arterial hypertension, myocardial infarction, ulceration of gastrointestinal tract, immunodeficient conditions.

7.6. Memory, its types and mechanisms

Memory is the ability of an individual to perceive, record, store, and reproduce information about past experience.

Memory as the basis of processes of education and thinking includes four closely connected processes: retention, storage, recognition, reproduction. During a human life-time memory becomes a depository of a huge quantity of information: within 60 years of active creative activity a person is capable to perceive 10^{13}–10^{16} bits of information using however no more than 5–10 %.

The types of memory are subdivided according to several attributes (figure 7.10):

1. By its origin:

- *individual memory:*
- *specific memory.*

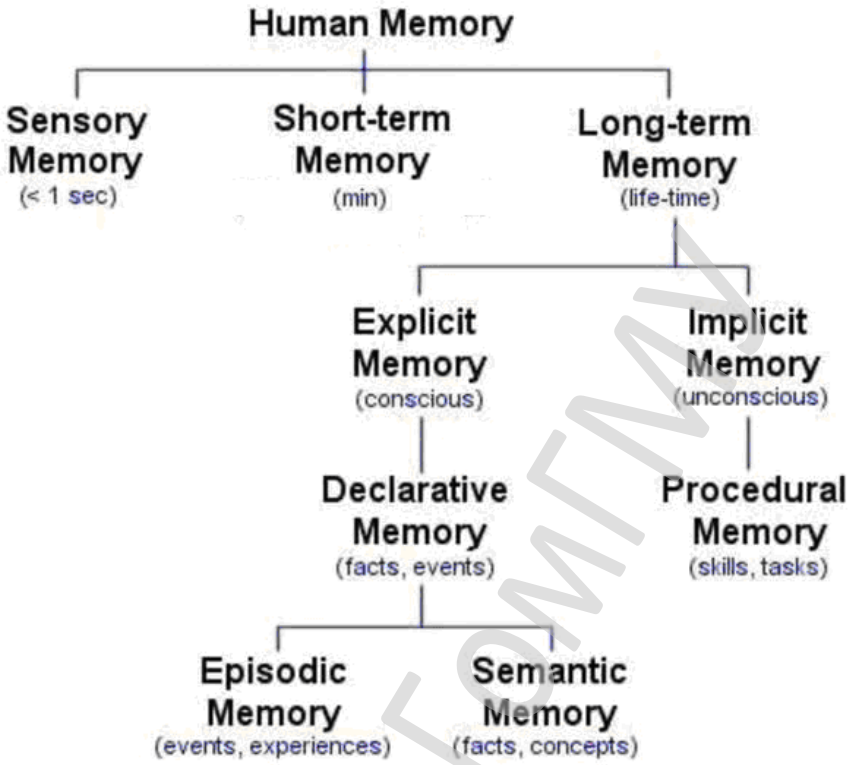


Figure 7.10– Types of memory

Individual memory retains data on personal life experience. *Specific (hereditary, genetic) memory* is present at birth and provides storage and transfer of experience which has been saved up by a species during its evolution. It provides formation of unconditioned reflexes and instincts and is based on the idea that common experiences of a species become incorporated into its genetic code.

2. By its psychological features:

- *declarative (verbal) memory;*
- *procedural memory;*

Declarative memory provides storage of information that is consciously declared by means of speech. Procedural memory is the memory of skills, particularly the use of objects or movements of the body, such as tying a shoelace, playing the guitar or riding a bike. These memories are typically acquired through repetition and practice and are composed of unconscious automatic sensorimotor behavioral acts that are so deeply embedded that we are no longer aware of them.

3. Our five senses make up the 5 types of sensory memory: *visual, auditory, tactile, olfactory, gustatory and also motor (impellent).* Basic amount of information (up to 80 %) gets into the brain from the visual system, and visual memory possesses a very high capacity.

4. By the duration of information preservation:

- *instantaneous (iconic, direct print, sensory image) memory;*
- *short-term memory;*
- *long-term memory.*

Instantaneous memory lasts about one second. It is the result of the properties of both peripheral (presented by sensory organs), and central (presented by the CC) ends of analyzers. At the level of the sensory organs this mechanism consists in the fact that activation of sensory receptors is kept for a short period of time (about 1 sec) after the action of a stimulus. In primary memory, containing huge amount of information, an image or event is kept for a short period of time. This property of the analyzers promotes conjoint perception of cinema- and television images.

