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 1

HUMAN PHYSIOLOGY

In two parts
Part 1

Гомель
ГомГМУ
2021

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

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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. 1. — 306 с.
ISBN 978-985-588-210-8

Первая часть учебного пособия содержит краткую информацию об истории развития физиологии, предмете и методах физиологических исследований. Освещены вопросы системы крови, возбудимых тканей, нервной и гуморальной регуляции физиологических функций, физиологии дыхания. 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 978-985-588-210-8 (Ч. 1)
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

FOREWORD

The present textbook contains educational material on Normal Physiology for English-medium students. The textbook has been written according to the State Educational Standard and the existing Model Program on Normal Physiology for Students of Higher Medical Educational Institutions specializing in "General Medicine."

The number of students studying at higher educational institutions of the Republic of Belarus in both Russian and English mediums increases every year. However, at the same time, the use of available high-quality foreign (English-language) physiology textbooks as basic in the educational process is complicated due to a great number of such textbooks, the presence of elements of pathological physiology, and some differences in their content. Therefore, while planning to write the textbook, the authors aimed to facilitate the mastering of the theoretical foundations of human physiology necessary for the study of clinical subjects and future medical career by English-medium students.

The textbook presents a brief history of the development of physiology in Russia and Belarus, describes the relevance of the study of this discipline by future doctors, the peculiarities of the functioning of the human organs and systems in detail, which is sequentially covered in 13 chapters with sections and subsections in two parts of the textbook. Theoretical descriptions of all the sections are supplemented by relevant illustrated material, including color pictures, and tables, which promotes the visibility of the presented questions. Each topic concludes with tests, which makes it possible to check the understanding of the material studied by students. At the end of the chapters, key questions for self-control of knowledge are suggested. The textbook enlists the basic constants of the physiological systems according to the International System of Physical Units (SI).

The textbook has medical orientation, meets the educational and methodological requirements of teaching, takes into account modern views and scientific approaches to normal physiology, as the most important source in understanding the functioning of all the organs and systems. The authors would be very grateful to everyone who would find it possible to give critical comments about the proposed textbook, which will be perceived as a willingness to help improve it in the subsequent reprinting. We consider it necessary to express our sincere gratitude to the reviewers for the thorough work they have done reviewing this textbook aimed at its improvement.

UNIT 1
SUBJECT AND PROBLEMS OF PHYSIOLOGY. BRIEF HISTORY. VALUE OF PHYSIOLOGY IN MEDICAL EDUCATION

1.1. Subject and problems of physiology. Branches of modern physiology

The main subject of **physiology** is the functioning of living organisms, their separate systems, organs, tissues, cells. Physiology studies the nature and development of the functions of living organisms, evolution within their individual development, mechanisms of their interaction with the environment and the functioning of living organisms in various conditions.

Physiology is a biological discipline; it is closely connected with and based on the headway of biology, anatomy, and histology. Physiology is based on the achievements and methods of various sciences, mainly biochemistry, biophysics, mathematics, cybernetics, and philosophy. Physiology is the basis for theoretical medical disciplines: pathological physiology, pharmacology, and together with these disciplines it creates the theoretical basis for clinical medicine.

Branches of modern physiology. Physiology is divided into interrelated branches: general, special, and applied physiology.

General physiology focuses on scientific data describing general aspects of the vital activities: metabolism, mechanisms of regulation, properties of biological membranes, separate cells, and tissues, as well as general laws of the reactions of the organism and its structures to stimulation, excitation, inhibition. This branch of physiology includes age, comparative, evolutionary physiology.

Special physiology studies properties of separate tissues (muscular, nervous, glandular, connective), organs (heart, liver, etc.), systems (circulatory, respiratory, digestive).

Applied physiology studies the human body functions in particular working conditions (aviation, space physiology) or in a particular climatic environment.

Physiology is divided into **normal** and **pathological**. Pathological physiology studies vital activities of sick individuals, the nature, course, and extent of diseases, and develops methods of experimental therapy.

1.2. Methods of investigation in physiology

Physiology is an experimental science, its basic method is experiment, which makes it possible to study the main mechanisms of the functions of organs, cells, systems, the mechanisms of regulation and maintenance of the vital activities.

All experiments are divided into *acute* and *chronic*.

Acute experiments are performed without aseptic or antiseptic rules and are lethal for animals.

Chronic experiments are performed over a long period of time (may last for years) with aseptic or antiseptic rules and are not lethal for animals, e. g., the fistula experiment.

Each separate case involves a particular method depending on the aims of research:

a) Suppressing of functions till their complete termination. For example, suppressing of the functions of the thyroid gland.

b) Stimulation of functions with the help of physical (electric current, pressure, temperature, etc.) and chemical agents (hormones, drugs, etc.).

c) Registration of electrical potentials (ECG, EEG).

d) Modeling.

Optional methods of physiology.

1. Transplantation:

a) Autotransplantation —transplantation of tissue from one region into another within the body of the same individual.

b) Homotransplantation — transplantation of an organ or tissue from one induvidual to another.

c) Allotransplantation — transplantation of an organ or tissue in twins.

d) Heterotransplantation — transplantation of an organ or tissue from one species of animals to another.

2. Deinnervation.

a) Surgical dissection.

b) Drug action.

3. Method of vascular anastomoses (used in organ dysfunction).
4. Radiotelemetry.
5. Catheterization.
6. Method of radioactive atoms.

Physiology has had several stages of its development: *empiric, anatomic-functional, functional*. All the stages of the study of physiological processes have included *analytical* and *synthetic* directions.

The **analytical** direction is focused on the study of particular processes in organs, tissues or cells as independent. This direction gives complex information about the mechanisms of the given process

This approach in physiology was replaced by **the synthetic one,** which was proposed by Academician I.P. Pavlov. That period of experimental physiology was characterized by the tendency to study the body functions in natural conditions considering numerous factors of the organism`s interaction with the environment.

1.3. General concepts about the structure and physiological properties of the organism

The human organism is an independent structural functional unit of inorganic and organic nature which closely interacts with the environment. The organism has a *set of attributes and properties characterizing and determining any living system*: ***metabolism, growth, development, reproduction, variability, heredity, reactivity, reliability***. The reliability of the body functions is ensured by the reserve structures, plasticity of processes, ability to adaptation, compensation of affected functions, duplication, interchangeability of elements, ability to regeneration.

The human organism has the following levels of organization: ***cellular, tissular, organ, system, and whole organism levels***. The structures of the human organism are in strict hierarchical relations directed to reach the optimal interaction of the organism and the environment. Any living organism is an open thermodynamic system exchanging energy and information with the environment. The environment provides the organism with nutrients, light, thermal energy, and influences its sensory systems. However, the functions of a healthy organism are optimal till some external impacts or its own internal processes do not hinder the stability of homeostasis (constancy of the organism`s internal environment), optimal conditions of metabolism, physical and chemical constants of the organism (Figure 1.1).

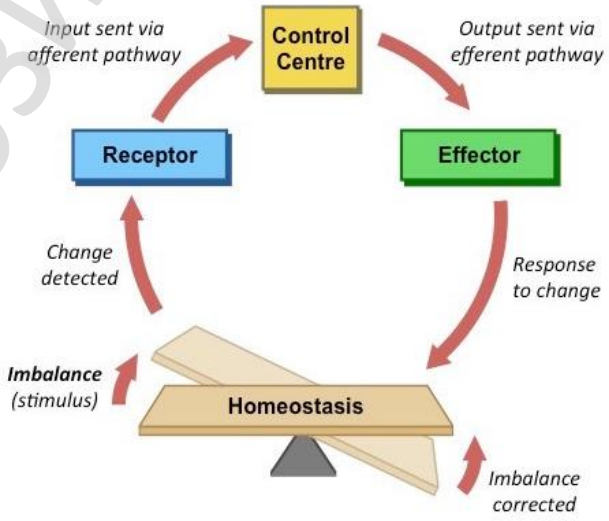


Figure 1.1 — Homeostatic control system (from picgalleria.com)

1.4. General principles of physiological regulation of the body functions

Nervous and humoral regulation.

Physiological regulation is the control over the functions of the organism in order to adapt it to the environment. The regulation of the body functions is the main source of the organism`s stable environment and its adaptation to changing conditions of an existing environment. It is performed by the principle of self-regulation by means of the formation of functional systems.

There are two main kinds of regulation: humoral and nervous.

Humoral regulation is performed through the body liquids (blood, lymph, intercellular and cerebrospinal fluids) with the help of various *biologically active substances* secreted by specialized cells, tissues or organs. This kind of regulation can be carried out at the level of organ structures — local self-regulation, or to provide generalization effects through the system of hormonal regulation. Blood accepts chemical substances formed in specialized tissues. These substances can act either locally or distantly. Hormones *regulate metabolism and stimulate the morpho-formation processes, differentiation, growth, metamorphosis of cells, etc.*

The humoral way of the regulation is rather slow, the speed of responses depends on the period of the formation and secretion of hormones, their penetration into the blood and lymph, velocity of the bloodstream. The period of the action of hormones depends on the speed of their destruction in the organism. In various body cells including the brain there are neuropeptides, which determine the body functions and regulate hormone secretion.

Nervous regulation is carried out via the nervous system, it is based on data processed by neurons and their transmission along the nerves. It has the following features (Table 1.1):

- high speed of action;
- precise connections;
- high specificity — only a definite number of components are needed for a certain reaction.

Table 1.1 — Characteristics of nervous and humoral regulation

Neural regulation	**Humoral regulation**
Information transfer through nerve fibers	Information transfer through fluids (blood0
Fast	Slow
Short time period	Long time period
Depends of nerve fibers and synapses	Depends of blood flow and transport proteins

The process of evolution led to the integration of the nervous and humoral mechanisms of physiological regulation.

The division of the regulatory mechanisms into nervous and humoral is conditional, as within the organism these mechanisms are inseparable.

1.5. Reflexes as a principle of physiological regulation of the body functions

The basis of the activity of the central nervous system (CNS) is the reflex principle. ***Reflexes*** are an organism`s natural reactions to changes of external and internal environments. These reactions are determined by the *participation of the nervous system* in the formation of responses to the stimulation of receptors. Reflexes set up the balance of the activity of organs within the system, the system within the organism, the organism in its interrelations with the environment. The structural basis of reflexes is the ***reflex arc***. It includes the following:

1) sensory receptors receiving stimulation from external and internal environments;

2) afferent (sensitive) nerve fibers;

3) nerve centres;

4) motor (efferent) nerve conductors;

5) effector (executing organs).

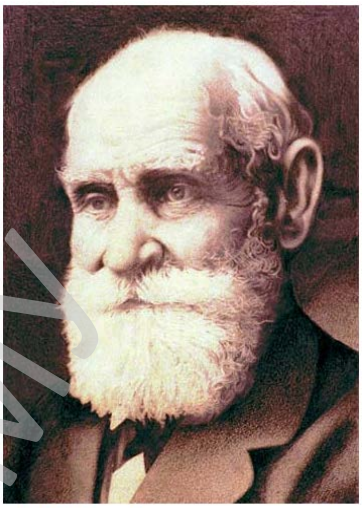
An obligatory element of all reflexes is the feedback between the CNS and executing organs.

1.6. Brief history of physiology

M.V. Lomonosov

In Russia physiology started its development after the Russian Academy of Sciences was established in 1724 in Saint-Petersburg. In 1738 physiology became a discipline at Saint-Petersburg University, in 1776 the Physiology Departments were established at Moscow University and Saint-Petersburg Medical-Surgical Academy. A great contribution to the development of physiology was brought by M.V. Lomonosov, who formulated the law of preservation of matter and energy, developed the hypothesis of three-component color vision, the theory of heat formation in living organisms, gave the classification of gustatory sensations.

The following Russian scientists gave great contribution to the development of physiology: I. P. Pavlov, I. M. Sechenov, A. I. Babuhin, F. V. Ovsyannikov, V. J. Danilevsky. The physiology of higher nervous activity received its fundamental development in the scientific experiments of I. P. Pavlov. The result of his work was the most important contribution to the physiology of the cardiovascular system, higher nervous activity, digestion (in 1904 he was awarded the Nobel Prize for this work). I. P. Pavlov discovered conditioned reflexes.



I.P. Pavlov

I. M. Sechenov investigated the gas composition of blood, discovered the phenomenon of summation and inhibition in the CNS.

I. M. Sechenov

The development of physiology was the most rapid in the 20th century. W.Kennon developed the doctrine of homeostasis, created the basis of cybernetics in biology. C. Sherrington was the first to explain the concepts of synapses and the receptor field. R. Magnus described the mechanisms of posture maintenance.

The development of physiology in Belarus is connected with the foundation of Belarussian University in 1922, Republican Academy of Sciences in 1929 and the organization of the Belarussian Society of Physiologists, Biochemists and Pharmacologists in 1936 headed by I. A. Vetokhin in 1936–1956. In 1937 I. A. Vetokhin headed the Institute of Experimental Physiology of the Academy of Sciences of Belarus; the physiology of blood circulation, digestion, and conditioned reflexes were investigated there.

I. A. Bulygin made important contribution to the development of physiology in Belarus. From 1953 to 1984 he headed the Institute of Physiology of the Academy of Sciences of Belarus. The basic directions of the activities of this institute included the study of the laws and mechanisms of interoreceptive exchange reflexes (1959), central and circular neurohumoral mechanisms of visceral reflex reactions (1970), new principles of the organization of the vegetative ganglia (1976), etc. From 1985 to 2005 the Institute was headed by Academician V. N. Gurin, whose main research was connected with the central mechanisms of thermoregulation and lipid metabolism.

Great research work in various directions of physiology is performed at the medical universities of Vitebsk, Grodno, Gomel, and Minsk.

1.7. Value of physiology in medical education

1. Physiology gives fundamental scientific knowledge about the vital functions of a healthy human organism.

2. Physiology sets up the norm of the body functions. The norm is a quantitative indicator of the intensity of the system functioning based on the investigation of statistically significant groups. The norm in medicine is of a great diagnostic and predictive value. Deviations from the norm help to determine the diagnosis, severity of a disease, helps to monitor the effectiveness of treatment, to prognose the outcomes of diseases and to correct the treatment.

3. Physiology is the basis for pharmacology. It studies the mechanisms of the action of drugs, the ways of drug biotransformation in the organism, the mechanisms of metabolite excretion from the organism.

4. Practically all the methods of functional examinations were created and used for the first time during physiological experiments.

5. Physiological data were used for creation of artificial organs (heart, kidney, systems of lung ventilation, etc.).

Review questions

1. What is the main subject of physiology? Name the branches of physiology and describe them.

2. List the methods of investigation in physiology. Decribe acute and chronic experiments.

3. Name the properties characterizing all living systems. What are the levels of organization of the human organism? Give the definition of "homeostasis".

4. Give the comparative characteristics of the nervous and humoral mechanisms of physiological regulation of the body functions. Give the definition of "reflex" and name the components of the reflex arch.

5. What are key steps in the development of physiology in Russia and Belarus. What is the value of the work of Academician I. P. Pavlov in the development of physiology?

6. Explain the value of physiology in medical education.

UNIT 2
PHYSIOLOGY OF BLOOD

2.1. Composition, amount, and properties of blood

2.1.1. The concept of the blood system

Blood along with interstitial fluid and lymph is an important component of an organism`s internal environment, the relative constancy of which, including physical and chemical parameters (pH, osmotic pressure, temperature, etc.), is a prerequisite for the organism`s vital activity. The changes of the physical and chemical properties of blood, which are important mechanisms in the pathogenesis of many diseases, are used for their diagnostics, assessment of the efficacy of treatment and prognosis.

The blood system, as proposed by G. F. Lang (1939), includes:

1. *Blood* (in the blood vessels).

2. *Organs of hemopoiesis* (red bone marrow, lymph nodes, spleen, thymus gland).

3. *Organs of blood destruction* (liver, bone marrow, spleen).

4. *Neurohumoral apparatus*.

The main site in the human body where blood cells are manufactured is *the red bone marrow*. Also, here the destruction of cells (erythrocytes), iron recycling, Hb synthesis, and maturing of B-lymphocyte populations, being the factors of humoral immunity, occur.

The production of T-lymphocytes takes place in the *thymus gland*. Besides, the spleen, lymph nodes, and other lymphoid formations (Peyer's plaques, tonsil, appendix, etc.) take part in the development of the immune components (Figure 2.1).

Lymphocytopoiesis, Ig synthesis, destruction of erythrocytes, leucocytes, thrombocytes, the deposition of blood are carried out in *the spleen*.

2.1.2. Basic functions of blood

1. *Transportation* (transition of various substances).

2. *Respiratory* (transition of oxygen from the respiratory organs to tissues, and CO_2 in the reverse direction).

3. *Trophic or nutritional* (transition of nutrients from the digestive truct to cells and the use of blood components by the cells of tissues and organs for plastic and energy needs).

4. *Excretory* (transition of waste and harmful substances to the excretory organs: the end products of metabolism, excessive mineral and organic substances formed during metabolism or ingested with food).

5. *Temperature control* (blood is warmed up in the internal organs, where a lot of energy is formed, and is cooled down at the upper layers of the body).

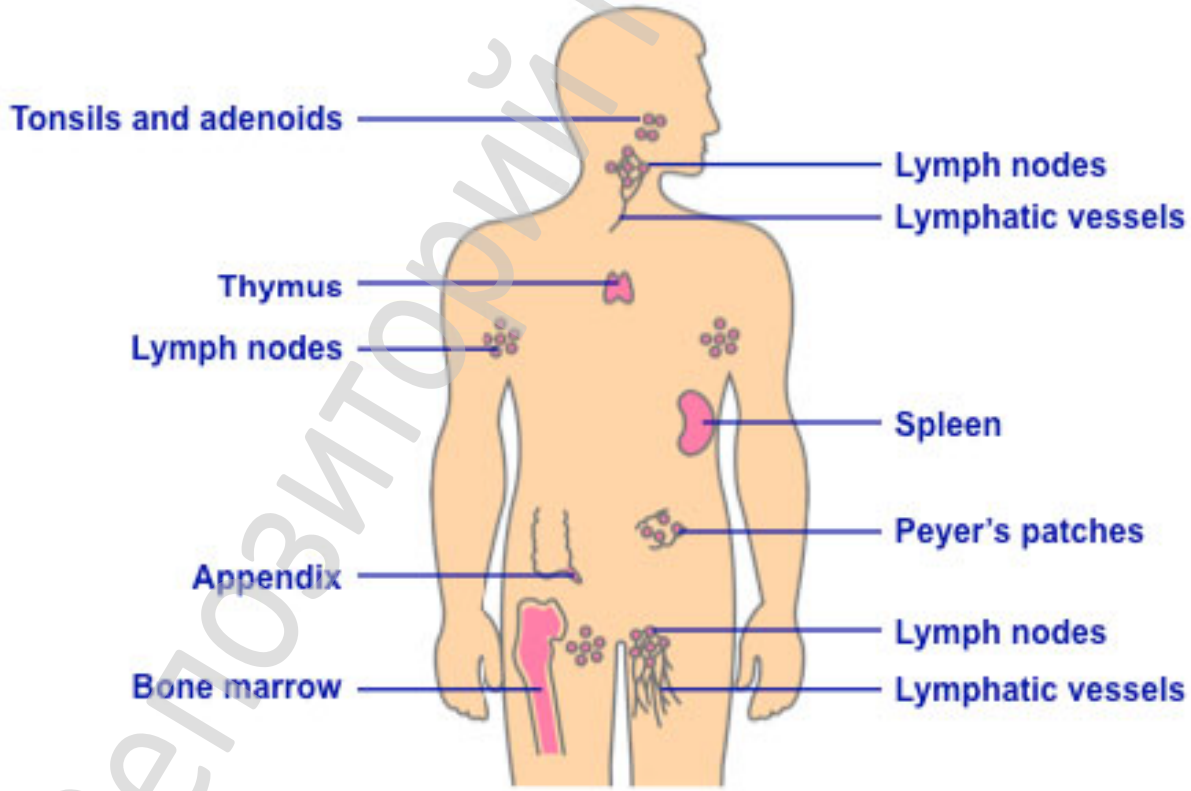
6. *Homeostatic* (along with interstitial fluid and lymph, blood forms the internal environment and participates in the maintenance of its constancy).

7. *Provides the water-salt exchange* between blood and tissues.

8. *Protective* (blood contains the factors of humoral and cell-mediated immunity: antibodies, phagocytes, coagulation factors, interferon, T- and B-lymphocyte populations, etc.).

9. *Correlative* (blood transfers biologically active substances which provide interconnections among various organs and tissues thus ensuring that the organism functions as a whole).

10. *Maintenance of constant acid-base balance* due to the buffer system.



Fugure 2.1 — Main organs of hemopoiesis (from picgalleria.com)

2.1.3. Composition and volume of blood

Blood consists of *plasma* and *the formed elements*: erythrocytes, leucocytes, thrombocytes (platelets) (Figure 2.2).

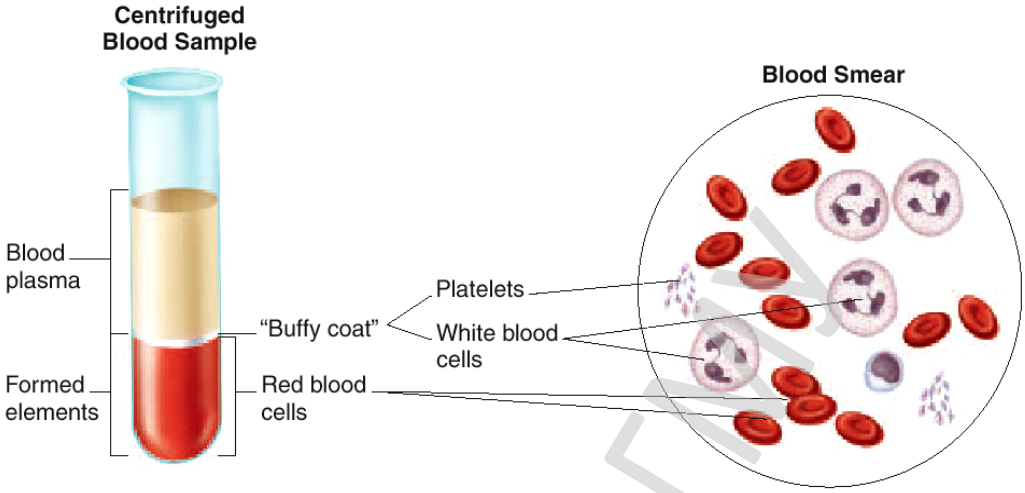


Figure 2.2 — Blood composition (from slideplayer.com)

Between the counts of the formed elements and plasma there is a certain interrelation which is called the hematocrit value (Figure 2.3). The hematocrit measures the count of red blood cells (RBCs) compared to the total blood count (red blood cells, white blood cells, platelets, and plasma). In norm, the erythrocyte count in males constitutes 42–52 %, plasma count — 48–58 %. To transform it into SI (International System of Units), the obtained number is multiplied by 0.01. The normal value for males is 0.42–0.52, for females — 0.37–0.47. In newborns, the hematocrit is 10 % higher.

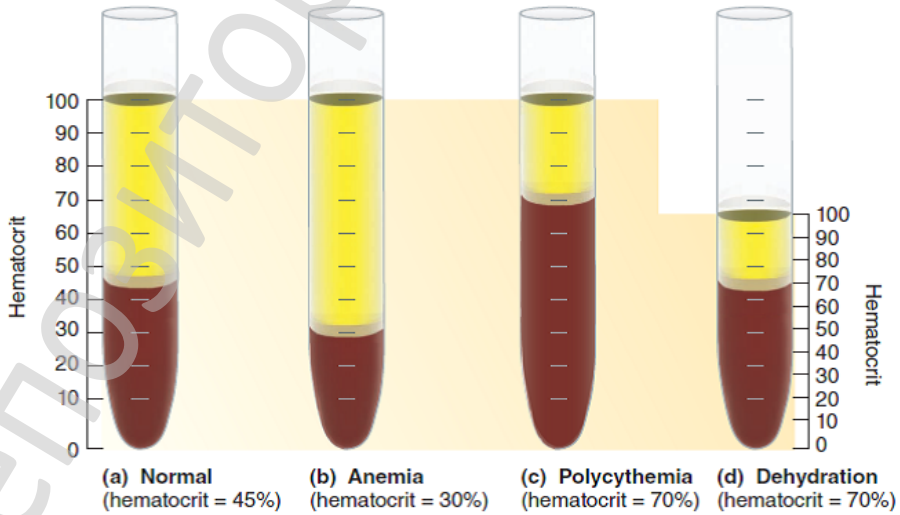


Figure 2.3 — Hematocrit values under various circumstances (from picgalleria.com)

Blood volume

In adults, the absolute blood volume is approximately 4.5–6 liters. Its relative content corresponds to 6–8% of body weight (in newborns — 15 %).

The normal total blood volume is called *normovolemia*. There are simple, oligocythemic, and polycythemic types of normovolemia (Table 2.1).

Simple normovolemia is the normal interrelation between the volume of the formed elements and plasma.

Table 2.1 — Changes of blood volume

Interrelation between the formed elements and plasma	Variants of volemia	Hematocrit value
	NORMOVOLEMIA	
FE 0.45 % plasma 0.55 %	simple	normal
FE 0.35 % plasma 0.65 %	oligocythemic	below normal
FE 0.55 % plasma 0.45 %	polycythemic	above normal
	HYPOVOLEMIA	
FE 0.45 % plasma 0.55 %	simple	normal
FE 0.35 % plasma 0.65 %	oligocythemic	below normal
FE 0.55 % plasma 0.45 %	polycythemic	above normal
	HYPERVOLEMIA	
FE 0.45 % plasma 0.55 %	simple	normal
FE 0.35 % plasma 0.65 %	oligocythemic	below normal
FE 0.55 % plasma 0.45 %	polycythemic	above normal

Notes: FE — formed elements of blood

Oligocythemic normovolemia can be observed in anemia as a result of blood loss when the volume of blood is restored due to its fluid part (transition of the interstitial fluid into the blood vessels), and the number of the formed elements is not yet restored.

Polycythemic normovolemia can be observed during transfusion of small amounts of erythrocytic mass.

Increased blood volume (hypervolemia, plethora) is observed:

1. After administration of a large amount of blood.
2. During intensive hemopoiesis (increased erythrocyte count).
3. Due to water retention in the body (kidney diseases).
4. After an excessive water intake.

Decreased blood volume (hypovolemia) is caused by:

1. Acute blood loss.
2. Anemia.
3. Body fluid loss (body dehydration), e. g., in profuse diarrhea, continuous vomiting.

Kinds of hypervolemia:

➢ *Simple* — proportional increases of the volumes of the formed elements and plasma (in hemotransfusion). The hematocrit value is normal.

➢ *Oligocythemic* — increased blood volume due to an increase of its fluid part (administration of blood-substituting fluids, kidney dysfunction). The hematocrit value is low.

➢ *Polycythemic* — increased blood volume due to an increased number of the formed elements (compensatory character in populations living in mountainous areas). The hematocrit value is low.

Kinds of hypovolemia:

➢*Simple* — proportional decreases of the volumes of the formed elements and plasma (it is short-term in acute hemorrhages). The hematocrit value is unchanged.

➢ *Oligocythemic* — decreased blood volume due to a decreased number of the formed elements after blood loss (when the volume of blood is restored owing to the interstitial fluid getting into the blood vessels). The hematocrit value is low.

➢ *Polycythemic* — decreased blood volume due to a decrease of the fluid part of blood (blood clotting in dehydration, e. g., in profuse diarrhea, continuous vomiting, hyperhidrosis). The hematocrit value is high.

By the degree of its participation in the circulation, there is *deposited blood* (45–50 %) and *circulating blood* (50–55 %).

The depots of blood:

➢ *Liver.* A large amount of blood is deposited here (up to 20% of its total volume) but is not excluded from the total blood flow completely (opposed to the spleen).

➢ *Spleen*. In the spleen up to 500 mL (10–16 %) of blood can be deposited (excluded from the blood flow).

➢ *Skin*. Blood is deposited in the capillaries and veins (about 10 %), which is connected with thermoregulation.

➢ *Lungs*. Blood is deposited due to the change of the volume of the arteries and veins.

➢ *Venous system* (regarded as the depot of the fluid part of blood containing a significant amount of lymph).

Lymph in the lymphatic vessels may be regarded as the depot of the fluid part of blood.

Deposited blood can transfer into circulating blood due to:

1. An emotional state.
2. A physical strain.
3. Low oxygen (hypoxia).
4. Hemorrhages.

Value of the depots of blood. The ability of organisms to increase the mass of circulating blood becomes vital in concrete conditions which require urgent satisfaction of the organism`s oxygen need (in mountaineering, physical exercise and other states connected with high oxygen consumption).

Hemorrhages and their effects. For a healthy person a single loss of 1/3 or even 1/4 of the volume of circulating blood is life-hazardous (low blood pressure, hypoxia). A sudden loss of 50 % blood leads to death, a slow loss (within a few days) of this amount of blood is not lethal, as in this situation there is enough time for the organism to mobilize the compensatory mechanisms directed to the stabilization of blood pressure and elimination of hypoxia.

Babies and newborns are especially sensitive to hemorrhages (compensatory mechanisms are not yet well developed). The sensitivity to hemorrhages increases in narcosis, hypothermia, pain, and shock.

Review questions

1. Name and describe the main components of the blood system (by G. F. Lang).

2. What are the main functions of blood? Explain them.

3. Name the main components of blood. Give the definition of the "hematoctit" and its normal values. What is the normal blood volume in adults and newborns? Describe the kinds and causes of hypervolemia and hypovolemia.

4. List the organs which contain the depot of blood. When is the transfer of deposited blood into circulating blood observed?

2.1.4. Blood plasma

Blood plasma is a colloid-polymeric solution of organic and inorganic substances (electrolytes, nutrients, proteins, hormones, etc.) with an addition of dissolved blood gases. Colloidal components are proteins and their compounds. Plasma is the fluid portion of blood (its volume is approximately 2.8–3.0 L). The composition of plasma: H_20 (90–92 %), being a solvent, and solid (dense) residue (8–10 %), which includes dissolved substances such as salts and low-molecular organic compounds (Table 2.2).

Table 2.2 — Composition and functions of blood plasma

Components				Amount	Functions
Water				90–92 %	solvent for other substances
Dry residue	Organic substances	Proteins:	albumins	35-55 g/L	• form 80 % of the colloid-osmotic pressure • participate in the regulation of water-salt balance. • participate in the transport of many substances • bind some hormones • form protein reserve

Components				Amount	Functions
			globulins	20–35 g/L	• transport of hormones, vitamins, microelements • Immune function (γ-globulins)
			Fibrino-gen	2-4 g/L	• participates in blood coagulation
		Glucose		3.3–6.1 mmol/L	• mainly energetic function
		Triglycerides		0.55–1.65 mmol/L	• they are present in the blood mainly in the forms of lipoproteins and chylomicrons — forms which transport lipids to different organs and tissues
		Cholesterol		3.0–6.2 mmol/L	
		Urea		2.5–8.3 mmol/L	• end product of protein metabolism which is transported to the organs of excretion
		General bilirubin		3.4–20.5 micromole/L	• pigment which is the product of hemoglobin degradation
	Inorganic substances	Na^+, K^+, Ca^{2+} chlorides, phosphates, hydrocarbonates		0.9 %	• participate in the maintenance of the osmotic pressure; • participate in the processes of excitation and contraction of cells • participate in blood coagulation (Ca2+); • participate in the regulation of acid-base balance

I. *Organic part*:

Proteins (albumins, globulins, fibrinogen) — 65–85 g/L.

1. ***Albumins*** (35–55*g/L*).

➢ They form 80 % of the colloid-osmotic pressure (high concentration, a relatively small size of molecules).

➢ They participate in the regulation of water-salt balance.

➢ They transport many substances (bilirubin, fats acids, exogenous substances, including drugs — antibiotics, sulfanilamids, mercury, and others).

➢ They bind hormones (for example, thyroxine).

➢ They are a protein reserve.

2. ***Globulins*** (*20–35g/L*) — α_1 -, α_2 -, $\beta_1 - \beta_2$ - and *Y*-fractions:

α-globulin — thyroxinbinding protein;

— transcobalamin (B_{12});

— cortisolbinding protein.

ß-globulin – is a transferring agent of lipids, lipoids, and polysaccharides:

— transport of Cu, Fe (transferrin).

Y-globulins — (IgA, IgD, IgE, IgG, IgM) perform immune functions and are better known as antibodies or immunoglobulins. The agglutinins of blood are related to this fraction.

3. ***Fibrinogen*** (*2*–4 *g/L*) — participates in blood coagulation.

Formation of proteins:

a) albumins, fibrinogen are produced in the liver;

b) globulins are produced in the bone marrow, spleen, lymph nodes, cells of the mononuclear phagocytic system.

The role of plasma proteins:

- They exert a part of the osmotic pressure, so-called the colloid-osmotic pressure of plasma protein, or oncotic pressure.
- They maintain pH (buffering action).
- They maintain blood viscosity (important for blood pressure).
- They prevent erythrocyte sedimentation (stabilization).
- They participate in blood coagulation (fibrinogen, etc.).
- They perform the factors of immunity (immunoglobulins).
- They transport substances which are poorly soluble in water (transport of hormones).
- They perform the nutrient (plastic) function.
- They regulate the concentration of free ions, for example, Fe^{++} (transferrin).
- They may inhibit the action of some proteases (antitrypsin — inhibitor of trypsin).
- They regulate metabolic functions (protein hormones, enzymes).
- They provide redistribution of water between tissues and blood (1 g of albumin binds 0.35 g of water and during swelling it can bind up to 18 mL of water). In hypoproteinemia (decrease of protein to 55 g/L) — edemas occur. Hunger edemas, for example, are caused by starvation.

Glucose. Glucose concentration in adults:

- Whole blood — 3.30–5.55 millimole/L.
- Plasma — 3.30–6.10 millimole/L.
- Glucose concentration in newborns — 1.70–4.20 millimole/L.

The blood glucose test is commonly used to diagnose diabetes mellitus.

Not protein nitrogen-containing substances (polypeptides, amino acids, urea, urinary acid, creatine, creatinine, bilirubin, etc.). Not protein (residual) nitrogen —14.3–28.5 millimole/L.

Urea is the end product of protein metabolism which is transported to the organs of excretion. The blood urea nitrogen test is used mainly for diagnosis of renal disorders. The normal concentration of urea in the blood ranges 2.5–8.3 millimole/L.

General bilirubin — 3.4–20.5 micromole/L. Bilirubin is an orange-yellow pigment which is produced after the breakdown of hemoglobin and is excreted by the liver. High bilirubin blood level results in the yellow pigmentation of the

skin and sclera, which is known as jaundice (icterus). The evaluation of the bilirubin concentration may be used to diagnose liver diseases, hemolytic anemia.

Cholesterol and **triglycerides** are present in the blood mainly in the forms of lipoproteins and chylomicrons. Triglycerides — 0.55–1.65 millimole/L. Cholesterol — 3.0–6.2 millimole/L.

Also, plasma contains hormones, vitamins, and enzymes.

II. *Inorganic part*: gases (O_2, nitrogen, CO_2) and mineral substances.

Mineral substances — 0.9 % (ions of potassium, sodium, chlorine, calcium, HCO^-, HPO^-, etc.). The basic cations of plasma are Na^+, K^+, Ca^{++}, which play an important role in the maintenance of the osmotic pressure, redistribution of water between blood and tissues, blood coagulation, excitability and contraction of cells, etc. The basic anions of plasma are Cl^-, sodium hydrogenums HCO^3, phosphates, which play an important role in the regulation of pH, acid-base balance, excitability of cells, etc.

2.1.5. Physical and chemical properties of blood

The osmotic pressure is formed mainly by dissociated salts and is equal to 290 ± 10 mosm/L. The osmotic pressure has an important value in the maintenance of the concentrations of various substances dissolved in the body fluids and promotes distribution of water among blood, cells, and tissues.

There are isotonic, hypotonic, and hypertonic solutions depending on the value of the osmotic pressure.

An isotonic solution is a solution whose osmotic pressure *is equal* to that of blood (e.g., 0.85 % NaCl solution). Erythrocytes placed in such a solution do not change, as the osmotic pressure in them is the same as in the solution (Figure 2.4). This solution is called physiological. It is used as a blood-substituting solution, solvent for many medications for parenteral administration. Over 60 % of the osmotic pressure of blood is provided by NaCl. Totally, inorganic substances provide 96 % of the osmotic pressure.

A hypotonic solution is a solution whose osmotic pressure *is lower* than that of blood (for example, 0.3 % NaCl solution). Erythrocytes placed in such a solution swell and burst (i.e., get hemolyzed) as a result of transition of water into cells, as the osmotic pressure in erythrocytes is higher than in the solution (Figure 2.4.).

A hypertonic solution is a solution whose osmotic pressure *is higher* than that of blood (for example, 2 % NaCl solution). Erythrocytes placed in such a solution, shrink as a result of the output of water from the cell, as the osmotic pressure in erythrocytes *is lower* than in the solution (Figure 2.4).

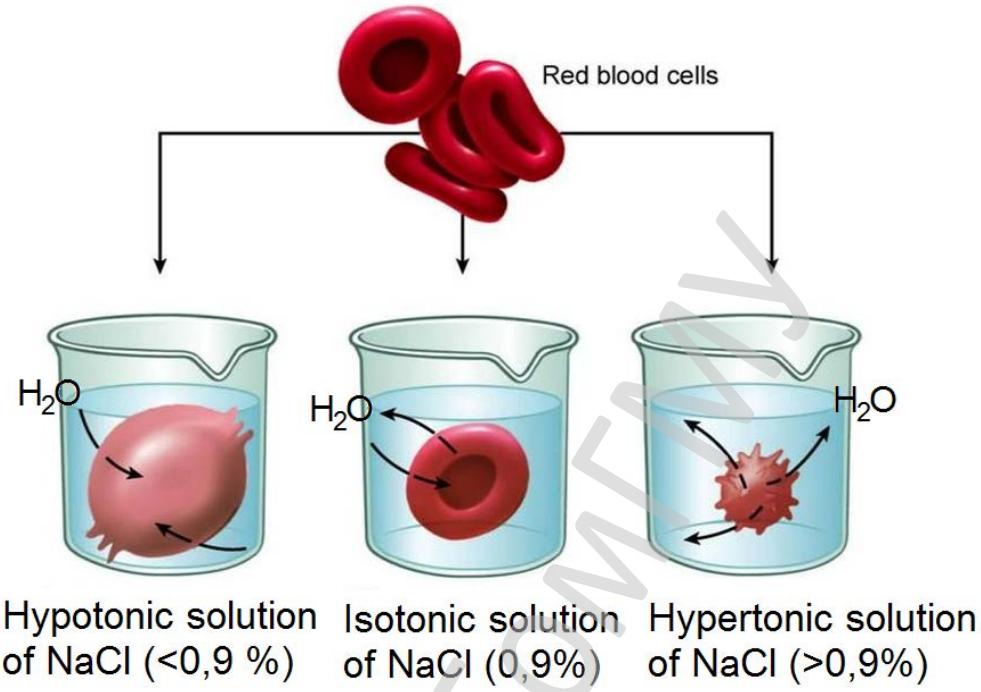


Figure 2.4 — The state of erythrocytes in solutions with different NaCl concentrations (in the hypotonic solution there is osmotic hemolysis) (from slideplayer.com)

The human osmotic pressure is rather constant. The excretory organs (kidneys, perspiratory glands) participate in its neurohumoral regulation. The osmotic pressure changes are perceived by special osmoreceptors located both on the periphery (in the endothelium of the blood vessels) and in the center (in the hypothalamus).

Oncotic pressure. The osmotic pressure formed by proteins is called oncotic (due to their ability to draw H_2O).

The portion of the osmotic pressure formed by proteins is 25–35 mm Hg.

More than 80 % oncotic pressure is caused by albumins due to small sizes of their molecules and their high number (as compared with fibrinogen and globulins).

The oncotic pressure is important for:

1. The formation of the interstitial fluid.
2. The formation of lymph.
3. The formation of urine.
4. The adsorption of H_2O in the intestines.
5. The redistribution of H_2O between blood and tissues.

Proteins have a big size of molecules and, therefore, are unable to pass through the endothelium of capillaries (they remain in the blood flow). They keep a certain amount of water in the blood.

Blood viscosity is a physicochemical property of blood related to the internal friction. At laminar blood flow the force of internal friction appear, that interferes blood flow.

In medicine, the viscosity of blood is usually measured in centipoise (cP). The viscosity of water is equall to 1 at 20.3 °C.

The viscosity of blood:

— whole blood— 4.5–5 cP;

— plasma — 1.7–2.2 cP.

Blood viscosity is determined by plasma viscosity, hematocrit and properties of erythrocytes such as deformability and aggregation.Plasma viscosity is determined by water content and macromolecular components (especially plasma protein concentration and types of proteins in plasma).

The hematocrit and the amount of erythrocytes have the strongest impact on whole blood viscosity (Table 2.3). High counts of red blood cells lead to high blood thickness.

Table 2.3 — Dependence of blood viscosity on the erythrocyte count

Number of erythrocytes	Blood viscosity
4.5×10^{12}/L	5.0
6.7×10^{12}/L	6.4
7.4×10^{12}/L	8.1
9.3×10^{12}/L	20.9

High blood viscosity is caused by:

— body dehydration (profuse diarrhea, continuous vomiting);

— high count of the formed elements in the blood (polycythemia, leukosis);

— accumulation of CO_2;

— increased content of proteins, especially fibrinogen.

High blood viscosity leads to slow blood flow and high hydrodynamical peripheral resistance in the blood vessels, which forces the heart to work harder to pump the blood, increasing the risk for heart diseases.

Low blood viscosity is caused by:

— body hydration (intake of too much water, water retention in kidney diseases),

— anemias, hypoproteinemias,

— decreased rate of blood coagulation (under the influence of administered heparin).

Low blood viscosity leads to accelerated blood flow.

Blood behaves like a non-Newtonian fluid whose viscosity varies with shear rate (shear rates indicates how fast the fluid layers are sliding past one another). The non-Newtonian characteristics of blood come from erythrocyte deformability and erythrocyte aggregation. Erythrocyte aggregation is a reversible dynamic

phenomenon. At low shear rates and in the presence of fibrinogen and other plasma proteins, erythrocytes tend to aggregate, and blood viscosity increases. At high shear rates the aggregates of erythrocytes break down.

The relative density (specific gravity) of blood depends on the content of proteins, salts, and erythrocytes. The relative density of whole blood changes within rather narrow limits (1.050–1.060), plasma (1.025–1.034), and relative density of erythrocytes is higher than that of whole blood and plasma (1.090).

The reaction of blood (acid-base balance). The active reaction of blood (pH) is caused by the interrelation of hydrogen (H^+) and hydroxyl (OH^-) ions. It is one of the rigid parameters of homeostasis.

— the pH of arterial blood is 7.37–7.45;

— the pH of venous blood is 7.34–7.43 (it has more carbonic acid);

— the pH inside cells is 7.0–7.2 (acidic metabolic products).

— the pH ranges compatible with life are 7.0–7.8. But a long-term pH shift of 0.1–0.2 can be hazardous for life. Any pH shift, first of all, influences the activity of enzymes.

Despite the fact that CO_2, lactic acid, and other acidic components constantly get into the blood, which may affect its pH level, the active reaction (pH) remains constant. It is provided by the buffer properties of blood and activity of the excretory organs (excretion of CO_2 by the lungs, excretion of acidic and containment of alkaline products by the kidneys).

2.1.6. Buffer systems of blood

The buffer systems (also buffer solutions or buffer mixtures), are solutions which maintain the constancy of the concentration of hydrogen ions, both after addition of acids or alkalis, and their dilution. They consist of a mixture of weak acids with salts of these acids and strong alkali. Due to the buffer systems, the active reaction of blood (pH), the major parameter of the constancy of the internal environment, is maintained.

The buffer systems of blood:

1. Bicarbonate (H_2CO_3+$NaHCO_3$) and (H_2CO_3+$KHCO_3$). Acidic components which come into the blood cooperate with bicarbonate ones. Coming into the blood, the alkaline components cooperate with H_2CO_3, thus forming the salt and H_2O (removed by the excretory organs).

2. *Phosphate* (NaH_2PO_4+Na_2HPO_4) NaH_2PO_4 has the property of an acid and reacts with alkaline components, and Na_2HPO_4 having the properties of alkalinity reacts with the acidic components.

3. *Protein.* It is caused by the amphoteric properties of plasma proteins. In an acidic medium they behave like alkali, in an alkaline medium — like acids, binding acids in the former, and alkalis in the latter.