A great amount of information by means of impulses going from sensory receptors reaches the brain. However, on the way to the higher centers of the CC most information is eliminated, and some of its blocks cannot pass in general. Probably, there are some levels of the system controlling selectivity of information passing to its structures, which ensures its storage and comprehension. At least, parts of this controlling system are the reticular formation, limbic areas and some departments of the CC. In the mechanisms of selective storage dominating motivation plays an important role. It directs attention of humans to perception of information which is important for realization of decisions and actions aimed at satisfaction of needs.

Attention is the state of active wakefulness which is characterized by orientation of mental activity on perception and analysis of a certain kind of events and information. Therefore, importance of attention concentration on a studied subject is obvious to its perception and storage. The orientation of attention can be defined at the level of subconsciousness (involuntary attention) and thanks to a will-power effort of a person. The stage of perception of information includes such events as:

1) active selection of new information;

2) definition of its novelty on the basis of comparison to the past experience;

3) emotional estimation of perceived information;

4) classification of information.

For the further preservation of the received information mechanisms of short-term memory should be activated.

Short-term memory is formed on the basis of instantaneous memory and provides preservation of a limited part of information perceived by the sensory organs. It may last from units of seconds up to 30 minutes and its capacity is small. For example, the number of objects an average human can hold in

memory (known as memory span) is between 5 and 9. Short-term memory is supported owing to the presence of impulses circulating in the circuits of neurons. Due to the electrochemical transfer of impulses across synapse gaps to receptors, the communicative strength of certain circuits of neurons in the brain is reinforced. One of the major evidences of the electrophysiological nature of short-term memory is the presence of the phenomenon of retrograde amnesia after brain concussion, contusion. Retrograde amnesia is a form of memory loss that affects memory about past events or experience (within the limits of 30 min) due to a traumatic brain injury or onset of a disease. Retrograde amnesia is caused by electrical or mechanical damage to the memory-storage areas of the brain in various brain regions which leads to terminated circulation of excitation in the circuits of neurons. Repeated rhythmic arrivals of impulses to the same neurons are requisite for conversion of short-term memory to long-term memory.

Long-term memory is intended for long-term storage and reproduction of information (Figure 7.11). Transition of short-term memory into long-term is named *memory consolidation*. Memory consolidation occurs on the basis of the circulation of impulses through the CC, hippocampus, mamillary bodies, and thalamus. This closed pathway is called the corticohippocampal circuit. The circulation of impulses creates conditions for better transfer of excitation in synapses and synthesis of specific proteins (in particular, protein S-100 and cholinoreceptic protein), selectively changing the excitability of neurons and properties of their membranes, causing appearance of new processes and synaptic communications among neurons. Thus, morphofunctional and biochemical mechanisms are the basis for long-term memory. They provide the process of retaining of information in the engrams of memory — structural and functional associations of neurons in various areas of the brain whose activation causes certain ideas, emotional experience, images. It is revealed that administration of a number of biologically active substances (adrenocorticotropic hormone, intermedin, vasopressin) noticeably improves memory storage. Memory storage occurs more quickly if information has a vital value or if it often repeats.

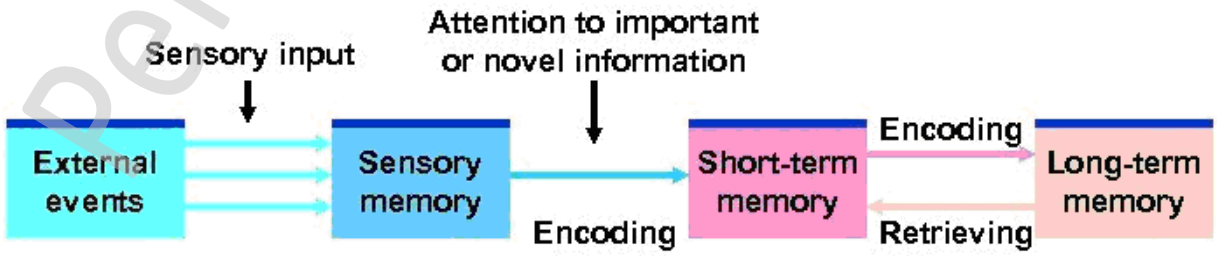


Figure 7.11 – Simplified memory model (from studylib.net)

Alongside with the processes of perception, processing, storing and retaining of information an important role in the mechanisms of memory belongs to the processes of reproduction of information.

Reproduction consists in extraction (reading) of information from systems or blocks of memory. It, as well as storage, can be voluntary and involuntary. Involuntary reproduction occurs unintentionally. It can be persuasive and can be caused by events linked to information stored in memory.

Owing to voluntary reproduction there is selective extraction of certain information from memory. It demands activation of attention and in some cases — significant efforts. Reproduction is broken the earliest in various brain lesions.

Not everything that is perceived, experienced or done by a person is kept in memory, as a significant part of received information after some time is forgotten. Forgetting is the impossibility to recognize, remember something or erroneous recognition, anamnesis. Forgetting can be caused by different factors connected with negative influences of stimuli operating directly after learning (the phenomenon of retroactive inhibition, depression of memory). The process of forgetting appreciably depends on the biological value of perceived information, the kind and character of memory. Forgetting in some cases can have a positive character, for example, memory of negative signals, unpleasant events.

Under favorable conditions previously forgotten information can be reproduced and can become accessible for consciousness.

7.7. Consciousness

Consciousness is a set of mental processes of human awareness of internal or external existence. Consciousness is the highest form of reflection of reality characteristic only for humans.

Consciousness develops on the basis of interaction of peoples, life experience and is connected with speech. Consciousness makes it possible to transfer knowledge to other people by means of language. Owing to this the continuity of experience and better knowledge about one`s environment is provided, the opportunity for active adaptation to a changing environment, manufacture of products and subjects for maintenance of life is created.

At every moment of time, conscious processes in the zone of optimal cortical activity coexist with unconscious activity.

The subconscious category includes automated unconscious skills and forms of behaviour. In the course of long evolution, the subconscious mind was developed as a means of protecting consciousness from unnecessary work and mental overload. Conservatism is one of the characteristics of consciousness.

The second group of the unconscious forms of brain activity consists of the mechanisms of creativity, the formation of hypotheses, guesses, assumptions, creative insights (intuition), and is called **superconsciousness.** This is the stage of initial creativity.

The highest form of consciousness is *abstract thinking*, which makes it possible for humans with one another and to realize their ideas. Consciousness also includes forms of concrete-picturesque thinking: sensations, perceptions, representations, and feelings connected with motives and emotions.

All the structures of the central nervous system participate in the formation of consciousness at the leading part of the CC and nearest subcortical formations. Activating influences of the reticular formation on the CC have a great importance. Consciousness is possible only for human beings in an awake condition and in the presence of a complex of continuously varying excited and inhibited neural ensembles. Consciousness is lost in deep narcosis, oxygen or glucose deprivation, excessive excitation of the nervous system (epileptic attack).

The attributes of consciousness are: presence of sensations, an opportunity of speech or sign contact to other people, presence of orientation in environment and time, self-estimation and self-identification.

To estimate the level of consciousness, the following factors should be taken into account:

1) presence of attention and ability to concentrate on various phenomena;
2) possibility to predict results of an action, ability to make prediction;
3) presence of ethical values;
4) memory, emotions, motives.

The presence of consciousness is an obligatory attribute of wakefulness.

7.8. Thinking

Thinking is the maximum level of human knowledge, process of reflection of the surrounding real world in the brain based on two essentially different psycho- physiological mechanisms: formation and continuous increase of the number of concepts, representations and making of new judgements and conclusions. Thinking allows to receive knowledge about objects, properties, and attitudes of the surrounding world which cannot be directly perceived by means of the first signal system. Forms and laws of thinking are the subject for the study of logic, and psycho-physiological mechanisms, accordingly, — for psychology and physiology.

Human thinking is closely connected with the second signal system. Two processes are the basis for thinking: transformation of thoughts into speech (written or oral) and extraction of thoughts (contents) from its certain verbal form. The thought (idea) is a form of the most complicated generalized abstracted reflection of reality caused by some motives; it is a specific process of integration of certain representations and concepts in concrete conditions of social development. Therefore, the thought as an element of higher nervous activity represents the language result of processing of information based on individual socio-historical development.

Thus, thinking is based on our sensory experience and knowledge accumulated in the process of our past experience. It is divided into imaginative and abstract.

Imaginative thinking is the operation of information obtained using the first signal system, stored in memory sensations, perceptions, and representations. Such thinking is important for various types of human activity: work, sports. It is the basis of a visual teaching method that is necessary for creative imagination of artists, musicians, etc. This type of thinking is common for humans and higher animals. However, in humans, it becomes more complex.