4. *Hemoglobin*. Low Hb is an acid which is weaker than H_2CO_3 and thus gives it its K^+ ions, attaching H^+ and becoming a low-dissociated acid.

The buffer systems are also present in tissues (the main ones are protein and phosphatic).

During metabolism more acidic products are formed than basic ones, therefore the danger of a pH shift to the acidic side exists. In the human body the total daily acidity of HCl, lactic, pyruvic, carbonic, and other acids is equal to 20 – to 30 liters of 1.0 normality of HCl. Despite this, the organism lives and the constant pH value is maintained. The buffer systems of blood and tissues ensure high sustainability to the action of acids. Therefore, to shift the pH value:

— to *the alkaline* side — it is necessary to add alkalis whose amount is 40–70 times higher than that of water;

— to *the acidic* side — it is necessary to add acids whose amount is 327 times higher than that of water.

The alkaline salts of the weak acids kept in blood form the *alkaline reserve* of blood.

Shifts of the active reaction of blood either to acidic *(acidosis)* and to alkaline *(alkalosis)* sides are possible (Figure 2.5).

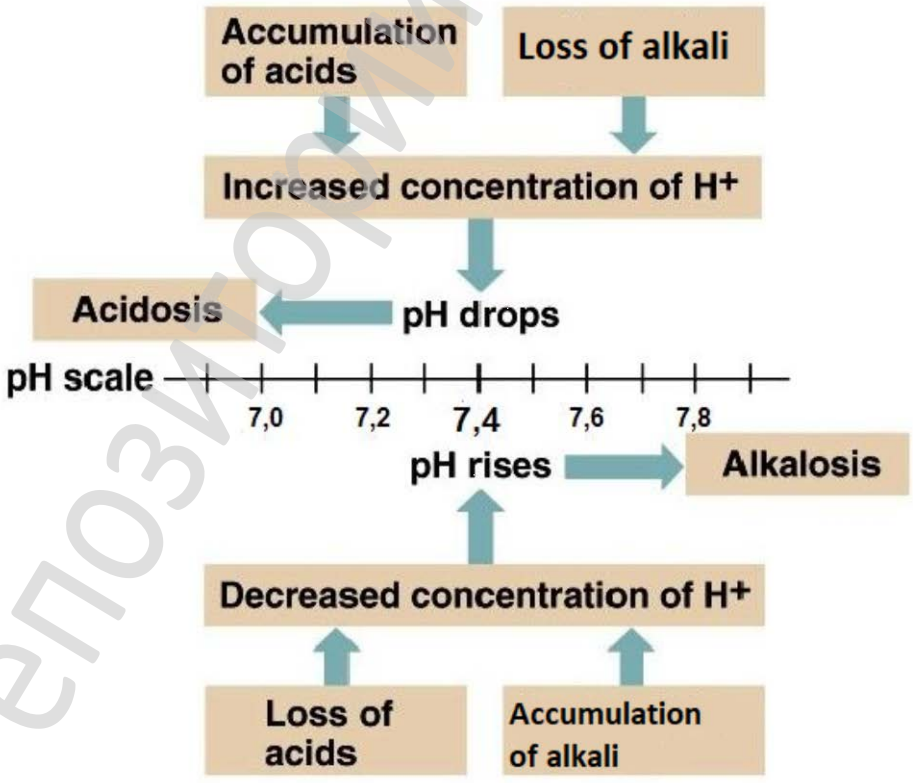


Figure 2.5 — Acidosis and alkalosis (from slideplayer.com)

By the degree of its intensity, acidosis can be compensated and non-compensated.

In compensated acidosis the accumulation of acids in the blood results only in the depletion of the alkaline reserve without pH changes. Despite the chemical and functional shifts in the body, the pH is maintained due the action of the buffer systems. Due to the exhaustion of the alkaline reserve and failure of the protective mechanisms, the pH is shifted outside the limits, and *non-compensated acidosis* develops.

By their origin there are:

1. Gaseous acidosis and gaseous alkalosis.
2. Non-gaseous acidosis and non-gaseous alkalosis.

Gaseous (respiratory) *acidosis* refers to high levels of the acid (H_2CO_3) in the blood. Its common causes are:

1. Malfunction of external respiration.
2. Circulatory insufficiency.
3. Inhalation of air (admixture) with an increased concentration of CO_2.

Gaseous (respiratory) *alkalosis* is a medical condition in which hyperventilation elevates the blood pH beyond the normal range (7.34–7.45) with a concurrent reduction of carbon dioxide in the arterial levels (mountain sickness, excessive artificial respiration).

Non-gaseous (metabolic) *acidosis* is caused by excess accumulation of acidic products. Its common causes are:

1. Excessive formation of acidic products in dysbolism (diabetes, starvation).
2. Affected excretion of acidic products from the body (nephrites).
3. Alkali loss (in profuse diarrhea, fistulas of the intestines).
4. Excessive administration of mineral substances (poisoning by acetic acid).

Non-gaseous (metabolic) *alkalosis* is caused by excess accumulation of alkaline products. Its common causes are:

1. Administration of a big amount of alkaline products into the body (baking soda, alkaline water abuse).
2. Loss of a large amount of gastric juice (in continuous vomiting, stomachal fistula).
3. Hyperproduction of glucocorticoids or treatment with the preparations of adrenal hormones.

Review questions

1. Name the main organic and inorganic components of blood plasma, their amount and functions.

2. Describe the groups of plasma proteins and explain their functions.

3. What is the volume, determining factor, and physiological role of the osmotic pressure of blood? Explain what hyper-, hypo- and isotonic (physiological) solutions are. What is the volume, determining factor, and physiological role of the oncotic pressure of blood plasma?

4. Name the values, determining factor, and physiological role of blood viscosity and relative density of blood.

5. What is the active reaction (pH) of blood? Give the normal pH values of arterial and venous blood. Name and describe the buffer systems of blood.

6. Give the definitions of "acidosis" and alkalosis". What is the alkaline reserve of blood? Describe the types of acidosis and alkalosis and the factors causing them.

2.2. Formed elements of blood

2.2.1. Erythrocytes, their structure, properties and functions

The erythrological system is a physiological system including erythrocytes circulating in the blood, organs of their production and destruction, incorporated into the system of neuroendocrinological regulation.

In humans and mammals, erythrocytes do not contain nuclei. The absence of nuclei presumes that erythrocytes consume 200 times less oxygen for their own needs than nucleus-containing representatives (erythroblasts, normoblastes).

The size of erythrocytes: diameter — 7.7 micrometers (μm), thickness — 2.2 μm (Figure 2.6).

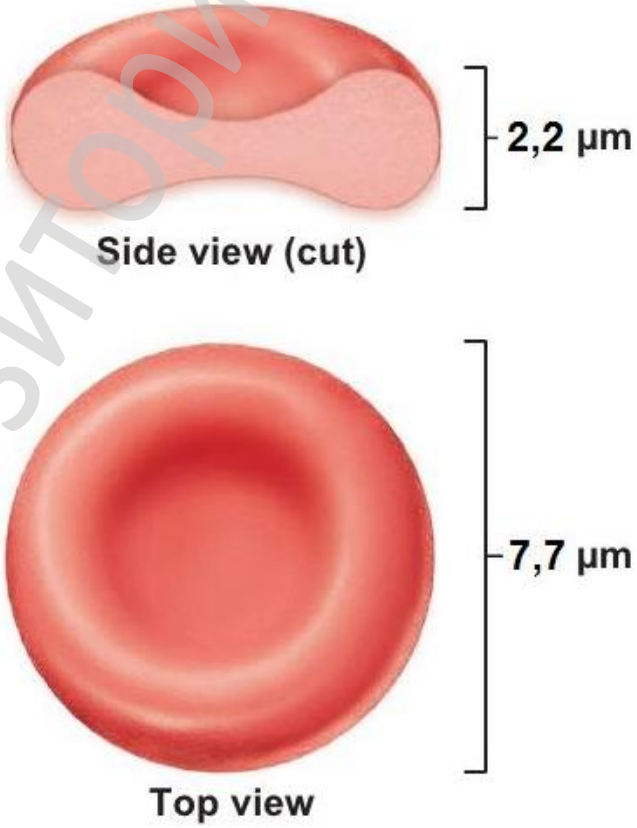


Figure 2.6 — The shape and size of erythrocytes (by Elaine N. Marieb, 1989)

One important feature of erythrocytes is that they are biconcave disks: plump at their periphery and very thin in the center.

The biconcave shape of erythrocytes:

- It provides a greater surface area (by 20 %) in comparison with the same diameter of a sphere.
- It performs one of the basic functions — transition of O_2 and CO_2.
- It increases the ability for reversible deformation (plasticity) during the passage through narrow and bent capillaries.

In some pathology (anemia), there are erythrocytes of various shapes (crescent, pear-shaped, etc.) named *poikilocytosis,* and also of various sizes — *anisocytosis* (Figure 2.7).

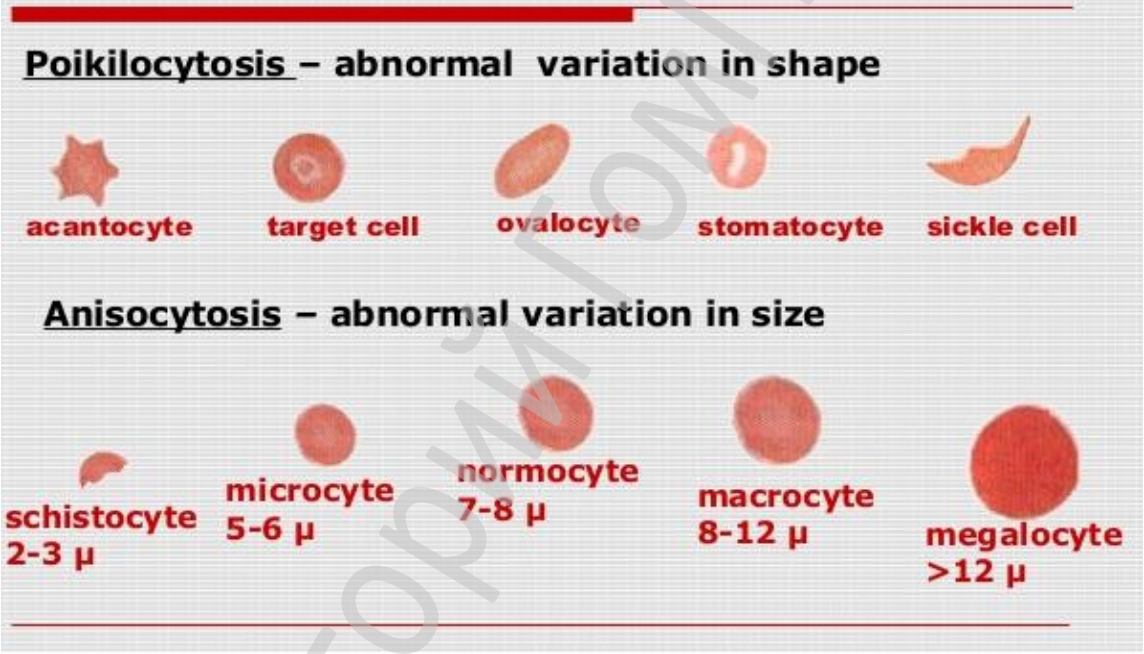


Figure 2.7 — Poikilocytosis and anisocytosis (from picgalleria.com)

Erythrocytes consist of the skeleton of the cell — stroma, and the upper layer — membrane. The thickness of the membrane is 10 nanometers.

The membrane of the erythrocyte consists of 4 layers:

- External, which is formed by glycoproteins.
- Average 2 layers — bi-lipid layers.
- Internal layer — protein.

The chemical composition of erythrocytes: 60 % — H_2O, 40 % — dry sediment (almost 90 % of which is hemoglobin (Hb)).

The functions of erythrocytes:

- Transition of O_2 (participation of hemoglobin).
- Transition of CO_2 (participation of hemoglobin).
- Protection (absorption of harmful substances, production of antibiotic — eritrin).

- Regulation of the water-and-salt exchange.
- Transition of nutrients.
- Participation in the regulation of erythrogenesis.
- Creative. It presumes the transition of macromolecules ensuring information links of the body (see «Main Functions of Blood»).
- Participation in the regulation of acid-base balance (hemoglobin buffer).
- Participation in blood coagulation (erythrocytes contain thromboplastin, released during their destruction. The presence of destroyed erythrocytes in the blood induces hypercoagulation and thrombus formation. Along with it, they are heparin bearers being anticoagulants).

The erythrocyte count in the blood:

— in males — $4.5–5.1 \times 10^{12}$/L;

— in females — $3.7–4.7 \times 10^{12}$/L.

A condition characterized by an increased number of red blood cells is called erytrocytosis.

A condition characterized by a decreased number of erythrocytes is called erythropenia. Erythropenia is observed in anemia (in combination of low Hb).

The life span of erythrocytes is 130 days.

The production of erythrocytes occurs in the red bone marrow (160×10^6 cells are produced per minute), and their destruction — in the spleen, liver, red bone marrow.

2.2.2. Hemoglobin, its structure, behavior, varieties, compounds and functions

One of the major functions of blood is the transmission of oxygen to organs and tissues and transport of carbonic gas (CO_2).

The important role in this process is played by erythrocytes due to the presence of the red blood pigment — hemoglobin.

The advantages of Hb localization in erythrocytes:

- it provides low blood viscosity;
- It reduces the oncotic pressure, preventing water loss in tissues;
- It prevents Hb loss during blood filtration in nephrones.

Hemoglobin is a chromoproteid consisting of a protein called globin (96 %) and the prosthetic group of hemes (4 %). There are 4 heme groups. The heme represents protoporphyrin with an ion of iron (Fe2+) in the centre (Figure 2.8).

The key role in Hb activity is played by Fe^{++} ions.

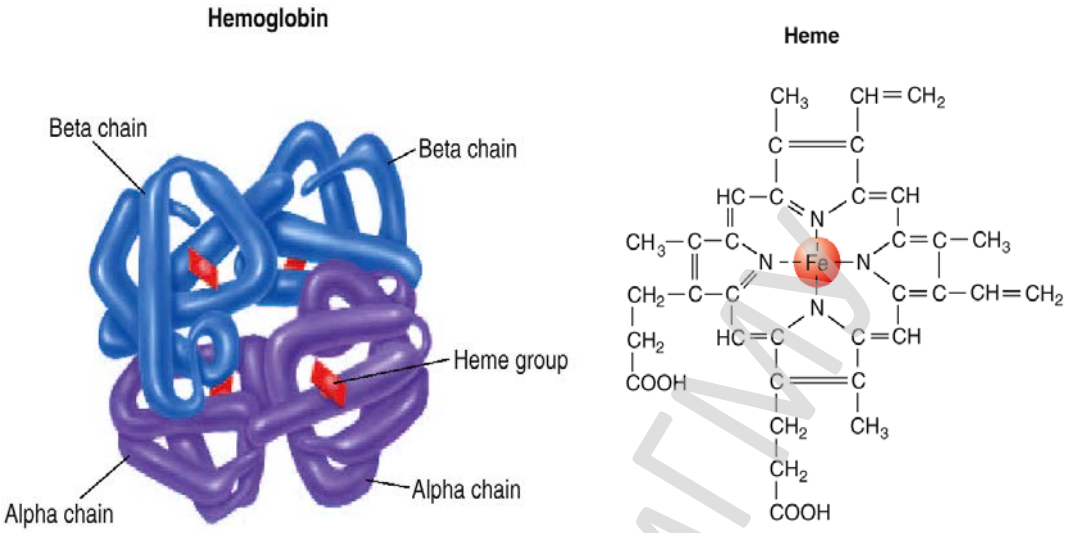


Figure 2.8 — Structure of hemoglobin (from slideplayer.com)

The functions of hemoglobin:

➢ Transport of O_2 — oxyhemoglobin ($HHbO_2$). One molecule of Hb attaches 4 oxygen molecules. 1 g of Hb binds 1.34 mL of O_2.

➢ Transport of CO_2.

➢ Participation in the maintenance of acid-alkaline balance (hemoglobin buffer).

Bonds of Hb:

1. **Oxyhemoglobin** ($HHbO_2$). Hemoglobin is bound to O_2. Arterial blood contains about 98 % $HHbO_2$, and venous — about 60 %. The form of Hb after oxygen is released in tissues is called *restored or reduced* hemoglobin. Hemoglobin has high affinity for oxygen.

2. **Carbohemoglobin** ($HHbCO_2$) is a stable formation of hemoglobin with carbon dioxide (CO_2).

3. **Methhemoglobin** (MetHb). It is formed under the influence of strong oxidants (permanganates of potassium, aniline, nitrites, pyrogallol, etc.). Thus, Fe^{2+} turns into Fe^{3+}). This bond is stable and can not be disconnected.

4. **Carboxyhemoglobin** (HHbCO) is a stable formation of hemoglobin with carbon monoxide (CO). This bond is 150–200 times stronger than that of $HHbO_2$. In 0.1 % CO concentration in the air, 80 % Hb turns into carboxyhemoglobin. The 1 % CO concentration causes death within a few minutes.

The physiological bonds of Hb are $HHbO_2$ and $HHbCO_2$.

Myoglobin is a respiratory pigment, or muscular hemoglobin contained in skeletal muscles and myocardium. It has higher affinity for oxygen in comparison with hemoglobin. It binds up to 14 % O_2 in the body. Its role is to supply muscles with oxygen during muscle contractions when capillaries are pressed and tissues do not receive blood. At this moment the main source of oxygen is myoglobin, which during the phase of muscle relaxation is filled with oxygen.

Hb synthesis takes place in the bone marrow erythroblasts. Hemoglobin metabolism after erythrocyte destruction is shown in Figure 2.9.

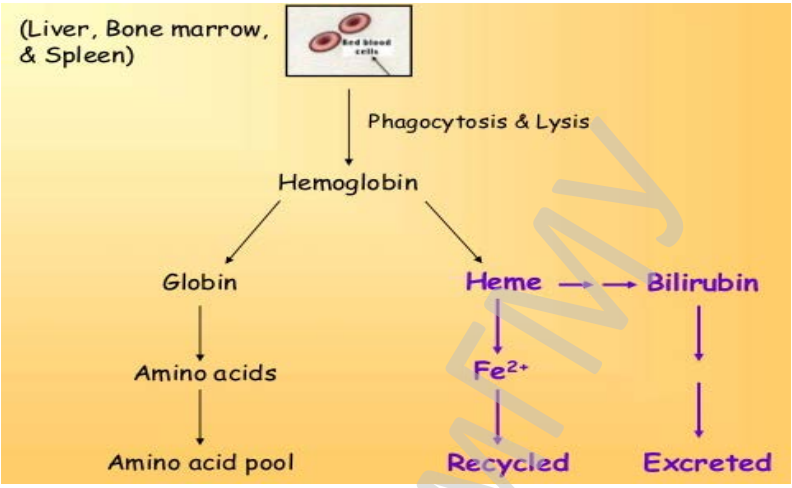


Figure 2.9 — Hemoglobin metabolism (from picgalleria.com)

A condition characterized by a low amount of Hb per unit of blood volume (more often in low red blood cell count) is called *anemia.*

Anemia is observed when the Hb amount is less than 130 grams per liter in males, and less than 120 grams per liter in females (in pregnant females — less than 110 grams per liter).

Types of Hb:

- *HbP* — primitive — is formed during 7–12 weeks of intra-uterine development.
- *HbF* — fetus — during the 9th week of intra-uterine development.
- *HbA* — hemoglobin of adults appears before birth.

HbF has high affinity for O_2 and binds 60 % O_2 at such partial pressure of O_2 (pO_2), whereas HbA is only 30 %. Due to the given property, HbF supplies tissues with oxygen in the conditions of low pO_2 in the arterial blood of a fetus. Within the first year of life, HbF is almost completely replaced by HbA.

Normal Hb ranges in the blood of males vary within 130–160 grams per liter, in females — 120–140 grams per liter.

The color index (CI) reflects the relative saturation of erythrocytes with hemoglobin and is calculated with the formula:

$$CI = \frac{Hb(g/l) \times 3}{A}$$

where:

Hb — hemoglobin amount, g/L:

A — amount of erythrocytes per microliter (first three digits).

The color index has been a useful clinical method to diagnose anemia.

Its normal ranges are 0.85–1.05. Erythrocytes having such an index are called normochromal. If the parameter is above 1.5, erythrocytes are called hyperchromal and if under 0.85 — hypochromal.

2.2.3. Hemolysis and its varieties

Hemolysis refers to the destruction of the erythrocyte membrane accompanied by the release of Hb into blood plasma (laky blood, or pellucid blood).

Kinds of hemolysis:

1. *Mechanical* (in vivo excessive mechanical forces, in vitro in vial blood stirring).

2. *Thermal* (in vivo in burns, in vitro in blood freezing and de-freezing).

3. *Chemical* (in vivo under the influence of chemical substances, aspiration of volatiles (acetone, benzene, chloroform), destruction of the erythrocyte membrane, in vitro under the influence of acids, alkalis, heavy metals, etc.).

4. *Electrical* (in vivo due to damage caused by electric currents, in vitro during the transit of an electric current through the blood in the vial). On the «+» anode hemolysis is an acid, on the «–» cathode — alkaline.

5. *Biological.* Under the influence of biological factors (hemolysins, venoms of serpents, fungal poisons).

6. *Osmotic*. In hypotonic solutions hemolysis begins in 0.48 % sodium chloride (NaCl) solution, and in 0.32 % — full hemolysis of erythrocytes is observed.

The osmotic resistance of erythrocytes (ORE) is their susceptibility to hemolysis in hypotonic solutions.

The minimal ORE is determined by the concentration of a NaCl solution (0.48–0.46 %) in which hemolysis begins.

The maximal ORE is determined by the concentration of a NaCl solution (0.34–0.32 %), in which all erythrocytes have been hemolysed.

The ORE depends on the degree of their maturity and form.

The young forms of erythrocytes which come from the bone marrow into the blood are more resistant to hypotonia.

7. *Immune hemolysis* occurs in transfusion of incompatible blood or if there are immune antibodies to erythrocytes.

8. *Physiological hemolysis* is the hemolysis of erythrocytes at the end of their life cycle (in the liver, spleen, red bone marrow).

2.2.4. Erythrocyte sedimentation rate

The sedimentation of erythrocytes is observed when a blood sample with an anticoagulant (which prevents the blood from coagulation) is placed in a tall,

thin, vertical tube. The erythrocyte sedimentation rate test is a hematological test which measures the rate of erythrocyte sedimentation, which is reported as the millimeters of plasma that are present at the top portion of the tube after one hour Figure 2.10.

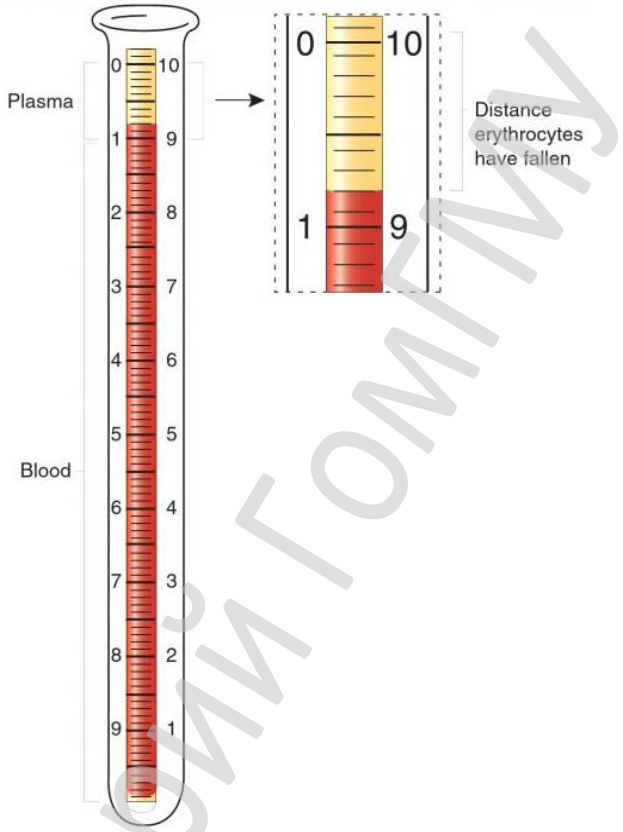


Figure 2.10 — ESR measurement (from slideplayer.com)

Normal erythrocyte sedimentation rates (ESR) are:
in males 1–10 mm / hour;
in females 2–15 mm / hour;
in newborns 1–2 mm / hour.
The ESR depends on:
The properties of plasma:

- The ESR accelerates due to an increased concentration of the molecules of large globulins and fibrinogen in particular. Their concentration rises due to inflammatory processes, pregnancy. They reduce the electrical charge of erythrocytes, promoting cohesion of erythrocytes and formation of monetary columns.
- The ESR decreases in an increased erythrocyte count (for example, the sedimentation of erythrocytes can stop completely owing to high blood viscosity). Anemia is responsible for accelerating ESR.
- The ESR goes down if the shape of erythrocytes changes (drepancytic anemia).

➢The ESR slows down in a low pH value and, vice versa, accelerates in a high pH.

➢ The ESR increases in a high hemoglobin level.

Review questions

1. Describe the structure and properties of erythrocytes. What is the physiological role of the biconcave shape of erythrocytes? Give the definitions of "poikilocytosis" and "anisocytosis". Name the functions of erythrocytes. What is the normal erythrocyte count in the blood? What are erythrocytosis and erythropenia?

2. Describe the structure and functions of hemoglobin. List and describe the bonds of hemoglobin. What is the normal range for hemoglobin in the blood? Give the definition of "anemia". List the types of hemoglobin. What is the diagnostical value of the color index of blood?

3. Give the definition of "hemolysis". Name and describe its types. What is the osmotic resistance of erythrocytes? Explain its diagnostic value.

4. What are the normal values and diagnostic importance of the erythrocyte sedimentation rate? Explain what factors increase and decrease the erythrocyte sedimentation rate.

2.2.5. Leukocytes, their classification, features and functions

Leukocytes, or white blood cells, opposite to erythrocytes, have nuclei and other structural elements peculiar to cells. The size of leukocytes is 7.5–20 micrometres.

The functions of leukocytes:

➢ *Protective* (participation in the maintenance of nonspecific and cell immunity).

➢ *Metabolic* (release of nutrients into the digestive system, their seizure and transmission into the bloodstream. Especially, it has an essential value in the maintenance of immunity in newborns during their breast feeding).

➢Dissolution of damaged tissues;

➢ *Morphogenetic* — destruction of various malformations during the embryonic period.

Leukocytes also provide the *regulatory function* due to the production and secretion of cytokines, growth factors and other substances which regulate haemopoiesis and immune responses.

Leukocytes are capable to move towards the source of chemical substances formed in inflamed tissues. This processs is known as chemotaxis.

The classification and functions of leukocytes (Table 2.4).

Table 2.4 — Types of leukocytes

Type of cells		Amount (in %)	Functions	Morphology of the cell
Granular leucocytes	Neutrophils: myelocytes metamyelocytes stab neutrophils segmentonuclear	 0 0-1 1–6 47–72	• possess high bactericidal activity, perform phagocytosis • have receptors to IgG, to proteins of complement on their membrane	segmentonuclear neutrophil
	Eosinophils	0.5–5	• phagocytosis • neutralization of toxins of the albuminous nature • destruction of alien proteins and antigen-antibody complexes • production of plasminogen (participate in fibrinolysis) • cytotoxic effect on helminthes, their eggs	eosinophil
	Basophils	0–1	• production of histamine (it dilates capillaries) and heparin (it prevents blood coagulation) • regulation of the aggregate state of blood, microcirculation and permeability of capillaries. • have receptors to IgE	 basophil
Agranular leucocytes	Lymphocytes T — lymphocytes (provide cell-mediated immunity): B — lymphocytes (provide humoral immunity) Zero lymphocytes (nature killers)	19–37	• antibody formation • destruction of alien cells • provide the reaction of transplant rejection • keep immune memory • destruction of the body`s own mutant cells • sensitization	 lymphocyte
	Monocytes	2–11	• turn into tissue macrophages in tissues • perform phagocytosis of microorganisms, dead leucocytes, damaged tissue cells • perform the antigen-presenting function	 monocyte

1. *Agranular:*

a) **Monocytes** — 2–11 % of all leukocytes (macrophages). Monocytes turn into tissue macrophags in tissues. Monocytes are the largest blood cells. They have bactericidal activity, appear in the damaged area after neutrophils and perform phagocytosis of:

- Microorganisms.
- Dead leucocytes.
- Damaged tissue cells.

Thus they clear the damaged area.

Macrophages also perform the antigen-presenting function, they can present phagocyted antigen fragments to lymphocytes to initiate a specific immune reaction.

b) **Lymphocytes** — 19–37 % of all leucocytes.

Lymphocytes enter the circulatory system continually. After a few hours, they pass back into tissues through diapedesis, then re-enter the lymph and return to the blood again and again; thus, there is continual circulation of lymphocytes through tissues. The life span of lymphocytes is from several days, as in other leucocytes, to 20 and more years.

Lymphocytes are the central part of the immune system. They provide genetic constancy of the organism.

They perform the following functions:

- Antibody formation.
- Destruction of alien cells.
- Provide the reaction of transplant rejection.
- Keep immune memory.
- Destruction of the body`s own mutant cells.
- Sensitization.

There are three main types known as T cells, B cells, and natural killer cells.

T-lymphocytes (provide cell-mediated immunity):

a) T-helpers (the major regulator of immune functions due to production of interleukins and other regulatory substances);

b) T-cytotoxic (or T-killers, these cells are capable of killing microorganisms);

c) T-cells of immune memory;

d) T-regulatory cells and others.

B-lymphocytes or bursacytes (provide humoral immunity). They differentiate into plasma cells which secret immunoglobulins (antibodies).

Lymphocytes are produced from common stem cells. The differentiation of T-lymphocytes occurs in the thymus gland, and bursacytes — in the red bone marrow, tonsils, lymph nodes, appendix.

Natural killer cells (NK-cells). They make 5–10 % of circulating lymphocytes and play a major role in immune reactions against tumour cells and virally infected cells.

2. Granular:

a) **Neutrophils** are the most common of all leucocytes (comprise 50–70 % of the total leucocyte count). They possess high bactericidal activity. They are carriers of receptors to IgG, to complement proteins. They are the first to appear in the damaged area and destroy harmful agents. One neutrophil is capable to destroy 20–30 bacteria.

b) **Eosinophils** typically represent 0.5–5 % of the total leucocyte count and are stained with eosin. They stay in the blood for some hours and then migrate into tissues where they are destructed.

The functions of eosinocytes:

1. Phagocytosis.
2. Neutralization of toxins of albuminous nature.
3. Destruction of alien proteins and antigen-antibody complexes.
4. Production of plasminogen, i.e. participation in fibrinolysis.
5. Protection against parasitic infections.

High counts of eosinophils are typical of patients experiencing allergies and some autoimmune diseases. Eosinophils migrate toward the inflamed allergic tissue, detoxify some inflammation-inducing substances and also destroy allergen-antibody complexes, thus preventing the excess spread of a local inflammatory process. They are particularly effective against parasitic worms and their eggs.

c) Basophils are the least common leukocytes, typically comprising less than one percent of the total leukocyte count. They produce histamin and heparin (they are called heparinocytes). Heparin prevents blood coagulation, and histamin dilates capillaries, promotes resorption and wound healing.

The functions of basophils:

1. Regulation of the aggregate state of blood.
2. Regulation of the local blood flow (microcirculation) and permeability of capillaries.

Basophils and mast cells play an important role in some types of allergic reactions. Immunoglobulin E (IgE), which causes allergic reactions, has a special propensity to become attached to mast cells and basophils. Then, when specific antigens interreact with IgE, basophils release large quantities of histamine, heparin, and other substances which contribute to inflammation, cause local vascular and allergic reactions.

The normal count of leukocytes is $4–9 \times 10^9$ per liter.

The leukocyte formula (the differencial white blood cells count) is the percentage of each type of leukocytes. A high number of immature leukocytes in peripherial blood is known as the left shift of the leukocyte formula. It is most often found in infectious and inflammatory processes.

A high leukocyte count is called leukocytosis. There are physiological and pathological causes of leukocytosis.

Physiological leukocytosis is caused by the redistribution of leukocytes among the blood vessels and organs.

The physiological causes of leukocytosis are:

1. *Nutrition*. After meals leukocytes leave the depot and enter the bloodstream. They accumulate in the sub-mucous layer of the intestines, where they carry out the protective function.

2. *Muscular.* Under the influence of intensive muscle work the number of leukocytes increases by 3–5 times.

3. *Pregnancy*. Leukocytes are accumulated in the sub-mucous layer of the uterus.

4. *Newborns* (metabolic function).

5. *Pain*.

6. Emotional strain.

The pathological causes of leukocytosis are connected with diseases, tissue damage, infections, purulent, inflammatory, septic, and allergic processes.

Leukosis is the excess production of leukocytes. Leukocytes in these cases are poorly differentiated and do not carry out the physiological functions.

Leukocytopenia is an abnormally low number of leukocytes (less than 4×10^9 per liter).

The life span of various leukocytes differs (from 2–3 days till 2–3 weeks). Long-living lymphocytes (cells of immune memory) live for decades.

2.2.6. Thrombocytes, their structure, behavior and functions

Thrombocytes (blood platelets) have an irregular round shape and are 1–4 μm long and 0.5–0.75 μm deep (Figure 2.11).

Their amount in the blood is $150–450 \times 10^9$/L. They are formed in the red bone marrow by means of separation from the part of the protoplasm of megakariocytes. One megalokariocyte forms 3–4 thousand thrombocytes. 2/3 thrombocytes circulate in the blood, the others are located in the spleen. Their life span in the blood is 5–11 days, then they are destroyed in the liver, red bone marrow, and spleen.

The plasma membrane of thrombocytes contains glycoproteins (receptors), which are required for adhesion and aggregation. Thrombocytes contain

no nuclei. The range of the cytoplasm directly adjoining to the environment is not structured. The central part of the cytoplasm contains granules. There are 3 types of granules:

• α-granules (alpha granules) — contain proteins and glycoproteins which participate in blood coagulation (fibrinogen, fibronectin, Willebrand factor and others).

• δ-granules (delta or dense granules) — contain serotonin, calcium, ADP, ATP.

λ-granules (lambda granules, lysosomes) – contain lysosome enzymes.

Thrombocytes are capable of englobing non-biological foreign bodies, viruses, cell-bound immune complexes, i. e. participate in the nonspecific protective system of the body.

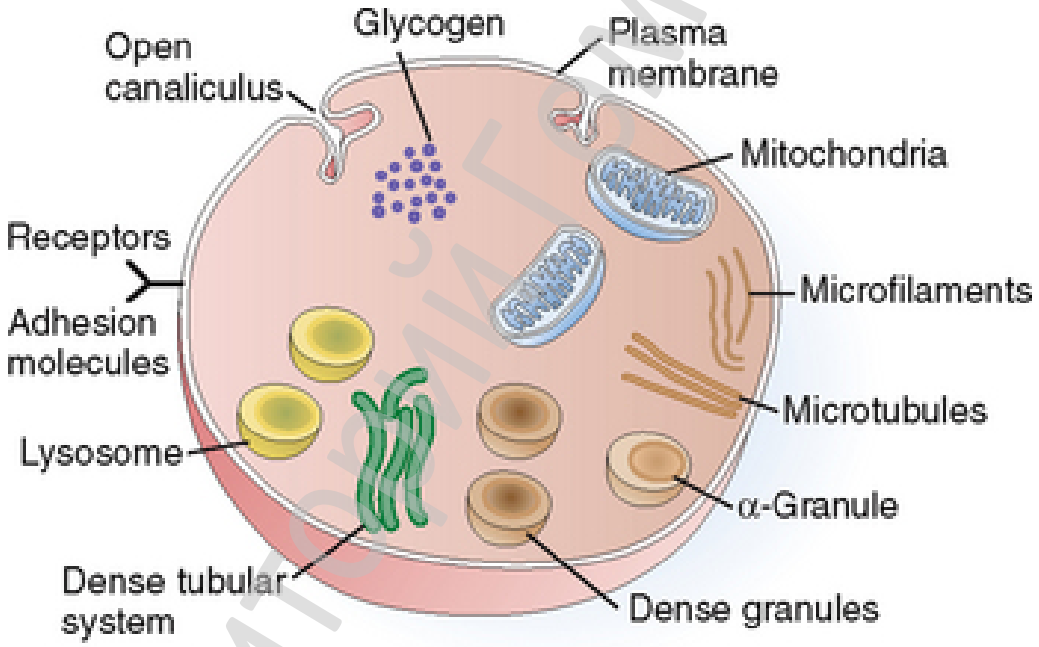


Figure 2.11 — Strucure of thrombocytes (from bianoti.com)

The destruction of thrombocytes leads to the release of substances which:

— participate in blood coagulation;

— promote angiospasm (serotonin (F10), adrenalin, noradrenalin);

— produce adhesion and aggregation of thrombocytes.

There are daily fluctuations of the thrombocyte count: in the afternoon it increases, during night-time — it goes down. One of the basic functions of thrombocytes is their participation in blood coagulation.

Review questions

1. What are the main functions and properties of leukocytes? Give the classification of leukocytes. Name the functions of different types of leukocytes.

2. What is the leukocyte formula? Explain its diagnostic value.

3. What is the normal leukocyte count in the blood? Give the definition of "leukocytosis" and name its types. Give the definition of "leukopenia".

4. Describe the structure and properties of thrombocytes. What is the normal number of thrombocytes in the blood? Name the functions of thrombocytes.

2.3. Hemostasis

2.3.1. Blood coagulation system

The maintenance of blood in a fluid state and its ability to circulate in the blood vessels within the confines of the circulatory system is a necessary condition for the organism`s homeostasis. It is ensured by *the system regulating the fluid state of blood (the system of hemostasis)* (Figure 2.12).

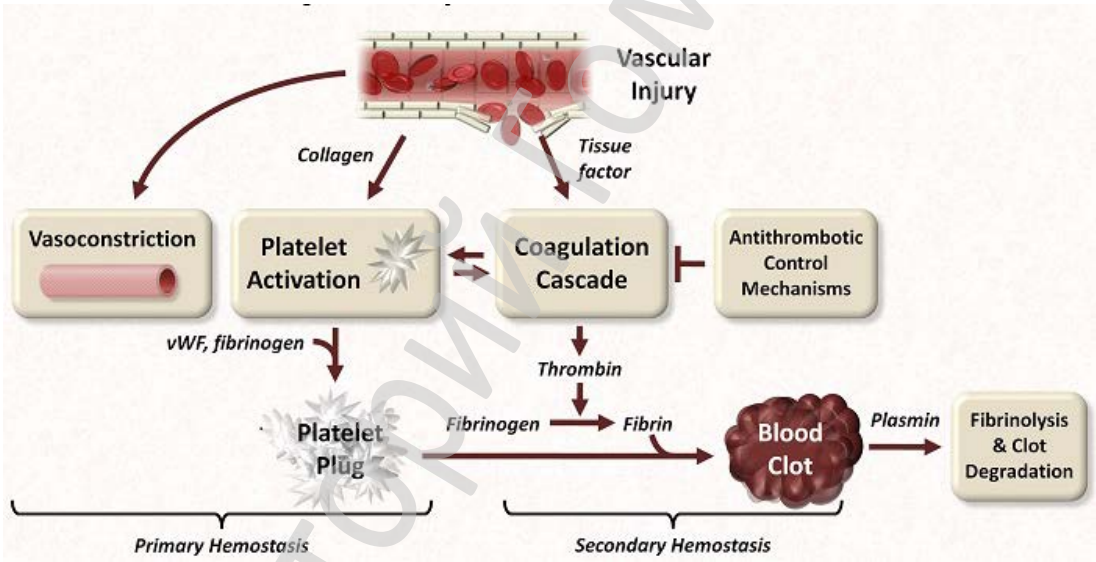


Figure 2.12 — The system regulating the fluid state of blood (from biology.reachingfordreams.com)

This system includes:

• Coagulation system of blood (microvascular and coagulation hemostasis).

• Anticoagulation system of blood (anticoagulants and fibrinolysis).

• Mechanisms of regulation.

Blood coagulation disorders lead to severe human diseases.

The term "hemostasis" means a complex set of reactions which lead to prevention and termination of bleeding or hemorrhage in ruptured blood vessels.

Hemostasis is achieved by several mechanisms:

- vascular constriction,
- formation of a platelet plug,
- blood coagulation and formation of a blood clot.

The system of hemocoagulation includes:

• Blood and tissues which produce and secrete substances participating in the above process.

• Neuro-humoral regulatory mechanisms.

2.3.2. Vascular platelet (initial, primary) hemostasis (Figure 2.13)

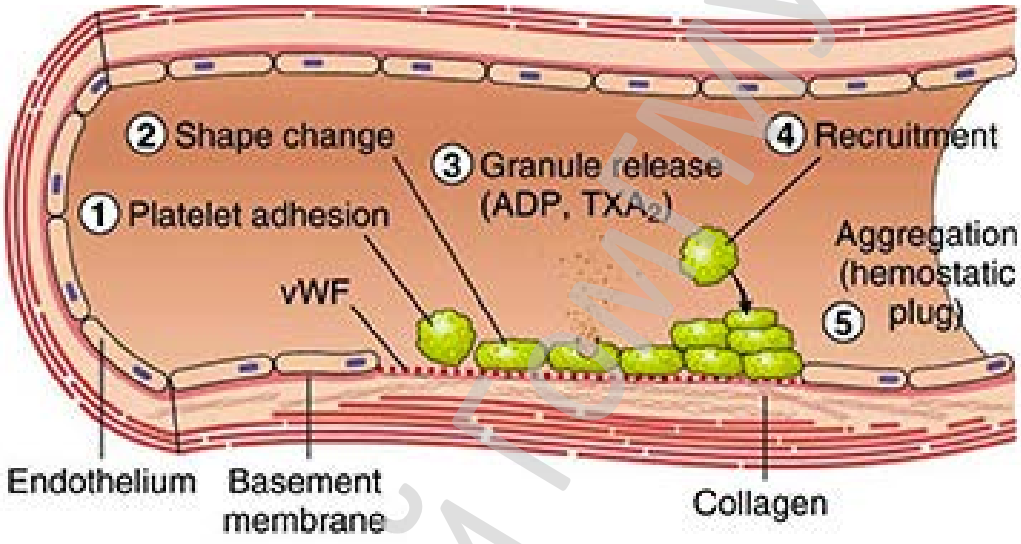


Figure 2.13 — Vascular-platelet hemostasis (by Kumar, V, 2009)

Notes: Platelets are attached to collagen fibers in the damaged area of the blood vessel (1). Platelets are activated, undergoing a shape change (2) and granule release (3). Released adenosine diphosphate (ADP) and thromboxane A_2 (TXA_2) induce additional platelet aggregation (4) and formation of the primary hemostatic plug (5).

In a healthy person the termination of bleeding in the microcirculatory flow with low arterial pressure is caused by the realization of the processes including:

1. Reflex spasm of the damaged blood vessel (the constriction of the vessel is caused by the release of noradrenalin, adrenalin, serotonin due to stimulation of receptors). It is known as *the initial angiospasm*.

2. Adhesion (attaching) of thrombocytes to the damaged surfaces (the injured area becomes positively (+) charged and thrombocytes have a negative electrical charge (-)). With participation of receptors they are attached to collagen in the damaged area of the blood vessel.

3. Accumulation and aggregation of thrombocytes on the damaged area. The stimulators of the given process are adrenalin, thrombin, Ca^{++}, thromboplastin, released from thrombocytes and erythrocytes (*internal system*), and collagen, released from the tissue cells of the damaged blood vessel (*external system*). As a result, the platelet plug is formed. The aggregation of thrombocytes at this stage is a reversible process.

4. Irreversible aggregation of thrombocytes. Thrombocytes flow into uniform mass, forming a thrombus, which is not permeable to blood plasma. The reaction is influenced by thrombin. The destruction of thrombocytes results in the release of physiologically active substances: adrenalin, noradrenalin, serotonin, nucleotides, coagulation factors (or clotting factors). They promote *a secondary vascular spasm*. Secreted in such a way, F3-platelet thromboplastin (thrombo-plastic factor) triggers the mechanism of coagulating hemostasis. A small amount of fibrin is produced.

5. Compression of the platelet plug. The compression of the platelet plug (thrombus) is ensured by the proteins of thrombocytes — thrombostenin (F6) and fibrin. It results in the termination of the bleeding.

In small blood vessels, the process of hemostasis stops at this stage. This hemostasis is called initial, or microvascular hemostasis.