Abstract (word-logical) thinking is a form of higher nervous activity peculiar only to human, which is based on the operation of the system of speech signals – audible, visible, or not externally manifested. In the process of abstract thinking, concepts, judgments, and conclusions are used. They show generalization of properties, objects, and phenomena. They are used for intellectual activity – a chain of sequential, logically connected processes that provide the reflection of the surrounding world that is detached from direct perception.

Human creative thinking is linked to the formation of new concepts. The word as a signal of signals is a dynamical complex of concrete stimuli generalized in the concept expressed by the given word and having wide context with other words and other concepts. During life a person continuously fills up the contents of formed concepts by expanding contextual communications of words and word-combinations. Any learning process, as a rule, is associated with a widening of meaning of old concepts and formation of new concepts.

The verbal basis of thinking activity in many aspects defines the character of the development and formation of the processes of thinking in children and is manifested in the formation and perfection of the

nervous mechanism of maintenance of an individual system using logic laws of making conclusion and reasoning (inductive and deductive thinking). The first speech-motor time communications appear by the end of the first year of life; at the age of 9–10 months the word becomes a significant element and component of a complex stimulus, but yet does not represent an independent stimulus. Word interactions in consecutive complexes, in separate semantic phrases are observed by the end of the second year of life.

The depth of thinking activity defining intellectual features and human intellect in many respects is caused by the development of generalizing function of the word.

In formation of generalizing function of a word at the person they distinguish following stages of integrative function of a brain.

During the first stage of integration, the word replaces sensual perception of a certain subject (phenomenon, event). Any word represents a conditional sign of one concrete subject; and the generalizing function of the word uniting all identical subjects of this class is not yet expressed. For example, the word «doll» for a child means particularly the doll which they have, but not a doll in a shop window, in a day nursery, etc. This stage occurs by the end of the 1-st — beginning of the 2-nd year of life.

During the second stage, the word replaces several sensual images uniting similar subjects. The word «doll» for a child becomes a generalizing concept of various dolls which they see. Such understanding occurs by the end of the 2-nd year of life.

During the third stage, the word replaces a number of sensual images of heterogeneous subjects. Children are able to understand the generalizing sense of words: for example, the word «toy» means both a doll, a ball, and a cube, etc. This level of operating by words is reached during 3-rd year of life.

During the last, ***the fourth stage*** of the integrative function of the word, characterized by verbal generalizations of the second-third order, is formed during the 5-th year of life (children are able to understand that the word «thing» designates integrating words of the previous level of generalization, such as «toy», «meal», «book», «clothes», etc.).

The stages of the development of the integrative generalizing function of the word as a component of thinking are closely connected with the stages and periods of the development of cognitive abilities. The first initial stage occurs during the stage of the development of sensor-motor coordination (at the age of 1.5–2). The following period of preoperational

thinking (age of 2–7) is defined by the development of language: children start to use sensor-motor schemes of thinking. The third period is characterized by the development of coherent operations: the ability to apply logic reasoning with the use of concrete concepts (age of 7–11) develops. At the beginning of this period verbal thinking and activation of internal speech start to prevail in children. The last, the finishing stage of the development of cognitive abilities is the period of formation and realization of logic operations on the basis of the development of elements of abstract thinking, logic of reasoning and conclusions (11). At the age of 15–17 the formation of the neuro- and psycho-physiological mechanisms of cogitative activity basically comes to its end. Further development of mind and intelligence is reached due to quantitative changes, all the basic mechanisms defining the essence of human intellect, are already generated.

Thinking as a decision-making process requires the involvement of the temporal and frontal lobes of the ***cerebral cortex***. As the process of information storage is provided by the *parieto-occipital parts* of the cortex, and as the compliance of solutions to developed criteria — by the *frontal, temporal,* and *limbic parts of the cortex,* which provide inclusion of emotions in the assessment of the situation.

The main role in the organization of thinking belongs to the *associative zones* of the cortex of the hemispheres, which ensure the integration of multi-modal information coming from the primary projection zones, and compare it with information contained in memory. The most important role belongs to the associative zones of *the frontal lobes*. It consists in interpreting sensory stimuli depending on a specific situation, and also in selecting a goal and predicting events.

Human intelligence as a general property of mind and talents is commonly assessed by IQ scores – a parameter of intellectual development, determined by psychological IQ tests.

The studies proving correlations between the level of mental capabilities, depth of thinking processes and corresponding structures of the brain still remain unsuccessful. Even such an integrated and objective parameter as the weight of the brain, is not defining. So, many outstanding minds differed significantly in terms of the weight of the brain (I. S. Turgenev's brain weighed 2012 g, I. P. Pavlov — 1,653 g, D. I. Mendeleyev — 1,571 g, A. F. Koni — 1,100 g, A. France — 1,017).

Review questions

1. What are motives? How are they classified?

2. What are emotions? What is the role of emotions? How are they classified? Give their characteristics. What parts of the brain participate in the formation of emotions?

3. What are the parts of the functional system of behavior? Draw the scheme of the functional system of behavior, describe it and give examples of the formation of a behavioral act.

4. What is memory? What are the kinds of memory? What is the role of various departments of the brain in perception, storage, and reproduction of information? What are the mechanisms of short-term and long-term memory?

5. What is consciousness? What are the physiological bases of consciousness? What are the medical criteria for the evaluation of human consciousness?

6. What is thinking? What are the stages of the integrative function of the brain in the development of the generalizing function of the word in humans? What are the stages of the development of cognitive abilities in children?

Multiple Choice Questions
HIGHER NERVOUS ACTIVITY

1. Who discovered the reflex character of the activity of the higher departments of the brain?

Variants of answer:

a) K. M. Bykov.;
b) P. K. Anohin;
c) I. P. Pavlov, I. M. Sechenov;
d) G. F. Lang;
e) N. E. Vvedensky.

2. The basis for higher nervous activity is…

Variants of answer:

a) unconditioned reflexes;
b) conditioned reflexes;
c) conditioned and unconditioned reflexes;
d) vegetative reflexes;
e) alimentary reflexes.

3. A reflex which appears during evolution and is hereditarily fixed is called…

Variants of answer:

a) a dynamic stereotype;
b) an unconditioned reflex;
c) a conditioned reflex;
d) a reflex of the second or third order;
e) higher nervous activity.

4. A reflex which appears during ontogenesis under the condition of a numerous combination of an unconditioned stimulus with an indifferent signal is called…

Variants of answer:

a) a protective reflex;
b) a spinal reflex;
c) a conditioned reflex;
d) a vegetative reflex;
e) a reflex of the second or third order.

5. The total sum of the most complex unconditioned reflexes is called…

Variants of answer:

a) a dynamic stereotype;
b) an instinct;
c) higher nervous activity;
d) a reflex of the second or third order;
e) motivation.

6. Unconditioned reflexes are …

Variants of answer:

a) acquired, constant, individual;
b) acquired, temporary, individual;
c) innate, constant, specific;
d) innate, temporary, individual;
e) acquired, specific, temporary.

7. Conditioned reflexes are …

Variants of answer:

a) acquired, constant, individual;
b) acquired, temporary, individual;
c) innate, constant, specific;
d) innate, temporary, individual;
e) acquired, specific, temporary.

8. To develop a conditioned reflex, basically, it is necessary, that …

Variants of answer:

a) an unconditional stimulus should precede the action of a conditional one;
b) conditional and unconditional stimuli should act simultaneously;
c) a conditional stimulus should precede the action of an unconditional one;
d) only conditional stimuli should act;
e) only unconditional stimuli should act.

9. The participation of the cerebral cortex is necessary for the formation of…

Variants of answer:

a) instincts;
b) conditioned reflexes;
c) unconditioned reflexes;
d) vegetative unconditioned reflexes;
e) all the answers are correct.

10. The connection between the cortical centers of conditioned and unconditioned reflexes is called…

Variants of answer:

a) dominating connection;
b) time connection;
c) return connection;
d) direct connection;
e) positive connection.

11. The pupillary light reflex is …

Variants of answer:

a) conditioned;
b) unconditioned;
c) artificial;
d) vegetative;
e) positive.

12. The ocular-cardiac reflex is...

Variants of answer:

a) a reflex of the second order;
b) a conditioned reflex;
c) an unconditioned reflex;
d) a somatic reflex;
e) a positive reflex.

13. Pupillary narrowing under the effect of light is …

Variants of answer:

a) a conditioned reflex;
b) a reflex of the second order;
c) an unconditioned reflex;
d) a somatic reflex;
e) a positive reflex.

14. Salivary secretion in a person who is hungry caused by food images is…

Variants of answer:

a) an unconditioned reflex;
b) a reflex of the second order;
c) an artificial reflex;
d) a conditioned reflex;
e) a positive reflex.

15. The reflex of tachypnea in runners before the start is…

Variants of answer:

a) conditioned;
b) statokinetic;
c) unconditioned;
d) posture;
e) rhythmic.