In large blood vessels with high blood pressure, the platelet plug is not able to stop hemorrhage. In these vessels a stronger thrombus is formed as a result of other mechanism — coagulation cascades, or secondary hemostasis.

2.3.3. Secondary hemostasis

Secondary hemostasis includes the following:

• Plasma blood-coagulation factors.

• Blood-coagulation factors of the formed elements of blood.

• Tissue blood-coagulation factors.

I. Plasma factors (marked chronologically in the Roman numerals).

• **FI** — *fibrinogen*, the protein of plasma. Its concentration in the blood is 3 g/L, and it is produced in the liver. It is used as a basis for thrombus formation.

• **FII** — *thrombinogen (prothrombin)*. It is synthesized in the liver with the presence of vitamin K.

• **FIII** — *thromboplastin*. It is a phospholipoprotein, which is the part of the membranes of blood and tissue cells.

• **FIV** — *calcium ions* (Ca^{++}). About 1/2 Ca^{++} are not connected with the protein and 1/2 are in the complex with plasma proteins. FIV is necessary for all the phases of blood coagulation. It promotes the aggregation of thrombocytes and binds heparin.

• **FV** — *proaccelerin*. It is produced in the liver. It participates in the 1^{st} and 2^{nd} phases of blood coagulation.

• **FVI** — it has been excluded from the classification.

• **FVII** — *proconvertin*. This is a glycoprotein which is produced in the liver with the presence of vitamin K. It is necessary for the formation of thromboplastin (tissue factor).

• **FVIII** — *antihemophilic globulin A.* It is produced in the liver, spleen, and leukocytes. It activates prothrombin. It ensures the optimum conditions for the interaction of factors IX and X. It is necessary for the adhesion of thrombocytes and activation of prothromboplastin. If this factor is absent, hemophilia develops.

• **FIX** — *antihemophilic globulin B*, a plasma protein (glycoprotein) and a vitamin K-dependent factor. The absence of this factor causes hemophilia B.

• **FX** —*Stuart-Prower factor*, a vitamin K-dependent factor. It is a part of tissue and blood thrombokinase.

• **FXI** — *Antihemolytic factor C (plasma thromboplastin antecedent)*. It is necessary for the activation of thromboplastin and FIX. The absence of this factor results in hemophilia C.

• **FXII** — *Hagemun factor* — is activated during contact with an alien surface (for example, a site of the damaged blood vessel), that is why it is named the contact factor. It is the initiator of the formation of blood thromboplastin and all the processes of hemocoagulation. The absence of this factor results in hemophilia D.

• **FXIII** — *Fibrin-stabilizing factor.* It is contained in plasma, cells, and tissues. It is necessary for the formation of final or unsolvable fibrin. It is activated by thrombin and Ca^{++}. If the given factor was absent, wounds would heal very badly.

The phases of secondary hemostasis (Figure 2.14):

• **1st phase** — formation of **active thromboplastin** (tissue and blood). The process goes with the participation of the tissue and plasma factors: IV, V, VII, VIII, IX, X, XI, XII. The formation of thromboplastin takes place as a result of the interaction of the lipid factor with plasma factors. Blood thromboplastin is produced from destroyed blood cells (*internal system*). Tissue thromboplastin is released from the damaged cells of the walls of the blood vessels and tissues (*external system).* Active thromboplastin is necessary for the activation of thrombinogen.

• **II phase** — activation of inactive thrombinogen into the active form — **thrombin**. This process is influenced by FV — proaccelerin (accelerin**),** FX, Ca^{++} and some factors of thrombocytes.

• **III phase** — the process of the transformation of soluble fibrinogen into its unsoluable form — **fibrin**. Thrombin is necessary for the proteolysis of a fibrinogen molecule, transforming it into fibrin. Fibrinogen is produced in the liver. Vitamin K is necessary for its synthesis. Under the influence of thrombin with the presence of Ca^{++} the process of the formation of insoluble fibrin goes in 3 stages:

1. Influenced by thrombin, fibrinogen is splitted into fibrin-monomers.

2. After the polymerization of fibrin-monomers, the molecule of the soluble fibrin-polymer «S» is formed. For the polymerization the presence of calcium ions is necessary.

3. Under the influence of the fibrin-stabilizing factor (FXIII) insoluble fibrin («I») is formed.

The formed elements of blood get stuck in the fibrin nets, thus forming a blood thrombus. This thrombus is subjected to compression under the influence of the protein trombostenin. During the compression of the thrombus the wound closes.

The time of blood coagulation is 5–7 min.

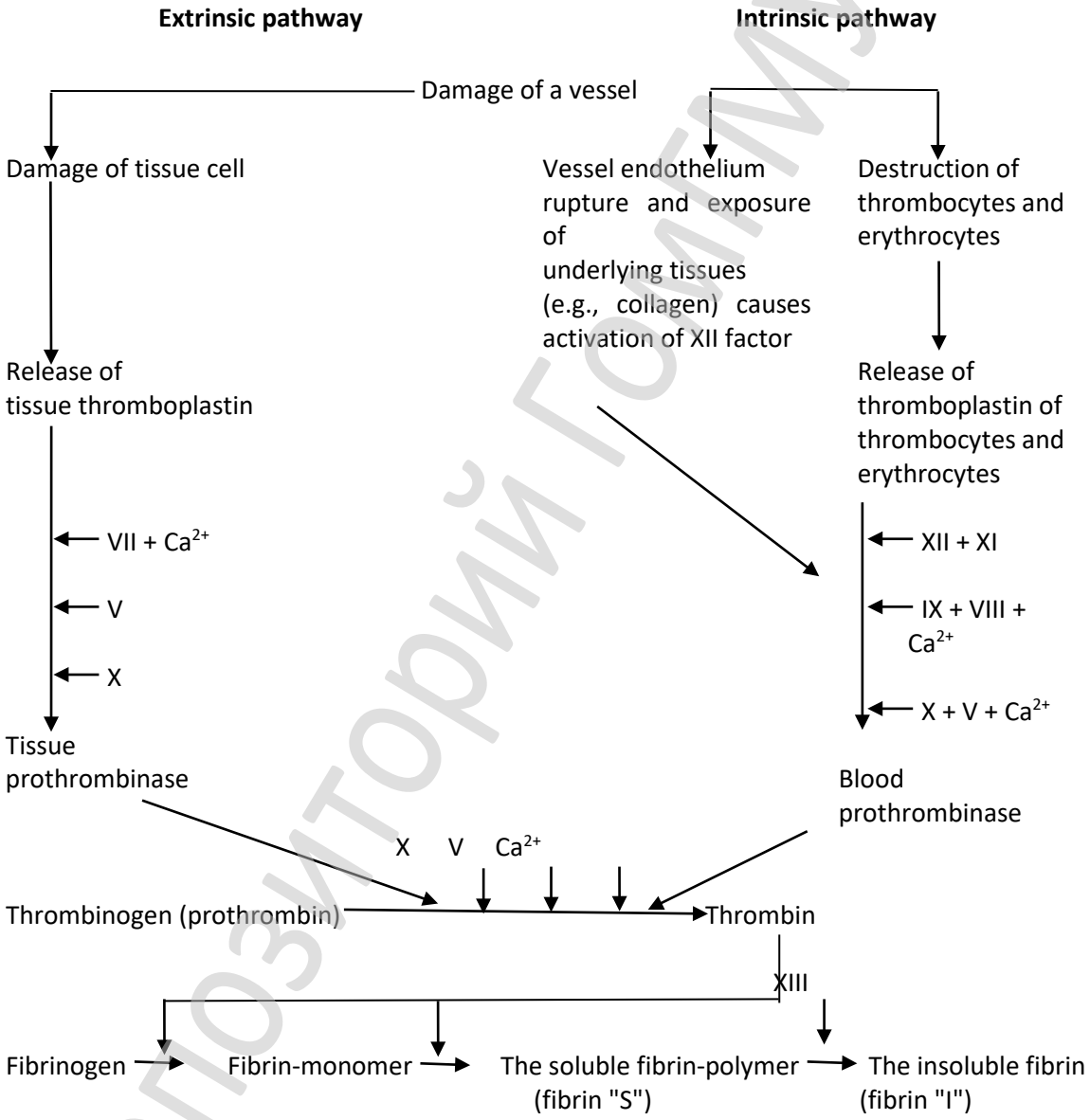


Figure 2.14 — Secondary hemostasis (scheme)

2.3.4. Blood anticoagulation system

Despite the fact that all the factors necessary for blood coagulation constantly circulate in the bloodstream, it remains fluid. It is one of the parameters of homeostasis.

The mechanisms of the maintenance of blood fluidity:

• Smooth surface of the blood vessels (prevents the activation of the Hagemun factor and aggregation of thrombocytes).

• Negative charges of the vessel wall and the formed elements of blood which provide their repulsion from each other.

•The blood vessel wall is coated with the thin layer of soluble fibrin, having the ability to adsorb active blood-coagulation factors.

• High blood flow rate (interferes the concentration of the coagulation factors).

• Presence of natural anticoagulants.

There are 2 groups of anticoagulants in the organism:

1. *Initial* (they are present in the blood constantly).

2. *Secondary* (they are formed during coagulation or fibrinolysis).

Initial anticoagulants — antithromboplastins, antithrombins:

• Antithrombin II (heparin). It inhibits all the phases of hemocoagulation.

• Antithrombin III — plasma factor of heparin. It transforms thrombin into inactive metathrombin.

• Antithrombin IV.

• Protein C — vitamin K-dependent protein. Activates fibrinolysis.

• Prostacyclin — inhibits thrombocyte aggregation.

Secondary anticoagulants**.** The function of secondary anticoagulants consists in restriction of intravascular coagulation.

• Antithrombin I (fibrin) is capable to bind with significant (up to 90 %) amounts of thrombin.

• Anticoagulants formed during fibrinolisis (products of degradation of thrombinogen, fibrinogen, and fibrin).

The anticoagulants which are used in laboratory clinical practice are:

1. Heparin.

2. Citric acid and its 0.5 % salt solutions.

The factors accelerating blood coagulation:

• Damage of the blood vessel walls.

• Augmentation of thromboplastin formation.

• Augmentation of vitamin K absorption.

• Augmentation of fibrinogen formation.

• High temperature.

• Increased amounts of amino acids in the blood.

• Decreased fibrinolysis.

The factors decreasing coagulation:

• Decreased thromboplastin formation.

• Decreased vitamin K absorption.

• Increased development of anticoagulants.

• Decreased fibrinogen formation.

Types of hemophilia

•Type A hemophilia — terminated phase I of coagulation (disturbance of thromboplastin formation). If FVIII is absent, phases II and III are also terminated.

• Type B hemophilia — absence of FIX.

• Type C hemophilia — absence of FXI (plasma predecessor of thromboplastin).

• Type D hemophilia — absence of FXII.

Hemophilia occurs more commonly in males than in females.

2.3.5. Fibrinolysis

Fibrinolysis is the process of dissolution of a blood thrombus. It is considered that in the blood there is constant transformation of a small amount of fibrinogen into fibrin, which is exposed to dilution — fibrinolysis.

During the damage of tissues the process of fibrin formation dominates over fibrinolysis and local blood coagulation takes place. The main function of fibrinolysis is the restoration of the lumen of the blood vessel.

Fibrinolysis starts immediately upon thrombus compression in 2 phases (Figure 2.15):

I phase — plasminogen transformation into *plasmin*.

II phase — plasmin-influenced dissolution of fibrin (thrombus) with the formation of peptides and amino acids.

Figure 2.15 — The activation of fibrinolysis (by Korobkov A. V., Chesnokova S. A., 1986)

The factor providing fibrinolysis is plasminogen, which under the influence of tissue and blood factors transforms into the active form — plasmin.

The main activators of plasmin formation are the blood and tissue plasminogen activators. The other factors which stimulate fibrinolysis are the active plasma factor XII, kallikrein-kinin system, urokinase, acid and alkaline phosphatases, trypsin, complement C_1, streptokinase.

Excessive fibrinolysis is prevented by plasmin inhibitors (antiplasmins) and inhibitors of the plasminogen activator.

2.3.6. Regulation of the aggregate state of blood

Normally, there is no intravascular blood clotting or it occurs to a small extent. The fragile process of the regulation of blood coagulation involves many factors and systems:

• Presence of the inhibitors of pro-coagulants in plasma.

• Many factors are in the inactive state.

• The concentration of pro-coagulants decreases due to fibrinolysis. Therefore, a thrombus is not formed in the blood vessels of fast blood flow but develops in the blood vessels of low blood flow.

• Pro-coagulants are inactive in the blood.

On the whole, the mechanism of the regulation of coagulation is neurohumoral. In the body there are special chemoreceptors reacting to the concentrations of thrombin, plasmin, and other factors of the coagulation and anticoagulation systems in the blood.

The stimulation **of the sympathetic** nervous system increases the speed of blood coagulation (hypercoagulation). It is pronounced in stress, pain, and is accompanied by the collateral release of adrenalin.

Under the influence of *adrenalin*:

• Thromboplastin is released from the vascular wall.

• FXII (the contact factor) is induced, which activates prothromboplastin.

• Phospholipids are released from erythrocytes.

• Glucocorticoids, somatotropic hormone, antidiuretic hormone, calcitonin, testosteron, progesteron initially cause hypercoagulation but then activate fibrinolysis.

Blood coagulation is prevented by the action of the complex anticoagulation mechanism:

•When thrombin is slowly formed in the blood vessels, it is neutralized by the plasma anticoagulants (antithrombins, heparin).

• Heparin (prevents the formation of thromboplastin and thrombin, activating fibrinolysis).

Review questions

1. What does the system regulating the fluid state of blood include? Give the definition of “hemostasis”. Name and describe the phases of primary hemostasis.

2. List the plasma factors of secondary hemostasis. Name and describe the phases of secondary hemostasis. How long does blood coagulation take in norm?

3. What are the mechanisms maintaining the fluid state of blood? Name the main initial and secondary anticoagulants. What are the factors which decrease and accelerate blood coagulation?

4. Give the definition of "fibrinolysis". Name and describe the phases of fibrinolysis.

5. Describe the main mechanisms of neuro-humoral regulation of coagulation and fibrinolysis.

2.4. Blood groups (types). Regulation of the blood system

2.4.1. Blood groups (types). Fundamentals of blood transfusion

In 1901 Karl Landsteiner observed that blood transfusions in different people in some cases caused erythrocyte agglutination, and in some did not. His further research and also that of J. Jansky allowed to discover the major human blood groups which differ from one another by the presence or absence of erythrocyte antigens (agglutinogens) and antibodies (agglutinins) in blood plasma (Table 2.5).

Table 2.5 — Blood groups (types) of the AB0 system

Blood groups	Erythrocytes	Plasma or serum
	Agglutinogen	Agglutinin
I (0)	0	**α,** ß
II (A)	**A**	ß
III (B)	**B**	**A**
IV (AB)	**AB**	**0**

The agglutinogens of erythrocytes are **A** and **B**. In blood plasma there are γ-globulin-natured specific antibodies (agglutinins α and ß). They have 2 centers of linkage that provide an opportunity of the formation of bridges between two erythrocytes and formation of erythrocyte conglomerates.

Normally, there are no agglutinins corresponding to agglutinogens, and everyone has their individual panel of erythrocyte agglutinogens (Figure 2.16).

In the blood of neonates there are no antibodies of the ABO system and antigens, which are absent in newborns, are formed within the first year of life.

For blood transfusion the blood is selected to avoid meeting similar agglutinogens of the donor with agglutinins of the recipient (e. g. A and α, B and ß). Donor agglutinins are not considered since they dilute in the recipient blood and thus they cannot cause agglutination of the recipient erythrocytes (in transfusion of small amounts of blood of 200–500 mL). During transfusion of a big amount (4–5 L) of blood plasma of 0 (I), a large number of agglutinins come

into the recipient blood. Thus, the dilution effect is lost and therefore the donor agglutinins may cause agglutination of the recipient erythrocytes.

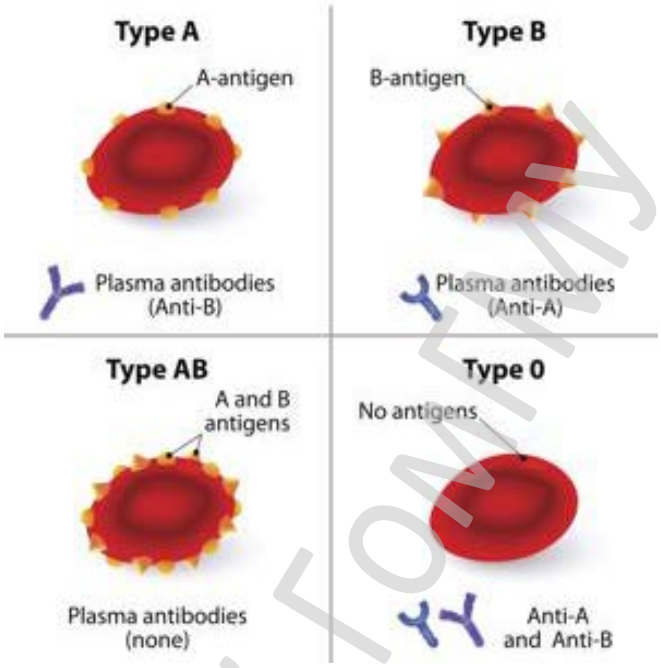


Figure 2.16 — ABO blood groups (from dreamstime.com)

As a rule, to avoid possible transfusion reactions, it is best to transfuse only matching blood types (that is, a type B+ recipient should ideally receive blood only from a type B+ donor and so on). In emergency situations, blood transfusions may be performed under the scheme (Figure 2.17.) of blood groups compatibility (Table 2.6).

Table 2.6 — Compatibility of various blood groups

Serum group	Erythrocyte group			
	I (0)	II (A)	III (B)	IV (AB)
I α, ß	–	+	+	+
II ß	–	–	+	+
III α	–	+	–	+
IV	–	–	–	–

Note: «+» — presence of agglutination (group incompatibility);
«–» — absence of agglutination (group compatibility).

Individuals with I (0) blood type are known as universal donors, those with blood type IV (AB+) are universal recipients.

To avoid complications duiring blood transfusions:

1. A blood group is determined with the application of the standard sera of I, II and III groups by blending a drop of each serum type with a drop of the

examined blood. The group compatibility is determined by the presence or absence of agglutination. To avoid mistakes, the examination is performed at a temperature of 15–25 °C. The drop of blood brought into the serum should be 3–5 times less than the serum drop. In case of indistinct results, the examination is repeated with the serum of other series.

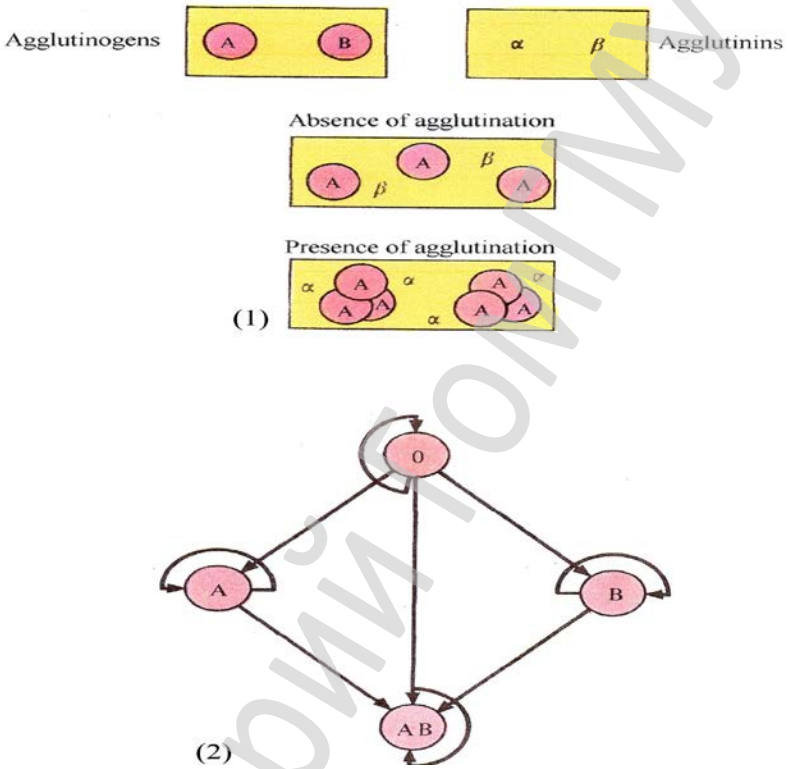


Figure 2.17 — Blood groups (by Korobkov A. V., Chesnokova S. A., 1986)

Notes: (1) Mechanism of agglutination. (2) Possible variants of transfusion of erythrocyte mass of different groups.

2. ***Direct and indirect tests***.

Direct test. The donor erythrocytes are mixed on a slide with the recipient plasma or serum at 37 °C. The purpose is to determine the presence of antibodies in the recipient serum to the donor erythrocytes. If there is no agglutination, the **indirect test** is carried out. The recipient erythrocytes are placed into the donor serum in order to reveal antibodies in the donor serum to the recipient erythrocytes.

3. ***Biological test***. First, a stream intravenous introduction of 10–15 mL donor blood is performed, and after 3–5 min the recipient is examined for the presence or absence of complications (high heart and respiration rates, shortbreath, heavy breathing, facial hyperemia, etc.). This introduction is repeated for *three times*. In absence of any complications, the rest of the blood is administered.

People with I (0) blood group have anti-A and anti-B immune agglutinins (ά and ß) present in blood plasma. Transfusion of large amounts of this blood is prohibited since in these cases the donor agglutinins are not diluted in the recipient plasma, which can cause agglutination of erythrocytes in the recipient. Besides, people with I (0) blood group have **antigen H** on the surface of erythrocytes which can interact with anti-H-antibodes frequently present in the blood plasma of II (A) and IV (AB) groups and less in III (B) group. In these cases blood transfusion of I (0) group to individuals having other blood groups can result in hemolytic shock (hemotransfusion shock). Therefore, universal donors are called *dangerous* universal donors.

The presence of H-antigen on the surface of erythrocytes ensured the name of the AB0 system as ABH.

The prevalence of the blood groups: I (0) — 40–50 %, II (A) — 30–40 %, III (B) — 10–20 %, IV (AB) — 5 %. Geography: 40 % people in Central Europe have blood group II (A), 90 % in North America — I (0), more than 20 % in Central Asia — III (B). I (0) blood group is present in all nationalities, II (A) — dominates in inhabitants of Europe, Middle East, China, Japan, IV (AB) — dominates in inhabitants of India, Central Asia.

Apart from agglutinogens A and B (systems AB0), more than 400 agglutinogens are known, 140 from which (M, N, S, P, Di, C, K, Ln, Le, Fy, Ik, etc.) make almost 20 groups or systems.

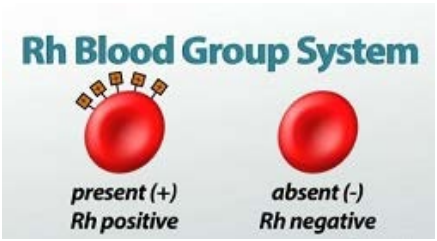
From them, it is possible to note systems: MNSS, P, Lutherans, Lewis, Kidd, etc. For example, the Kell-Cellano system consists of 2 agglutinogen K and k and forms 3 groups — КК, кк and Кк. The given system of blood is present in 100 % people.

Fortunately, the antigenic properties of the majority of these antigens are poorly expressed and neglected during blood transfusions. However, these systems matter in frequent blood transfusions. Therefore, it is not recommended to repeat blood transfusions from the same donor.

Alongside with agglutinins, blood plasma may contain *hemolysins* (marked agglutinins α and ß respectively).They are mainly IgM antibodies and their binding with similar agglutinogens results in erythrocyte hemolysis. Their action is revealed at a temperature of 37–40 °C and within 30–40 seconds the hemolysis of erythrocytes happens.

2.4.2. Rhesus-factor

The Rh-factor (Rh) was discovered in 1940 by Landsteiner and Wiener. The Rh-factor is an antigen located on the surface of erythrocytes. In Europe 85 % people have this factor, in 15 % it is absent. People whose blood has the Rh-factor are called rhesus- positive (Rh+), those who do not have it are rhesus-negative (Rh-) (Figure 2.18).



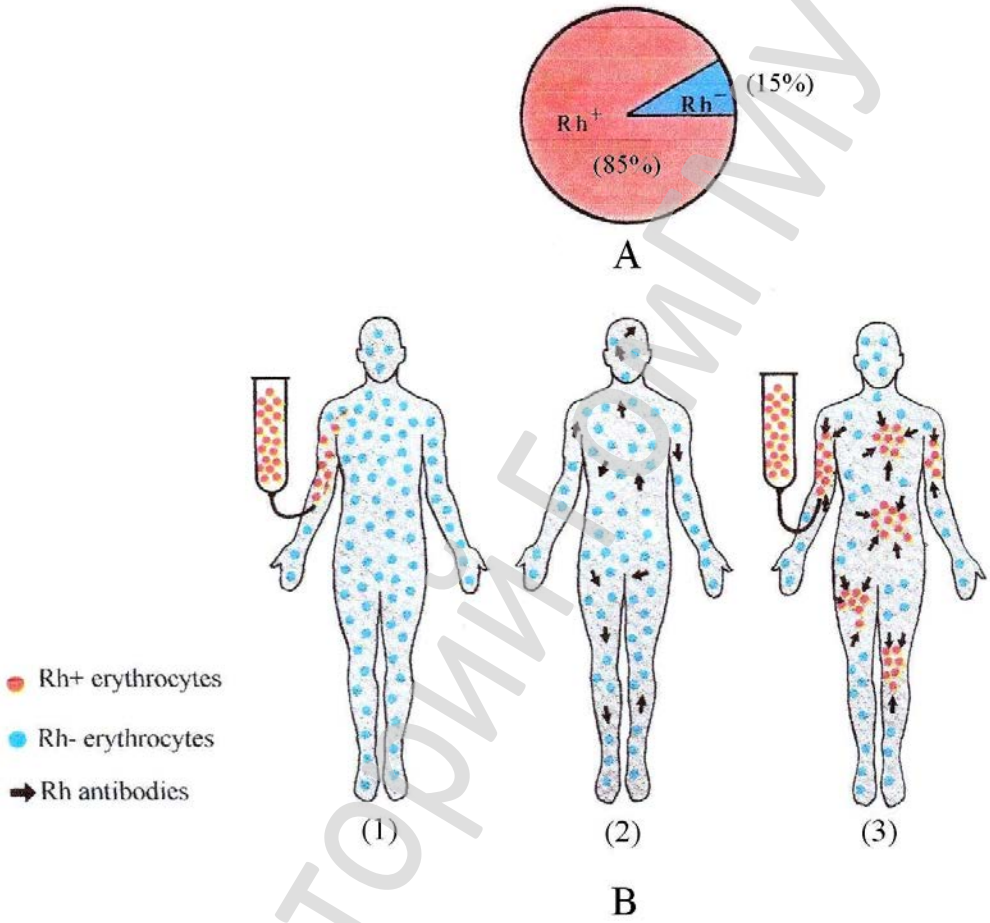


Figure 2.18— Rhesus factor (Rh) (by Korobkov A. V., Chesnokova S. A., 1986)

Notes: A — frequency of Rh+ and Rh– people. B — «Rhesus conflict». (1) — transfusion of Rh+ blood to a Rh– recipient. (2) — the production of Rh antibodies in the organism of the recipient. (3) — the second transfusion of Rh+ blood to the Rh– recipient causes agglutination

The Rh-factor includes 6 basic antigens: C, D, E, c, d, e. Among them, the most powerful is D (it possesses high antigenic properties).

In Rh^+ blood transfusion to a Rh^- person the agglutinins are formed in the recipient slowly (within several months). That is why a single transfusion does not lead to any hemotransfusion complications. A repeated transfusion causes rhesus-incompatibility (rhesus-conflict) with serious complications: formation of erythrocyte conglomerates and their hemolysis, intensive intravascular blood coagulation, many organs are affected, the kidneys in particular.

It is important to take into account the rhesus-factor of a woman during pregnancy. If a fetus inherits the Rh-positive blood from its father, and the mother is Rh-negative, the mother's organism develops antibodies to Rh^+ erythrocytes of the fetus (Figure 2.19). Rh formation in the fetus starts only from the 3rd month of the antenatal period and becomes active by the end of the pregnancy. During this period the mother`s organism has no time for Rh sensitization. The formation of antirhesus-agglutinins lasts slowly (3–5 months). Therefore, pregnancy complications usually do not occur during an Rh-negative woman's first pregnancy with an Rh-positive fetus, because her body does not have a chance to develop a lot of antibodies. Rh incompatibility develops in a second and further pregnancies (also Rhesus disease or Rh factor disease), which causes the antibodies in the mother`s blood attack and destroy the fetus`s erythrocytes, which can result in its severe health problems or even intra-uterine death.

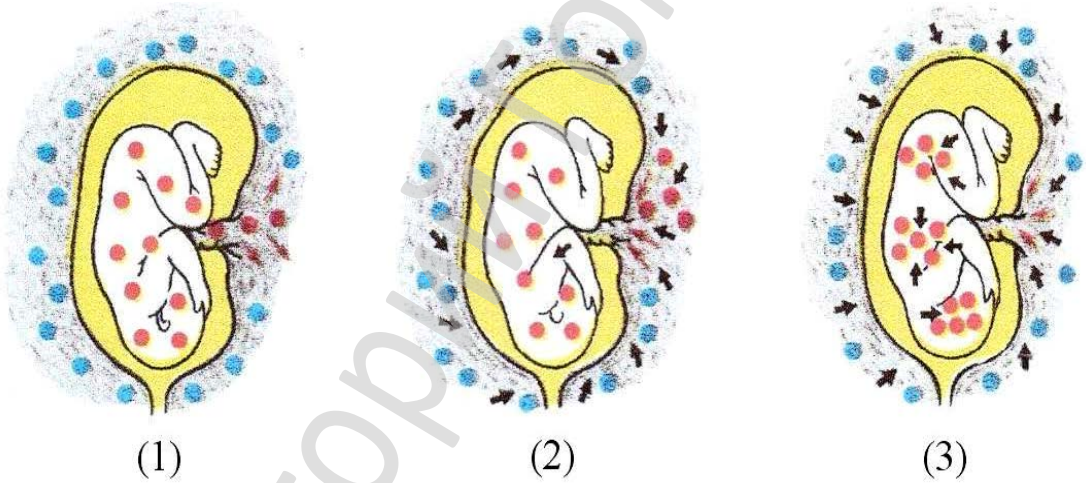


Figure 2.19 — Rh incompatibility between a Rh-negative pregnant woman and a Rh-positive fetus (by Korobkov A. V., Chesnokova S. A., 1986)

Notes: 1 — immunization of the Rh- mother by the Rh+ erythrocytes of the fetus. 2 — production of Rh antibodies in the mother`s organism. 3 — agglutination of the Rh+ erythrocytes of the fetus by the mother`s antibodies.

The development of antibodies in Rhesus-negative women can be prevented by injections of immune serum containing 'anti-D gamma globulin' (anti-D administration) instantly after the delivery of a rhesus-positive baby. Anti-D gamma globulin' destroys fetal Rh^+ erythrocytes which got into the mother`s blood, i.e. the factor causing antibody formation and their accumulation is prevented.

2.4.3. Regulation of the blood system

Hemopoiesis is regulated by the neuro-humoral mechanism (Table 2.7).

Table 2.7 — Humoral factors which regulate hemopoesis

Humoral factors which regulate erythropoiesis		**Humoral factors which regulate leukopoiesis**		**Humoral factors which regulate thrombocytopoiesis**	
Factor	**The role of the factor**	**Factor**	**The role of the factor**	**Factor**	**The role of the factor**
Iron	In the structure of hemoglobin there is the iron-containing heme group	Products of leucocyte destruction	The more destruction of leucocytes is, the higher is their formation	Thrombocytopoietins of short action	They are formed in the spleen and stimulate the release of thrombocytes into the blood
Vitamin B_{12}	It is necessary for normal formation, growth of erythrocytes	Tissue destruction products	They stimulate leukopoiesis		
Kastle's antanmic factor	It is necessary for the absorption of vitamin B_{12} in the intestine	Microbes and their toxins	They stimulate leukopoiesis	Thrombocytopoietins of long action	They are contained in blood plasma and stimulate the formation of thrombocytes in the bone marrow
Ascorbic acid	It promotes converting Fe+++ into Fe++ and iron absorption in the intestine	The colony-stimulating factors	They stimulate leukopoiesis		
Erythropoietins	They influence the cells-predecessors of erythrocytes, stimulate their proliferation, synthesis of hemoglobin	Adrenalin, hydrocortisone	They cause leukocytosis due to the release of leukocytes from the blood depot (but glucocorticoids decrease the formation of eosinophils and lymphocytes)		
Products of erythrocyte destruction	They stimulate erythropoiesis (autoregulation). The number of destroyed erythrocytes is equal to that of newly formed erythrocytes (self-control)	Interleukins	They stimulate leukopoiesis		
Andrgens adrenlin, thyroxin, somatotropic hormone	They stimulate erythrogenesis				
Estrgens	They decrease erythrogenesis				

Erythropoiesis

Neuro-humoral regulation of erythropoiesis. For normal erythropiesis (erythrogenesis process) adequate nutrition with sufficient amount of *ferrous lactate* is necessary. It is the limitation factor, and deficiency results in anemia.

Erythropoietins are manufactured in many organs (spleen, liver, bone marrow, salivary glands) but mostly in the kidneys. The basic starting mechanism is hypoxia or blood loss. Kidney tissue hypoxia leads to increased levels of *hypoxia-inducible factor-1 (*HIF-1), which serves as a transcription factor for a large number of hypoxia-inducible genes, including the erythropoietin gene.

Kastle's antianemic factor is the complex of vitamin B_{12} (external factor) and gastromycoproteid in the stomach (internal factor). This complex comes into the liver and from it into the bone marrow (Figure 2.20).

Ascorbic acid promotes absorption of ferrous lactose into the intestines converting it from Fe^{+++} into Fe^{++}. The daily need in ferrous lactose for normal erythrogenes is 20–25 mg.

The products of erythrocyte destruction stimulate hemopoiesis (autoregulation). The number of destroyed erythrocytes is equal to that of newly formed erythrocytes (self-control).

Hormones. Androgens increase and estrogens decrease erythropiesis. That is why the count of erythrocytes in men's blood is higher than in women`s.

Erythropiesis is stimulated by adrenalin, thyroxin, somatotropic hormone.

Figure 2.20 — Factors which stimulate erythropoiesis
(by Korobkov A. V., Chesnokova S. A., 1986)

The role of the nervous system. The stimulation of the nerves going to the bone marrow enforces erythropiesis. Nervous and hormonal factors affect the red bone marrow through erythropoietins.

The role of the cerebral cortex. It is possible to develop a conditioned reflex resulting in the decreased formation of erythrocytes.

Leukopoiesis.

Neuro-humoral regulation of leukopoiesis.

1. Stimulation of leukopoiesis *by the products of leukocyte destruction* (self-control). The more the destruction is, the more leukocytes are produced (FIgure 2.21).

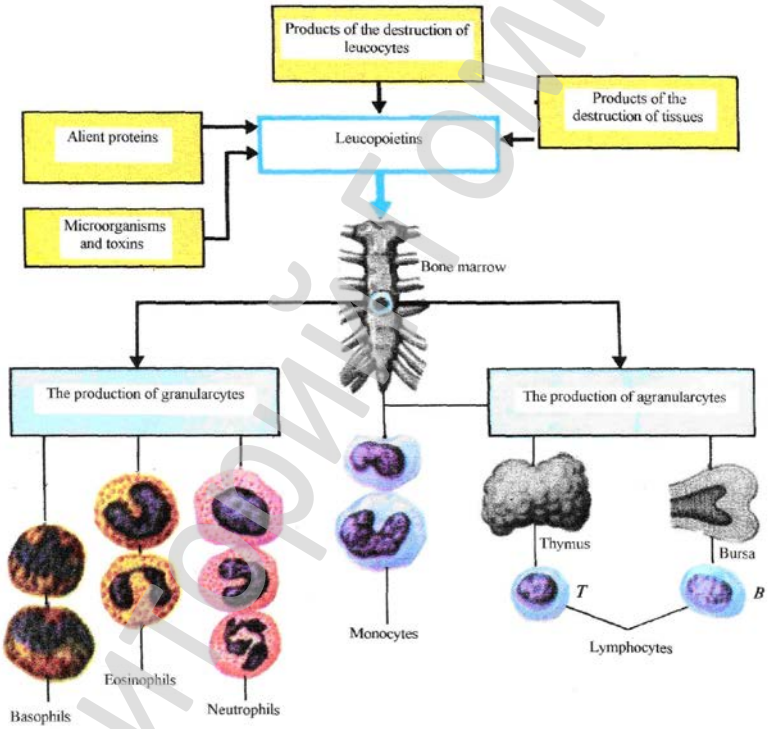


Figure 2.21 — Factors which stimulate leucopoiesis
(by Korobkov A. V., Chesnokova S. A., 1986)

2. S*timulation by tissue destruction products,* especially by their proteins.

3. *Stimulation by microbes and their toxins*.

4. *Stimulation of leukopoiesis by leukopoietins.*

5. Stimulation of leukopoiesis by the colony-stimulating factors. These factors are produced by macrophages, endothelium and a number of other immune cells. The colony-stimulating factor (GM-CSF) stimulates both granulocyte and monocyte production; the other two, namely the granulocyte colony-stimulating factor (G-CSF) and monocyte colonystimulating factor (M-CSF), stimulate granulocyte and monocyte production, respectively.

6. Interleukins (IL) are produced by leukocytes (mainly by T-helper lymphocytes and activated macrophages) and promote the development and differentiation of leukocytes and hemopoetic cells. For example, IL-3 stimulates the production of granulocytes and monocytes, IL-5 regulates the growth of eosinophils, IL-2, IL-4, IL-6 and IL-7 regulate growth and differentiation of T- and B-Lymphocytes.

7. *Hormones.* The release of adrenalin and hydrocortisone results in leukocytosis due to the release of neutrophils, monocytes, and lymphocytes from the blood depot (leukocytosis caused by stress, emotional excitation).

The role of the nervous system. The stimulation of the sympathetic nervous system increases the number of neutrophils. The stimulation of the vagus reduces the number of leukocytes in peripheral blood.

Thrombocytopoiesis

Thrombocytopoietins can be of short or long action. The former are produced in the spleen and stimulate the release of thrombocytes into the blood. The latter are contained in blood plasma and stimulate the formation of thrombocytes in the bone marrow.

Thrombocytopoiesis increases after blood loss. The number of thrombocytes can increase within a few hours and can exceed their normal number twice.

2.4.4. Blood-substituting solutions

In hemodynamic disorders caused by blood loss, apart from blood transfusion various blood-substituting solutions (blood fluids) are used (Table 2.8).

Blood-substituting solutions should conform with the following requirements:

- Their physico-chemical properties should be close to the basic parameters of blood (isotonic, isoionic, etc.).
- Absence of the influence on the basic biological properties of blood.
- Absence of toxicity.
- Long-term stay in the vascular system.
- It is possible to maintain sterilization and long storage of solutions.
- They should not produce sensitization and their reintroduction should not lead to anaphylaxis.

Salt solutions (Saline solution, Ringer-Locke solution and others) have a low molecular weight, compared with protein and colloid solutions and thus are quickly removed from the bloodstream, i. e. they can replace the volume of the lost blood within a short period of time (dehydration, acute blood loss, intoxication etc).

Table 2.8 — Blood-substituting solutions

Kind of the solution	Examples of the solutions	Positive property of the solutions	Negative property of the solutions	The cases of using the solutions
Salt solutions	Saline solution — (0.85–0.9 % NaCl), Ringer-Locke solution	They do not cause any allergic reactions (sensitization)	They are quickly removed from the blood vessels	They can replenish the volume of the lost blood within a short period of time. They can be used for normalization of the water-salt exchange and acid-base balance
Synthetic colloid solutions	Reopoliglucin, Macrodex, Haemodez	They stay in the blood vessels for a long period of time. They can bind toxic substances	They can cause allergic reactions (sensitization)	They can replenish the volume of the lost blood within a long period of time. They can be used to improve hemodynamics and have the most pronounced effect in shock and intoxication.
Protein preparations	Solution of albumin (5 %), Solution of gelatin (8 %) Native, preserved and fresh frozen plasma	– // – – // –	The preparations of plasma can contain dangerous infections agents (for example – HIV, hepatitis B virus)	– // – – // –
Blood components	Preserved blood and plasma, Erythrocyte mass, Leukocytes (fresh), Thrombocytes (fresh)	Different kinds of preparations have special qualities according to the components of preparation	Blood fluids may contain dangerous infectious agents (for example — HIV, hepatitis B) Blood fluids have antigenic qualities and can cause posttransfusion complications	Different kinds of preparations can be used according to what is necessary for a patient (for example, a low count of thrombocytes calls forth their transfusion)

The drawback of synthetic *colloid* solutions (plasma substitutes) is their ability to induce allergic responses.

Protein preparations:

- Native, preserved and fresh frozen plasma (FFP).

- 5 % albumin solution.
- Protein — it is an albuminous preparation of isogenic human plasma.

They have a high molecular weight and are slowly removed from the bloodstream (applied in shock, blood loss, burns, and in the treatment of pathological processes accompanied by dehydration). Their introduction does not cause pathological reactions but bind toxic materials. Their intravenous introduction increases the volume of circulating blood.

Whole blood transfusions are no longer common. The blood components *necessary for the organism* (plasma, erythrocyte mass, etc.) are mainly used for transfusions.

Blood components: preserved blood, plasma, erythrocyte mass, washed erythrocytes, leukocytes (fresh), thrombocytes (fresh).

Review questions

1. What factors determine the human blood groups? Describe the AB0 blood group system. What are the basic principles of hemotransfusion? Describe how the determination of the blood groups with the application of standard serum is performed. Name and describe the tests used for the determination of blood compatibility (cross-matching).

2. What is the Rh-factor? Name the Rh-factor antigens. In what situations is rhesus-incompatibility (rhesus-conflict) observed? Describe the mechanism of its development. What is anti-D administration?

3. What are the main requirements for blood-substituting solutions? Name and describe the types of blood-substituting solutions and their positive and negative aspects.

4. Name and describe the main nervous and humoral mechanisms of the regulation of erythropoiesis, leukopoiesis, and thrombocytopoiesis.

Multiple Choice Questions
PHYSIOLOGY OF BLOOD

1. A set of reactions which provide the maintenance or restoration of the constancy of an organism`s internal environment is...

Variants of answer:

a) hemopoiesis;

b) homeostasis;

c) hemostasis;

d) hemolysis;

e) hematocrit.

2. In 1939 G. F. Lang formulated the notion of blood as the system including...

Variants of answer:

a) peripheral blood, organs of hemopoiesis, organs of blood destruction;

b) peripheral blood, organs of hemopoiesis, organs of blood destruction, humoral mechanism of regulation;

c) peripheral blood, organs of hemopoiesis, organs of blood destruction, neurohumoral apparatus of regulation.

d) peripheral blood, organs of hemopoiesis, organs of blood destruction, nervous mechanism of regulation;

e) peripheral blood, organs of blood destruction, neurohumoral apparatus of regulation.

3. Which function of blood is caused by the presence of antibodies and phagocytosis of leukocytes?

Variants of answer:

a) protective;

b) trophic;

c) transport;

d) respiratory;

e) regulatory.

4. The respiratory function of blood is provided by...

Variants of answer:

a) heparin;

b) plasma;

c) hemoglobin;

d) thrombin;

e) histamine.

5. The hematocrit characterizes...

Variants of answer:

a) the system of hemostasis;

b) the volumetric ratio of the formed elements and whole blood;

c) the quantitative ratio of the formed elements of blood;

d) the ratio of the formed elements and serum of blood;

e) the percentage ratio of the number of platelets to the total blood volume.

6. How will the oncotic pressure of blood change, if the amount of general protein in the blood is not changed and the amount of albumins is low?

Variants of answer:

a) it will increase;

b) it will not change;

c) it will decrease;

d) it can either decrease or increase;

e) it will not depend on the protein content.

7. Which pressure is created by the proteins of blood plasma?

Variants of answer:

a) osmotic;

b) hydrostatic;

c) oncotic;

d) hemodynamic;

e) atmospheric.

8. Which protein of blood plasma provides iron transport?

Variants of answer:

a) albumin;

b) transferrin;

c) transcobolamin II;

d) transducin;

e) none of the above.

9. What factors participate in the maintenance of the acid-alkaline balance of blood plasma?

Variants of answer:

a) osmotic pressure;

b) buffer systems;

c) ions and nutrients;

d) plasma blood-coagulation factors;

e) all the answers are correct.