16. Due to the conditioned reflex, blood pressure…

Variants of answer:

a) cannot change;
b) can change if the corresponding conditioned reflex develops;
c) always increases;
d) always decreases;
e) disappears.

17. A reflex which is formed in the combination of a new conditioned stimulus with a conditioned stimulus of the already developed reflex is…

Variants of answer:

a) a dynamic stereotype;
b) an instinct;
c) a conditioned reflex of the second order;
d) an orientation reflex;
e) a statokinetic reflex.

18. The congenital kind of inhibition which arises without preliminary development and can make both conditioned and unconditioned reflexes disappear is called…

Variants of answer:

a) internal;
b) external;
c) lateral;
d) reverse;
e) dorsal.

19. Inhibition which arises in the nerve centers of conditioned reflexes and demands preliminary development is…

Variants of answer:

a) differentiating inhibition;
b) protective inhibition;
c) reciprocal inhibition;

d) conditioned inhibition;
e) lateral inhibition.

20. Owing to which inhibition does a dog stop eating if an unknown person enters the room?

Variants of answer:
a) reciprocal;
b) external;
c) conditional brake;
d) differentiating;
e) lateral.

21 Exorbitant inhibition is called…

Variants of answer:
a) late inhibition;
b) differentiating inhibition;
c) a conditioned brake;
d) protective inhibition;
e) fading inhibition.

22. What is the role of «the fading brake»?

Variants of answer:
a) it allows to save power resources;
b) it allows to distinguish stimuli which are similar by their character;
c) it switches an organism to research the importance of stimuli;
d) it inhibits unnecessary reflexes;
e) all the answers are correct.

23. The inhibition of reflex activity due to the influence of a strong stimulus is called...

Variants of answer:
a) differentiating inhibition;
b) a conditioned brake;
c) late inhibition;
d) protective inhibition;
e) «the fading brake».

24. Conditioned inhibition is…

Variants of answer:
a) reciprocal, lateral;

b) fading, differentiating, conditional brake, late;
c) protective;
d) postsynaptic, presynaptic;
e) all the answers are correct.

25. Differentiating inhibition...
Variants of answer:
a) protects the nervous centers from excess of information;
b) allows to save power resources;
c) allows to distinguish stimuli which are close by character.
d) inhibits digestive reflexes;
e) all the answers are correct.

26. What kind of inhibition develops if in a combination with a conditional stimulus another conditional stimulus is added and this combination is not supported?
Variants of answer:
a) conditioned brake;
b) fading inhibition;
c) late inhibition;
d) differentiating inhibition;
e) protective inhibition.

27. What kind of inhibition appears in a dog if a food stimulus is always given one minute after ringing the bell?
Variants of answer:
a) the conditioned brake;
b) fading inhibition;
c) lagging inhibition;
d) differentiating inhibition;
e) protective inhibition.

28. What value for an organism do external and internal inhibition of conditioned reflexes have?
Variants of answer:
a) an organism is protected from superthreshold stimuli;
b) all the answers are correct;
c) they provide concentration on the most important activity;
d) the activity of an organism is adapted to varying conditions of environment;
e) allows to save power resources.

29. The system of conditioned reflexes which are carried out in a strictly certain sequence is called…

Variants of answer:

a) dynamic stereotyping;

b) an instinct;

c) a conditioned reflex of the fourth order;

d) rhythmic reflexes;

e) posture reflexes.

30. How is the ability to perceive and say words arising during social human life provided?

Variants of answer:

a) by means of instincts;

b) by means of the first signaling system;

c) by means of the second signaling system;

d) by means of dynamic stereotyping;

e) by means of motivation.

31. The left part of the brain dominates in the performance of the following functions…

Variants of answer:

a) regulation of the functions of the left half of the body;

b) analysis and synthesis of the signals of the first signaling system;

c) speech, writing, and calculation;

d) regulation of vegetative functions;

e) all the answers are correct.

32. The right part of the brain dominates in the performance of the following functions…

Variants of answer:

a) regulation of the functions of the right half of the body;

b) analysis and synthesis of the signals of the first signaling system;

c) speech, writing, and calculation;

d) regulation of vegetative functions;

e) all the answers are correct.

33. The most exact method for the determination of HNA types in animals and humans is…

Variants of answer:

a) observation;

b) psychological testing;
c) self-questionnaire;
d) conditioned reflexes;
e) radiotelemetry.

34. What types of higher nervous activity are distinguished by I. P. Pavlov?

Variants of answer:

a) introvert, extrovert;
b) choleric, sanguine, phlegmatic, melancholic;
c) strong, unbalanced, impatient; strong balanced, lobile; strong, balanced, inert; weak;
d) asthenic, hypersthenic, normosthenic;
e) all the answers are correct.

35. According to Hippocrates, which temperament does the person have if they have the ability to form conditioned reflexes quickly and strongly?

Variants of answer:

a) choleric;
b) melancholic;
c) phlegmatic;
d) sanguine;
e) extrovert.

36. According to Hippocrates` classification, which temperament does the strong unbalanced impatient type by I. P. Pavlov's classification correspond?

Variants of answer:

a) to phlegmatic;
b) to melancholic;
c) to sanguine person;
d) to choleric person;
e) to extrovert.

37. Which cerebral hemisphere and signaling system dominate in individuals of the «artistic type» by I. P. Pavlov?

Variants of answer:

a) the left cerebral hemisphere, first signaling system;
b) the right cerebral hemisphere, first signaling system;
c) the left cerebral hemisphere, second signaling system;
d) the right cerebral hemisphere, second signaling system;
e) the left cerebral hemisphere, first and second signaling systems.

38. Which cerebral hemisphere and signaling system dominate in individuals of the «intellectual type» by I. P. Pavlov?

Variants of answer:

a) the left cerebral hemisphere, first signaling system;

b) the right cerebral hemisphere, first signaling system;

c) the left cerebral hemisphere, second signaling system;

d) the right cerebral hemisphere, second signaling system.

e) the left cerebral hemisphere, first and second signaling systems.

39. Sleep is a sum of functional conditions of the CNS which…

Variants of answer:

a) is the decrease of conscious activity;

b) is the decrease of reaction on stimuli;

c) includes certain wave phases of electroencephalogram;

d) is distinguished from wakefulness and characterized by loss of consciousness.

e) all the answers are correct.

40. How does duration of sleep change with aging?

Variants of answer:

a) it increases;

b) it does not change;

c) it decreases;

d) it disappears;

e) at first it increases, then it decreases.

41. Which EEG rhythm is characteristic for active wakefulness?

Variants of answer:

a) alpha;

b) delta;

c) beta;

d) teta;

e) sigma.

42. Which EEG rhythm is characteristic for quiet wakefulness (for a person at rest whose eyes are closed)?

Variants of answer:

a) alpha;

b) delta;

c) beta;

d) teta;

e) sigma.

43. Which EEG rhythm is characteristic for deep sleep?

Variants of answer:

a) alpha;

b) delta;

c) beta;

d) teta;

e) sigma.

44. The biological value of the phase of fast sleep is…

Variants of answer:

a) activation of the plastic processes in the nervous system;

b) processing and keeping of information in long-term memory, restoration of mental processes;

c) increased sensitivity to external stimuli;

d) increased synthesis of DNA and RNA in an organism;

e) all the answers are correct.

45. During which phase of sleep are dreams observed?

Variants of answer:

a) phase of falling asleep;

b) phase of fast sleep;

c) dreams do not depend on the phase of sleep;

d) phase of superficial sleep;

e) phase of mild deep sleep.

46. Short-term memory is a kind of memory which…

Variants of answer:

a) keeps sensory information during milliseconds and seconds;

b) has a small volume of 7±2 units;

c) keeps nonverbal information for several days;

d) provides preservation of information for a long time (months, years);

e) all the answers are correct.

47. Long-term memory is a kind of memory which…

Variants of answer:

a) keeps sensory information during milliseconds and seconds;

b) has a small volume of 7±2 units;

c) keeps nonverbal information for several seconds and minutes;

d) provides long storage and reproduction of information;

e) all the answers are correct.

48. The delta waves are found during...

Variants of answer:

a) deep sleep;
b) REM sleep;
c) awake state;
d) stage A of orthodox sleep;
e) all the answers are correct.

49. Which statement about paradoxical sleep is true?

Variants of answer:

a) the delta waves are dominant;
b) the alpha waves are dominant;
c) paradoxical sleep is also known as non-REM sleep;
d) it has low amplitude, mixed frequency waves;
e) all the answers are correct.

50. Structures which directly participate in the formation of emotions are…

Variants of answer:

a) the structures of spinal cord (motoneurons and vegetative centers);
b) the limbic system and vegetative centers of spinal cord;
c) the structures of cerebellum and vestibular nuclei;
d) the hypothalamic structures, cerebral cortex, limbic system;
e) all the answers are correct.