10. The buffer properties of proteins provide...

Variants of answer:

a) the maintenance of the osmotic pressure;

b) the decreased concentration of hydrogen ions in the blood;

c) metabolism in the blood;

d) the maintenance of the constant concentration of hydrogen ions in the blood;

e) blood coagulation.

11. Which buffer system does not exist?

Variants of answer:

a) hemoglobin;

b) phosphate;

c) chloric.

d) carbonate;

e) protein.

12. Carboxyhemoglobin is...

Variants of answer:

a) a bond of hemoglobin with CO_2;

b) a bond of hemoglobin with H_2CO_3;

c) a bond of hemoglobin with CO;

d) a bond of hemoglobin with Ca_2CO_3;

e) a bond of hemoglobin with O_2.

13. What does the color index of blood reflect?

Variants of answer:

a) the total amount of hemoglobin in the blood;

b) the amount of hemolysed erythrocytes;

c) the amount of erythrocytes per 1 liter of blood;

d) relative saturation of erythrocytes with hemoglobin;

e) the number of red blood cells in the organism.

14. Destruction of the membrane of erythrocytes and hemoglobin release into blood plasma under the action of various factors is called...

Variants of answer:

a) plasmolysis;

b) hemolysis;

c) fibrinolysis;

d) hemostasis;

e) homeostasis.

15. How does the erythrocyte sedimentation rate (ESR) change due to an increased number of large protein molecules (globulins and fibrinogen) in blood plasma?

Variants of answer:

a) the ESR does not decrease;
b) the ESR does not change;
c) the ESR does not decrease sharply;
d) the ESR increases.
e) the proteins do not influence the ESR.

16. Which function is not performed by leukocytes?

Variants of answer:

a) phagocytosis;
b) synthesis of collagen and elastin;
c) active movement;
d) migration on the gradient of chemical factors;
e) humoral and cell-mediated immunity.

17. Which cells are differentiated into macrophages after they leave the blood vessels and enter the surrounding tissues?

Variants of answer:

a) eosinophils;
b) basophils;
c) T-lymphocytes;
d) monocytes;
e) B-lymphocytes.

18. Neutrophils provide mainly...

Variants of answer:

a) the production of specific antibodies;
b) heparin transport;
c) the phagocytosis of microorganisms;
d) the activation of lymphocytes;
e) histamine synthesis.

19. The function of eosinophils is...

Variants of answer:

a) the transport of carbonic gas and oxygen;
b) the maintenance of the osmotic pressure;
c) the production of antibodies;
d) desintoxication in allergic reactions;
e) the maintenance of the oncotic pressure.

20. Which blood cells contain active histaminase?

Variants of answer:

a) basophils;
b) monocytes;
c) eosinophils;
d) erythrocytes;
e) B-lymphocytes.

21. Which cells produce histamin during their stimulation?

Variants of answer:

a) neutrophils;
b) eosinophils;
c) basophils;
d) monocytes;
e) lymphocytes.

22. How is the percentage ratio of all the kinds of leukocytes called?

Variants of answer:

a) the color index;
b) the hematocrit;
c) the leukocyte formula;
d) leukocytosis;
e) leukopenia.

23. The increased count of leukocytes in peripheral blood is called ...

Variants of answer:

a) leukocytosis;
b) leucopoiesis;
c) leukopenia;
d) thrombocytosis.
e) anemia.

24. How does the leukocyte count change after food intake, muscle work, in pregnancy, in strong emotions?

Variants of answer:

a) it decreases;
b) it does not change;
c) it increases;
d) it decreases after food intake, muscle work, but increases in pregnancy, strong emotions;
e) it decreases in pregnancy, strong emotions, but increases after food intake, muscle work.

25. Agglutinins are a component of...

Variants of answer:

a) erythrocytes;

b) plasma;

c) leucocytes;

d) thrombocytes;

e) hemoglobin.

26. Agglutinogens are a component of...

Variants of answer:

a) plasma;

b) leukocyte nuclei;

c) thrombocytes;

d) erythrocyte membranes;

e) hemoglobin.

27. Which combination of agglutinogens and agglutinins does I blood group have?

Variants of answer:

a) AB and 0;

b) B and alpha;

c) 0 and alpha, beta;

d) A and beta;

e) AB and alpha, beta.

28. In an individual having III blood group, plasma contains …agglutinin.

Variants of answer:

a) beta;

b) alpha;

c) alpha, beta;

d) there are no alpha and beta agglutinins.

e) delta.

29. In an individual having IV blood group, erythrocytes contain... agglutinogens

Variants of answer:

a) A;

b) B;

c) 0;

d) AB;

e) all the answers are correct.

30. Which blood group of the ABO system does not contain A and B agglutinogens?

Variants of answer:

a) the first;
b) the second;
c) the third;
d) the fourth;
e) the third and the fourth.

31. Which variant has the impossible combination of agglutinogens and agglutinins in the ABO system?

Variants of answer:

a) B and alpha;
b) 0 and alpha, beta;
c) B and beta;
d) AB and 0;
e) A and beta.

32. Is it possible to transfuse the blood of the same donor to the patient repeatedly, and if no, then why?

Variants of answer:

a) it is possible without restrictions;
b) it is possible at small amounts;
c) it is possible for the first group of the ABO blood group system;
d) it is impossible, because each person has the individual blood group;
e) it is possible for the fourth group of the ABO blood group system.

33. It is possible to transfuse ... to an individual with I blood group.

Variants of answer:

a) any group blood;
b) IV group blood;
c) I group blood;
d) II group blood;
e) III group blood.

34. An individual with A (Rh^+) blood group can be a donor for people having the blood group of...

Variants of answer:

a) A, Rh^-;
b) 0, Rh^+;
c) B, Rh^+;
d) A, Rh^+;
e) B, Rh^-.

35. Which blood group is determined, if the mixing of a blood sample with all the standard sera does not lead to agglutination?

Variants of answer:

a) II (A) blood group;

b) I (0) blood group;

c) III (B) blood group;

d) IV (AB) blood group;

e) all the answers are correct.

36. Which blood group is determined, if the mixing of a blood sample with all standard sera of I, II, III groups leads to agglutination?

Variants of answer:

a) II (A) blood group;

b) I (0) blood group;

c) III (B) blood group;

d) IV (AB) blood group;

e) all the answers are correct.

37. The Rhesus antigen is a component of...

Variants of answer:

a) plasma;

b) erythrocyte membranes;

c) leukocyte nuclei;

d) thrombocyte membranes.

e) hemoglobin.

38. In which situation can Rh incompatibility (Rhesus conflict) be observed?

Variants of answer:

a) mother — Rh^+; father — Rh^-, a fetus — Rh^-;

b) mother — Rh^-; father — Rh^+, a fetus — Rh^-;

c) mother — Rh^+; father — Rh^-, a fetus — Rh^-;

d) mother — Rh^-; father — Rh^+, a fetus — Rh^+;

e) mother — Rh^+; father — Rh^+, a fetus — Rh^-.

39. The system of hemostasis provides...

Variants of answer:

a) the maintenance of the fluid state of blood;

b) blood coagulation inside the blood vessels;

c) the maintenance of the fluid state of blood and blood coagulation in the damaged blood vessels;

d) the compression of fibrin thrombus;

e) the maintenance of the constancy of the internal environment.

40. Which factor transforms from a soluble state into insoluble one during blood coagulation?

Variants of answer:

a) fibrinogen;
b) antigemophilic globulin A;
c) prothrombin;
d) tissue thromboplastin;
e) proaccelerin.

41. For the course of all the hemocoagulation phases the participation of … ions is necessary:

Variants of answer:

a) sodium;
b) potassium;
c) calcium;
d) fluorine;
e) copper.

42. Which factor provides the transformation of soluble fibrin-polymer into insoluble fibrin?

Variants of answer:

a) IV-ions of Ca^{++};
b) VII-proconvertin;
c) XIII-fibrinstabilization factor;
d) XI-antigemophilic globulin C;
e) VIII-antigemophilic globulin A.

43. What is plasmin and what is it necessary for?

Variants of answer:

a) it is the dry residual of plasma;
b) it is a plasma protein;
c) it is a protease, which activates fibrin formation;
d) it is a protease, which splits fibrin;
e) it is a protease, which activates thrombin **.**

44. The substances which prevent blood coagulation and which have the fibrinolytic action are called...

Variants of answer:

a) coagulants;
b) factors of blood coagulation;
c) anticoagulants;
d) homostatins;
e) myorelaxants.

45. How does the initial anticoagulants differ from the secondary anticoagulants?

Variants of answer:

a) they are activated by thrombin;

b) they are formed in the body constantly and do not depend on the processes of blood coagulation;

c) they are formed in the body changeably and depend on the processes of blood coagulation.

d) they do not exist in the body;

e) they are activated by thrombostenin.

46. Give the correct sequence of the processes of vascular-platelet hemostasis:

Variants of answer:

a) a reflex spasm of the damaged blood vessels — aggregation of thrombocytes — adhesion of thrombocytes — compression of a blood thrombus;

b) a reflex spasm of the damaged blood vessels — compression of a blood thrombus — adhesion of thrombocytes — aggregation of thrombocytes;

c) a reflex spasm of the damaged blood vessels — adhesion of thrombocytes — aggregation of thrombocytes — compression of a blood thrombus.

d) adhesion of thrombocytes — a reflex spasm of the damaged blood vessels — aggregation of thrombocytes — compression of a blood thrombus;

e) compression of a blood thrombus — a reflex spasm of the damaged blood vessels — adhesion of thrombocytes — aggregation of thrombocytes.

47. Give the correct sequence of the processes of coagulating hemostasis:

Variants of answer:

a) formation of prothrombinase — transformation of fibrinogen into fibrin — formation of thrombin;

b) formation of prothrombinase — formation of thrombin — transformation of fibrinogen into fibrin;

c) transformation of fibrinogen into fibrin — formation of thrombin — formation of prothrombinase.

d) formation of thrombin — transformation of fibrinogen into fibrin — formation of prothrombinase;

e) formation of thrombin — formation of prothrombinase — transformation of fibrinogen into fibrin.

48. Give the correct sequence of the processes of fibrinolysis:

Variants of answer:

a) transformation of plasminogen into plasmin — splitting of fibrin to peptides and amino acids — formation of the blood activator of plasminogen;

b) splitting of fibrin to peptides and amino acids — formation of the blood activator of plasminogen — transformation of plasminogen into plasmin;

c) formation of the blood activator of plasminogen — transformation of plasminogen into plasmin — splitting of fibrin to peptides and amino acids.

d) formation of the blood activator of plasminogen — splitting of fibrin to peptides and amino acids — transformation of plasminogen into plasmin;

e) transformation of plasminogen into plasmin — formation of the blood activator of plasminogen — splitting of fibrin to peptides and amino acids.

49. How will a decrease of Ca^{2+} amount in blood plasma influence the duration of hemostasis?

Variants of answer:

a) the duration of hemostasis will increase;

b) the duration of hemostasis will decrease;

c) the duration of hemostasis will not change;

d) Ca^{2+} does not influence the duration of hemostasis.

e) Ca^{2+} can both increase and decrease the duration of hemostasis.

50. How does the composition of lymph differ from that of blood plasma?

Variants of answer:

a) it has a larger protein concentration;

b) their phospholipid concentrations are different;

c) it has a smaller protein concentration;

d) it has a larger concentration of the formed elements;

e) it has a larger concentration of vitamins.

51. Albumin is an important factor for the maintainance of the oncotic pressure, because it has…

Variants of answer:

a) relatively low molecular weight and high blood concentration;

b) relatively low molecular weight and low blood concentration;

c) high molecular weight and low blood concentration;

d) high molecular weight and high blood concentration;

e) albumin is not important for the maintainance of the oncotic pressure.

52. Which of the following is not a transport or binding protein?

Variants of answer:

a) hemoglobin;

b) ceruloplasmin;

c) lactoferrin;

d) transferrin;

e) erythropoietin.

53. Helper and cytotoxic cells belong to…

Variants of answer:

a) T cells;
b) B cells;
c) monocytes;
b) macrophages;
e) eosinophils.

54. Thrombosthenin is …

Variants of answer:

a) a thrombosis preventing protein;
b) a contractile protein;
c) a coagulation protein of blood plasma;
d) a protein regulating the production of platelets;
e) a transport protein.

55. Which of the following coagulation factors causes cross linking and stabilization of clots?

Variants of answer:

a) factor XIII;
b) thrombin;
c) factor VIII;
d) factor IX;
e) factor VII.

56. All the coagulation factors of the hepatic origin are vitamin K- dependent except….

Variants of answer:

a) II;
b) VII;
c) VIII;
d) IX;
e) X**.**

57. The action of the VIII procoagulant factor is deficient in…

Variants of answer:

a) haemophilia A;
b) haemophilia B;
c) idiopathic thrombocytopenic purpura;
d) sickle cell anemia;
e) megaloblastic anemia.

58. Heme synthesis requires…
Variants of answer:
a) ferrous iron;
b) glycine;
c) alanine;
d) thrombin;
e) fibrinogen.

59. Iron absorption is increased by…
Variants of answer:
a) fibre diet;
b) vitamin C;
c) phosphate;
d) Kastle's antianemic factor;
e) insulin.

60. Erythropoiesis is promoted by all of the following except…
Variants of answer:
a) androgens;
b) thyroxine;
c) estrogen;
d) activation of the sympathetic nervous system;
e) products of erythrocyte destruction.

CORRECT ANSWERS
PHYSIOLOGY OF BLOOD

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

UNIT 3
PHYSIOLOGY OF EXCITABLE TISSUES

3.1. Laws of stimulation and assessment of excitability

3.1.1. Membrane-ionic theory of the origin of the resting membrane potential

All tissues are excitable, but conventionally they are divided into excitable and non-excitable. ***Nervous, muscular, and glandular*** tissues are excitable, as impulses which appear in them go across the membrane. These impulses have an important diagnostic value (for example, in electrocardiography, electroencephalography, electromyography, etc.).

Excitability is a property of a cell, allowing it to respond to stimulation by rapid changes in membrane potential produced by ion fluxes across the plasma membrane.

Conduction is the ability of cells to conduct generated impulses along the cell membrane.

Lability is the frequency of the development of the response to a stimulus.

The cell membrane is known to have an electric charge. Its external surface at rest is charged positively "+" and the internal one — negatively "–".

The difference between the charges of the external and internal membrane sides is called the ***resting membrane potential***.

The formation of the resting membrane potential (RMP) depends on the concentrations of K^+, Na^+, Ca^{2+}, Cl^-, as well as on the features of the cell membrane.

The basic structure of the cell membrane is a ***lipid bilayer*** which is composed of phospholipid molecules and cholesterol molecules (Figure 3.1).

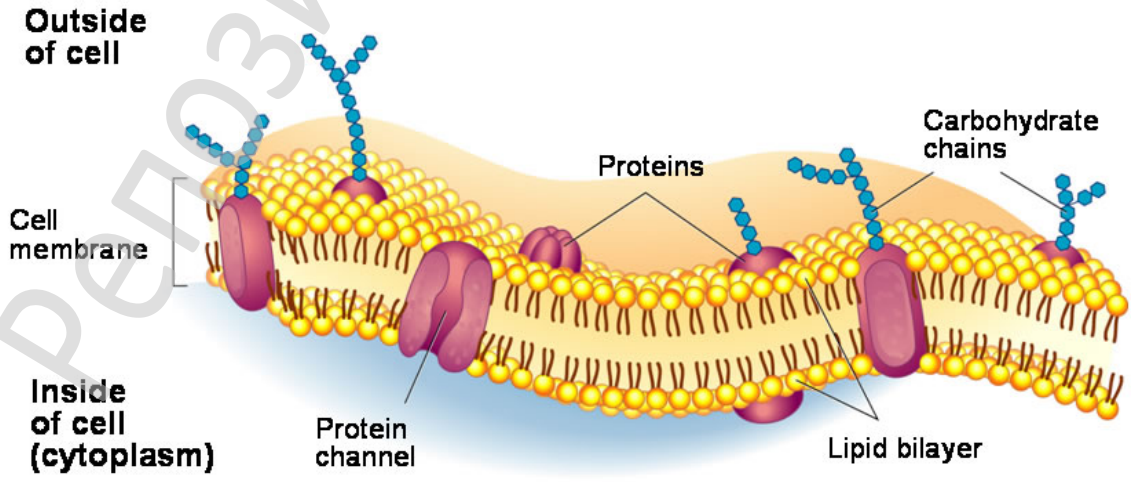


Figure 3.1 — Structure of the plasma membrane (from studylib.net)

The membrane also contains ***membrane proteins***: *integral proteins which* protrude all the way through the membrane and *peripheral proteins* which are attached only to one surface of the membrane. Many integral proteins provide structural channels through which water molecules and watersoluble substances, especially ions, can diffuse between the extracellular and intracellular fluids.

The carbohydrate layer (glycocalyx) is the external layer and contains membrane carbohydrates mainly in the combination with proteins or lipids in the form of glycoproteins or glycolipids.

Transport through the cell membrane occurs by means of different mechanisms:

— passive transport is the transport of biochemicals and other atomic or molecular substances across membranes down gradients without energy expenditure (simple diffusion, facilitated diffusion. osmosis, filtration, etc.)

— active transport is the transport against gradients which requires energy input (for example, sodium-potassium pump);

— co-transport (secondary active transport) is the combined transport of Na+ and glucose; Na+ and amino acids.

The membrane has channels which have the properties of:

1. *Selectivity* — the channels are divided into 4 groups: *sodium, potassium, calcium, chloric*. Selectivity is not obligatory yet preferable.

2. Electroexcitability.

Many channels can be opened or closed by gates that are regulated by electrical signals or chemicals that bind to the channels. The gating of protein channels provides a means to control their ion permeability (Figure 3.2).

Classification of ion channels:

1) By the amount of ions to which the channel is permeable:

— *Selective ion channels* (permeable to one type of ions).

— *Non-selective ion channels* (permeable to several types of ions).

By the type of ions the selective channels are divided into K^+, Na^+, Ca^{2+}, Cl^- channels.

2) By the type of regulation (gating):

— V*oltage-gated channels.* They react to the changes of the membrane potential. When the potential reaches a certain value, the channel becomes activated and ions pass through it down the concentration gradient.

— *Chemically-gated channels (ligand-gated channels).* In these channels the gates are opened by the binding of a chemical substance (a ligand) with receptors.

— *Mechanically-gated channels.* In these channels the permeability is changed if there are some mechanical actions on the membrane (these channels are present in the membrane of the mechanoreceptors of the blood vessels, skin, etc).

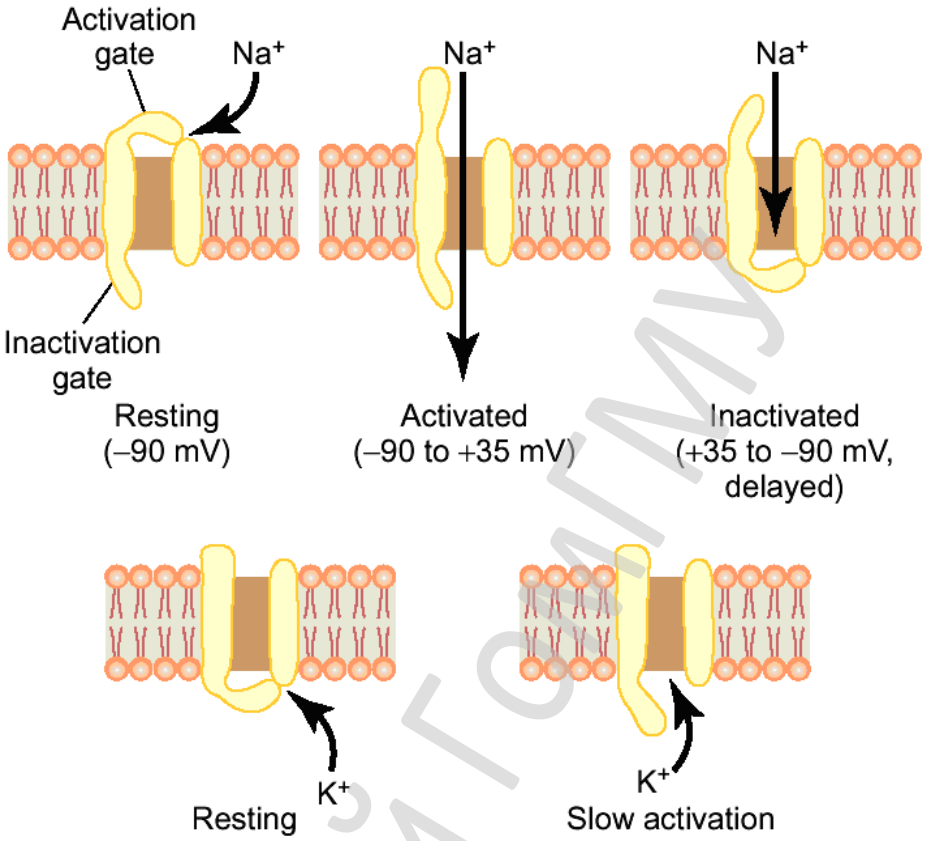


Figure 3.2 — Sodium and potassium channels (by C. Guyton and John E. Hall, 2016)

Notes: Characteristics of the voltage-gated sodium and potassium channels, showing successive activation and inactivation of the sodium channels and delayed activation of the potassium channels when the membrane potential is changed from the normal resting negative value to a positive value.

In cells at rest all sodium channels are closed. There are *leakage channels* (non-specific), which are permeable to all elements but are most permeable to potassium. They are always open, and potassium ions move through these channels down the concentration and electrochemical gradients. According to the **membrane-ionic theory,** the presence of the ***resting membrane potential*** **(RMP)** is caused by:

1. Unequal ion concentration inside and outside the cell.
2. Different permeability of the channels to these ions.

There are many K^+ ions inside cells and few outside them, opposite to Na^+. There are slightly more Cl^- ions outside cells than inside them. There are *a great number of organic anions* inside cells.

The membrane of cells at rest is only permeable ***to K^+ ions***. At rest, potassium ions constantly move outside cells, where there is a high Na^+ concentration. Therefore, in cells at rest, the external surface of the membrane is ***positively*** charged. ***High-molecular organic anions (proteins)*** are concentrated on the internal surface of the membrane and determine its ***negative*** charge. Due

to electrostatics they keep K^+ ions on the other side of the membrane. **The basic role in the formation of the RMP belongs to K^+ ions** (Figure 3.3.).

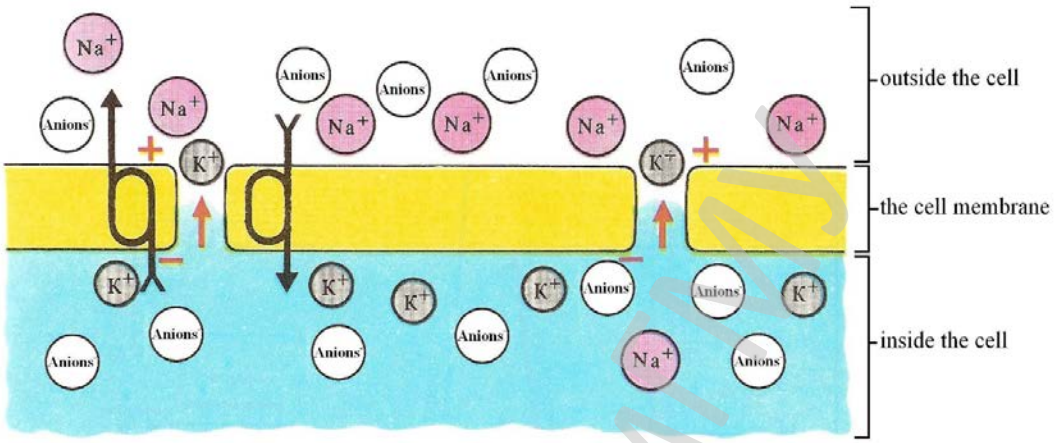


Figure 3.3 — Ionic mechanism of the formation of the resting membrane potential (by Korobkov A. V., Chesnokova S. A., 1986)

Despite the streams of ions coming through the leakage channels, the ion concentrations are not equivalent, i. e. they are always constant. This does not happen because of the existence of ***Na^+-K^+-pumps*** in the membranes (Figure 3. 4).

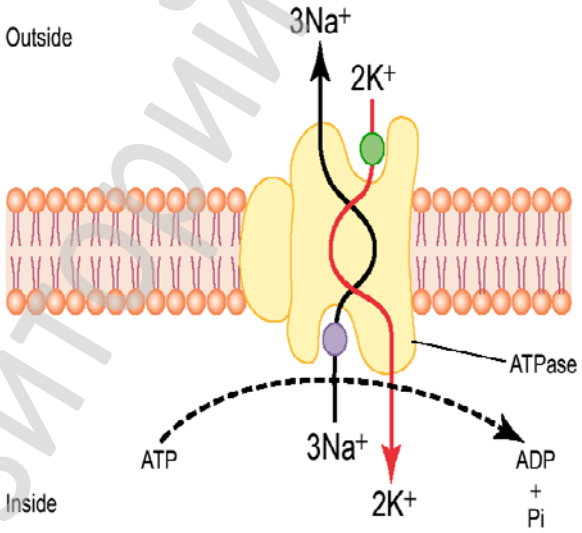


Figure 3.4 — Structure of the sodium-potassium pump (by C. Guyton and John E. Hall, 2016)

They continuously pump Na^+ out of cells and pump K^+ against the concentration gradient into the cytoplasm. For 3 Na^+ ions removed from a cell, 2 K^+ ions are introduced into it. The transmission of ions against the concentration gradient is carried out by active transport (with energy input).

Membrane potentials in different tissues at rest are characterized by different values: the highest one is in muscular tissue — 80–90 mV, in nervous — 70 mV, in connective — 35–40 mV, in epithelial — 20 mV.

When the internal charge of the membrane becomes less negative, it is known as membrane *depolarization*. If the internal charge of the membrane becomes more negative, it is called *hyperpolarization.*

3.1.2. Membrane action potential (AP)

Being imposed by a threshold stimulus, the permeability of the membrane changes, and an ***action potential (AP)*** or excitation occurs (Figure 3.5.). AP is rapid fluctuations of the membrane potential during excitation.

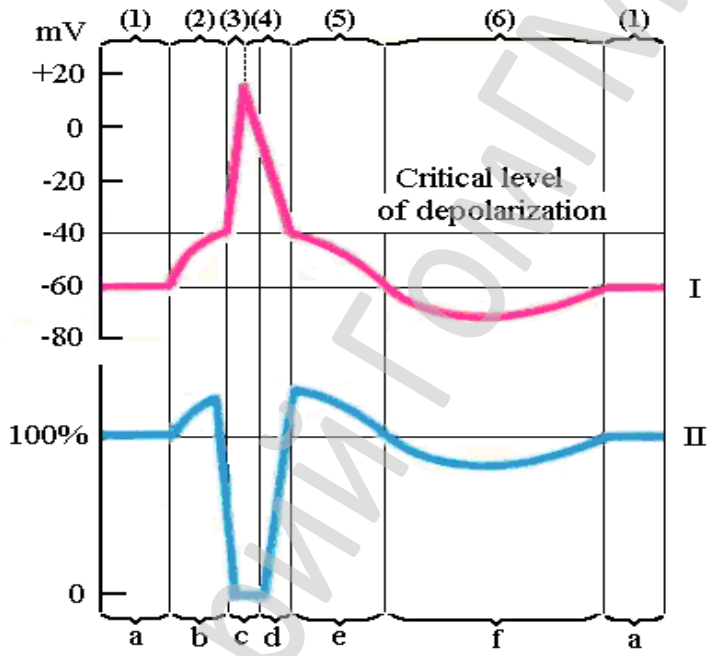


Figure 3.5 — Changes of the membrane potential and excitability during excitation (by Korobkov A. V., Chesnokova S. A., 1986)

Notes:

I — Changes of the membrane potential:	**II — Changes of excitability:**
(1) Resting membrane potential	
Phases of the membrane action potential:	(a) Normal excitability
(2) Slow depolarization;	(b) Hyperexcitability
(3) Fast depolarization.	(c) Absolute refractory period
(4) Fast repolarization;	(d) Relative refractory period
(5) Slow repolarization	(e) Supernormal or exaltation period
(6) Hyperpolarization	(f) Subnormal period

The threshold stimulus is the minimal strength which leads to the generation of a response. To characterize the threshold stimulus, the concept of *rheobase* (in Greek, the root *rhe* translates to "current or flow", and *basi* means "bottom or foundation") is used.

Apart from the threshold stimulus, there are *subthreshold stimuli* which cannot generate responses but induce a shift in cell metabolism. Besides, there are *superthreshold stimuli.*

Having arisen, AP goes along the membrane.

It has the following phases:

1. Slow depolarization (See figure 3.5. «2»);
2. Fast depolarization (See figure 3.5. «3»).
3. Fast repolarization (See figure 3.5. «4»);
4. Slow repolarization or negative afterpotential (See figure 3.5. «5»).
5. Hyperpolarization or positive afterpotential (See figure 3.5. «6»).

Mechanism of the AP origin (Figure 3.6.).

Under the effect of the *threshold stimulus,* the cell membrane becomes permeable to ***Na^+ ions,*** which stream inside the cell at a high speed (the flow of Na^+ ions into cells is higher than the flow of K^+ ions outside cells). ***The internal side of the membrane becomes positive, and on its surface a negative charge is formed***. The changes of the charges on the internal and external surfaces of the membrane correspond to the ***depolarization*** phase (See figure 3.6. «1»).

Figure 3.6 — Ionic mechanism of the formation of the membrane action potential (by Korobkov A. V., Chesnokova S. A., 1986)

Afterwards the sodium channels close, and the potassium channels which have been partially closed open. K^+ ions go out of the cell. This AP phase is called ***repolarization*** (See figure 3.6. «2»)

The action of the Na^+-K^+-pump and the RMP are restored (See figure 3.6. «3»).

The basic role in the formation of AP belongs to Na^+ ions.

3.1.3. Changes of excitability during excitation

During the development of AP (excitation), the excitability of cells changes (Figure 3.5.).

The development of the slow depolarization phase ***raises the excitability*** (hyperexcitability) creating conditions for a response. Further, when the slow depolarization phase is replaced by the fast one, the ***excitability rapidly reduces*** and, when the repolarization phase occurs, it starts ***to recover again***.

There are several periods of excitability:

1. Refractory period:

a) absolute;

b) relative.

2. Supernormal or exaltation period.

The *refractory period* is an interval of time during which a cell cannot respond to the action of a stimulus. The sodium channels are inactivated. During the ***absolute refractory period,*** the cell does not respond to the action of threshold or superthreshold stimuli.

The membrane repolarization leads to the reactivation of the sodium channels. This is the ***relative refractory period.*** During this period, a response may appear under the action of the superthreshold stimulus.

During the ***supernormal period,*** excitability exceeds the initial level. At this state the cell can respond to a stimulus the strength of which is a bit lower than the threshold one. The threshold of excitation is decreased because the values of the membrane potential are close to the critical level.

3.1.4. Laws of stimulation and assessment of excitability. Lability

The excitability of tissue depends on the threshold of its irritability *(rheobase)*. ***Rheobase*** is the minimal strength of a stimulus that is able to cause excitation of tissue and induce the minimal response if the duration of the action of the stimulus is long enough.

The lower the strength of the threshold stimulus is, the higher the excitability of tissue is. However, the response of tissue depends on the strength of the stimulus to a certain extent.

The response of the cell also depends on the duration for which the stimulus is applied. The threshold strength of the stimulus is in the inverse relation with its duration.

The interrelations between the strength and duration of the stimulus are demonstrated by the ***strength-duration curve***. If the strength of the current is «1», to induce a response from tissue, the duration of the stimulus must be «a» (Figure 3.7.).

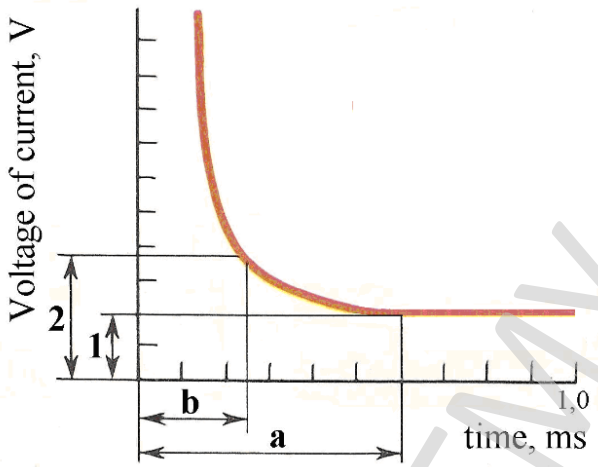


Figure 3.7 — The strength-duration curve (by Korobkov A. V., Chesnokova S. A., 1986)
Notes: 1 — rheobase; 2 — double rheobase; a — useful time; b — chronaxie

The shortest duration for which a stimulus equal to rheobase should react to induce a response is called ***the useful time*** (Figure 3.7.). If to double the strength of the stimulus («2» — two rheobases), the duration of the stimulus necessary to induce the response decreases («b») (Figure 3.7.).

The shortest duration for which a stimulus equal to double rheobase should be applied on tissue to cause a response is called ***chronaxie*.**

If the strength of a stimulus is equal to half of rheobase (half of «1»), no response will arise regardless of the duration of the stimulus. For example, the reflex of withdrawing hands away from a cold iron will not occur.

If tissue is exposed to a stimulus whose strength is equal to triple rheobase, but whose duration is too short (half of «b»), no response will arise either. For example, if to touch a hot iron very quickly, it is impossible to feel its temperature (Figure 3.7).

Chronaxie characterizes the rate of excitation generation. In different tissues it varies, which is used for medical purposes, e.g. to determine the damage of motor nerves.

Lability

To characterize the development of single APs, the concept of *lability* is used. ***Lability*** is the frequency of the development of the response to a stimulus (single APs). The higher lability is, the more APs tissue can make per unit of time. The measure of lability is the highest number of stimuli to which tissue can respond by generating APs per unit of time. The maximal rhythm of excitation is limited by the duration of the absolute refractory period. If the refractory period lasts for 0.5 msec, the maximal rhythm is 1,000 impulses per second and more.

Nervous tissue possesses the highest lability. It can generate up to 1,000 impulses per second. Muscular tissue can conduct up to 500 impulses per second. Synapses are least labile. However, tissues cannot function at the maximum rhythm for a long time. In natural conditions tissue reacts to the excitation of a lower rhythm which can be kept for a long time. This rhythm is produced during the supernormal period and is therefore called ***optimal.*** In nerve fiber it is 500 impulses per second, in muscle fiber — 200 impulses per second.

During rhythmic excitation, lability can increase or decrease. Decreased lability leads to the development of the processes of inhibition and its increase determines the properties of tissues to adjust to a ***new higher rhythm*** of impulses. The adjustment to the higher rhythm is the ability of excitable tissue to change the number (frequency) of generated impulses in a long action of stimuli. The adjustment to the higher rhythm is connected with the pumping of Na^+ ions out from the cytoplasm during excitation. Thus, muscles are capable to adjust to a more frequent rhythm of impulses coming to them from nerve fibers.

3.2. Physiology of nerve tissue

3.2.1. Physiology of nerve fiber

Nerves specialize on the conduction of stimuli and connect the nerve centers with executing organs. Nerves consist of myelinated and unmyelinated fibers, which are coated with the connective tissue membrane (Table 3.1.).

Table 3.1 — Properties of different nerve fibers

Type of fibers	Diameter, mcm	Speed of conduction, m/sec	Functions
Aα (myelinated)	**13–22**	**70–120**	Efferent fibers conduct excitation to skeletal muscles, afferent fibers conduct excitation from muscle receptors
Aβ (myelinated)	**8–13**	**40–70**	Afferent fibers conduct excitation from touch and tendinous receptors
Aγ (myelinated)	**4–8**	**15–40**	Afferent fibers conduct excitation from touch and pressure receptors, efferent fibers conduct excitation to skeletal spindles
B (myelinated)	**1–3**	**3–14**	Preganglionic fibers of the vegetative nervous system
C (unmyelinated)	**0.5–1.0**	**0.5–1.0**	Postganglionic fibers of the vegetative nervous system, afferent fibers conduct excitation from pain, temperature, and pressure receptors

The surface of the axial cylinder of nerve fiber is coated with the plasma membrane, which performs the main role in the generation and conduction of excitement.

Myelinated fibers have an intercept sheath, which is formed by myelin segments 1–2 mm long (the myelin sheath). The gap between the two segments is called the ***node of Ranvier*** (Figure 3.8).

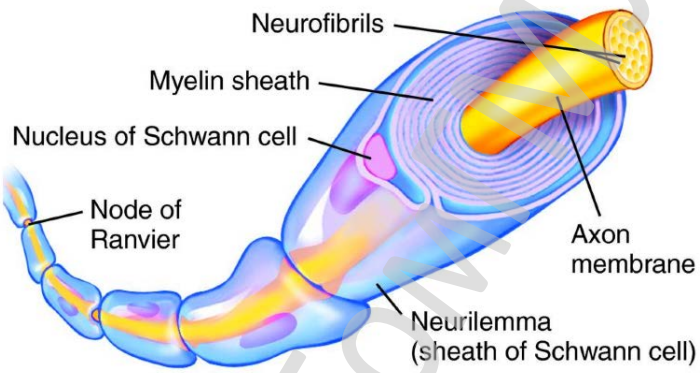


Figure 3.8 — Structure of myelinated fiber (from biology.reachingfordreams.com)

The myelin sheath is deposited around the axon by Schwann cells. The membrane of Schwann cells first envelops the axon. Then Schwann cells rotate around the axon many times, laying down the multiple layers of the Schwann cell membrane. Myelin is highly resistant and besides it performs the isolating function and takes part in the metabolism of nerve fibers. A signal along myelinated fiber goes only through the *nodes of Ranvier,* as they have many sodium channels.

Unmyelinated fibers are of the similar structure but have no myelin. Their surface is coated with Schwann cells.

If to dissect nerve fiber, its peripheral end after a while loses the ability to conduct signals and degenerates. Myelin undergoes fatty degeneration and transforms into fatty drops. The central end of nerve fiber is able to regenerate. A growth bulb is formed on it and grows towards the periphery (from 0.4 to 4.5 mm a day) and reaches the corresponding organ or tissue. Therefore, their innervations are recovered. Thus, the first signs of the regeneration of muscle innervations can appear after 5–6 weeks.

3.2.2. Laws of excitement conduction

1. ***The anatomical and physiological integrity of fibers*** is essential. Dissection or compression affects the conductivity of nerves. If to cut a nerve and separate both the ends of the cut at a distance of 1 mm, excitation can skip from one end to the other only through myelinated fibers.

2. ***Signals may propagate along nerves in both the directions***. This law is typical only for fibers isolated from the body, as inside the body signals are transmitted through synapses which conduct APs only in one direction.

3. ***Isolated signal conduction,*** i.e. a signal from one nerve fiber cannot skip to another one located in parallel.

3.2.3. Mechanisms of signal formation and conduction in myelinated and unmyelinated fibers

The mechanism of signal conduction in unmyelinated fibers. The action of the threshold stimulus on the unmyelinated fiber membrane changes its permeability to Na^+ ions, a great number of which flow inside the fiber. In this area the charge of the membrane changes (the internal becomes positive, the external — negative). It generates circular currents (movements of charged particles) from «+» to «–» along the whole fiber (Figure 3.9., «a»).

Features of signal conduction along unmyelinated fibers:

1. Signals go continuously and the whole fiber is seized with excitation.

2. Signals go at a low velocity.

Along unmyelinated fibers signals go to the internal organs from the nerve centers. However, the low velocity of the signals and their fading are not always beneficiary to the human body. That is why nature made an additional mechanism: the conduction of signals along myelinated fibers.

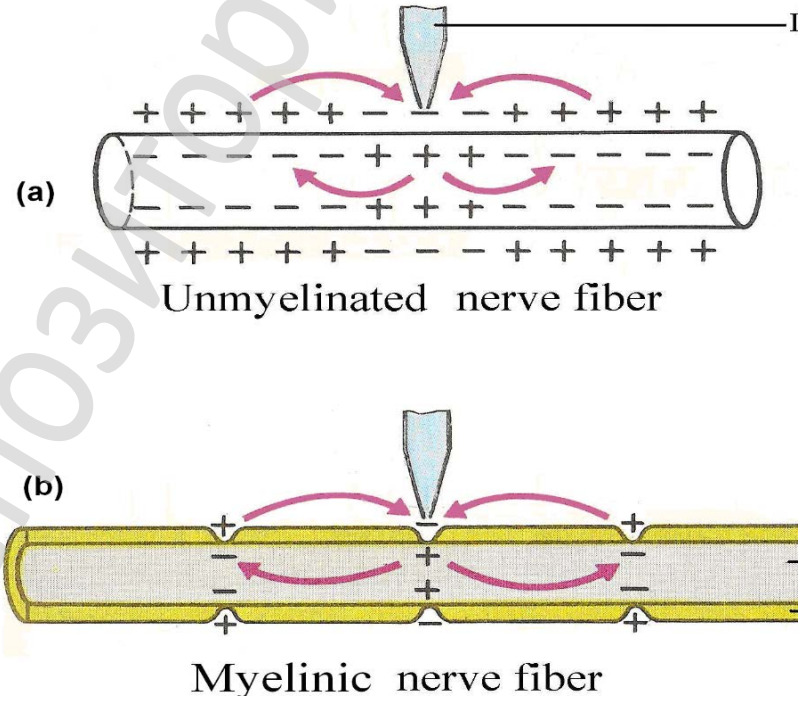


Figure 3.9 — Conduction of excitation in nerve fibers (by Korobkov A. V., Chesnokova S. A., 1986)

Notes: «a» — unmyelinated nerve fiber; «b» — myelinated nerve fiber

The mechanism of signal conduction in myelinated fibers (Figure 3.9., «b»). The action of the threshold stimulus on the membrane of myelinated fibers at the Ranvier's node changes the permeability to Na^+ ions, which go inside the fiber. In this part the charge of the membrane changes, which also generates circular currents. These currents go through the intercellular fluid to the adjacent node, where the charge changes again. Thus, the excitation transmits from one part to another. The reverse movement of the signal is impossible, as the part through which it has passed, is at the absolute refractory phase.

Thus, in myelinated fibers action potentials occur only at the nodes of Ranvier. *The action potentials are conducted from node to node,* and this is called saltatory conduction. Saltatory conduction is important for two reasons. Firstly, this mechanism increases the velocity of transmission of nerve impulses. Secondly, saltatory conduction conserves energy for the axon because only the nodes depolarize, therefore requiring less energy for re-establishing the difference between the sodium and potassium concentrations across the membrane after a series of nerve impulses.

Features of signal conduction along myelinated fibers:

1. Signals go in intermittent motion (saltatory conduction).

2. Signals go at a high velocity.

In myelinated fibers signals are transmitted from analyzers to the CNS, skeletal muscles i.e. where a high speed of responses is required.

3.2.4. Parabiosis

The scientist ***N.E.Vvedensky*** proved that a part of a nerve changes its lability under the effect of an alterant (irritant). This happens due to the fact that excitation lasts longer within this part and, therefore, at a certain stage of the alteration, the excitation is not transmitted through the nerve.

The condition of low lability, i.e. damage of the normal vital activity of the nerve is called ***parabiosis***. Parabiosis can be observed under the action of anesthetics, cold or heat, under the influence of currents and other stimuli.

The phenomenon of parabiosis was studied on the example of a nerve-muscle specimen which consisted of nervous cells, nerve fibers, and muscles, which reflected all the changes happening in nerve fibers (Figure 3.10). During the experiment, a stimulus (for example, some narcotic on cotton wool) was applied on some part of nerve fiber. Through this part the stimulus transferred and some changes could be observed.

As a result of the experiment, 3 phases (Figure 3.11.) of parabiosis were detected:

1. ***Provisional or equalizing phase***. If to irritate nerve fiber with stimuli of various strength (weak and strong), the response of the muscle will always be identical.

2. If the narcotic continues its action, there comes the second phase — ***paradoxical.*** In this case strong stimuli induce weak responses, and, on the contrary, weak stimuli —strong ones.

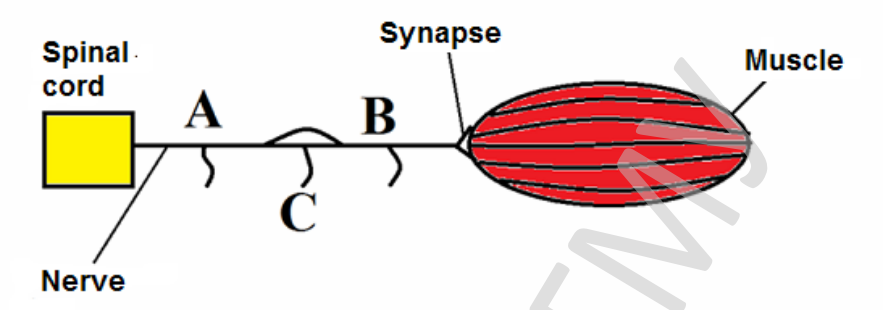


Figure 3.10 — The scheme of the nerve-muscle specimen of parabiosis

Notes: A,B,C — electrodes: A — experimental, B — control, C — in the area of the alteration influence

3.If the effect of the narcotic is not stopped, neither strong nor weak stimuli can induce a response. This stage is called ***inhibitory.***

Then, if to terminate the effect of the narcotic and to wash the damaged part of the nerve, its properties are recovered in the inverse sequence.

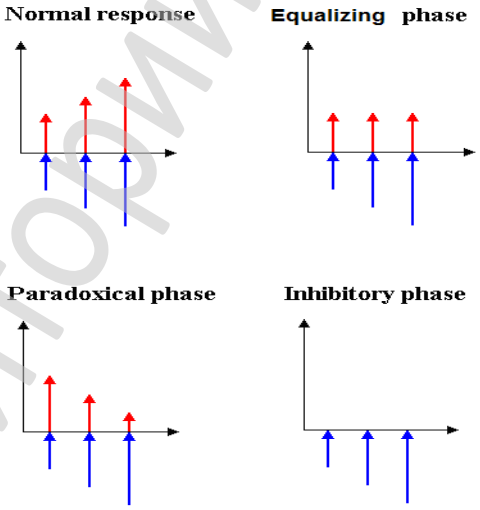


Figure 3.11 — Phases of parabiosis

Notes: The arrows above show the strength of the response (the force of the muscle contraction). The arrows below show the strength of the stimulus (current)

3.3. Physiology of synapses

3.3.1. Synapses. Structure of synapses

Synapses are specialized structures which provide the transmission of excitation from one neuron to another or to target effector cells.

The functional role of synapses:

1. They provide functional contacts between nerves and organs.

2. They promote the regulatory activity of the CNS.

3. They have plasticity (the amount of signal which passes through a synapse can change, which is of an important functional value).

4. They participate in the formation of memory (chemical synapses).

The structure of chemical synapses

Nerve fibers approaching a cell form a thickening which contacts with the cell. This part is the ***presynaptic membrane***. The opposite membrane is ***postsynaptic***. Between them there is a ***cleft*** filled with a plasma-like fluid. In the presynaptic terminal, there are ***neuromediators*** *(transmitters),* which are capable to excite or inhibit the innervated cell (Figure 3.12).

Myelinated nerve fibers approaching skeletal muscles make fanlike branchings into end fibers (terminals). The area of the synapse formation between the nerve terminations and muscles is called the ***motor end plate.*** The postsynaptic membrane of muscle fibers is thicker and forms regular folds which increase the surface area of the postsynaptic membrane. Therefore, a big amount of the mediator may contact the postsynaptic membrane of muscle fiber.

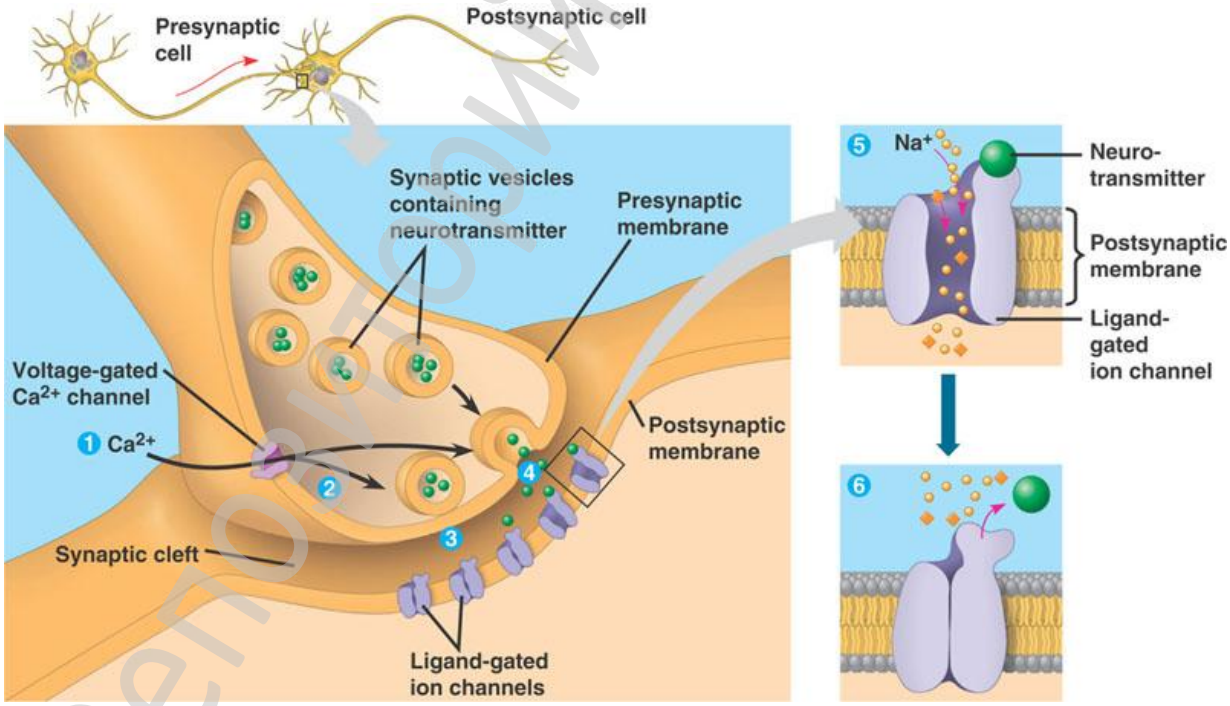


Figure 3.12 — Structure of the synapse (from studylib.net)

3.3.2. Classification of synapses

1. By the location:

a) peripheral: neuro-muscular, neuro-secretory, receptor-neuronal;

b) central: axoaxonic, axosomatic, axodendritic, dendrodendritic, somatodendritic (Figure 3.13).

2. By the effect:

a) excitants;

b) inhibitors.

3. By the mechanisms of signal conduction:

a) chemical;

b) electrical. They conduct excitation without participation of the mediator at a high speed and have bilateral signal conduction. The structural basis of electrical synapses is the nexus. These synapses are located in the endocrine glands, epithelial tissue, CNS, and heart.

c) mixed.

In some organs excitation can be transmitted both through chemical and electrical synapses.

4. By the type of the secreted mediator, chemical synapses are classified into:

a) adrenergic (the mediator is noradrenalin);

b) cholinergic (the mediator is acetylcholine);

c) serotoninergic;

d) glycinergic and others.

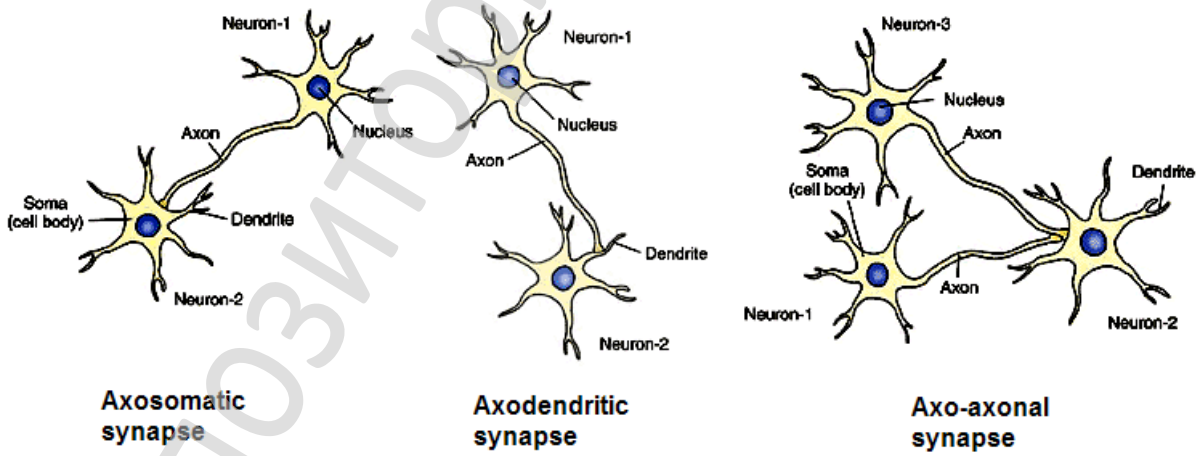


Figure 3.13 — Classification of synapses (from picgalleria.com)

In chemical synapses, the membrane of the postsynaptic neuron contains large numbers of receptor proteins for binding with neuromediator.

There are two types of receptors.

1) *ionotropic receptors* are transmembrane ion channes that allow passage of specified types of ions through the membrane; when a neuromediator substance activates an ion channel, the channel usually opens.

2) *metabotropic receptors* are receptors which act through a "second messenger" Such receptor is a molecule that activates one or more substances inside the postsynaptic neuron. These substances serve as "second messengers" to increase or decrease specific cellular functions.

Chemical synapses have some common properties:

- Excitation in synapses is transmitted only in one direction. This is provided by the structure of synapses: the mediator is released only from the presynaptic part and it interacts with the receptors of the postsynaptic membrane.
- The transmission of excitation in synapses is slower than that in nerve fibers (synaptic delay).
- Excitation is transmitted with the help of special chemical substances – mediators (neurotransmitters).
- In synapses the transformation of the excitation rhythm occurs.
- Synapses have low lability.
- Synapses have rapid fatigability.
- Synapses have high sensitivity to chemical substances (including pharmacological drugs — blockers and others).

3.3.3. Mechanisms of signal transmission in chemical synapses (on the example of nerve-muscular synapses)

1. Release of the mediator into the synaptic cleft.

When APs reach the nerve termination (pre-synaptic membrane), they generate its depolarization. As a result, ***calcium ions*** go inside the terminal. The increase of the calcium concentration in the nerve termination promotes the release of ***acetylcholine*** into the synaptic cleft.

2. Diffusion of the mediator to the postsynaptic membrane and binding with receptors. The mediator reaches the postsynaptic membrane and binds with cholinoreceptors located on the postsynaptic membrane.

3. The occurrence of excitation in muscle fiber. As a result of the interaction of acetylcholine with the receptors, sodium ions go through the postsynaptic membrane into the cell and depolarize the membrane (Figure 3.14.).

If the initial level of the RMP is — 85 mV, it can decrease to 10 mV, i.e. partial depolarization occurs, the excitation does not go further, it stays in the synapse. These mechanisms cause a synaptic delay, which may last 0.2–1 ms. Partial depolarization of the postsynaptic membrane is called an ***excitatory postsynaptic potential (EPP)***.

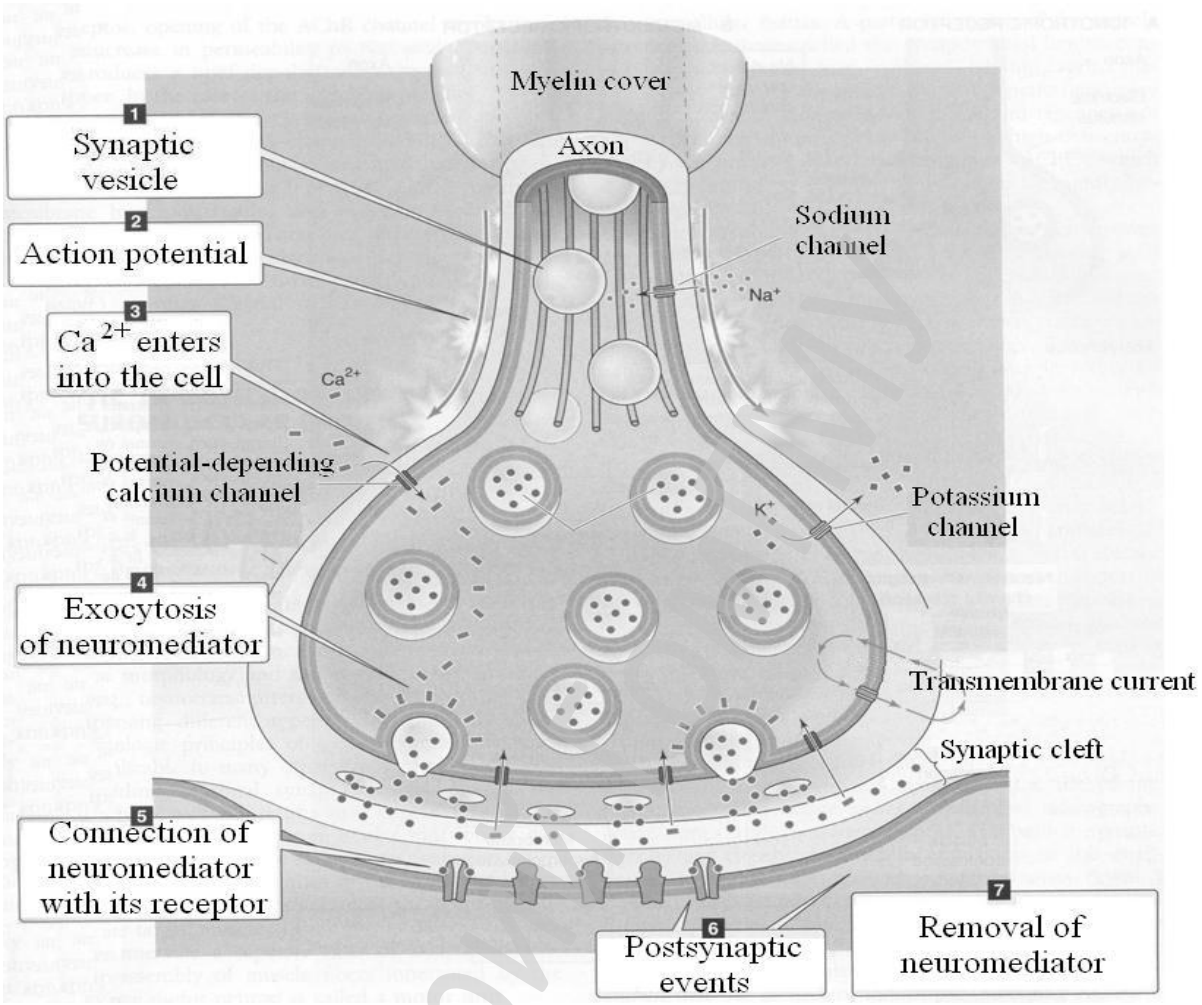


Figure 3.14 — Stages of signal transmission in the synapse (by Orlov R.S., Nozdrachev A. D., 2005)

Influenced by the ***EPP*** in the next part of the membrane of muscle fiber, there arises a ***propagating AP,*** which produces a muscle contraction.

In synapses the mediator depending on the chemical structure can cause depolarization of the postsynaptic membrane (the excitatory postsynaptic potential is formed, which provides the exciting effect) or hyperpolarization of the postsynaptic membrane (the inhibitory postsynaptic potential is formed, which provides the inhibitory effect).

4. The removal of acetylcholine from the synaptic cleft. The enzyme **acetylcholinesterase** is located on the external surface of the postsynaptic membrane. This enzyme disintegrates acetylcholine and inactivates it.

Some poisons and toxins like botulin can block the conduction of signals through synapses. For example, the poison *curare* contacts the receptors of the postsynaptic membrane and interferes their interaction with acetylcholine.

3.3.4. Principles and features of excitation transmission in interneuronic synapses. Perception of external stimuli (reception)

The main principles of excitation transmission in interneuronic synapses is similar to those in neuromuscular synapses. However, they have their specific features:

1. Many synapses are inhibiting.

2. EPP in depolarization of one synapse it is not enough for the excitation and generation of a spreading action potential, i.e. entry of signals to nerve cells from many synapses is necessary.

Perception of external stimuli (reception)

Receptors are specific formations which transform energy of a stimulus into an electrochemical potential and then into the form of nervous excitation.

Classification of receptors.

By the character of sensations:

1) Visual.
2) Auditory.
3) Olfactory.
4) Gustatory.
5) Tactile.

By location:

1) Exteroreceptors — external (acoustic, visual).
2) Interoreceptors — internal (vestibular and proprioreceptors).

By the character of stimuli:

1) Photoreceptors — (visual).
2) Mechanoreceptors — (touches and pressure).
3) Thermoreceptors — (cold and warmth).
4) Olfactory.
5) Gustatory.
6) Painreceptor.

By the location of stimuli:

1) Distant — (auditory, visual).
2) Contact — (gustatory, temperature, receptors of pressure).

All the receptors have adaptation***. Adaptation*** is decreasing sensitivity to the long effect of a stimulus.

3.3.5. Transformation of stimulus energy

The contact of a stimulus with the receptor membrane causes the increased membrane permeability to ions (in most receptors – to sodium ions),

and these ions diffuse into the sensory terminal, which is depolarized, and **a receptor potential (RP)** is formed. The primary transformation of a stimulus into the receptor potential is called **transformation.**

By the structural features, all receptors are divided into ***primary-sensitive receptors*** (they are endings of the dendrites of sensory neurons) and ***secondary-sensitive receptors*** (they have the specialized receptor cell between the stimulus and the first neuron, these receptor cells contact with the endings of sensory nerves).

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 RP amplitude.

In the secondary-sensitive receptors during the RP formation, the receptor cell secretes the mediator, which causes the formation of a generator potential on the postsynaptic membrane of the sensory neuron, followed by the appearance of a nerve impulse (AP).

A set of receptors that cause excitation of one of their own neurons is called ***the receptive field***; and the areas of the concentration of receptors belonging to certain sensory systems are called ***the reflexogenic zones***.

Review questions

1. What tissues are called excitable? Describe the structure of the plasma membrane. Give the classification of the ionic channels of the membrane.

2. What is the resting membrane potential? Explain the mechanism of its maintenance according to the membrane-ionic theory.

3. What is the membrane action potential? List its phases. Explain the mechanism of their origin.

4. What are the phases of the changes of excitability during excitation? Describe them.

5. Give the definition of "rheobase". Describe how the appearance of a cell response depends on the duration of a stimulus. Give definitions of "useful time" and chronaxie". What is the value of chronaxie in clinical practice? Explain what lability is.

6. Describe the structure of myelinated and unmyelinated nerve fibers. Give the classification of the types of nerve fibers (by diameter and velocity of signal conduction) and characterize each type.

7. Name the laws of excitement transmission along nerve fibers and explain them. Describe the mechanisms and features of signal conduction in myelinated and unmyelinated fibers. What is parabiosis according to N. E. Vvedensky? De-

scribe the experiment during which the phenomenon of parabiosis was studied. Name and describe the phases of parabiosis.

8. What are synapses? What is the functional role of synapses? Give the classification of synapses. Describe the structure of chemical synapses. Explain the mechanism of signal transmission in chemical synapses.

9. What are receptors? Give their classification. Explain how the transformation of the stimulus energy into receptor potentials and nerve impulses occurs in the *in the primary-sensitive and in the secondary-sensitive receptors*. Give the definitions of the "receptive field" and "reflexogenic zones".

3.4. Physiology of muscles

3.4.1. Forms and types of muscle contractions

Muscle tissues in the human body are divided by structure and physiological properties into 3 types:

1. Skeletal.
2. Smooth.
3. Cardiac.

All the types of muscles possess some properties:

1. Excitability.

2. Conduction.

3. Contractility, — change of length or strain, — and ability to relax.

In natural conditions the activity of muscles have the reflex character. The electric activity of muscles can be recorded by means of electromyography, which is widely used in sports medicine.

There are several forms and types of muscle contractions (Table 3.2.).

1. ***Dynamic form***. In this form of contractions the length of the muscle changes but its strain does not. This form includes two types:

a) *Isotonic*, or concentration type (the muscle is shortened but does not change its strain). E.g., walking.

b) *Eccentric type*. If a load on a muscle is higher than its strain, the muscle is stretched. E.g., lowering of a heavy object.

2. ***Static form***. This form is observed during posture maintenance or overcoming of terrestrial attraction.

This form includes one type of muscle contractions — *isometric*, when the muscle changes its strain but does not change its length.

3. ***Auxotonic or mixed***.

The division into forms and types of muscle contractions is conditional, since all contractions are mixed. However, one type predominates.

Table 3.2 — Forms and types of muscle contractions

Form	Type	Characteristics of the type	Example
Dynamic form	Isotonic type	The muscle is shortened but does not change its strain	Walking
	Eccentric type	If a load on a muscle is more than its strain, the muscle is stretched, but does not change its strain	Lowering of a heavy object
Static form	Isometric type	The muscle changes its strain but does not change its length	Posture maintenance or overcoming of terrestrial attraction.
Auxotonic or mixed	—	The muscle changes its strain and length	Most contractions are mixed.

3.4.2. Mode of muscle contractions

The character or the mode of muscle contractions depends on the frequency of signals coming from motoneurons.

There are single and tetanic muscle contractions (Figure 3.15.).

If a muscle is imposed by a ***single signal***, a single muscle contraction (Figure 3.15., «a») appears and it has several periods:

1. *Latent period* — the time from the action of the stimulus till the beginning of a contraction.

2. *Shortening period* in isotonic contractions or *strain period* in isometric contractions.

3. *Relaxation period*.

Single muscle contractions are characterized by minor fatigability, yet the muscle is not capable to realize its capabilities.

Tetanic muscle contractions. If muscle fiber is influenced by two signals quickly following each other, contractions are overlapped to induce strong contractions.

The process when two signals following each other are overlapped is called ***summation.***

There are two types of summation (Figure 3.15 «b».):

1. If a second stimulus comes at the moment when the muscle starts to relax, the curve's peak is separated from the peak of the first contraction. This type of summation is called ***incomplete***.

2. If a second stimulus comes at the moment when the muscle contraction has not yet reached its peak, i.e. the muscle has not started to relax, both the contractions unite as a whole. This type is called ***complete***. Long and strong

muscle contractions influenced by the rhythm of signals with consequent rapid relaxation are called ***tetanus***. In the human body tetanus can develop if signals come at a frequency of 30–100 sgn/sec.

There are two types of tetanus (Figure 3.15. «c»):

1. *Dentate*, arising at a low frequency of signals. It is formed due to the incomplete summation of muscle contractions)

2. *Smooth*, arising at a high rhythm of signals. It is formed due to the complete summation of muscle contractions.

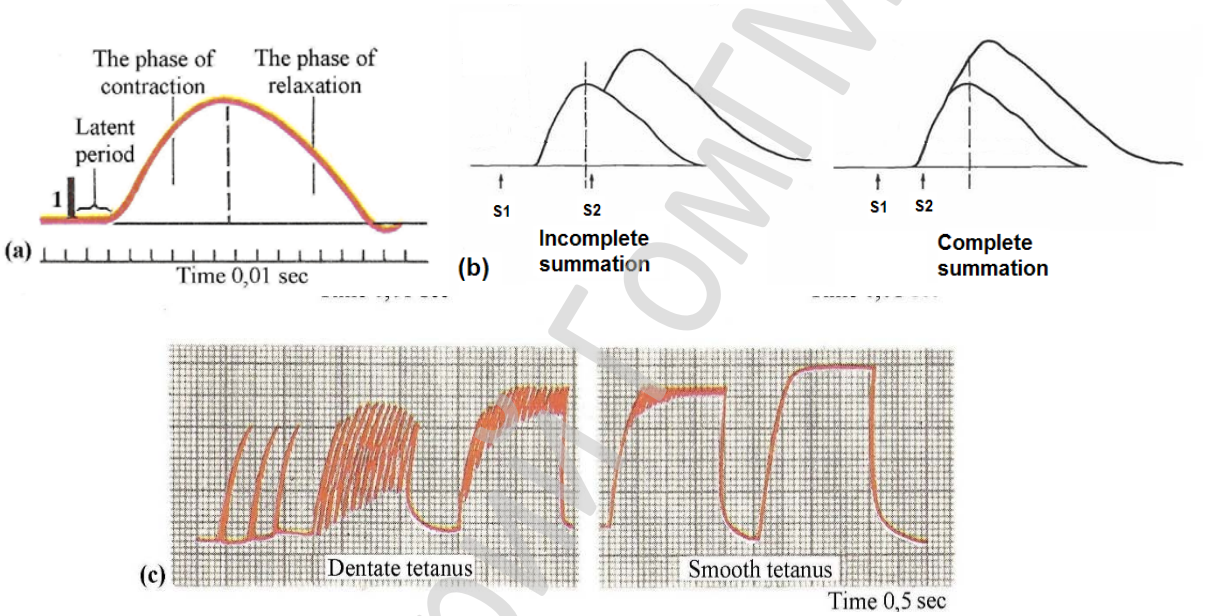


Figure 3.15 — Single muscle contraction (a), summation (b), tetanus (c)
(by Korobkov A. V., Chesnokova S. A., 1986)

Notes: S1 — the moment of the first stimulus signal. S2 — the moment of the second stimulus signal

There are optimal and pessimal rhythms of the work of muscles.

Thus, if the rate and strength of signals produce the maximal contracting effect, this is the ***optimal rhythm*** of the work. It is formed during the exaltation phase (i.e. supernormal).

If the rate of signals and strength of stimuli are higher than the optimal rhythm, it decreases the contracting force. This rhythm is called ***pessimal.*** This muscle work rhythm is formed during the absolute refractory phase.

Sometimes, steady continuous stationary reversible contractions of muscles with their strongly prolonged relaxation can be observed. These muscle contractions are called ***contracture (cramps).*** It differs from tetanus, as there are no action potentials extending along muscles.

There are 3 kinds of contracture:

1. *Potassium* contracture. It appears if the fluid surrounding muscle fiber accumulates many potassium ions.

2. *Caffeine* contracture. Influenced by a high concentration of caffeine, calcium ions come inside muscle fiber and induce long muscle contractions.

3. *Post-tetanic contracture*. This is the residual contraction of muscles after the action of stimuli. For example, if you carry a heavy bag for a long time not changing your hands, you cannot unbend your fingers instantly after you get rid of the bag.

3.4.3. Strength and work of muscle fiber

Muscular strength is the amount of force a muscle can produce in a single effort. The force of contractions (muscular strength) depends on the morphological properties and physiological state of muscles:

1. **Length of muscles**. Muscles create great forces. The force of a muscle contraction depends on the initial length of the muscle, or its length at rest.

2. **Cross-section (diameter) of muscles**. There are two diameters:

a) *Anatomical diameter* being the cross-section of muscles.

b) *Physiological* area of the section, i. e. of the perpendicular section of each muscle fiber. The more the physiological section is, the greater strength the muscle has (Figure 3.16.).

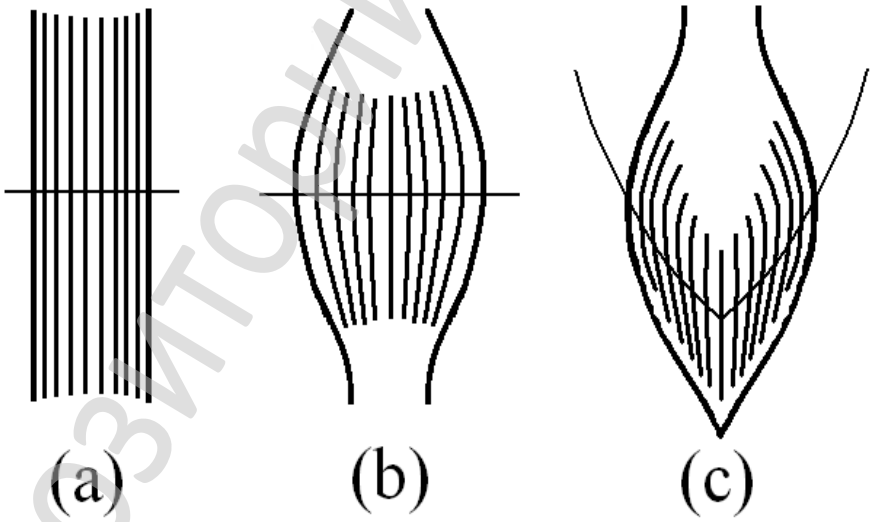


Figure 3.16 — The structure of different types of muscles and their physiological cross section (by Pokrovskiy V. M., Korotko G. F., 2000)

Notes: (a) Sartorius muscle; (b) Biceps brachii; (c) Gastrocnemius muscle

The strength of muscles is measured by the maximal lifted weight. It is measured in kilograms or newtons. The method of the measurement of muscular strength is called dynamometry.

There are two kinds of muscular strength:

1. *Absolute strength*, which is the relation of the maximal strength to the physiological diameter.

2. *Relative strength, which is the* relation of the maximal strength to the anatomical diameter.

During contractions muscles are capable to perform their work. The muscle work is measured by multiplying the mass of the raised cargo and the height at which it is raised. The muscle work is characterized by its power. The muscle power is determined by the amount of work done per unit of time and is measured in Watts. The greatest work and power are reached in average loads.

3.4.4. Motor units. Composition (structure of muscles)

Muscle contractions depend on the frequency of signals coming from motoneurons. The axons of motoneurons can branch and innervate a group of muscle fibers (Figure 3.17). One axon can innervate from 10 to 3,000 muscle fibers.

A motoneuron and the group of muscle fibers innervated by it compose a ***motor unit***.

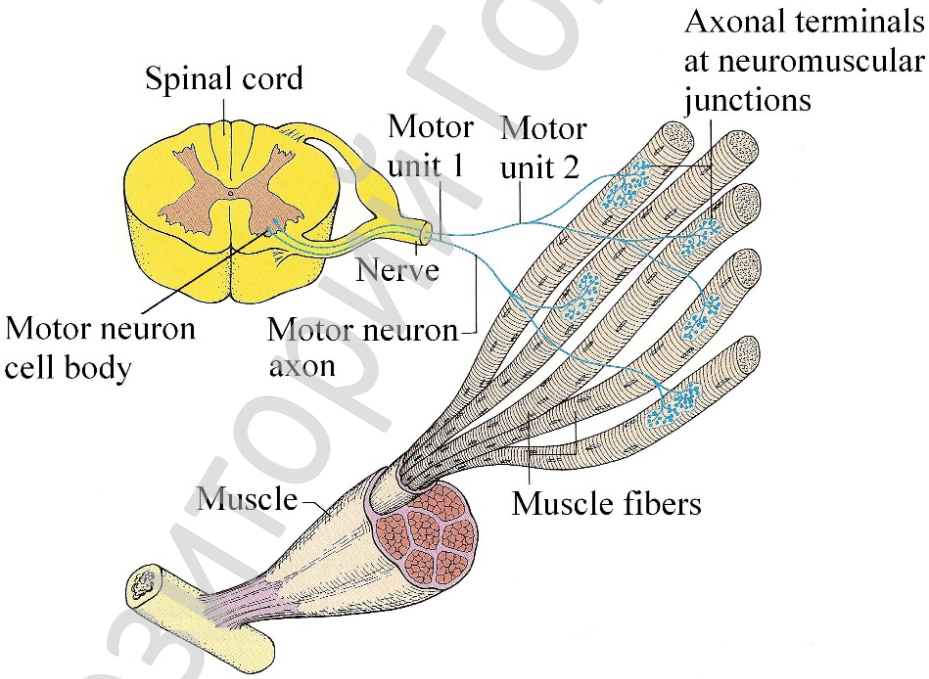


Figure 3.17 — Motor units (schematic view of the parts of two motor units) (from studylib.net)

There are motor units different in their structure and functions.

By their structure, motor units are divided into:

1. ***Small motor units*** which have a small motoneuron and a thin axon capable to innervate 10–12 muscle fibers. For example, facial muscles, muscles of fingers.

2. ***Big motor units***. They differ in the large body of a motoneuron, a thick axon which is capable to innervate more than 1,000 muscle fibers. For example, quadriceps.

By their functional value, motor units are divided into:

1. ***Slow motor units***. They include small motor units, and are easily excitable, characterized by the low velocity of the signal conduction, first involve into work but they almost never get tired, e. g., muscles of a marathon runner.

2. ***Fast motor units***. They consist of big motor units, are badly excitable, have high-velocity signal conduction, high speed and strength of responses. E.g., muscles of a boxer.

These features of motor units are ensured by a number of properties.

Muscle fibers included into the motor units have similar properties and differences. Slow twitch muscle fibers have:

1. Rich capillary network.
2. They contain a lot of myofibrils.
3. They contain a lot of myoglobin (i.e. capable to bind large amounts of oxygen).
4. They contain a lot of fats.
5. They contain a lot of mitochondria.

Due to the above features, these muscle fibers have high endurance and are capable to contract continuously for a long time.

Due to the reddish color of myoglobin, these fibers may be referred to as red fibers.

The distinctive features of fast twitch muscle fibers:

1. They contain more myofibrils than slow twitch fibers.
2. They have a greater rate and strength of contractions.
3. They contain few capillaries.
4. They contain little myoglobin.
5. They contain few fats.
6. They contain a lot of glycogen.

Due to the lack of myoglobin, fast twitch muscle fibers can be referred to as white fibers.

Accordingly, these muscle fibers get tired rapidly but have great strength and high speed of responses.

The ratio of slow and fast twitch muscle fibers in different muscles is unequal and varies in individuals.

The interrelation of muscle fibers is genetically determined. Transition of fast twitch muscle fibers into slow ones and vice versa during life-time is impossible.

In natural conditions muscles are hardly ever relaxed, as they are at the state of normal tonicity. The ability of muscles for constant low-level activity at the normal state of balanced tension and minimum energy consumption is called muscle tone or muscle tonus. For example, the muscles of the neck maintain the head the whole day. In some disorders of the nervous system muscle tone can be affected.

3.4.5. Structure of muscle fiber

The average length of muscle fiber is 12–14 cm. It contains many nuclei. Its membrane is called the ***sarcolemma*** and it has flexures inside fibers (Figure 3.18). The cytoplasm of muscle cells is called ***sarcoplasm*** and consists of myofibrils, myoglobin, glycogen, sarcoplasmic reticulum (a system of longitudinal tubules and extended saccules containing calcium).

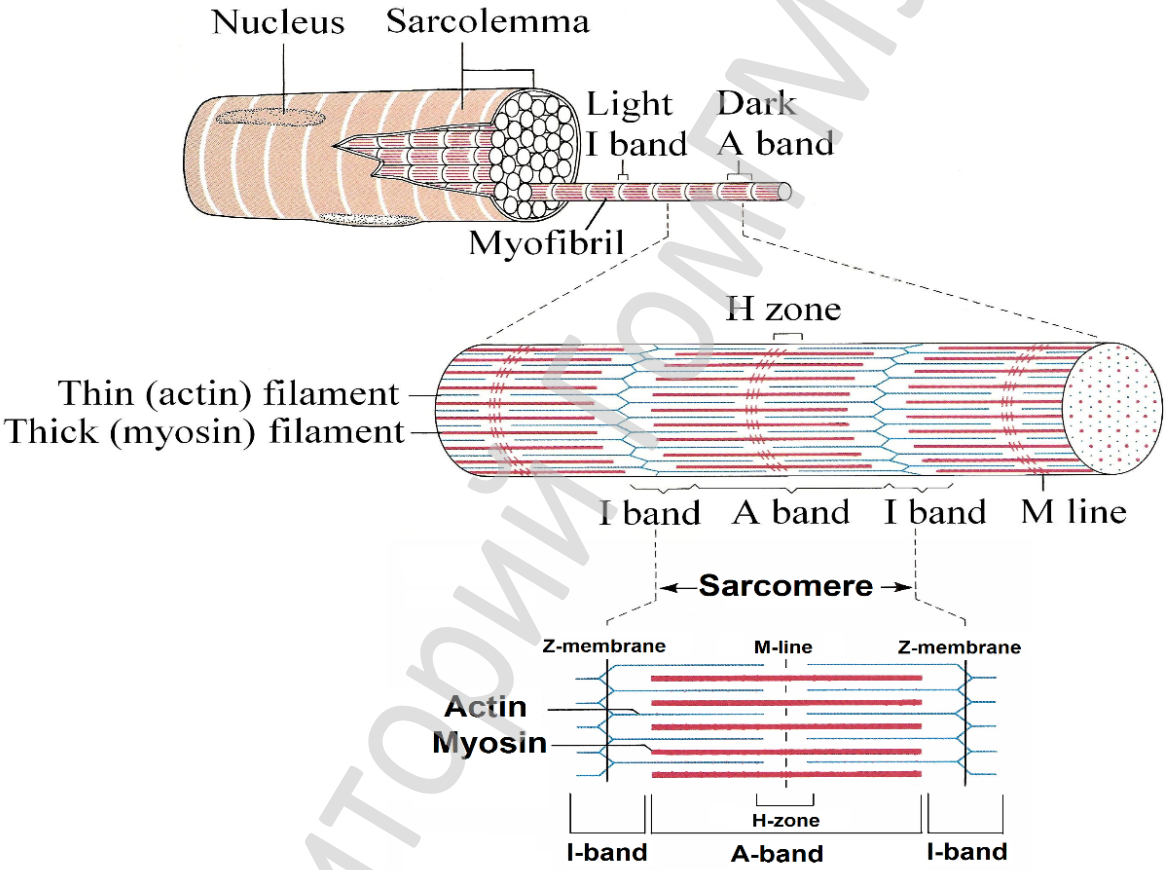


Figure 3.18 —Structure of muscle fiber and sarcomere (by Elaine N. Marieb, 1989)

Myofibrils are grouped into bundles and pass through the whole fiber without interruption. They are divided into dark and pale bands. The dark bands are called *anisotropic*, the pale ones — *isotropic*. The pale bands at the center have the Z-membrane, the dark bands have the H-strip (Figure 3.18.). The contractile unit of the myofibril between the two Z-lines is called the ***sarcomere***.

Each myofibril consists of ***actin (thin)*** and ***myosin (thick) filaments***. The proteins *troponin* (has high affinity for calcium ions) and *tropomyosin* are located on the actin filaments. Each myosin molecule is composed of two long protein chains with a globular head at one end. The myosin head attaches to the binding site on the actin filament. (Figure 3.19).

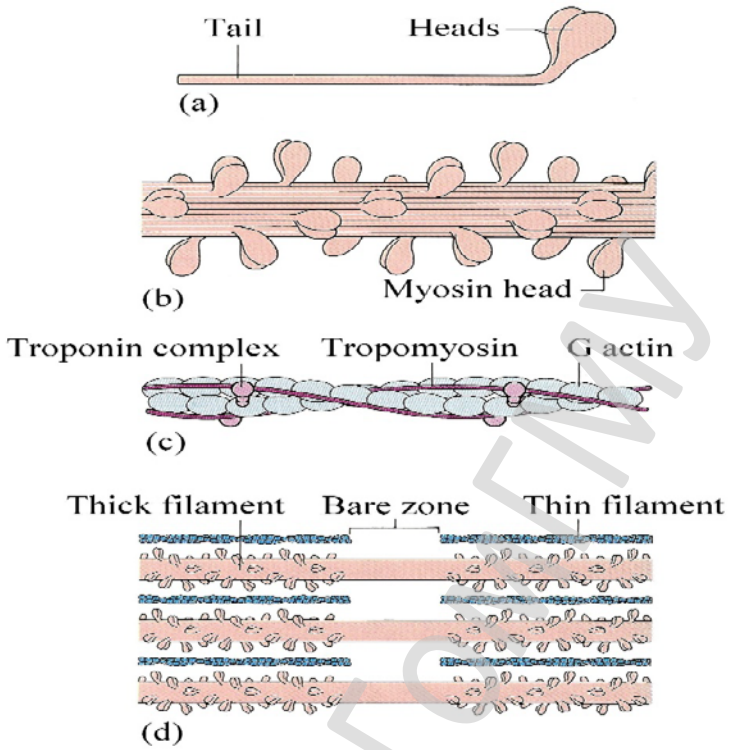


Figure 3.19 — Myofilament composition in skeletal muscle (by Elaine N. Marieb, 1989)
Notes: (a) Each myosin molecule has a stalk-like tail, from which two «heads» protrude. (b) Each thick filament consists of many myosin molecules. (c) The thin filament contains two strands of F actin twisted together. Each strand is made of G actin subunits. Tropomyosin molecules coil around the F actin. A troponin complex is attached to each tropomyosin molecule. (d) The arrangement of the filaments in the sacromere (longitudinal view).

3.4.6. Theory of muscle contractions (sliding of filaments)

A muscle contraction is connected with the appearance of an action potential on the muscle fiber membrane. Then AP is distributed along the sarcolemma and enters the fiber.

To cause a muscle contraction, a current must penetrate deeply into the muscle fiber. This is achieved by the transmission of action potentials along transverse tubules (T tubules), which penetrate all the way through the muscle fiber. The action potentials of the T tubules promote a release of calcium ions from the sarcoplasmic reticulum. In the sarcoplasmic reticulum, there are voltage-gated calcium channels. As these channels open, calcium reaches the cytoplasm down the concentration gradient.

Cross-bridge cycling.

1. The muscle contraction cycle is triggered by calcium ions released from the reticulum and binding to the protein complex troponin (Figure 3.19.). The troponin complex undergoes a conformational change, and tropomyosin mole-

cules move more deeply into the groove between the two actin strands. As a result of this, the obstacle inhibiting the interaction of the actin and myosin filaments is removed. The active actin sites become uncovered for binding with myosin.

2. The high-energy myosin head bridges the gap and attach to the binding sites on the thin actin filaments, forming a cross-bridge. ATP is split, but ADP and phosphate ion are bound to the head.

3. The heads of the myosin filaments perform a longitudinal pull. As a result, the sliding of the actin filaments between the myosin ones appears. The bond between the myosin head and the active actin site causes a conformational change in the head to a lower energy state, prompting the head to tilt. This provides the "power stroke" for pulling the actin filament. ADP and phosphate ions are released, but the cross-bridge is still in place.

4. ATP then binds to myosin, and the detachment of the myosin head from the actin active site takes place. The released energy is spent on breaking the connection of the actin-myosin cross bridge.

5. The ATP molecule is split (but ADP and phosphate ions are not released). The initial conformational state of the myosin head is restored, which allows the cross-bridge cycle to start again, leading to a new power stroke. Thus, these cycles can repeat till calcium ions and ATP are present in the sarcoplasm.

6. The calcium ions are pumped back into the sarcoplasmic reticulum. Calcium in the sarcoplasma activates CA^{2+} ATPase, which provides active transport of calcium into the sarcoplasmic reticulum. Thus, the tropomyosin-troponin complex covers the binding sites on the actin filaments and the contraction ceases.

3.4.7. Muscle fatigue. Hypertrophy and atrophy of muscles

Muscle fatigue is a temporal state of exhaustion or loss of strength and/or muscle endurance following strenuous activity which disappears after some rest.

Causes of muscle fatigue:

1. Accumulation of metabolic products (lactic acid) in muscles inhibiting generation of action potentials.

2. Oxygen starvation, i.e. muscles are deprived of adequate oxygen supply.

3. Energy exhaustion.

4. The central-nervous theory of muscle fatigue. According to this theory, the fatigue of nervous cells develops faster than that of muscles. The fatigue of synapses through which impulses are transferred to muscles also occurs.

On the whole, there is no first or last cause. All of them act simultaneously.

Hypertrophy and atrophy of muscles

Muscle hypertrophy involves an increase in the size of muscle fibers due to regular physical exercise. There are two types of hypertrophy:

1. ***Myofibrillary type*** develops due to static work (lifting of heavy objects). In this type of hypertrophy, the number of myofibrils increases and muscle strength is significantly enlarged, for example, in weight-lifters.

2. ***Sarcoplasmic type*** focuses more on increased muscle sarcoplasm storage (glycogen, phosphocreatine, myoglobin, number of capillaries). In this type of hypertrophy, muscle endurance develops, for example, in marathon runners.

Muscle atrophy develops due to low physical activity, e. g. it is common in those who wear a plaster bandage or are bedridden, or it may be caused when an injury or disease harms the nerve which attaches to the muscle (dissection of tendons, nervous disorders).

3.4.8. Smooth muscles

Smooth muscles are present in the walls *of the blood vessels, skin, and internal organs.*

Smooth muscles differ from transversal striated muscle fibers in irregular actin and myosin myofibrils. The junction of smooth muscles represents close continuous contacts between the membranes. These junctions are called ***nexuses***. Thus, they form a network acting as a whole.

Smooth muscles provide slow motions and continuous tonic contractions (e. g., pendulum-like and peristaltic contractions of the intestines). Smooth muscles provide the tonus of arteries and arterioles (Figure 3.20).