CORRECT ANSWERS
HIGHER NERVOUS ACTIVITY

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	14	d	27	c	40	c
2	b	15	a	28	b	41	c
3	b	16	b	29	a	42	a
4	c	17	c	30	c	43	b
5	b	18	b	31	c	44	b
6	c	19	d	32	b	45	b
7	b	20	b	33	d	46	b
8	c	21	d	34	c	47	d
9	b	22	c	35	d	48	a
10	b	23	d	36	d	49	d
11	b	24	b	37	b	50	d
12	c	25	c	38	c		
13	c	26	a	39	e		

BASIC PHYSIOLOGIC CONSTANTS

Constants of the cardiovascular system	
Heart rate in adults	60–80 beats / min
Heart rate in newborns	135–140 beats /min
Stroke volume	65–70 mL
Cardiac output for a person at rest	4.5–5.0 L/min
Cardiac output for a person during physical exercise	up to 30 L/min
Duration of the cardiac cycle	0.75–1.0 sec
Arterial pressure: max (systolic)	110–139 mm Hg
Arterial pressure: min (diastolic)	60–89 mm Hg
Constants of the digestive system	
Amount of secreted saliva	1.5 l/ per day
Normal pH range for saliva	5.8–7.8
Amount of secreted gastric juice	2.0–2.5 l/ per day
Normal pH range for gastric juice	1.5–1.8
Normal pH range for the juice of the small intestine	5.05–7.07
Amount of secreted pancreatic juice	1.5–2.0 l/ per day
Normal pH range for pancreatic juice	7.8–8.4
Amount of secreted bile	500–1,500 mL/ per day
Constants of metabolism and energy	
Daily consumption of proteins	80–100 g or 1g per kg of body weght (of them 30 % are of animal origin)
Daily consumption of fats	70–125 g
Daily consumption of carbohydrates	400–450 g
Water content in adults	60–65 %;
Water content in newborns	75–80 %
Water formation during oxidation:	
100 g of carbohydrates	55 mL
100 g of proteins	41 mL
100 fats	107 mL
Daily water balance	nearly 2.5 L
Caloric value:	
1 g of fats	39.0 kilojoule (9.0 kcal)
1 g of carbohydrates	17.1 kilojoule (4.1 kcal)
1 g of proteins	17.1 kilojoule (4.1 kcal)

Respiratory quotinent during oxidation:	
Carbohydrates	1.0
Fats	0.7
Proteins	0.8
Daily basal metabolism in adults	1 kcal/kg per hour
Daily basal metabolism in males	7,100 kilojoule (1,700 kcal)
Daily basal metabolism in females	6,400 kilojoule (1,500 kcal)
Constants of thermoregulation	
Axillary temperature	35.1–36.9 °C
Ioral temperature	36.4–37.2 °C
Rectal temperature	36.8–37.6 °C
Maximal daily temperature fluctuations	at 4–6 p.m.
Minimal daily temperature fluctuations	at 3–4 a.m.
Constants of excretion	
Effective filtration pressure	20 mm Hg
Renal blood flow	1,200 mL/minute
Renal plasma flow	650 mL/minute
Amount of primary urine	150–170 L/ per day
Amount of final urine	1.5 L/ per day
Relative density of urine	11.003-1.005 kg/L to 1.020-1.030 kg/L
Normal color of urine	from light yellow to amber or stramineous
Transparence	transparent
Normal pH range for urine	5.0–7.0
Constants of the sensory systems	
Sound frequencies heard by humans	16–20,000 Hz
The nearest point of clear vision	10 cm
Normal visual acuity	1.0 and higher

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Учебное издание

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ФИЗИОЛОГИЯ ЧЕЛОВЕКА
(на английском языке)

Учебное пособие
для студентов медицинских университетов,
обучающихся на английском языке

В двух частях

Часть 2

Редактор ***Т. М. Кожемякина***
Компьютерная верстка ***Ж. И. Цырыкова***

Подписано в печать 09.02.2021.
Формат 60×84 1/8. Бумага офсетная 80 г/м2. Гарнитура «Calibri».
Усл. печ. л. 36,74. Уч.-изд. л. 40,16. Тираж 100 экз. Заказ № 50.

Издатель и полиграфическое исполнение:
учреждение образования «Гомельский государственный медицинский университет».
Свидетельство о государственной регистрации издателя,
изготовителя, распространителя печатных изданий № 1/46 от 03.10.2013.
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