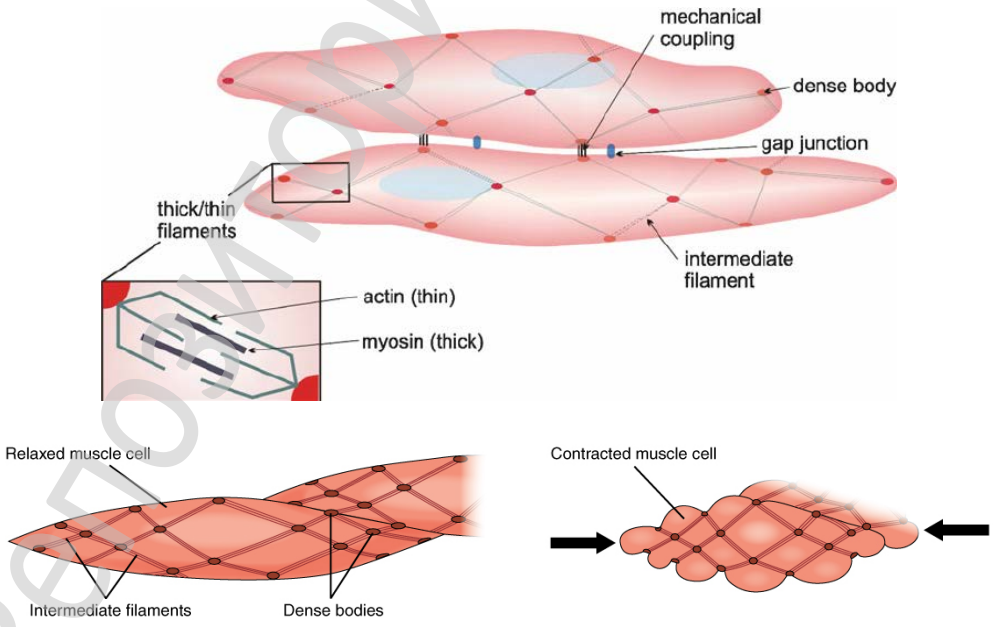


Figure 3.20 — Structure of smooth muscle cells (from bianoti.com)

By functional value, smooth muscles are divided into two types:

1. **Unitary (*visceral, single-unit)*** located in the gastrointestinal tract and urinary system.

2. **Multi-unit**, consisting of units containing a large number of muscle cells. Multi-unit smooth muscles are present in the walls of the blood vessels, in the pupil, lens, and skin.

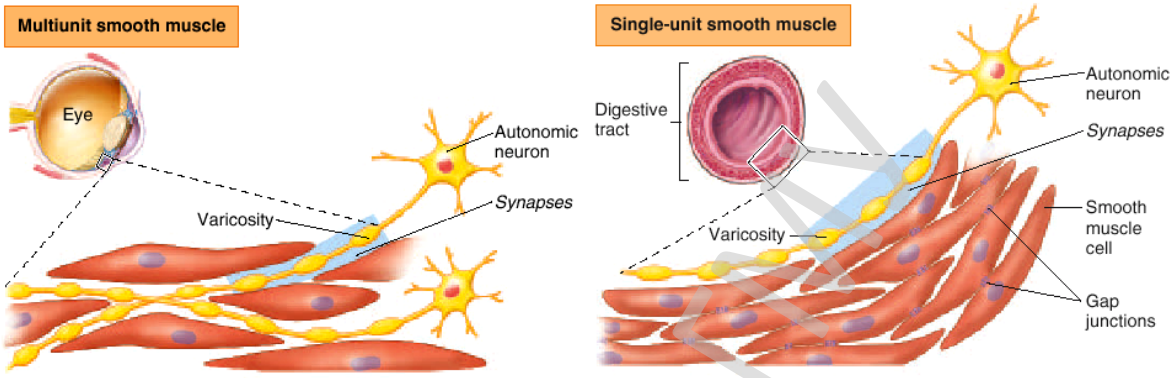


Figure 3.21— Types of smooth muscles (from biology.reachingfordreams.com)

The activity of smooth muscles is influenced by the sympathetic and parasympathetic parts of the autonomic nervous system.

Visceral smooth muscles are able to contract without direct nervous influences. The constant resting membrane potential in smooth muscles is absent, it continuously drifts and makes — 50 mV on the average. The drift is spontaneous, without any influences and, once the resting membrane potential has achieved the critical level, an action potential is generated, which induces a muscle contraction. The action potential lasts for a few seconds, therefore the contraction lasts for a few seconds, too. The excitation is distributed through the nexus to the next areas inducing their contractions.

The velocity of the signal conduction by the nerve fibers towards smooth muscles is 0.5–1 m/sec.

Spontaneous (independent) activity is connected with extension of smooth muscle cells and when they are stretched, an action potential is generated. The frequency of action potentials depends on the degree of fiber extension. For example, peristaltic contractions of the intestines strengthen because of the extension of its walls caused by the chyme.

Basically ***multi-unit muscles*** contract when they are influenced by nervous impulses, but sometimes spontaneous contractions are also possible. A single nervous impulse cannot induce a response. To induce a response, several impulses are required.

In all smooth muscles, the generation of excitation leads to the activation ***of calcium channels***, therefore in smooth muscles all processes go slower as compared with skeletal ones.

Humoral regulation of smooth muscle contractions. The force of smooth muscle contractions is influenced by *adrenalin*, which produces continuous

contractions. Smooth muscles can respond to the action of the biological substances of blood. Opposite to them, skeletal muscles respond to the action of the substances only through synapses.

Smooth muscles consume little energy and possess *plasticity*. **Plasticity** is the ability of muscles to store the given length with the strain unchanged. This property is very important for the functioning of the urinary bladder.

The action of the biologically active substances on smooth muscles located in various organs is not similar. Thus, ***acetylcholine*** excites smooth muscles of the internal organs but inhibits those of the vessels; ***adrenalin*** is capable to relax the uterus in a non-pregnant woman but produces contractions of the uterus in a pregnant one.

Review questions

1. What are the types of muscle tissues in the human organism? What properties do muscles have? Name and describe the forms and types of muscle contractions.

2. Name the phases of single muscle contractions. What is the summation of muscle contractions? Describe its types. What is tetanus? Explain the origin of dentate and smooth tetanus. Explain the concept of the optimum and pessimum of frequency. What is contracture? Name and describe its kinds.

3. What factors influence the force of muscle contractions? Name the types of the muscle diameter. Give the definition of "muscle strength". Name its kinds. Give the definitions of "muscle work" and "muscle power".

4. What are the motor units? Give the classification of the motor units by the structure and functional value. Name the features of slow-twitch and fast-twitch muscle fibers.

5. Describe the structure of muscle fibers and sarcomere. Explain the theory of muscle contractions (sliding of filaments) and the role of myosin, actin, ATP and calcium ions in muscle contractions.

6. What is muscle fatigue? Explain the mechanisms of its development. What are hypertrophy and atrophy of muscles? Name the types of hypertrophy and describe them.

7. What are the functions of smooth (unstriated) muscles? Where they are located? Name the types of smooth muscles. Describe the features of the structure and properties of smooth muscles. What is the plasticity of smooth muscles? Explain its value.

Multiple Choice Questions
PHYSIOLOGY OF EXCITABLE TISSUES
LAWS OF STIMULATION AND ASSESSMENT OF EXCITABILITY. PHYSIOLOGY OF NERVE TISSUES. PHYSIOLOGY OF SYNAPSES

1. Tissues that are capable to respond to the action of stimuli with an active physiological reaction are called …

Variants of answer:

a) relaxable;
b) contractive;
c) excitable;
d) conductive;
e) autonomic.

2. Excitable tissues are…

Variants of answer:

a) muscular, connective, glandular;
b) nervous, epithelial, connective;
c) glandular, connective, epithelial;
d) muscular, nervous, glandular;
e) fatty, epithelial, muscular.

3. The minimal strength of a stimulus that is capable to cause excitation is called…

Variants of answer:

a) subthreshold;
b) superthreshold;
c) threshold;
d) submaximal;
e) subminimal.

4. The threshold of tissue stimulation is a criterion of …

Variants of answer:

a) excitability;
b) inhibition;
c) conductivity;
d) contractility;
e) lability.

5. The difference between the charges of the internal and external surfaces of the cell membrane is called …

Variants of answer:

a) the membrane action potential;
b) the local response;
c) the membrane resting potential;
d) reversal inhibition;
e) electrotone.

6. In the excitable tissue cytoplasm of cells at rest, the concentration of … ions is the highest.

Variants of answer:

a) potassium;
b) chlorine;
c) sodium;
d) calcium;
e) magnesium.

7. The mechanism of the ion movement through the membrane down the concentration gradient without energy consumption is called …

Variants of answer:

a) passive transport;
b) pinocytosis;
c) endocytosis;
d) active transport;
e) exocytosis.

8. The mechanism of the ion movement through the membrane against the concentration gradient with energy consumption is called …

Variants of answer:

a) passive transport;
b) pinocytosis;
c) endocytosis;
d) active transport;
e) exocytosis.

9. The active mechanism providing the removal of sodium ions from cells and introduction of potassium ions into them is called …

Variants of answer:

a) the sodium selective pump;
b) the membrane action potential;
c) the critical level of depolarization;

d) the sodium-potassium pump;
e) diffusion.

10. The sodium-potassium pump transmits Na^+ and K^+ ions through the cell membrane …

Variants of answer:

a) down their concentration gradient;
b) without taking into account their concentration gradient;
c) against their concentration gradient;
d) down the osmotic gradient;
e) down the electrochemical gradient.

11. The change of the membrane potential to a less electronegative value is called …

Variants of answer:

a) hyperpolarization;
b) repolarization;
c) exaltation;
d) depolarization;
e) subnormality.

12. The change of the membrane potential to a more electronegative value is called …

Variants of answer:

a) hyperpolarization;
b) repolarization;
c) exaltation;
d) depolarization;
e) refractory period.

13. The correct order of the phases of the membrane action potential is:

Variants of answer:

a) slow depolarization — fast depolarization — fast repolarization — hyperpolarization — slow repolarization;
b) slow depolarization — fast depolarization — fast repolarization — slow repolarization — hyperpolarization;
c) fast depolarization — slow repolarization — slow depolarization — fast repolarization — hyperpolarization;
d) slow repolarization — slow depolarization — fast depolarization — fast repolarization — hyperpolarization;
e) slow depolarization — hyperpolarization — fast depolarization — fast repolarization — slow repolarization.

14. What happens to the charge of the membrane during the process of its depolarization when an AP is formed?

Variants of answer:

a) the negative charge of the internal surface of the membrane increases;

b) the positive charge of the external surface of the membrane increases;

c) the negative charge changes to the positive one;

d) the charge does not change at all;

e) the charge is absent.

15. During the phase of depolarization of the membrane action potential, the permeability of the membrane increases basically to … ions.

Variants of answer:

a) potassium;

b) chlorine;

c) sodium;

d) magnesium;

e) all the answers are correct.

16. The phase of repolarization of the membrane action potential is caused by the increased permeability of the membrane to … ions.

Variants of answer:

a) potassium;

b) chlorine;

c) sodium;

d) calcium;

e) all the answers are correct.

17. The correct order of the phases of the changes of excitability during excitation is:

Variants of answer:

a) hyperexcitability — absolute refractory — relative refractory — subnormal excitability — supernormal excitability;

b) hyperexcitability — relative refractory — absolute refractory — subnormal excitability — supernormal excitability;

c) hyperexcitability — absolute refractory — relative refractory — supernormal excitability — subnormal excitability;

d) hyperexcitability — subnormal excitability — absolute refractory — relative refractory — supernormal excitability;

e) hyperexcitability — subnormal excitability — relative refractory — absolute refractory — supernormal excitability.

18. What is the "absolute refractory period"?

Variants of answer:

a) it is a gradual increase of excitability;

b) It is a decrease of excitability during the period of hyperpolarization;

c) It is a period of full unexcitability;

d) it is a period of maximum excitability;

e) all the answers are correct.

19. The relative refractory period develops during the phase of…

Variants of answer:

a) depolarization;

b) hyperpolarization;

c) fast repolarization;

e) rest period.

20. When the phase of slow depolarization of the membrane develops, excitability is…

Variants of answer:

a) absolute refractory;

b) subnormal excitability;

c) relative refractory;

d) hyperexcitability;

e) all the answers are correct.

21. Which phase corresponds to the phase of fast depolarization of the membrane action potential?

Variants of answer:

a) supernormal excitability;

b) subnormal excitability;

c) absolute refractory;

d) relative refractory;

e) hypererethism.

22. The excitability during the phase of slow repolarization is characterized by …

Variants of answer:

a) the absolute refractory phase;

b) supernormal excitability;

c) the relative refractory phase;

d) subnormal excitability;

e) normal excitability.

23. What corresponds to hyperpolarization?

Variants of answer:

a) supernormal excitability;

b) subnormal excitability;

c) absolute refractory;

d) relative refractory;

e) hypererethism.

24. Parabiosis is...

Variants of answer:

a) a local long condition of excitation arising under the action of narcotic and other substances;

b) the dependence between the strength of a stimulus and its duration;

c) passive transport with the help of specialized structures;

d) the dependence between the strength of a stimulus and strength of a response;

e) all the answers are correct.

25. The correct order of the development of the phases of parabiosis is …

Variants of answer:

a) inhibitory, equaling, paradoxical;

b) paradoxical, inhibitory, equaling;

c) equaling, paradoxical, inhibitory;

d) inhibitory, paradoxical, equaling;

e) paradoxical, equaling, inhibitory.

26. The characteristics of the paradoxical phase of parabiosis are…

Variants of answer:

a) stimuli of various strength (weak and strong) induce identical responses;

b) stimuli of various strength (weak and strong) cannot induce responses;

c) strong stimuli induce weak responses, weak stimuli induce strong responses;

d) strong stimuli induce strong responses, weak stimuli induce weak responses;

e) all the answers are correct.

27. The minimal time during which a stimulus equal to rheobase should be applied to cause excitation is called…

Variants of answer:

a) chronaxie;

b) rheobase;

c) the useful time;
d) electrotone;
e) the local response.

28. The minimal time during which a stimulus equal to double rheobase should be applied to cause excitation is called…

Variants of answer:
a) rheobase;
b) the time of reaction;
c) the useful time;
d) chronaxie;
e) electrotone.

29. Lability is measured by…

Variants of answer:
a) the minimal strength of a stimulus which is necessary to cause excitation;
b) the minimal time during which the threshold stimulus should be applied to cause a response;
c) the maximum number of signals which a cell can produce per second according to the frequency of a stimulus;
d) the minimal time during which a stimulus equal to double rheobase should be applied to cause excitation;
e) all the answers are correct.

30. The adjustment of rhythm is…

Variants of answer:
a) the decreased lability of tissue during rhythmic stimulation;
b) the decreased excitability of tissue during rhythmic stimulation;
c) the increased lability of tissue during rhythmic stimulation;
d) the development of inhibition process in tissue during rhythmic stimulation;
e) all the answers are correct.

31. Why does the phenomenon «pessimum» appear?

Variants of answer:
a) as a result of getting of each following stimulus into the refractory phase;
b) as a result of getting of each following stimulus into the phase of super-normal excitability;
c) as a result of getting of each following stimulus into the phase of hyper-excitability;
d) in consequence of tissue necrosis;
e) all the answers are correct.

32. What is typical for the process of signal conduction in nerves?

Variants of answer:

a) anatomical integrity;

b) physiological integrity;

c) conduction in two directions;

d) isolation of signal conduction;

e) all the answers are correct.

33. What carries out the insulation and trophic function in myelinated nerve fibers?

Variants of answer:

a) neurofibers;

b) microtubulus;

c) axon membrane;

d) myelinated membrane;

e) all the answers are correct.

34. Excitation in unmyelinated isolated nerve fibers is conducted…

Variants of answer:

a) excitation skips from one part to another, and the whole fiber is not seized by excitation;

b) it spreads continuously and the whole fiber is seized with excitation;

c) following the movement of axoplasm;

d) at first it spreads continuously, and at the end of the nerve fibers excitation goes in intermittent motion;

e) at first excitation goes in intermittent motion, and at the end of the nerve fibers it spreads continuously.

35. Excitation in myelinated isolated nerve fibers is conducted …

Variants of answer:

a) it spreads continuously and the whole fiber is seized with excitation;

b) it goes in intermittent motion and the whole fiber is not seized by excitation;

в) following the movement of axoplasm;

г) at first it spreads continuously, and at the end of the nerve fibers excitation goes in intermittent motion;

e) all the answers are correct.

36. The velocity of signal conduction along myelinated nerve fibers in comparison with unmyelinated ones is…

Variants of answer:

a) slower;

b) identical;
c) higher;
d) does not have a constant rate;
e) all the answers are correct.

37. One-direction transmission of signals, synaptic delay, low lability, increased fatigability, transformation of excitation rhythm, high sensitivity to drugs and poisons are typical for…

Variants of answer:
a) electric synapses;
b) mixed synapses;
c) chemical synapses;
d) electric and mixed synapses;
e) all the answers are correct.

38. What appears on the postsynaptic membrane under the influence of excitatory neurotransmitters?

Variants of answer:
a) an inhibitory postsynaptic potential;
b) an excitatory postsynaptic potential;
c) inhibition of an excitatory postsynaptic potential;
d) no changes of the postsynaptic membrane occur;
e) an action potential.

39. How does the poison of curare affect synaptic conduction?

Variants of answer:
a) it facilitates the interactions of the postsynaptic membrane with the cholinergic receptor;
b) it causes blockade of the cholinergic receptor of the postsynaptic membranes;
c) the synaptic conduction is enhanced;
d) it does not affect the synaptic conduction;
e) it decreases the mediator synthesis.

40. The processes of fatigue of neuromuscular preparation earlier develop in…

Variants of answer:
a) synapses;
b) skeletal muscle;
c) nerve body;
d) nerve fiber;
e) simultaneously in all the structures.

41. Which statement about the Na^+-K^+ pump is true?

Variants of answer:

a) K^+ is pumped against the gradient;
b) $2K^+$ are exchanged with $5Na^+$;
c) it pumps out one Na+ for one K^+ ;
d) hypercalcemia causes arrest in the Na^+ K^+ pump;
e) it can transmit Na+ in and out of cells.

42. The resting membrane potential is formed mainly due to…

Variants of answer:

a) Na^+;
b) Ca^{2+};
c) Cl ;
d) Mg^{2+};
e) K^+.

43. Which statement about nerve impulses is true?

a) they travel in one direction through axons;
b) if currents increase too slowly, nerves respond rapidly;
c) they travel in one direction along synapses;
d) they travel at the speed of an electric current;
e) all the answers are correct.

44. A travelling nerve impulse does not depolarize the area immediately behind it, because this area …

Variants of answer:

a) is hyperpolarized;
b) is at the refractory period;
c) is not self-propagating;
d) the conduction is always orthodromic;
e) all the answers are correct.

45. The unidirectional conduction of nerve impulses is found in…

Variants of answer:

a) synapses;
b) axons;
c) dendrites;
d) all of the above-mentioned;
e) none of the above-mentioned.

46. Synaptic conduction is mostly orthodromic because:

Variants of answer:

a) the dendrities cannot be depolarized;

b) once repolarized, the area cannot be depolarized;
c) the strength of antidromic impulses is lower;
d) the chemical mediator is localized only in the presynaptic terminal;
e) all the answers are correct.

47. Which of the following statements is true about excitatory postsynaptic potentials?

Variants of answer:
a) they are self-propagating;
b) they induce no response;
c) they are proportional to the amount of the transmitter released by the presynaptic neuron;
d) they are inhibitory at presynaptic terminal;
e) none of the above-mentioned statements are true.

48. Nerve fibers involved in proprioception are:

Variants of answer:
a) type A fiber;
b) type B fiber;
c) type C fiber;
d) type IV fiber;
e) J fiber.

49. Type B nerve fibers are placed in:

Variants of answer:
a) muscle spindles;
b) fibers carrying pain sensation;
c) preganglionic autonomic fibers;
d) postganglionic autonomic fibers;
e) all the answers are correct.

50. The inhibitory neurotransmitter in the CNS neurons is…

Variants of answer:
a) glutamate;
b) aspartate;
c) gamma-amino butyric acid;
d) noradrenaline;
e) all the answers are correct.

PHYSIOLOGY OF MUSCLES

1. A motor unit is …

Variants of answer:

a) a group of quickly contractile muscle fibers;
b) a group of quickly and slowly contractile muscle fibers;
c) a motoneuron and a group of muscle fibers innervated by it;
d) a motoneuron;
e) one (single) contraction.

2. By their structure, motor units are divided into….

Variants of answer:

a) big and small;
b) fast and slow;
c) multi-unit and unitary;
d) sarcoplasmic and myofibrillary;
e) actinic and myosinic.

3. By the functional value and rate of contractions, motor units are divided into…

Variants of answer:

a) big and small;
b) fast and slow;
c) multi-unit and unitary;
d) sarcoplasmic and myofibrillary;
e) actinic and myosinic.

4. Muscle contractions with the constant length of muscles are called…

Variants of answer:

a) isometric;
b) isotonic;
c) auxotonic;
d) auxometric;
e) tonic.

5. What is typical for isometric contractions?

Variants of answer:

a) muscle changes its strain but does not change length;
b) muscle is shortened but does not change its strain;
c) lower muscle tension when muscle length is reduced;
d) constant muscle tension when muscle is elongated (stretched);
e) constant muscle tension at the constant length.

6. What is typical for isotonic contractions?

Variants of answer:

a) muscle changes its strain but does not change its length;
b) muscle is shortened but does not change its strain;
c) muscle tension is lower when the muscle length is reduced;
d) muscle length is constant in decreased muscle tension;
e) muscle tension is constant in constant muscle length.

7. Auxotonic (mixed) contractions are characterized by…

Variants of answer:

a) constant muscle strain when muscle is shortened;
b) constant muscle length when the size of muscle strain increases;
c) changes of the strain and length of muscle;
d) constant muscle tension when it is elongated (stretched);
e) constant muscle tension and length of muscles.

8. Muscle contractions with long intervals between stimuli are called…

Variants of answer:

a) smooth tetanus;
b) dentate tetanus;
c) single contractions;
d) pessimal contractions;
e) optimal contractions.

9. Which order of the phases of single muscle contractions is correct?

Variants of answer:

a) phase of relaxation, shortening phase, latent phase;
b) shortening phase, phase of relaxation, latent phase;
c) latent phase, shortening phase, phase of relaxation;
d) shortening phase, latent phase, phase of relaxation;
e) latent phase, phase of relaxation, shortening phase.

10. Contractions during frequent stimulation of muscles are called…

Variants of answer:

a) tetanus;
b) single contractions;
c) pessimum;
d) optimum;
e) maximum.

11. What is contracture (cramp)?

Variants of answer:

a) the time between the action of a stimulus and the beginning of a muscle contraction;

b) a steady continuous stationary reversible contraction of muscle with its strongly prolonged relaxation;

c) the ability of muscle to change its strain during stretching;

d) long and strong muscle contractions influenced by the rhythm of signals with consequent rapid relaxation;

e) the change of the length or strain of muscle.

12. During which phase of single muscle contractions is it necessary to influence the next stimulation in order to induce dentate tetanus?

Variants of answer:

a) during the latent period;

b) during the period of shortening;

c) during relaxation;

d) during the refractory period;

e) during any of the periods.

13. During which phase of single muscle contractions is it necessary to influence the next stimulation in order to induce smooth tetanus?

Variants of answer:

a) during the latent period;

b) during the period of shortening;

c) during relaxation;

d) during the refractory period;

e) during any of the periods.

14. Why does smooth tetanus arise in rhythmic stimulation of muscles with the high frequency?

Variants of answer:

a) incomplete summation of single muscle contractions occurs;

b) complete summation of single muscle contractions occurs;

c) there is separation of the phases of excitation and excitability;

d) summation of single muscle contractions does not occur;

e) all the answers are correct.

15. Which type of tetanus has the highest amplitude of muscle contractions?

Variants of answer:

a) smooth;

b) dentate;

c) mixed;
d) pessimal;
e) smooth and dentate.

16. The strength of muscle is …

Variants of answer:

a) the weight of the maximal load lifted at a height;
b) the maximal rate at which the muscle can be contracted;
c) the weight of the minimal load lifted at height;
d) the weight of the minimal load lifted at height and divided by the anatomical cross-section;
e) all the answers are correct.

17. The absolute force of muscle contractions depends on…

Variants of answer:

a) the anatomic cross-section of muscles;
b) the physiological cross-section of muscles;
c) the anatomic and physiological diameter;
d) the strength of the stimulus;
e) all the answers are correct.

18. How does the amplitude of a single muscle contraction depend on the strength of stimulation (threshold or superthreshold)?

Variants of answer:

a) the amplitude is higher under the influence of the superthreshold stimulus;
b) the amplitude is lower under the influence of the superthreshold stimulus;
c) the amplitude is identical in both the cases;
d) muscle fiber does not contract in either case;
e) all the answers are correct.

19. Does the force of contractions of skeletal muscles depend on the strength of stimulation?

Variants of answer:

a) yes;
b) no;
c) only for the suprathroshold stimulus;
d) yes, during physical activity;
e) yes, during mental activity.

20. Which rhythm of muscle work is called optimum?

Variants of answer:

a) when the work is maximal;

b) during which the maximum amount of energy is consumed;
c) during which the maximal force of muscles develops;
d) during which the maximum amount of oxygen is used;
e) all the answers are correct.

21. Muscles are capable to perform their maximal work if loads are?
Variants of answer:
a) minimal;
b) maximal;
c) average;
d) pessimal;
e) any loads.

22. Which order of processes which lead to a muscle contraction is correct?
Variants of answer:
a) stimulation — origin of an action potential — its conduction along the cell membrane — conduction of the action potential deep into fibers by transverse tubules — release of calcium from the sarcoplasmic reticulum — interaction between actin and myosin filaments;
b) stimulation — origin of an action potential — its conduction along the cell membrane — conduction of the action potential deep into fibers by transverse tubules — interaction between actin and myosin filaments;
c) origin of an action potential — stimulation — its conduction along the cell membrane — conduction of the action potential deep into fibers by transverse tubules — interaction between actin and myosin filaments — release of calcium from the sarcoplasmic reticulum;
d) stimulation — origin of an action potential — its conduction along the cell membrane — release of calcium from the sarcoplasmic reticulum — conduction of the action potential deep into fibers by transverse tubules — interaction between actin and myosin filaments;
e) stimulation — release of calcium from the sarcoplasmic reticulum — origin of an action potential — its conduction along the cell membrane — conduction of the action potential deep into fibers by transverse tubules — interaction between actin and myosin filaments.

23. What ions are released from the sarcoplasmic reticulum during excitation?
Variants of answer:
a) potassium;
b) chlorine;
c) sodium;
d) calcium;
e) all answers are correct.

24. What inhibits the binding of myosin with actin?

Variants of answer:

a) actin;
b) heavy meromyosin;
c) tropomyosin;
d) myosin;
e) all the answers are correct.

25. Muscle relaxation is caused by…

Variants of answer:

a) Ca^{2+} release from the sarcoplasmic reticulum;
b) blocking of ATPase;
c) active transport of Ca^{2+} into the sarcoplasmic reticulum;
d) the formation of bridges between actin and myosin;
e) all the answers are correct.

26. The energy of ATP is used in muscles for …

Variants of answer:

a) the work of the Na^{+}-K^{+}-pump;
b) the process of «sliding» of actin and myosin of filaments;
c) all the answers are correct;
d) the process of disconnection between actin and myosin;
e) active transport of Ca^{2+} into the sarcoplasmic reticulum.

27. What will happen to muscle tone after transection of the ventral roots of the spinal cord?

Variants of answer:

a) it will disappear;
b) it will not change;
c) the tone of extensor will increase;
d) the tone of flexors will increase;
e) it will increase.

28. What are the types of muscle hypertrophy?

Variants of answer:

a) presynaptic and postsynaptic;
b) myofibrillary and sarcoplasmic type;
c) big and small;
d) actinic and myosinic;
e) all the answers are correct.

29. Automaticity, lower resting potential, rather slow and long tonic contraction are typical for…

Variants of answer:

a) smooth muscles;

b) skeletal muscles;
c) cardiac muscles;
d) all the types of muscles;
e) none of the specified types of muscles.

30. The ability of smooth muscles to keep the given length without any change of strain is called…

Variants of answer:
a) automatism of muscles;
b) plasticity of muscles;
c) excitability;
d) dynamicity;
e) conductivity.

CORRECT ANSWERS
PHYSIOLOGY OF EXCITABLE TISSUES
LAWS OF STIMULATION AND ASSESSMENT OF EXCITABILITY. PHYSIOLOGY OF NERVE TISSUES. PHYSIOLOGY OF SYNAPSES

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

PHYSIOLOGY OF MUSCLES

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	9	c	17	b	25	c
2	a	10	a	18	c	26	c
3	b	11	b	19	a	27	a
4	a	12	c	20	a	28	b
5	a	13	b	21	b	29	a
6	b	14	b	22	a	30	b
7	c	15	a	23	d		
8	c	16	a	24	c		

UNIT 4
NERVOUS REGULATION OF PHYSIOLOGICAL FUNCTIONS

4.1. General physiology of the central nervous system

4.1.1. Reflex activity of the nervous system

The central nervous system (CNS) is responsible for coordinated activity of all the organs and systems, as well as for the organism`s adaptation to environmental changes and formation of goal-seeking behaviour.

The human nervous system is divided structurally into **central** (the brain and spinal cord) and **peripheral** (nerve fibers, nerve plexuses, nerve terminations). By its functions, the nervous system is divided into somatic and vegetative (autonomic).

The somatic nervous system:

— can be controlled by voluntary regulation;

— regulates the work of skeletal muscles;

— transmits sensory information from the external environment;

— its main centers are located in the cortex of the cerebrum.

The vegetative (autonomic) nervous system (sympathetic, parasympathetic, and metasympathetic):

— provides involuntary regulation;

— regulates the work of the internal organs, glands, heart, and blood vessels;

— the main vegetative centers are located in the hypothalamus.

The nervous system consists of nervous cells (neurons), which process information, and glia, which provide neurons with mechanical and metabolic support. Neurons form chains and nerve centers, which compound the functional systems of the brain.

The main components of the nervous cell are:

— cell body (soma);

— dendrites;

— axon;

— presynaptic axon terminal.

Each of these parts performs a certain function. The **soma** contains organelles requisite for normal neuronal activity. The cell body of the neuron usually gives rise to multiple dendrites and to one axon.

In most neurons the **dendrites** have many branches and their entire surface significantly exceeds the surface of the cell body. The dendrites are the

main structures which receive signals from body tissues or other neurons and pass them into the cell body.

The **axon** is a special cellular extension that arises from the cell body at a site called the axon hillock. The main function of the axon is to conduct signals to other nerve cells or innervated organs. The presynaptic axon terminal contains vesicles with the mediator, which, when released into the synaptic cleft, either excites or inhibits the postsynaptic membrane. Also, the membrane of the presynaptic terminal contains many calcium channels, and their activation provides an influx of calcium ions into the axon terminal.

Neurons differ by the size of the cell body, length, number of dendrites, and the length of the axon (Figure 4.1.).

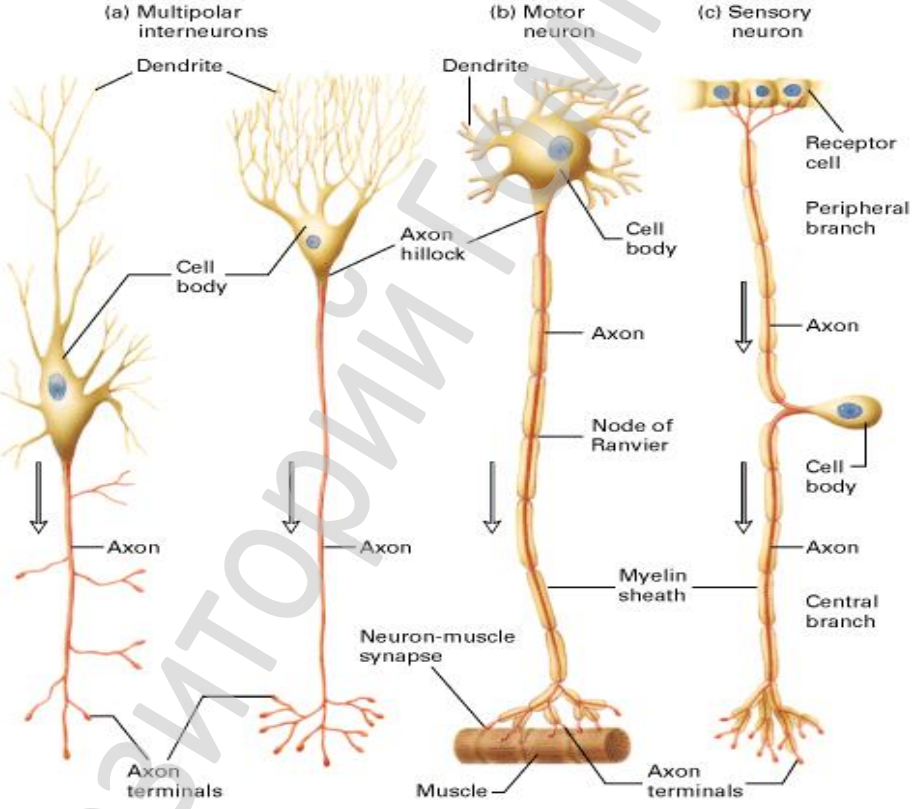


Figure 4.1 — Types of neurons (from biology.reachingfordreams.com)

By their localization and functions, neurons are divided into:

1. Afferent (sensory) — which transmit signals from receptors to nerve centers.

2. Interneurons — which do not go outside the CNS boundaries and provide connections between different afferent and efferent neurons.

3. Efferent (motor) – which transmit information to muscles or executing organs.

By the number of neuronal processes, neurons are divided into:

— unipolar;

— pseudounipolar;
— bipolar;
— multipolar.

Unipolar neurons have only one process extending from the cell body. In humans they are located only in the mesencephalic nucleus of the trigeminal nerve and provide the proprioreceptive sensitivity of masticatory muscles.

Pseudounipolar neurons have two processes: one process conducts signals from receptors and the other — to the CNS. These cells are located in the sensory ganglia and provide reception of sensory information (tactile, temperature, etc.).

Bipolar neurons are located mainly in the peripheral parts of the visual, acoustical, and olfactory systems. Their dendrites are connected with receptors, and axons – with the neurons of the next levels of the sensory system.

Multipolar neurons have several dendrites and one axon. There are about 60 different structural variations of multipolar neurons. Most neurons are multipolar.

The main function of the nervous system is performed by nervous cells. They are only 10 %, and the majority are of the ***glia cells*** (astrocytes, microglia, astrodendroglia, oligodendrocyte, Schwann cells). Astrocytes are located between the blood vessels and neuron bodies. Their processes contact capillaries and are components of the hematoencephalic barrier.

Temporary blood deficiency of the brain results in a loss of consciousness, as the brain is very *sensitive to any oxygen or glucose deprivation.* The brain consumes 20 % of oxygen from the total volume in the organism.

The main specific manifestation of the CNS activity is a reflex.

The reflex is a natural reaction of an organism to internal or environmental changes with the participation of the CNS. The value of reflexes and their mechanisms were studied by I. M. Setchenov and I. P. Pavlov.

The classification of reflexes:

I. *By biological signs:*

1. Food.
2. Defense.
3. Sexual.
4. Orientation.
5. Motor.
6. Parent, etc.

II. *By the location of receptors:*

1. Extero (from the skin surface).
2. Viscero (from the internal organs).

3. Proprio (from muscles).

4. Intero (from the blood vessels), i.e. the reflex chains originate from them.

III. *By the participation of the CNS parts:*

1. Spinal (the centers are located in the spinal cord).
2. Bulbar (the centers are located in the medulla oblongata) .
3. Mesencephalic (the centers are located in the midbrain).
4. Cortical, etc.

IV. *By the character of responses:*

1. Motor (the response is a muscle contraction).
2. Secretory (the response is the secretion of the glands).
3. Vasomotor (the response is the change of the vascular tone).

V. *By the adaptation value:*

1. Unconditioned.
2. Conditioned

Unconditioned reflexes are congenital (specific) reactions of the nervous system. They are carried out by relatively constant nerve pathways in response to adequate stimuli. The inferior parts of the CNS (excluding the cortex) participate in the formation of unconditioned reflexes.

Conditioned reflexes are acquired during ontogenesis. The reaction is carried out by temporary reflex pathways in response to any stimulus. They are formed on the basis of unconditioned reflexes.

The pathway along which signals go from receptors to the executing organ through the CNS (i.e. the pathway through which the reflex action occurs) is called the ***reflex arc.***

A set of neurons necessary for the regulation of the functions or execution of a certain reflex is called the ***nerve center (NC)***, e.g., respiratory, digestive, etc.

The nerve center possesses a ***number of properties***. Basically, they depend on the features of *synapses* and structure of neural networks.

1. **Summation of excitation** is the combination of two or several subthreshold stimuli which induce a response. A separate stimulus is not enough to induce a response. There are 2 kinds of summation (Figure 4.2.):

a) ***Temporal summation***. If several sub-threshold signals enter a single presynaptic terminal in turns over a short period of time (successively). The total amount of neurotransmitter released may exceed the threshold value of the postsynaptic neuron. The higher the frequency of the action potential, the more quickly the threshold may be exceeded.

b) ***Spatial summation.*** If two or more sub-threshold stimuli act simultaneously on different presynaptic terminals which form synapses on one neuron, and together release enough mediator to exceed the threshold of the postsynaptic neuron. For example, neuron A and neuron B may individually release insufficient neurotransmitter but when these quantities are combined, the threshold may be exceeded and an action potential generated.

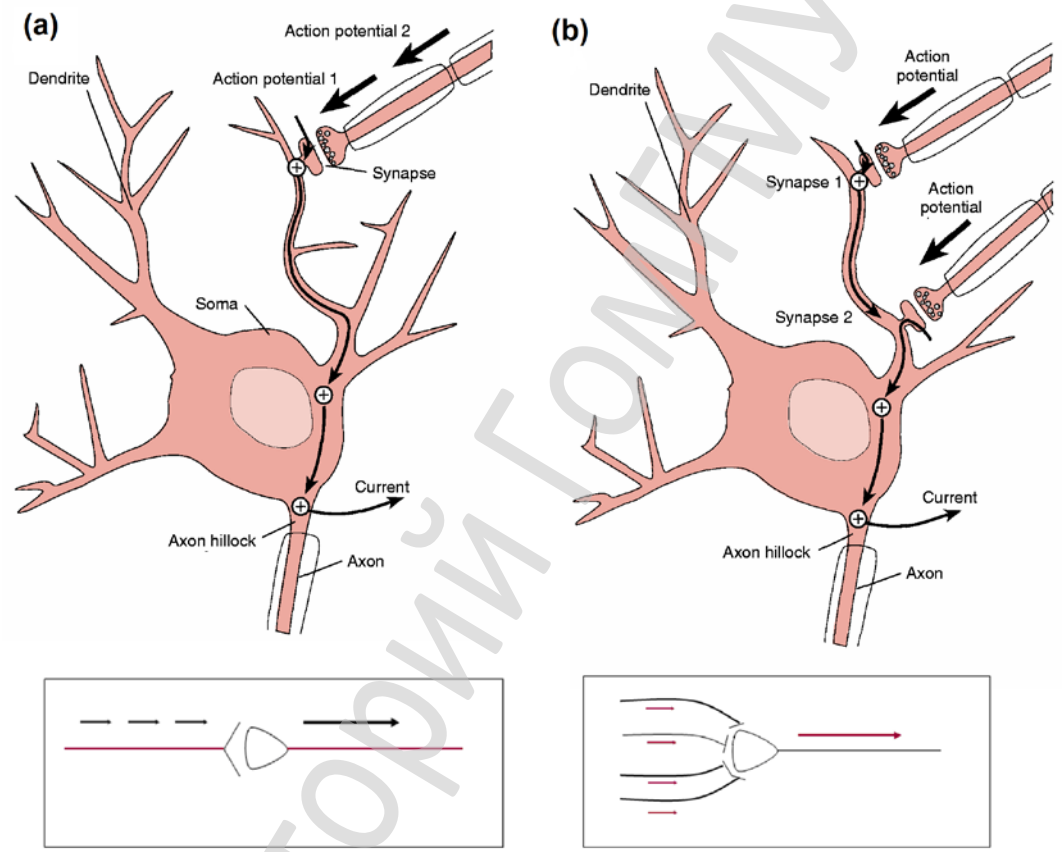


Figure 4.2 – Temporal (a) and spatial (b) summation (from studylib.net)

2. **Transformation of excitation rhythms**. The frequency of signals coming into the nerve center is not equal to the frequency of signals coming out of the nerve center (Figure 4.3.). It is explained by the fact that the postsynaptic potential appears to be very long or depends on the fluctuation of the afterpotentials of the membrane. If the negative afterpotential achieves the critical level, it is capable to induce a new AP.

3. **Posttetanic potentiation**. A temporary increase of the excitability of the nerve center and the strength of the reaction after rhythmic stimulation is called posttetanic potentiation. Low frequency stimulation of afferent nerves causes reflex reactions of certain intensiveness (force). If this nerve is imposed to rhythmic stimulation of high frequency (300–400 stimuli per second), then the following low frequency rhythmic stimulation will increase the reaction (Figure 4.4).

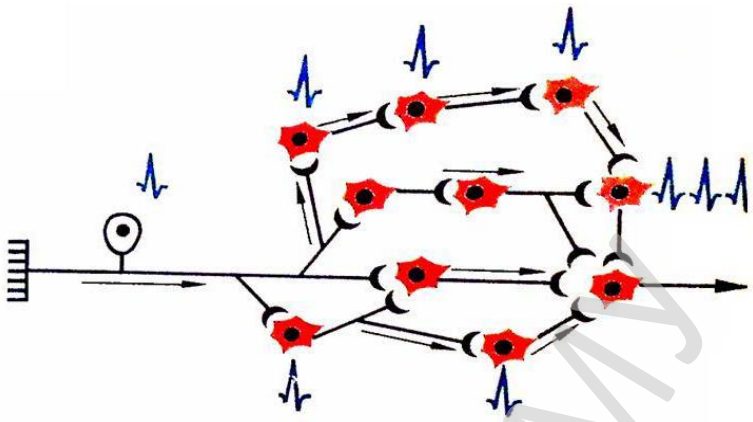


Figure 4.3– Transformation of excitation rhythms (from slideplayer.com)

It is explained by the fact that due to the previous excitation, the ions of Ca^{++} are accumulated inside the presynaptic terminal, which raises the efficiency of the work of the synapse. In a frequent excitation rate each subsequent potential induces secretion of a greater amount of the mediator quanta, which promotes the increase of the postsynaptic potential amplitude.

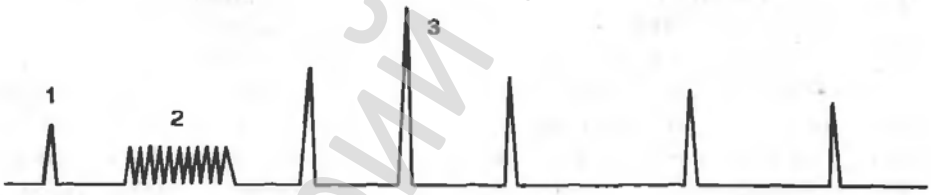


Figure 4.4 — Posttetanic potentiation:
1 — initial response; 2 — rhythmic stimulation; 3 — increased response of the nerve center

4. **The fatigability of the NC** is caused by impairment of signal transmission in interneuron synapses or a decrease of the post-synaptic membrane sensitivity to the mediator. Fatigue is also connected with the neuron sensitivity to a lack of oxygen. The brain consumes 50 ml of oxygen per minute (1/6 from all oxygen consumed by a person at rest). If the brain is not supplied with blood, the cells of the cortex die within 5–6 minutes; those of the brain stem — within 15–20 minutes, and the cells of the spinal cord are the least sensitive to hypoxia and die within 20–30 minutes. Hypothermia prolongs the period of tolerable hypoxia by slowing the cerebral metabolic rate for oxygen. The nerve centers are also sensitive to low glucose levels.

5. Neurons and synapses are selectively **sensitive to some chemical substances and poisons**. *Strychnine* blocks the functions of inhibiting synapses, i. e. increases the excitability of the NC. Some substances selectively affect the nerve centers. For example, *apomorphin* affects only the vomiting center, *lobiline* suppresses the respiratory center.

4.1.2. Main principles of excitation transmission in nerve centers

1. The ability of neurons to establish numerous synaptic links with other neurons is called ***divergence*** (Figure 4.5.), i. e. one cell influences a set of other cells and, therefore, each neuron is capable to redistribute electrical impulses (***irradiation of excitation***).

2. The junction of pathways in a neuron is called ***convergence*** (Figure 4.5.). Since a number of the pathways join in a motoneuron, Sherrington made up a conclusion that the motor neuron is the final common pathway of the motor system.

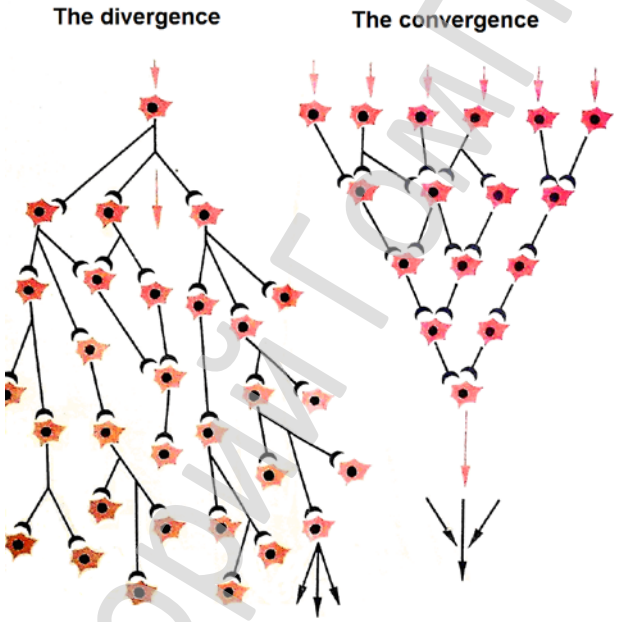


Figure 4.5 — Types of excitation transmission in the nervous system (from studylib.net)

3. Through the NC ***excitation is transferred only in one direction*** from the sensory neuron through the interneuron to the efferent one — the law of one-way transmission of signals. It is explained by the mechanism of the functioning of chemical synapses, when mediator is released only from the presynaptic terminal and influences the post synaptic membrane. For example: if to stimulate the posterior (dorsal) roots of the spinal cord, the action potential is registered on the ventral (anterior) roots; in the reverse direction excitation does not extend.

4. In the NC ***signals are transmitted slower than in nerve fibers***. It explains the relative duration of the reflex period. This period includes the following processes:

1) excitation of receptors;
2) conduction of excitation by afferent fibers;
3) conduction of excitation through interneurons;

4) conduction of excitation by efferent fibers;

5) transmission of excitation to the executing organ and its response.

The period during which the intracentral conduction of excitation occurs is called the ***genuine, or central time of the reflex***. For example: the knee reflex is the fastest, as there are no intercalary neurons.

5. The action of a reflex does not end as soon as the extension of excitation is over, but after some time. This is connected with the circulation of excitation in the chains of neurons (Figure 4.6). This process is called ***reverberation*** (the basis of short-term memory).

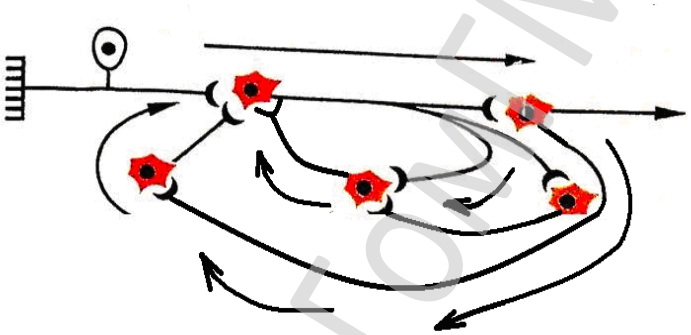


Figure 4.6 — Reverberation in the nerve center (from studylib.net)

4.1.3. Inhibition in the CNS. Inhibition mechanisms

Inhibition, an important property of the CNS, was studied by **I. M. Sechenov** (Figure 4.7.). He removed the cerebral hemisphere of a frog at the level of the thalamus. Then he stimulated the posterior leg of the frog, put it into the solution of sulfuric acid and measured the time of the reflex (the defense reflex). After that he put salt crystals on the thalamus and stimulated them with a weak electric current along with putting the posterior leg again into the solution — the time of the reflex was prolonged or absent.

Conclusion: the thalamus has nerve centers inhibiting spinal reflexes.

Later on, inhibition was studied by F. Holtz. He revealed that the defense reflex can be inhibited by strong mechanical stimulation of the other leg as the process of inhibition arises.

Conclusion: inhibition may develop in any part of the CNS when two or several stimulations coincide.

Inhibition is an active process resulting in weakened or depressed excitation.

The role of inhibition in the CNS:

— it decreases the irradiation of excitation and promotes its concentration;

— it protects the CNS from excessive overstrain;

— it switches off the activity of the nerve centers which are unnecessary at this moment.

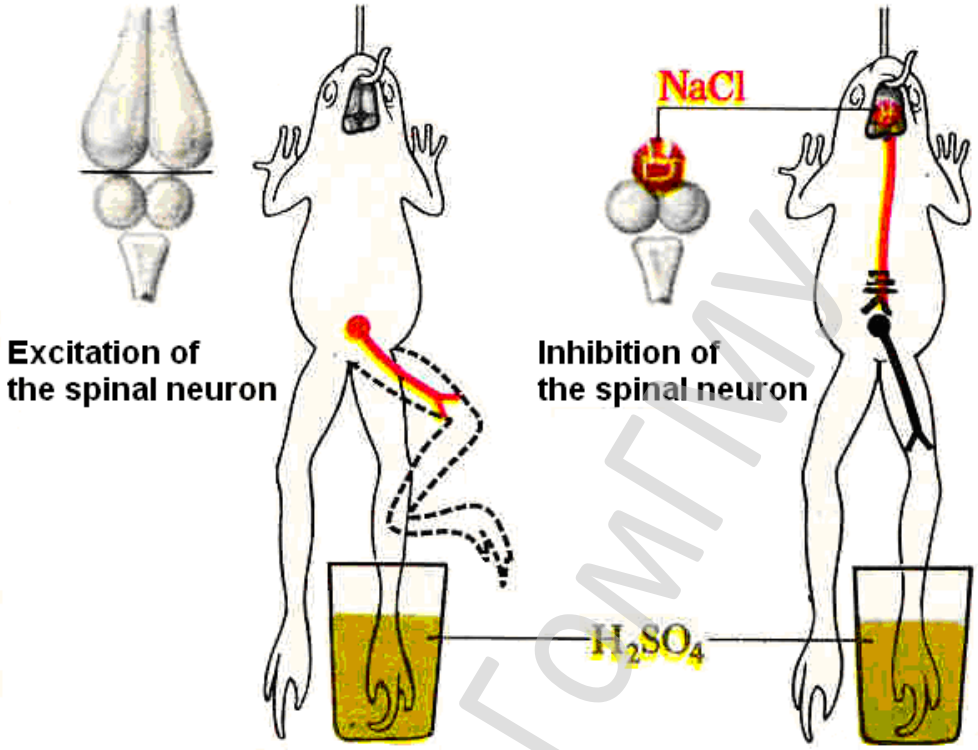


Figure 4.7 —The inhibition experiment (by I.M. Sechenov)

Kinds of inhibition

1. **Antidromic (recurrent):** signals from motoneurons together with the activation of muscles through the axon collaterals activate inhibiting cells (**the Renshaw cells**), which form synapses on motoneurons. Inhibition is carried out by the feedback principle (Figure 4.8.).

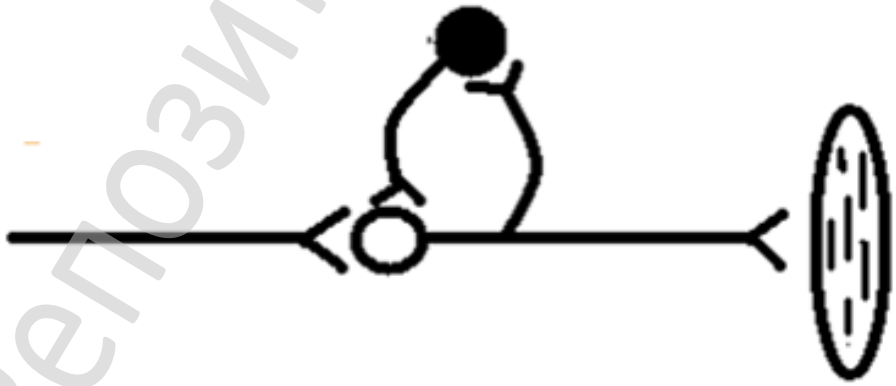


Figure 4.8 — Antidromic inhibition

2. **Reciprocal inhibition** (Figure 4.9.) is based upon the fact that one and the same afferent which stimulates one group of cells through intercalary inhibitory neurons may inhibit other cell groups.

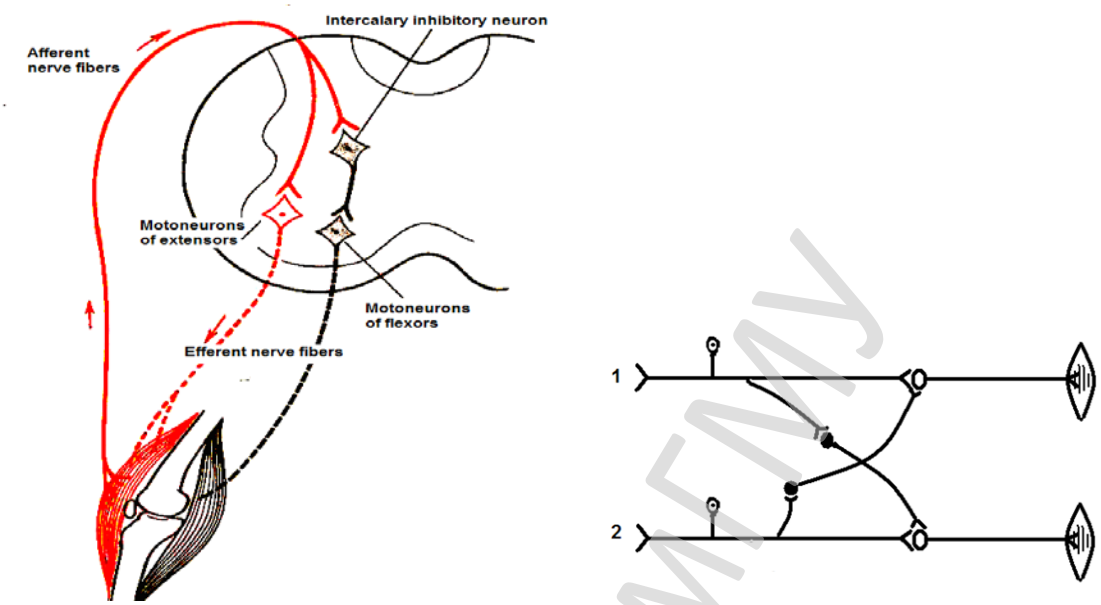


Figure 4.9 — Reciprocal inhibition (from biology.reachingfordreams.com)

3. **Lateral inhibition** (Figure 4.10) is performed by inhibitory interneurons in parallel nets of neurons. Interneurons can influence not only excitant cells but also closely located cells in which excitation is absent or weak.

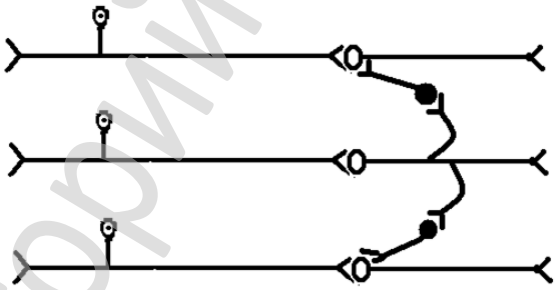


Figure 4.10 — Lateral inhibition

4. **Protective (exorbitant) inhibition** is generated by a stimulus exceeding the limit of the working capacity of neurons. It interferes the exhaustion of a neuron and results in strong shock.

5. **Cortical inhibition** is caused by inhibitory cortical inter-neurons (stellate cells), i.e. excitation does not expand from stellate cells.

6. **Pessimal inhibition** develops in excitant synapses as a result of strong de-polarization of the post-synaptic membrane under the influence of the excessive rhythm of impulses. This inhibition is observed in the spinal cord and reticulum.

7. **External and internal types of inhibition** are present in the cerebral cortex.

Inhibition mechanisms

In interneuronic synapses two mechanisms of inhibition are possible: post-synaptic and pre-synaptic.

Post-synaptic inhibition develops in response to the action of inhibitory mediators in the synapse (*gamma aminobutyric acid (GABA), glycine, taurine*) (Figure 4.11). The permeability of the post-synaptic membrane influenced by these mediators increases for potassium and chlorine ions, potassium is released and chlorine comes inside the cell thus generating ***hyperpolarization*** of the membrane, ***or inhibitory postsynaptic potential (IPP)***, i. e. the *threshold of excitation increases and the inhibiting postsynaptic potential arises*.

The second mechanism of post-synaptic inhibition. If the membrane potential of the post-synaptic membrane is beneath the norm (–50–60 mV), only chlorine ions come inside the cell and ***hyperpolarization, or IPP***, arises. If the membrane potential is high (–90 mV), chlorine ions come inducing partial depolarization, which also results in the development of IPP.

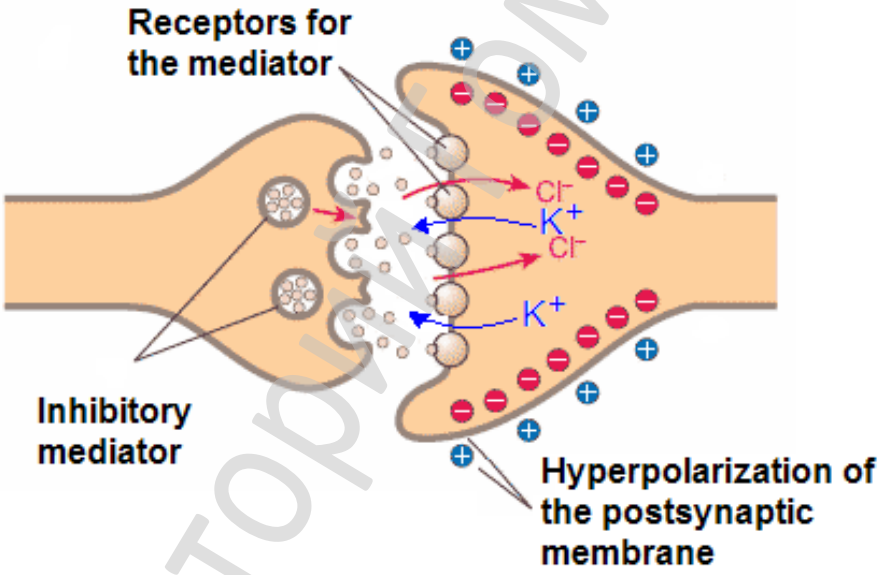


Figure 4.11 — Mechanism of post-synaptic inhibition (from studylib.net)

Pre-synaptic inhibition (Figure 4.12) arises before the excitatory synaptic contact. Its structural basis is the ***axo-axonal synapse***. The axon terminal of the inhibitory cell forms a synapse on the axon of the excitatory neuron and blocks the transmission of excitation. In the area of the presynaptic contact it causes the membrane ***depolarization***, which decreases the amplitude of the action potential taking place here. The basis: the inhibiting axon releases the inhibiting mediator, which enlarges the membrane permeability of the excitant axon for chlorine ions *coming from the excitant termination,* which *partially depolarizes*. This reduces the amplitude of the action potential and decreases the excitation intensity, because the decreased amount of the released mediator quanta in the excitant synapse is insufficient to induce a response.

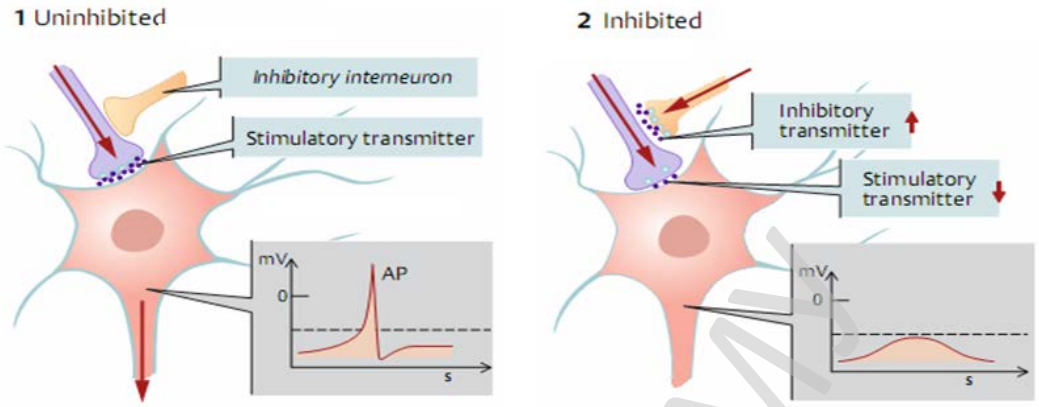


Figure 4.12 — Mechanism of pre-synaptic inhibition (from bianoti.com)

4.1.4. Coordination of reflexes. Dominant

The mechanism of each reflex depends on the state of the CNS at the given moment of time and on the set of intercentral interactions. The interaction of neurons, and, therefore, nervous processes, ensuring coordinated activity of the CNS, is called ***coordination***. Its basis is in the interrelations between excitation and inhibition. This question for the first time was studied by ***N. E. Vvedensky***.

The reciprocal principle. In his experiments on animals, N.E. Vvedensky developed the theory of reciprocal innervation of antagonist muscles: the excitation of the motor center of one muscle group is accompanied with ***reciprocal inhibition*** of the center of antagonist muscles. It happens because of the branching of the afferents in the spinal cord. One of them stimulates flexor motoneurons, others form inhibition synapses on extension motoneurons, that is why the excitation of the afferent simultaneously causes the excitation of the flexion center and inhibition of the extension center.

Induction. Induction is dynamic interactions of the nerve processes of excitation and inhibition. By its effect, induction may have two forms:

— positive;

— negative.

By its duration, induction may be:

— simultaneous***;***

— successive.

In reflex coordination the inverse change of the state of the nerve center after excitation or inhibition plays an important role. If inhibition in a group of nerve cells induces excitation, it is called ***positive successive induction***, and, conversely, if an initially produced process of excitation induces inhibition, it is known as ***negative successive induction.***

The inter-inhibitory influences of reflexes based on reciprocal inhibition are called ***simultaneous negative induction***.

Strong and long stimulation excite not only the neurons of this center but also those of other centers. This conduction of signals in the CNS is called ***irradiation***.

Hence, inhibition of the nerve centers proceeds due to induction (they are «switched off» from functions), and irradiation involves other nerve centers into this reflex.

Feedback principle.

Any reflex act is controlled due to feedback from the nerve center. The feedback consists in the secondary afferent impulses which come to the CNS from receptors which get excited when the functional activity of the executing organ changes. The afferent impulses arising as a result of the activity of the organs are called *secondary*. They carry out the feedback function and play an important role in the coordination of reflexes providing the interaction between the nerve center and the executing organ.

The feedback can be positive (it increases the reflex reaction which caused the secondary afferent impulses) and negative (it inhibits the reflex which caused the secondary afferent impulses).

Example. Any motor act arises under the influence of impulses from the nervous system to the executing organ. The motor act is accompanied with the excitation of ***proprioreceptors*** from which impulses go to the CNS. If the patient`s proprioceptive system is affected, their movements become jerky, there is no accuracy, i. e., the CNS control over the movements is lost.

The principle of the "final common pathway". It was discovered by C. Sherrington. One reflex (for example, muscle contractions) can be caused by stimulation of different receptors, because the same α-motor neuron of the anterior horns of the spinal cord is a part of many reflex arches (Figure 4.13.). Sherrington made up a conclusion that the motor neuron is the final common pathway of the motor system.

Occlusion. If two groups of afferents are stimulated simultaneously, and each of these afferents gives the contractive muscle reflex, it is possible to receive the effect of a smaller force than the sum of the volumes of these reflexes separately. For example: if each afferent excites separately, excitation covers 2 groups of 4 neurons; if two afferents are stimulated simultaneously, excitation covers 6 neurons instead of 8, as two of them, due to convergence, are innervated by both the afferents, and due to the overlap of the synaptic fields the general response is smaller (Figure 4.14.).

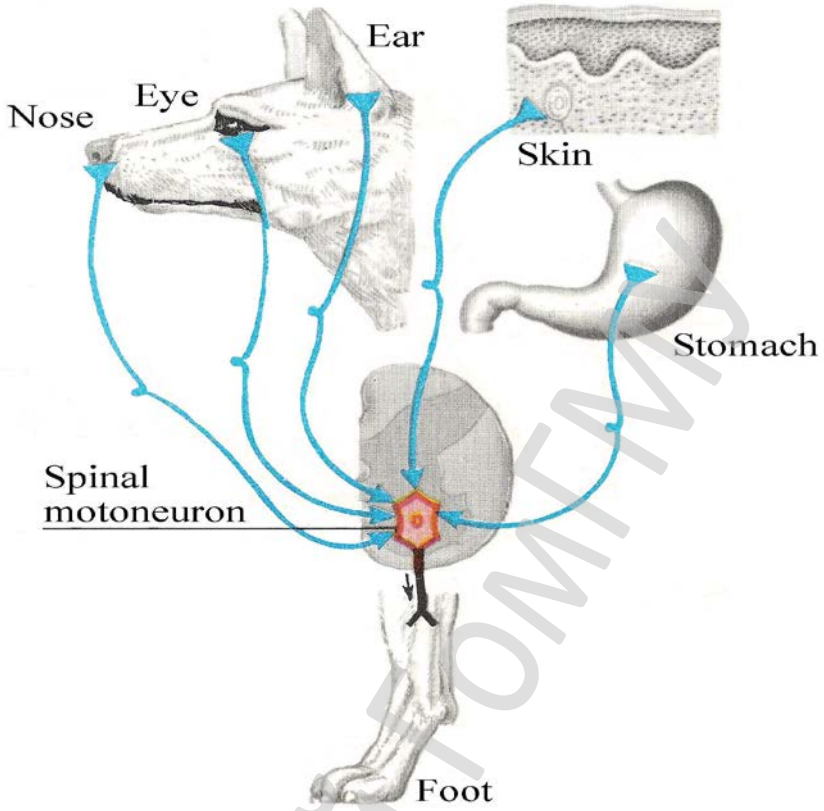


Figure 4.13 — The principle of the "final common pathway" (by Korobkov A. V., Chesnokova S. A., 1986)

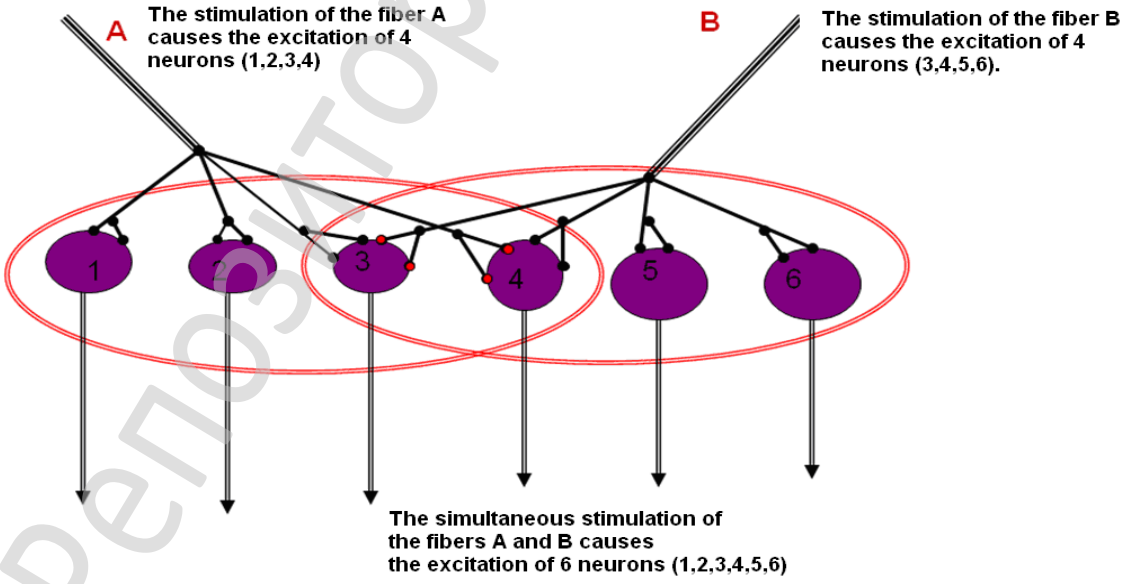


Figure 4.14 — Occlusion (from biology.reachingfordreams.com)

Weak stimulation of the afferents leads to summation (i. e. intensified excitation), and strong stimulation to — occlusion, i. e. suppression of excitation (clogging).

Dominant

Dominant is the prevailing focus of excitation changing and subordinating the work of all nerve centers. Once the dominant appears, stimulation of any receptors will induce a response typical of this dominant.

The dominant covers large systems of reflexes and is the basis for sexual, alimentary, defense, and other reflexes. But at once only one dominant which is the most essential is realized at the given moment of time and then a new one arises. For example: alimentary and protective reflex. The generation of the dominant always inhibits other centers (a person is thinking and does not hear that somebody is calling them).

The properties of the dominant:

1. Hyperexcitability.
2. Stability of excitation.
3. Ability to sum up excitation.
4. Inertia — ability to keep excitation for a long time once the action of a stimulant is over (hunger dominant).
5. Ability to disinhibit.
6. The ability to inhibit other reflexes in the “final common pathway”.

Review questions

1. What are the functions of the central nervous system? Name the parts of the CNS. Give the classification of neurons. Describe the functions of the structural elements of the neuron (soma, axon, dendrites).

2. What are reflexes? Give the classifications of reflexes. Describe the structure of the reflex arc.

3. What is the nerve center? Explain its properties (spatial and temporal summation, transformation of excitation rhythm, fatigability, and others).

4. Name and explain the main principles of the transmission of excitation in nerves centers.

5. What is inhibition? Explain its physiological role. Name and describe the types of inhibition. What are the mechanisms of post-synaptic and pre-synaptic inhibition?

6. What is the basis for the coordination of reflexes? Explain the principles of coordinated activity of the CNS (induction, feedback, reciprocal principle, and others). What is the dominant? Name the properties of the dominant.

Multiple Choice Questions

GENERAL PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM

1. A reflex is…

Variants of answer:

a) an organism`s response to the action of a stimulus with the participation of the CNS;

b) an organism`s response to the action of a stimulus without the participation of the CNS;

c) a sensitive structure which perceives stimuli from the external and internal environments;

d) a response of the external environment on the functions of the human body;

e) the contact between two neurons or between a neuron and an effector cell.

2. The duration of reflexes is estimated from the moment of the influence of a stimulus up to …

Variants of answer:

a) the occurrence of a response;

b) the termination of its action;

c) the termination of a response;

d) achievement of an useful adaptive result;

e) all the answers are correct.

3. When will a response arise if the receptors in the reflex arch are blocked?

Variants of answer:

a) within 1–3 seconds;

b) within 5–7 seconds;

c) no response will arise;

d) within 2–5 seconds;

e) within 5 minutes.

4. What are the basic physiological functions of the neuroglia?

Variants of answer:

a) support, trophic, insulating functions;

b) maintenance of the process of central inhibition;

c) ascending activating influence on the cerebral cortex;

d) transmission of nerve impulses;

e) all the answers are correct.

5. Temporal summation in the nerve center is caused by…

Variants of answer:

a) the simultaneous excitation of several closely located synapses;
b) the increased frequency of impulses;
c) the decreased strength of impulses;
d) the increased strength of impulses;
e) all the answers are correct.

6. Spatial summation in the nerve center is caused by…

Variants of answer:

a) simultaneous excitation of several closely located synapses;
b) the increased frequency of impulses;
c) the decreased frequency of impulses;
d) the increased strength of impulses;
e) all the answers are correct.

7. Under the influence of fatigue the duration of reflexes …

Variants of answer:

a) decreases;
b) does not change;
c) increases;
d) at first increases, then decreases;
e) all the answers are correct.

8. The ability of neurons to make many synaptic connections with various nervous cells is called…

Variants of answer:

a) convergence;
b) prolongation;
c) divergence;
d) summation;
e) transformation of rhythm.

9. The junction of various ways to the same nervous cell is called…

Variants of answer:

a) convergence;
b) prolongation;
c) divergence;
d) summation;
e) transformation.

10. Due to which process neurons can receive signals from several afferent neurons?

Variants of answer:

a) convergence;

b) afferent synthesis;

c) temporal summation;

d) divergence;

e) inhibition.

11. Spatial summation of signals is provided by…

Variants of answer:

a) divergence;

b) the presence of feedback;

c) convergence;

d) induction;

e) inhibition.

12. Excitation through the nerve centers is conducted faster than along nerve fibers.

Variants of answer:

a) it is true;

b) it is false;

c) it is identical;

d) it depends on the nerve center;

e) it depends on the types of nervous fibers.

13. Which reflexes have the minimum duration?

Variants of answer:

a) secretory;

b) vasomotor;

c) viscerovisceral;

d) tendinous;

e) viscerodermal.

14. What is reverberation?

Variants of answer:

a) chaotic distribution of excitation in the CNS;

b) increased or reduced number of signals in a closed neural network;

c) the ability of neurons to make many synaptic connections with various nervous cells;

d) long circulation of nervous signals in a closed neural network;

e) all the answers are correct.

15. Inhibition in the CNS is …

Variants of answer:

a) an active nervous process resulting in weakened or depressed excitation;
b) a passive process connected with the development of fatigue;
c) long circulation of nervous signals in a closed neural network;
d) chaotic distribution of excitation in the CNS;
e) all the answers are correct.

16. Which role does inhibition play in the work of the nerve centers?

Variants of answer:

a) it switches the reflex arch in response to stimulation;
b) it stimulates the work of the nerve centers;
c) it carries out protective, regulating, and coordinating functions;
d) it provides integration of the CNS cells in the nerve centers;
e) all the answers are correct.

17. The Renshaw cells are found in … and their functional value is...

Variants of answer:

a) the cortex of the cerebrum, stimulating action;
b) the cerebellum, coordination of complex motion activity;
c) the spinal cord, inhibiting action on motoneurons;
d) the medulla, to ensure the functioning of the vasomotor center;
e) all the answers are correct.

18. The inhibition of a neuron by the impulses of the inhibitory cell, which is activated by the axon collaterals of this neuron is called…

Variants of answer:

a) reciprocal;
b) forward;
c) recurrent;
d) lateral;
e) cortical.

19. Inhibition of the same afferent fibers causing excitation of one group of neurons and inhibition of the other group of neurons is called…

Variants of answer:

a) pessimal;
b) reciprocal;
c) antidromic.
d) lateral;
e) cortical.

20. A physiological process during which excitation of the pressor department of the vasomotor center is accompanied by inhibition of the depressor department is called…

Variants of answer:

a) convergence;
b) reciprocal inhibition;
c) divergence;
d) summation;
e) transformation of rhythm.

21. Presynaptic inhibition develops in…

Variants of answer:

a) axo-somatic synapses;
b) somatosomatic synapses;
c) axoaxonic synapses;
d) axodendritic synapses;
e) all the answers are correct.

22. The structural basis of presynaptic inhibition is…

Variants of answer:

a) axoaxonic synapses;
b) axo-somatic synapses;
c) axodendritic synapses;
d) somatosomatic synapses;
e) all the answers are correct.

23. The interaction of neurons, and, hence, nervous processes is called…

Variants of answer:

a) coordination;
b) plasticity;
c) divergence;
d) convergence;
e) reciprocal inhibition.

24. Which properties does the dominant have?

Variants of answer:

a) hyperexcitability;
b) inertia;
c) all the answers are correct;
d) the ability to sum up excitation;
e) the ability to disinhibit.

25. The phenomenon when the simultaneous action of two strong afferent signals causes a weaker effect than the sum of their separate effects is called…

Variants of answer:

a) inhibition;

b) occlusion;

c) lowering transformation;

d) convergence;

e) plasticity.

4.2. PARTICULAR PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM

4.2.1. Physiology of the spinal cord

The CNS is divided into parts by structure, development, and functions. By structure, the CNS is divided into the spinal cord, metencephal (myelencephalon, cerebellum, mesencephalon), mediate (thalamus, hypothalamus), and neoncephalon (basal nuclei, limbic system, cortex of the cerebrum).

4.2.1.1. Reflex activity of the spinal cord

The spinal cord is the most ancient structure of the CNS, which is proved by its segmentary structure. The segments are regions of the spinal cord with two pairs of dorsal and ventral roots growing from it. The spinal cord executes *two basic functions* (Figure 4.15.):

1. ***Reflex activity***.

2. ***Conductive function*** (innervates all musculation except for the head muscles).

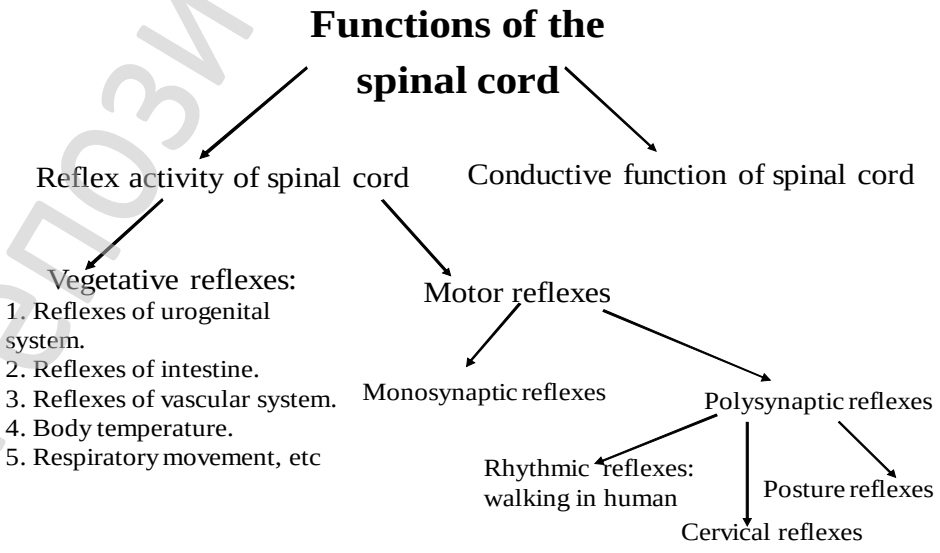


Figure 4.15 — Functions of the spinal cord

Along the spinal cord, there are 31 pairs of roots attached to it, i.e. the anterior (ventral) and posterior (dorsal) roots. The ventral roots contain efferents through which the axons of the following neurons pass: α-motoneurons to skeletal muscles, gamma-motoneurons to muscle proprioreceptors, preganglionic fibers of the vegetative nervous system, etc.

The dorsal roots represent the processes of neurons whose bodies are in the spinal ganglia. The ventral roots carry out motor functions, and the dorsal — sensitive ones.

The gray matter of the spinal cord contain the ventral and dorsal horns and also the intermediate region. The thoracal segments of the spinal cord have the lateral horns, too. Here, in the gray matter, there are many interneurons and Renshaw cells. The lateral and anterior horns contain preganglionic vegetative neurons, whose axons go to the corresponding vegetative ganglia. The top of the dorsal horn (also known as the posterior horn) creates an initial sensory region, as the fibers from exteroreceptors come here. Several ascending tracts originate from here.

In the anterior horns, motoneurons are concentrated and form motor nuclei. Segments with sensitive fibers of one pair of the dorsal roots form the metamere. The axons of one muscle go within the structure of several ventral roots, which provides stable functioning of muscles if any of the axons is damaged.

Reflex activity of the spinal cord

The functions which are carried out by the spinal cord are vital, as it takes part in the regulation of:

1. All motor reflexes (except for head movements).
2. Reflexes of the urogenital system.
3. Reflexes of the intestines.
4. Reflexes of the vascular system.
5. Body temperature.
6. Respiratory movements, etc.

The simplest reflexes of the spinal cord are ***the stretch***, or ***myotatic reflexes.*** The reflex arc of these reflexes does not contain interneurons, therefore, such reflexes are called ***monosynaptic***. These reflexes are of a great value in neurology, as they are easily invoked by the impact of the neurologic hammer by tendons and as result, muscle contractions occur. In clinical practice these reflexes are called *T-reflexes*. They are clearly marked in muscles-extensors. For example, the knee reflex, Achilles reflex, elbow reflex, etc.

The examination of these reflexes in clinical practice helps to determine:

1. At what *level of the spinal cord a pathological process is localized*. Thus, if to carry out tendon reflexes starting from the plantar and to rise gradually

upwards and know at what level the motoneurons of this reflex are localized, it is possible to determine the level of damage.

2. To determine the hypoexcitability or hyperexcitability of *excitation in the nerve centers.*

3. To determine the *side of the damage to the spinal cord*, i.e. if to define reflexes on the right and the left body sides, and if they are absent, it means this side is damaged.

There is a second group of reflexes carried out with the participation of the spinal cord which are more complex, as they include many interneurons and, therefore, are called ***polysynaptic***. There are three groups of these reflexes:

1. ***Rhythmic*** (for example, the scratch reflex in animals and walking in humans).

2. ***Posture*** (maintenance of posture).

3. ***Cervical or tonic reflexes***. They arise in the turning and nodding movements of the head resulting in the relocation of the muscle tone of the whole body.

Apart from somatic reflexes, the spinal cord carries out a set of the vegetative functions (vasomotor, urogenital functions, motility of the gastrointestinal tract, etc.) in the performance of which the vegetative ganglia located in the spinal cord take part.

4.2.1.2. Conductive function of the spinal cord

The conductive function of the spinal cord is connected with the transmission of excitation to and from the brain along the white matter consisting of fibers. The group of fibers of general constitution carrying out the general function organizes ***pathways***:

1. Associative (connect various segments of the spinal cord on one side).

2. Commissural (connect the right and left parts of the spinal cord at one level).

3. Projective (connect the lower parts of the CNS with the upper parts, and vice versa) (Table 4.1.):

a) Ascending (sensory) tract.

b) Descending (motor) tract.

The ascending tracts of the spinal cord are:

1. ***Tract of Goll***.

2. ***Wedge-shaped fascicle of Burdach***. The primary efferents of both the fascicles, without interruption, go to the medulla to the appropriate nuclei and are conductors of dermal and mechanical sensitivity.

3. ***The spinothalamic*** tract conducts impulses from dermal receptors.

4**. The s*pinocerebellar*** tract:

a) Dorsal.

b) Ventral. These tracts conduct impulses to the cerebellar cortex from the skin and muscles.

5. The tract of ***pain sensitivity*** is located in the ventral columns of the spinal cord.

The descending tracts of the spinal cord are:

1. ***The pyramidal (corticospinal) tract*** begins in the motor region of the cerebellar cortex. Some part of these fibers of the tract go to the medulla, where they are cross-directed and go to the lateral columns (lateral tract) of the spinal cord. The other part go directly and reach the corresponding segment of the spinal cord (direct pyramidal tract).

2. ***The rubrospinal tract*** is formed by the axons of the red nucleus of the midbrain. Some part of fibers go to the cerebellum and reticular formation, and the other — to the spinal cord, where they control muscle tone.

3. ***The vestibulospinal tract*** is formed by the axons of the neurons of Deuter's nucleus (lateral vestibular nucleus). It regulates muscle tone and coordinates movements, participates in the maintenance of equilibrium.

4. ***The reticulospinal tract*** begins from the reticular formation of the afterbrain, regulates the processes of movement coordination.

Table 4.1 — The basic conductive pathways

Conductive tracts	**Columns of the spinal cord**	**Physiological importance**
I. Ascending (sensory) tracts		
1. Tract of Goll	Posterior	Touch sensibility, sense of body position and passive movements, sense of vibration
2. Wedge-shaped fascicle of Burdach	-//-	-//-
3. Dorsolateral tract	Lateral	Tracts of pain and temperature sensitivity
4. Dorsal spinocerebellar tract of Flexig	-//-	Impulses from muscle proprioceptors, receptors of ligaments and tendons
5. Ventral spinocerebellar tract of Govers	-//-	-//-
6. Dorsal spinothalamic tract	-//-	Pain and temperature sensitivity
7. Spinotectal tract	-//-	Sensory tract of visual motor reflexes and pain sensitivity
8. Ventral spinothalamic tract	Front	Tactile sensitivity

Conductive tracts	Columns of the spinal cord	Physiological importance
II. Descending (motor) tracts		
1. Lateral corticospinal tract (pyramidal)	Lateral	Impulses to skeletal muscles Arbitrary movements.
2. Rubrospinal tract	-//-	Impulses supporting the tone of skeletal muscles.
3. Dorsal vestibulospinal tract	-//-	Impulses providing the maintenance of posture and body equilibrium.
4. Olivospinal tract	-//-	Unknown function
5. Reticulospinal tract	Front	Impulses support the tone of skeletal muscles, regulate the condition of the spinal vegetative centers and sensitivity of muscle spindles
6. Ventral vestibulospinal tract	-//-	Impulses providing the maintenance of posture and body equilibrium
7. Tectospinal tract	-//-	Impulses provide optic and acoustic reflexes
8. Ventral corticospinal tract (pyramidal)	Front	Impulses to skeletal muscles Arbitrary movements

The degree of the integration of the functions of the spinal cord with those of the brain is so strong, that impaired communication of the spinal cord with the brain results in spinal reflex disorders ***(the phenomenon of spinal shock)***, i. e. the excitability of the nerve centers sharply disappears below the damaged level. In spinal shock, the motor and vegetative reflexes are inhibited, which can be recovered within a long period of time.

The spinal shock is the loss of spinal reflexes after an injury of the spinal cord that appears in the muscles innervated by the cord segments situated below the site of the lesion. The majority of reflexes which regulate the movements and tone of skeletal muscles disappear, and the vegetative functions, acts of urination and defecation are disturbed. The blood pressure decreases, but comparatively earlier than other vegetative functions it starts to rise together with the restoration of some reflexes which regulate the blood redistribution between the vascular areas. If damage occurs above the 3rd cervical segment, it is accompanied by arrest of respiration and leads to death, if below the cervical segments — breath can be kept due to the contraction of the diaphragm. In modern clinical practice it is possible to preserve life of these patients.

4.2.2. Afterbrain

The afterbrain consists of the medulla and pons varolii (Figure 4.16.).

4.2.2.1. Medulla oblongata (medulla)

In the medulla, the gray matter is broken up into nuclei that are separated by nerve fibers. The white matter represents conducting tracts which connect the spinal cord with the upper regions of the CNS, and vice versa. The nuclei of the 5th–12th pairs of the cranial nerves are located in the medulla (Table 4.2.).

12th pair — ***sublingual nerve***. It is motor, innervates the tongue muscles.

11th pair — ***auxiliary nerve***. It is motor, innervates the neck muscles.

10th pair — ***vagus nerve***. It is mixed (both motor and sensory). It has 3 nuclei:

1. *Vegetative nucleus* innervating the larynx, gastrointestinal tract, heart, etc.

2. *Viscerosensory nucleus*. On this nucleus, fibers from the internal organs end and form a solitary tract (single).

3. *Somatomotor nucleus*. The neurons of this nucleus regulate the sequence of the muscle contractions of the pharynx and larynx.

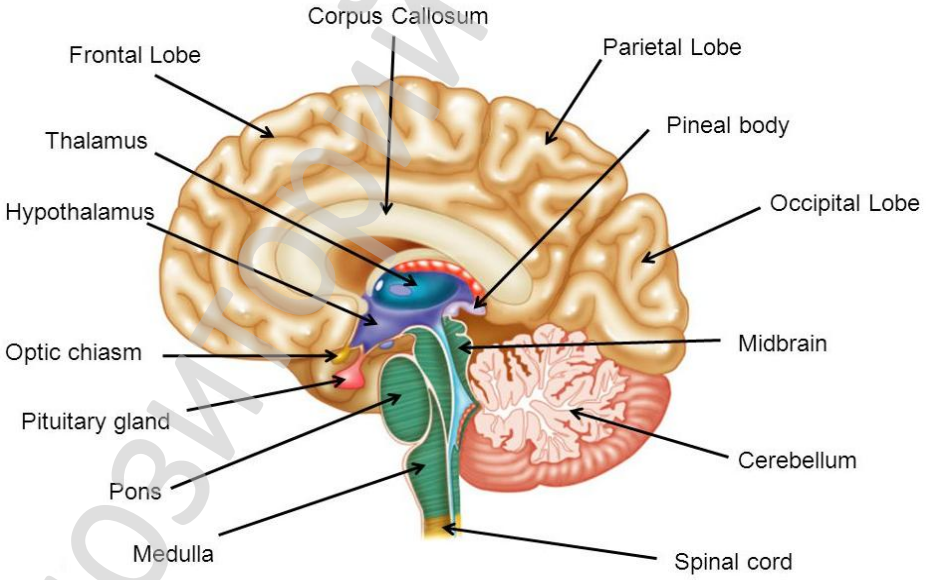


Figure 4.16 — Brain anatomy (from studylib.net)

9th pair — ***glossopharyngeal nerve***. It is mixed. Its motor fibers innervate the muscles of the bottom of the pharynx, and sensory fibers go from the gustatory receptors of the oral cavity. Vegetative fibers go to the parasympathetic ganglia and from them to the salivary glands.

8th pair — ***acoustic nerve***. It is sensory and has two branches: vestibular and acoustic. The vestibular branch begins from the semicircular canals of the internal ear and ends on the vestibular nuclei of the medulla (Deuter's and

Schwalbe's nuclei). The acoustic branch is organized by the afferents going from Corti's organ and ends on the ventral and dorsal acoustic nuclei.

In the center of the medulla, there is the reticular formation, which begins in the spinal cord and proceeds in the pons varolii and medulla. It is assumed that the reticular formation reaches the cortex of the cerebrum.

4.2.2.2. Pons varolii

The pons varolii contains nuclei of three pairs of cranial nerves (Table 4.2.).

Table 4.2 — Functional characteristics of cranial nerves

Name of cranial nerves	Effect of action	Function
XII n. hypoglossus	Motor	Innervates the tongue muscles
XI n. accessorius	Motor	Innervates the neck muscles
X n. vagus	Mixed	Afferent information goes from the internal organs Innervates the muscles of the gullet and larynx, internal organs, heart
IX n. glossopharyngeus	Mixed	Innervates the muscles of the gullet
VIII n. vestibulocochlearis	Sensory	Afferent information goes from the vestibular and auditory apparatus
VII n. facialis	Mixed	Afferent information goes from the gustatory receptors of the tongue Innervates the mimic muscles
VI n. abducens	Motor	Innervates eye muscles
V n. trigeminus	Mixed	Afferent information goes from the mucous membrane of the nose, teeth, tongue Innervates the masticatory muscles and muscles stressing the tympanic membrane
IV n. trochlearis	Motor	Innervates the eye muscles
III n.oculomotorius	Motor	Innervates the eye muscles
II n. opticus	Sensory	Innervates the retina
I n. olfactorii	Sensory	Innervates the mucous membrane of the nose

7th pair — ***facial nerve***. It is mixed. Afferents go to it from the gustatory receptors of the tongue, and efferents send signals to the facial mimic muscles.

6th pair — ***abducent nerve***. It is motor, and innervates the lateral rectus muscle of the eye.

5th pair — ***trigeminal.*** It is mixed. It contains sensory nuclei which occupy all the pons varolii, percepts toothache, receives impulses from the mucosa of the nose and tongue. The motor nucleus sends signals to the masticatory muscles and also to the muscles exerting the tympanic membrane.

Functions of the medulla and pons varolii

The afterbrain carries out several functions:

— *sensory function*, which consists in the primary analysis of information received from the skin, muscles, internal organs, acoustic and vestibular receptors;

— *conduction function* related to transmission of excitation in the ascending and descending pathways:

— *reflex function* allows performing of reflexes in response to the primary analysis of sensory information in the afterbrain:

— *integrative function* consists in the integration of different reflex reactions of an organism

The reflex function includes several groups of reflexes of the afterbrain.

1. Digestive motor reflexes:

The chewing reflex is performed by the mastication center, which includes the motor nuclei of V and XII cranial nerves.

The swallowing reflex is performed by the center which includes the nuclei of V, IX and X cranial nerves (both sensory and motor nuclei).

The sucking reflex is performed by the center which includes the motor nuclei of VII and XII cranial nerves.

2. Protective motor reflexes:

The cough reflex is performed by the center which includes the sensory nucleus of X cranial nerve and the motor nuclei of IX, X and XII cranial nerves.

The sneeze reflex is performed by the center which includes the sensory nucleus of V nerves and the motor nuclei of IX, X and XII cranial nerves.

The blink reflex, also known as **the corneal reflex**, arises under stimulation of the receptors of the eye cornea and conjunctiva and consists in contractions of m. orbicularis oculi. It is performed by the center which include the sensory nuclei of V cranial nerve and the motor nuclei of VII cranial nerve.

The tearing reflex is performed by the center including the sensory nucleus of V cranial nerve and the vegetative nucleus of VII cranial nerve.

The vomiting reflex is performed by the center which includes the sensory and the motor nuclei of X cranial nerve.

3. Vegetiative reflexes:

The salivary secretion reflex is regulated by the main center of salivation including the sensory nuclei of V,VII, IX cranial nerves and the vegetative nuclei of VII and IX cranial nerves.

The reflexes of respiration regulation provide changing of the phases of inspiration and expiration and regulation of respiration depth and are performed by the *respiratory center.*

The reflexes of the regulation of the cardiovascular system are performed by *the vasculomotor center*.

The centers of the medulla regulate the activity of the organs of the thoracal and abdominal cavities.

Damage to the structure of the medulla results in death.

4.2.3. Midbrain

The midbrain belongs to the brain stem. Its dorsal portions are represented with the tectum of the brain, and ventral — cerebral crus. The accumulation of neurons in the midbrain forms the following nuclei: *quadrigeminal plate, red nucleus, reticular formation, black substance, blue nucleus* (Figure 4.17.). ***The superior colliculi of the quadrigeminal plate*** are the initial visual centers, and ***the inferior*** ones — initial acoustic. At the level of the superior colliculi, there is the ***nucleus of the oculomotor nerve (III cranial)***, and at the level of the inferior colliculi — ***IV cranial (trochlear nerve)***. The oculomotor nerve innervates several eye muscles: superior rectus, inferior rectus, medial rectus, and inferior oblique muscles. The trochlear nerve innervates the superior oblique eye muscle.

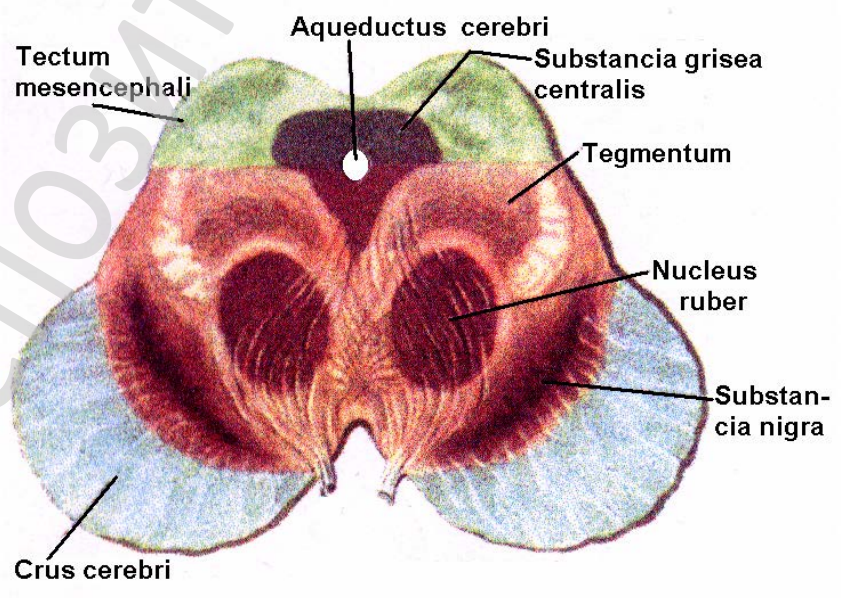


Figure 4.17 — Midbrain (from bianoti.com)

The ***red nucleus*** gives rise to axons that immediately decussate and descend the *rubrospinal tract* and thus regulates the tone of skeletal musculation. This nucleus is connected with the cortex of the cerebrum, cerebellum, reticular formation, spinal cord.

The ***black substance*** contains the pigment melanin of dark color, thanks to which it received its name. This substance is connected with the basal nuclei and reticular formation. It takes part in the reflexes of mastication, swallowing, regulation of the tone of the finger muscles. The neurons of the black substance synthesize ***dopamine,*** which is necessary for the control over complex movements. Dopamine enters the basal nuclei, where it performs an inhibiting influence. Damage to the black substance results in impaired function of finger movements, facial mimics (*Parkinson's disease*).

The ***blue nucleus*** represents dense accumulation of neurons, processes of which form divergent networks with one input. The mediator of the blue nucleus is *noradrenaline*, which regulates all emotional reactions. Surplus of this material results in serious stressful conditions, and its lack — in depression. The blue nucleus establishes connections with the cortex of the cerebrum, cerebellum, spinal cord, thalamus, and hypothalamus.

The functions of the midbrain:

The sensory function consists in the primary analysis of information received by the midbrain from the visual receptors and the secondary analysis of information from the acoustic receptors.

The conduction function is connected with the transmission of excitation by different conductive pathways.

The reflex function consists in the performance of reactions of the central analysis of sensory information in the midbrain.

The integrative function includes integration of different reflex reactions of an organism.

The reflexes of the midbrain are divided into several groups:

The orientative visual and acoustic reflexes are expressed in turns of the head and body in directions towards sources of light or sound. The nuclei of the quadrigeminal plate take part in the formation of ***watch reflex***, i. e. the tone of flexor muscles increases due to which preparation for a response to any new stimulus occurs. For example, high tone of flexor muscles in a cat occurs when there is rustle in silence.

The pupillary light reflex regulates the amount of light received by the retina. It is performed by the additional nuclei of the oculomotor nerve, which innervates the muscle constricting the pupil.

The accommodation reflex (or accommodation-convergence reflex) provides adaptation of lens curvature in response to focusing on a near object, then looking at distant object (and vice versa), comprising coordinated changes in vergence, lens shape and pupil size. It is performed by the additional nuclei of oculomotor nerve which innervates the ciliary muscle .

Reflexes of the brain stem

Also, there are some reflexes performed by the nuclei of the afterbrain and midbrain. These are static and statokinetic reflexes, connected with the maintenance of posture and execution of the chain reflexes.

There are two groups of reflexes connected to the maintenance of posture:

1. Static reflexes:

The static reflexes control the body position in space and arise under stimulation of the receptors of the vestibulum of the membranous labyrinth. They are divided into:

a) ***postural reflexes***. These reflexes provide redistribution of muscle tone when the position of the body is changed in space (inclinations, flexions);

b) ***reflexes of straightening***. These reflexes are connected with redistribution of muscle tone during regeneration of natural posture after it has been changed. For example, a person gets up from bed in a certain sequence (first, the head and only then the trunk and legs are raised).

2. **Statokinetic reflexes**. These reflexes are related to the maintenance of posture and orientation in space if the speed of movements is changed. The statikinetic reflexes arise under stimulation of the receptors of the semicircular canals.These reflexes are characterized by a great force and a high rate of response. The execution of these reflexes involves all musculation, especially the muscles of the eye. Besides, a large number of vegetative centers are activated. For example, the vagus nerve controls respiration, cardiac work, the tone of the blood vessels.

The reflexes of the brain stem are performed by the vestibular nuclei of the afterbrain with the participation of the subcortical visual and acustic centers of the midbrain.

Decerebrate rigidity. If to cut the brainstem in a cat above the medulla so that the red nucleus is remained above the section level, high tone of extensor muscles is observed, i. e. decerebrate rigidity develops (Figure 4.18.). In this case the impairment of the balance between the tone of antagonist muscles develops with the predominance of the tone of extensor muscles. The inhibitory influence of the red nucleus on extensor muscles disappears, but the excitatory influence on these muscles from the reticular and vestibular nuclei remains. After a secondary section of the brainstem at the level of the inferior border of the rhomboidal fossa, rigidity disappears, which is accompanied by the disappearance of the tone of all the muscles.

Figure4.18 — Decerebrate rigidity (from biology.reachingfordreams.com)

Decerebrate rigidity in humans results from a lesion of the upper parts of the brainstem and subcortical nuclei without midbrain damage and is manifested by high tone of flexor muscles and an exaggerated extensor posture of all extremities.

4.2.4. Cerebellum

The cerebellum is a part of the extrapyramidal system and consists of two hemispheres: vermis cerebelli and lateral lobes. The gray matter forms the trilaminar cerebellar cortex (Figure 4.19.):

1. *Molecular layer*. This layer consists of basket and stellate cells and nerve fibers.
2. *Ganglionic layer* consists of Purkinje's cells (piriform cells).
3. *Granular layer* consists of granule cells (grains cells) and Golgi neurons.

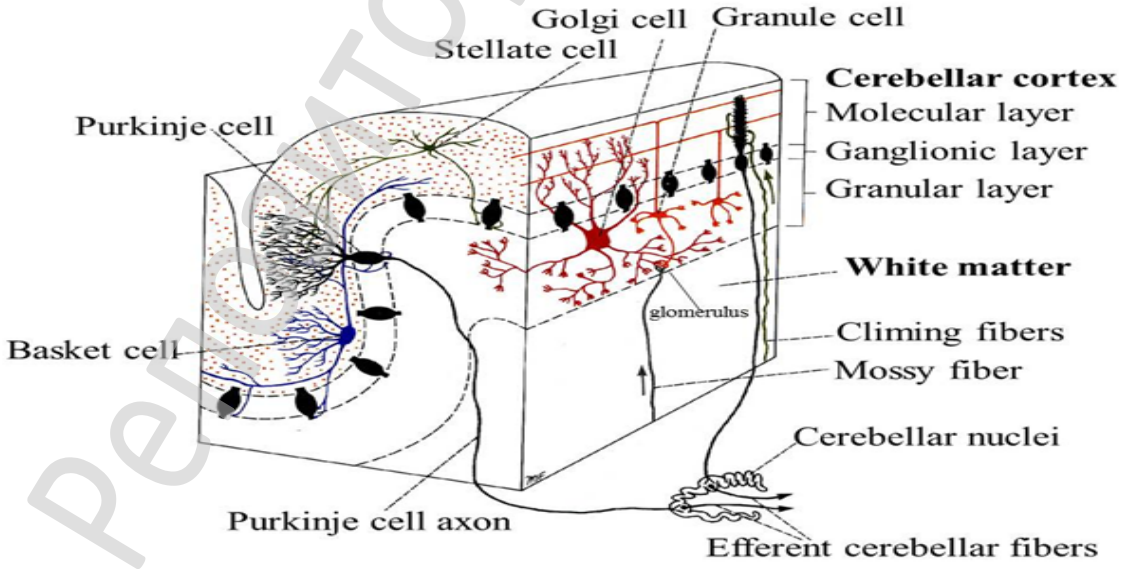


Figure 4.19 — Cerebellar cortex (from studylib.net)

In the white matter neurons form nuclei: ***dentate, emboliform, globose, and fastigial***.

The cerebellum has no direct connection with the organs. It is connected with the receptors of the skin, muscles, and tendons along the spinocerebellar tract. It receives signals from the medulla about the state of the vestibular apparatus, and visual and acoustic information from the midbrain. The cerebellum is connected with the cerebellar cortex by means of the cortex-cerebellar path. The cerebellum has big representation in the cortex. These regions of the cortex of the cerebrum are connected with the relevant fields of the cerebellum, thus providing coordinated activity of these structures of the brain in the control over its functions.

The cerebellum takes part in the regulation of motor activity, in the change and redistribution of muscle tone, i. e. together with the medulla it provides static and statokinetic reflexes. The cerebellum gives rise to the vestibulospinal tract and therefore controls basic commands coming to the spinal cord through the descending tracts.

Sensory influences come to the cerebellum along *climbing fibers*, *mossy fibers and from the neurons of the blue nucleus*. Contacts formed by these fibers are excitant. The climbing fibers come from the inferior olives of the medulla. Each climbing fiber contacts one Purkinje's cell. The nuclei of the pons varolii send afferent signals to the cerebellum along the mossy fibers. The cells of the mossy fibers form synapses on the great amount of inserted neurons; its fibers contact basket cells which form inhibiting synapses on Purkinje's cells. Also the mossy cells form synapses with Golgi cells and stellate cells, which are inhibiting cells.

Apart from grain cells, *all the neurons of the cortex of the cerebellum are inhibiting neurons*. No other part of the CNS contains such an amount of inhibiting cells.

The cortex of the cerebellum receives several types of nerve fibers, and only one pathway gets out — the axons of Purkinje's cells. All synapses which form these fibers are inhibiting. The axons of Purkinje cells form inhibitory synapses on the nuclei of the cerebellum and by decreasing of the tonic activity of these nuclei inhibit the activity of the vestibulo- reticulo- and rubrospinal tracts thus participating in the regulation of motor functions of an organism (coordination of movements, regulation of muscle tone, maintainance of posture and equilibrium).

The main functions of the cerebellum

1) regulation of posture and muscle tone;

2) correction of slow target movements and their coordination with the reflexes of posture maintainance;

3) correct performance of fast target movements in response to signals from the cortex of the cerebrum;

4) participation in the regulation of the vegetative functions.

The cerebellum affects a number of the ***vegetative functions,*** as it is connected to the reticular formation. For example, it changes the work of the *gastrointestinal tract, the level of blood pressure,* the *composition of blood*. The activity of the cerebellum is controlled by the cortex of the cerebrum.

Removal of the cerebellum or its anterior lobe in animals results in increased tone of the muscles of extensors, and the stimulation of the anterior lobe results in decreased tone.

The basic symptoms of damage to the cerebellum are connected with disorders of motor functions. Cerebellar deficiency is accompanied with the symptoms named in the table (Table 4.3).

Table 4.3 — Characteristics of cerebellar deficiency

Type of disorder	Characteristics
Asthenia	Increased fatigability of muscles, decreased force of muscle contractions
Astasia	Inability to stand due to a limitation or absence of muscular coordination (constant tremor of the head).
Dystonia	Involuntary increase or decrease of muscle tone
Tremor	Small by amplitude shaking movements arising synchronously in different parts of the body
Dysmetria	Inaccuracy in voluntary movements
Hypermetria	A form of dysmetria resulting in movements that overreach the intended goals (movement of the arm or hand beyond the object)
Hypometria	A form of dysmetria resulting in movements that fall short to the intended goals (movement of the arm or hand before the object)
Dysarthria	Disturbance of speech
Atony	Decreased muscle tone and deficiency of posture maintenance
Ataxy	Inability to coordinate voluntary muscle movements (their speed, orientation, and smoothness)
Adiadochokinesia	Inability to perform rapidly alternating muscle movements, as flexion and extension.

It is very difficult to diagnose cerebellar damage, since its failure can be compensated by other parts of the CNS, i. e. other regions of the brain can perform functions of the cerebellum in its dysfunction.

4.2.5. Reticular formation of the brain stem

The central part of the brain stem contains diffuse accumulation of cells interlaced by a set of fibers stretching in all directions. Under the microscope

this formation represents a network, that is why the scientist ***Deuters*** called it ***the reticular formation (network formation)***.

The reticular formation begins in the spinal cord and continues to the cortex of the cerebrum. The fibers of the reticular formation extend to the cortex of the cerebrum through the thalamus and form nonspecific pathways which sustain the activity of all the parts of the CNS. Through the descending reticular-spinal tracts the reticular formation can activate and inhibit the reflexes of the spinal cord.

Along the ascending nerve pathways the reticular formation activates the cortex of the cerebrum and maintains its wakeful state. Influenced by the reticular formation, reflexes become stronger and more precise.

The reticular formation acts as a filter and ***transmits only new and important information*** to the upper parts of the CNS.

The activity of the reticular formation is maintained constantly at a high level since signals from all receptors are transmitted through it.

The neurons of the reticular formation are ***very sensitive to the action of hormones and drugs*** which are capable to decrease its activity (aminazine, reserpin, serpasil, etc.).

The reticular formation receives signals from the cortex of the cerebellum, descending and ascending signals interact in its neurons. These signals constantly circulate in the chains of the neurons of the reticular formation and keep it in an active state, which is necessary to maintain the CNS tone and its readiness for work.

After introducing a microelectrode into the reticular formation with its subsequent stimulation with electric signals it was defined that the stimulation of this region of the brain induces the electrical activity of the brain, which is typical for awakening and waking states.

In lesions of the reticular formation and, in particular, its superior parts, an animal falls deeply asleep though afferent signals come into the cortex of the cerebrum along other nerve pathways. Animals with disorders of the reticular formation are constantly asleep and do not respond to any stimuli.

Thus, normal functioning of the cortex of the cerebrum to a greater extent depends on the influences of the reticular formation.

The majority of the neurons of the reticular formation are polysensoric, i. e. excitation may be induced in them by any stimulus (light, sound, tactile stimuli, etc.).

The reticular formation influences the tone of skeletal muscles, and elimination of this influence is one of the reasons for the appearance of the spinal shock followed by hyporeflexia. The activity of the reticular formation is controlled by the cortex of the cerebrum.

4.2.6. Diencephalon (thalamencephalon)

The diencephalon forms the walls of the third ventricle. Its main structures are the thalamus and hypothalamus. Deep in the diencephalon there are the nuclei of the lateral and medial geniculate bodies.

4.2.6.1. Thalamus

The neurons of the thalamus form nuclei which, ***by their anatomical features***, are divided into several basic groups:

1. Anterior.
2. Posterior.
3. Middle.
4. Lateral.
5. Central.
6. Ventral.
7. Intra-laminar.

By their physiology, all the nuclei of the thalamus can be divided into:

1. Nonspecific.
2. Specific.
3. Associative.
4. Motor.

The nonspecific nuclei represent continuation of the reticular formation. They send their signals through the axons to the whole cortex of the cerebrum. First, the signals are distributed from the nonspecific nuclei to the subcortical structures, and then go in parallel to all the regions of the cortex of the cerebrum, since the axons organize a set of collaterals. The nonspecific nuclei provide the activation influence on the cortex of the cerebrum, which is necessary for the maintainance of the necessary level of the activity of the cortical neurons in a person in awake state.

The nonspecific nuclei represent more ancient structures and include central and intra-laminar groups of nuclei.

The specific nuclei send their signals through the axons only to the cells of a certain area of the cortex of the cerebrum (for example, visual or acoustic areas). The fibers from all the ascending pathways end at the neurons of the specific nuclei. Then nerve signals along direct monosynaptic connections go to the sensory and associative areas of the cortex of the cerebrum.

The specific nuclei include:

The *ventro-basal nucleus (ventro-basal complex)* provides transmission of proprioceptive, tactile and interoceptive sensitivity mainly into the posterior central gyrus.

The lateral geniculated bodies receive signals from visual afferents and transmit signals into the cortical center of visual analyzes (occipital lobe); the lateral geniculated body is called the subcortical center of vision.

The medial geniculated bodies, whose neurons receive signals from the acoustic nuclei of the medulla and posterior colliculi of the quadrigeminal plate, provide conduction of impulses into the cortical center of the auditory analyzer (superior temporal gyrus); the medial geniculate bodies are called the subcortical center of audition.

The axons of the specific nuclei do not practically organize collaterals. All sensory information (except for the olfactory system) comes to the cerebellar cortex through the thalamus.

Inhibiting influences from the cortex of the cerebrum and other subcortical structures grab new important information, since the cortex of the cerebrum cannot accept all information at once.

The neurons of the nonspecific nuclei of the thalamus are effectively activated by pain signals, therefore it is assumed that the ***thalamus is the supreme center of pain sensitivity***. Damage to the thalamus is accompanied with unbearable pain and even its insignificant stimulation produces acute pain. Also, damage to a portion of the nonspecific nuclei of the thalamus results in a loss of consciousness. It means that signals from these nuclei maintain the necessary level of the activity of the cortex of the cerebrum necessary to maintain consciousness.

The associative nuclei of the thalamus receive signals from other nerve centers of the thalamus (from the specific nuclei) and have connections with the main associative regions of the cortex of the cerebrum.

The accociateive nuclei include:

The anterior group, which has connections with the limbic cortex

The medial group, which has connections with the associative zone of the frontal lobe of the cortex.

The posterior group, which has connections with the associative zones of the temporal and parietal lobes.

The neurons of the associative nuclei are polysensory (a neuron can receive impulses of different modalities from the centers providing visual, tactile and painful sensitivity) and provide an opportunity of integrated processes as a result of which the signals transferred into the associative zones of the cortex of the cerebrum are formed. These impulses provide manifestation of such mental processes, as recognition of subjects, coordination of speech, visual and motor functions, formation of concept about the pose and position of the body.

With the participation of the nuclei of the thalamus, conditioned reflexes may be formed without participation of the cortex of the cerebrum.

The motor nuclei receive impulses from the basal nuclei and cerebellum and send impulses to the motor zone of the cortex thus participating in the regulation of the motor functions. The ventrolateral nucleus is related to the motor nuclei.

4.2.6.2. Hypothalamus

The structure of the hypothalamus includes a group of nuclei situated at the base of the brain close to the hypophysis (Figure 4.20.). These nuclei are the superior subcortical centers of the autonomous nervous system and all the vital body functions.

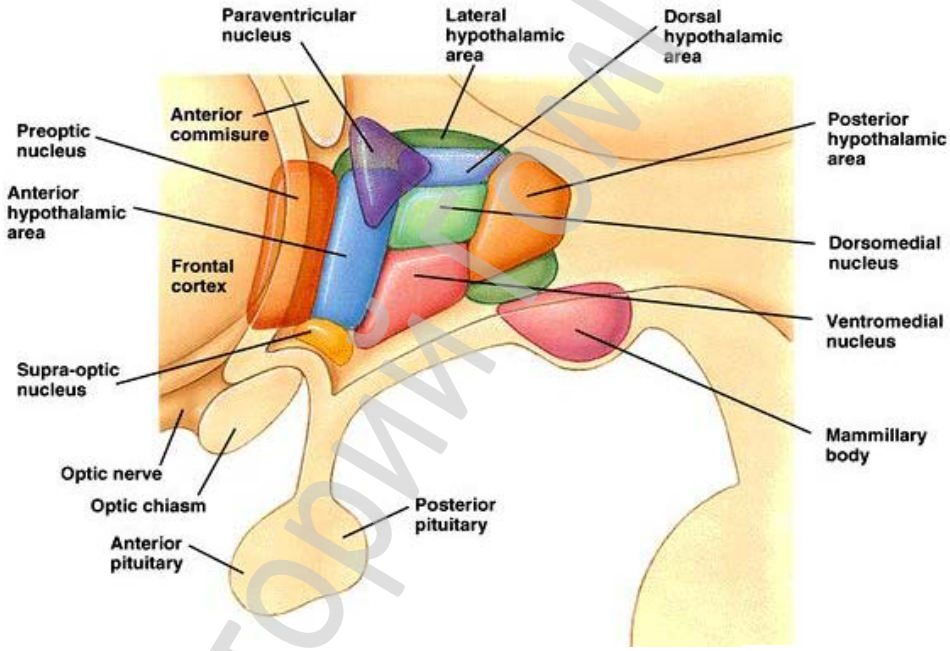


Figure 4.20 — The nuclei of the hypothalamus (from studylib.net)

The nuclei of the hypothalamus are divided into some basic groups:

1. Anterior group (supraoptic and paraventricular nuclei).
2. Middle group.
3. Posterior group.
4. External group.
5. Preoptic group.

These nuclei have complex afferent and efferent connections. *Afferent* signals come to the hypothalamus *from the cortex of the cerebrum, basal ganglia, and thalamus*, and *efferent* signals go from the hypothalamus to the *midbrain, thalamus, and other subcortical structures*.

The supraoptic and paraventricular nuclei of the hypothalamus are connected with the hypophysis with a special system of fibers which conduct electrical impulses and neurosecretion products of the neurons of these nuclei.

The majority of the hypothalamic nuclei have no borders (except the supraoptic and paraventricular nuclei), that is why other nuclei of the hypothalamus are divided into regions depending on their functional value.

There are three regions of the hypothalamus:

1. ***The hypophysotropical region*** includes the preoptic and anterior groups of nuclei whose neurons produce *liberins (stimulators)* and *statins (inhibitors),* thus regulating the activity of the adenohypophysis.

2. ***The medial region*** includes the middle group of nuclei and contains neurons which react to *changes of the body temperature, water-electrolytic composition of blood, the amount of hormones in the blood, and also controls the activity of the hypophysis*.

3. ***The lateral region*** is a denuclearized region where nerve fibers are located.

On the whole, the hypothalamus is an integrative ***center of the vegetative, somatic and endocrine functions*** of the organism.

The ***posterior part*** of the hypothalamus ***regulates heat production***. Stimulation of this part results is intensified metabolism, increased heart rate, appearance of shivering, which altogether leads to increased thermogenesis. If the posterior part of the hypothalamus is damaged, an animal cannot stand low temperature.

The ***anterior part*** of the hypothalamus (paraventricular nucleus) is responsible for ***heat loss***. If to stimulate this region of the hypothalamus, the skin vessels are dilated, sweat release increases. If the anterior part of the hypothalamus is affected, an animal cannot stand hot temperature.

In the region of the middle and lateral nuclei, there are the ***centers of hunger and satiety, thirst, centers regulating sexual behavior, aggression***. These regions of the hypothalamus take part in the ***change of the phases of sleep and wakefulness***, and their damage makes a person fall into lethargic sleep.

The secretory cells of the supraoptic and paraventricular nuclei produce ***vasopressin*** and ***oxytocin***. These hormones come through axons into the neurohypophysis.

The hypothalamus produces ***enkephalins*** and ***endorphins,*** which possess morphine-like action, and thus take part in the regulation of behavior, and also regulate the vegetative functions. The hypothalamus produces a number of other biologically active substances. The activity of the hypothalamus is regulated by the cortex of the cerebrum.

Functions of the hypothalamus:

1) regulation of different physiological functions (activity of the cardiovascular system, respiration system, gastrointestinal tract, metabolism and others);

2) thermoregulation function (performed by the centers of heat production and heat loss);

3) regulation of adenohypophysis function (due to liberins and statins) and production of hormones released by the neurohypophysis (vasopressin and oxytocin);

4) participates in the regulation of different behavioral reactions:

-food behavior (due to the centers of hunger and satiety);

- emotional sexual behavior;

- behavior directed to satisfaction of thirst ;

- regulation of aggressive behavior ;

- regulation of wakefulness (posterior region) and sleep (medial region).

Review questions

1. What structure does the spinal cord have? Name the main functions of the spinal cord. What vegetative and motor reflexes are performed by the spinal cord? What reflexes are called monosynaptic? Name the main clinically important spinal reflexes and their diagnostic value. What are the main conduction pathways of the spinal cord? What is the spinal shock?

2. The nuclei of which cranial nerves are located in the medulla oblongata? Describe their functions. The nuclei of which cranial nerves are located in the pons varolii? Describe their functions. What groups of reflexes responsible for the maintenance of posture are connected with the functions of the afterbrain? Name the vegetative functions regulated by the medulla.

3. Name the main structures of the midbrain. The nuclei of which cranial nerves are located in the midbrain? What reflexes are performed with the participation of the midbrain? Describe the functions of the red nucleus, black substance, blue nucleus. What is the decerebrate rigidity?

4. What are the main structures of the cerebellum? Name and describe the layers of the cerebellar cortex. Signals from which receptors does the cerebellum receive? What are the main functions of the cerebellum? Name disorders which occur in cerebellar deficiency and describe them.

5. What is the reticular formation of the brain stem? What are the main descending influences of the reticular formation on the activity of the spinal cord and the ascending influences on the cortex?

6. Name the basic groups of the thalamus according to its anatomical features and physiological classification. What are the functions of the nonspecific, specific and associative nuclei of the thalamus? Name the basic groups of the hypothalamic nuclei. What are the main vegetative centers of the hypothalamus? Where are they located? What hormones and biological active substances are produced by the hypothalamus?

4.2.7. Limbic system of the brain

The limbic system is a functional set of the brain structures and connections located in the mediobasal part of hemispheres.

The limbic system includes (Figure 4.21):

1. ***The ancient cortex,*** which includes the *rhinencephalon*.

2. ***The old cortex*** including the *hippocampus and cingulate gyrus*.

3. ***The subcortical structures*** (*amygdaloid complex, anterior thalamic nucleus, mamillary bodies*).

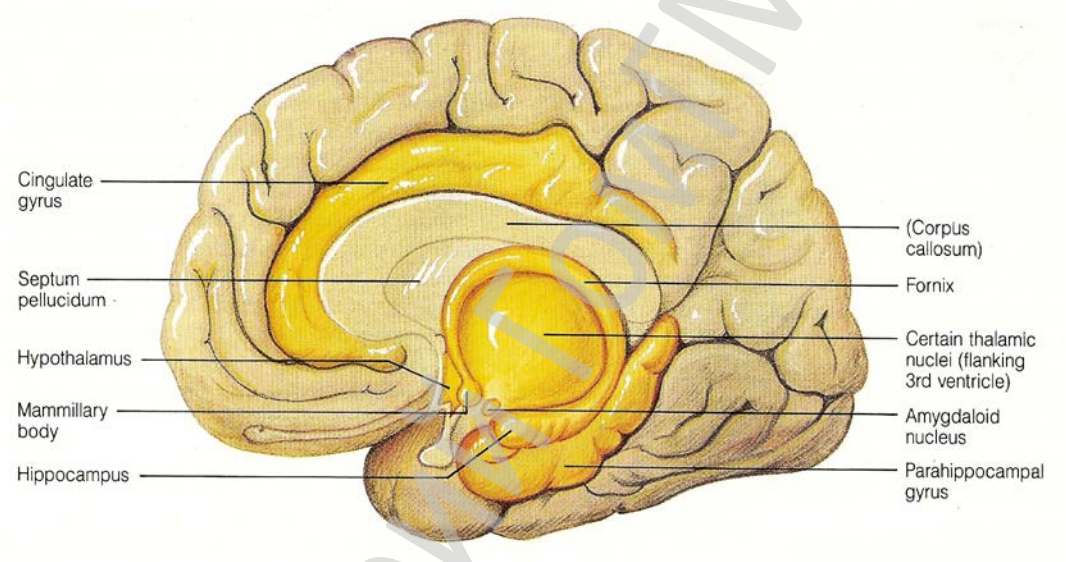


Figure 4.21 — The main structures of the limbic system (from slideplayer.com)

The limbic system is a ring-like structure which surrounds the base of the forebrain and is the border between the neocortex and brain stem. The limbic system is characterized by a set of bilateral connections. These connections inside the system and with other parts of the CNS are very complex and complicate the treatment of the diseases of the limbic system.

The connections between the brain structures organizing circuits having functional specificity are well-known nowadays. For example, the ***Papez circuit*** (*hippocampus — mamillary body — anterior nuclei of the thalamus — cortex of the cingulate gyrus — parahippocampal gyrus — hippocampus*). This circuit is connected with memory and leaning processes. Other circuits regulate defense-aggressive behavior.

The limbic system influences the cortex of the cerebrum and subcortical structures establishing necessary conformity of their activity.

The main functions of the limbic system:

1) it participates in the organization of emotion and motivated behavior (at the states of fear, aggression, hunger, thirst), which can be accompanied by the corresponding motor reactions);

2) it participates in the formation of complex forms of behavior (instincts, alimentary, sexual, defensive behavior);

3) it participates in orientaive reflexes; reactions of attention;

4) it participates in the formation of memory and dynamics of learning (formation of individual behavioral experience);

5) it participates in the regulation of biological rhythms (changes of the phases of wakefulness-sleep cycle);

6) it participates in the regulation of homeostasis by regulating the vegetative functions.

The participation of the limbic system in the ***regulation of vegetative reactions*** (stimulation or inhibition) is well-defined. The limbic system controls the activity of the internal organs through the lower located parts of the CNS (thalamus and hypothalamus). The limbic system changes the excitability of the nerve centers of these structures and aims the vegetative reactions towards a necessary direction.

In animals stimulation of the nuclei of the ***amygdaloid complex,*** located in the main temporal gyrus, results in the *appearance of fear, anger, or aggression depending* on where the impulse gets to. The bilaterial removal of the temporal lobe with the amygdaloid complex and hippocampus affects the emotional sphere and causes psychic blindness, i. e. the inability to evaluate visual and acoustical information correctly. For example, if an animal has got an electric shock, it will continue moving in the same direction though it will be shocked again.

The limbic system is responsible ***for storage of received information*** i. e. memory formation. The removal of the ***hippocampus*** in humans leads to a complete loss of short-term memory. *Stimulation of the* ***hippocampus*** recalls the latest events which a person cannot remember in usual conditions. ***The removal of the hippocampus*** in animals results in affected internal inhibition, i.e. they lose the ability to fade conditioned reflexes which have lost their value for the vital activity of the organism.

The limbic system influences the functioning of the cortex of the cerebrum due to the formation of an emotional background which ***regulates the rate of the formation of conditioned reflexes***.

Thus, the limbic system together with other structures of the brain forms a system coordinating the somatic and vegetative functions of the organism.

4.2.8. Basal ganglia

The forebrain includes the basal ganglia and the cortex of cerebrum.

Basal ganglia (Figure 4.22)

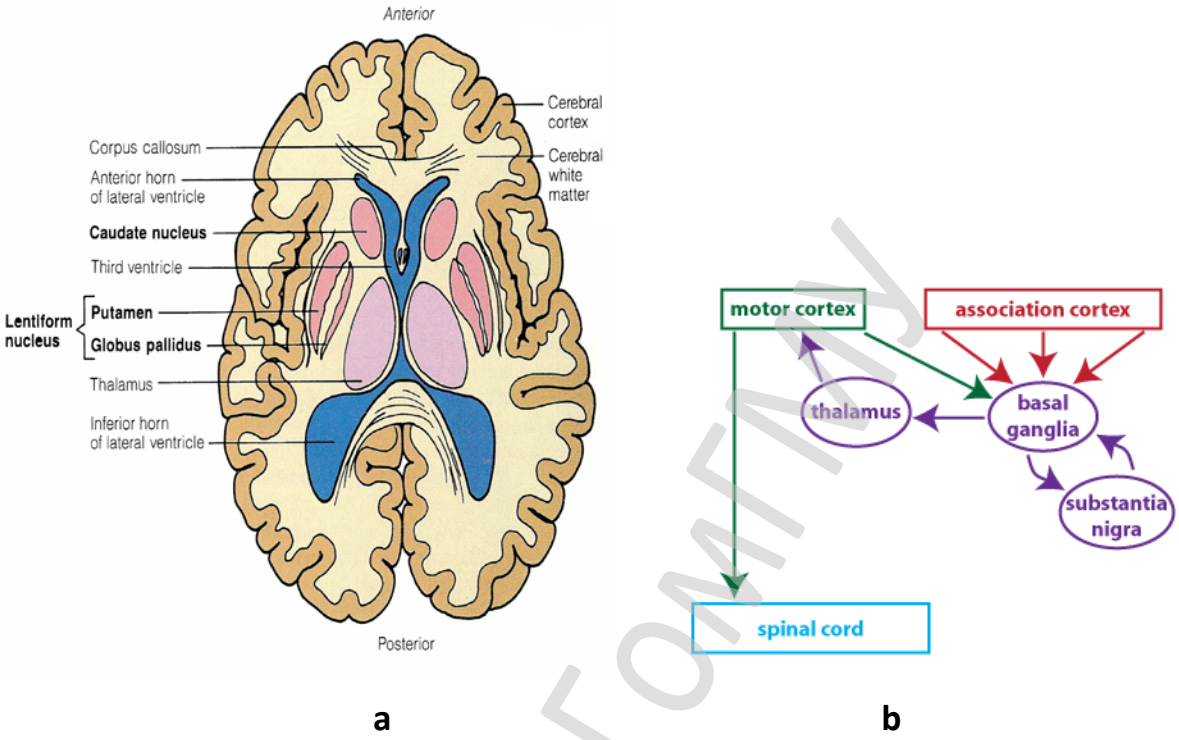


Figure 4.22 — Basal ganglia (from biology.reachingfordreams.com)

Notes: a — the relationship of the basal ganglia to the thalamus and the lateral and third ventricles **(**by Elaine N. Marieb, 1989) ; b – afferent and efferent connections of the basal ganglia.

The basal ganglia are nuclear structures located above the white matter inside the forebrain, mainly in the frontal lobes. They include the ***caudate nucleus, putamen, globus pallidus, and claustrum***. By functions and phylogenesis, it is divided into:

1. ***Paleostriatum*** — more ancient structures (*globus pallidus*).

2. ***Neostriatum*** — consists of the *caudate nucleus and putamen*. These two structures are interconnected anatomically and are called the ***corpus striatum***. The axons of its cells go to the globus pallidus and substantia nigra of the midbrain. The corpus striatum is a collector of afferent entries going to the basal ganglia. Impulses reaching the basal ganglia *come from the sensomotor cortex, the substantia nigra, and nonspecific nuclei of the thalamus*.

The globus pallidus forms efferents from the basal ganglia. Signals from these brain structures go along some efferents *to the diencephalon and red nucleus of the midbrain*. Other efferents go from the globus pallidus to the thalamus, then to the motor cortex of the cerebrum.

The fibers going from the cortex of the cerebrum and thalamus form *excitant synapses* on the neurons of the corpus striatum, and the fibers of the substantia nigra form *inhibiting synapses*.

Functions of the basal ganglia. The basal ganglia take part in ***coordination of motor activity.*** Damage to the corpus striatum results in ***athetosis*** — slow vermiform movements of the wrist and fingers; ***chorea*** — convulsive movements of mimic muscles and extremities.

Damage to the basal ganglia is related with the appearance of ***Parkinson's disease,*** which is accompanied by the following signs:

1. ***Akinesia*** — small motility.
2. Wax rigidity — ***hypertonus***.
3. ***Static tremor***, which is observed in the extremities and head.

These signs are connected with increased activity of the basal ganglia output nuclei which appears as a result of the damage of a dopaminergic pathway, i. e. the inhibiting influence from the substantia nigra of the midbrain disappears.

Also, the basal ganglia take part in ***the development of a program of targeted movements***, i.e. they receive information from the cortex of the cerebrum and send it to the forebrain, where it is integrated with information from the cerebellum. After that the information comes to the motor region of the cortex of cerebrum thus resulting in realization of the motor program through the influences on the spinal cord.

4.2.9. Physiology of the cerebral cortex

4.2.9.1. Morpho-functional characteristics of the cerebral cortex

The cerebral cortex is the most recent structure regarding its evolutionary development. The cortex is 1.3–4.5 mm thick. It contains 10–18 billion nervous cells. The area of the cortex surface is 2,200 cm^2. The basic cells of the cortex are *pyramidal, stellate, and fusiform*. All the cells of the cortex contain information and if they are not overloaded with it, they die.

As per the phylogenetic development, the cortex consists of:

1. ***The archicortex,*** which consists of the *rhinencephalon*.
2. ***The paleocortex,*** which consists of the *cingular gyrus, hippocampus, amygdaloid body*.
3. ***The neocortex,*** which has typical 6-layer structure (1^{st} layer — molecular, 2^{nd} layer — external granular, 3^{rd} — external pyramidal, 4^{rd} layer — internal granular, 5^{th} layer — internal pyramidal, 6^{th} layer — polymorphic).

The main efferents from the neocortex start from the cells of the 5^{th} layer (pyramidal cells) and stretch outside the cortex forming the pyramidal tract.

The main afferents come to the cortex along the fibers of the thalamocortical tract.

The cerebral cortex is characterized by numerous interneuronic contacts whose amount intensively increases till the age of 18. The final development of the cortex ends by 22–23.

By the location, density, and form of neurons, Brodman divided the cortex into 53 cytoarchitectonic fields.

The functional unit of the cortex is the ***vertical column,*** which performs a certain function. It consists of large pyramidal cells with above-and under-located neurons which organize functional unification. All the neurons of the column respond to the stimulation of the same receptor with identical reactions and together create the efferent response. Signal conduction from one column to the next one is limited by lateral inhibition. For example, each column of the somatosensory cortex innervates only one spinal motoneuron. Under the activation of the column this motoneuron is excited and induces contractions of muscles connected with this motoneuron.

4.2.9.2. Main regions of the cortex. Communication of the peripheral formations with the cortex

It has been revealed that removal of certain fields of the cortex results in termination of some functions, whereas stimulation of the cortex with electric shock results in their appearance. Thus, each region of the cortex is responsible for the performance of a definite function. Regarding this, the cortex has several regions (Figure 4.23):

1. ***Sensory regions.*** Specific afferent impulses come here from periphery receptors.

2. ***Motor regions.*** Once stimulated, various movements appear.

3. ***Associative regions***. They receive information from various receptor areas of the cortex.

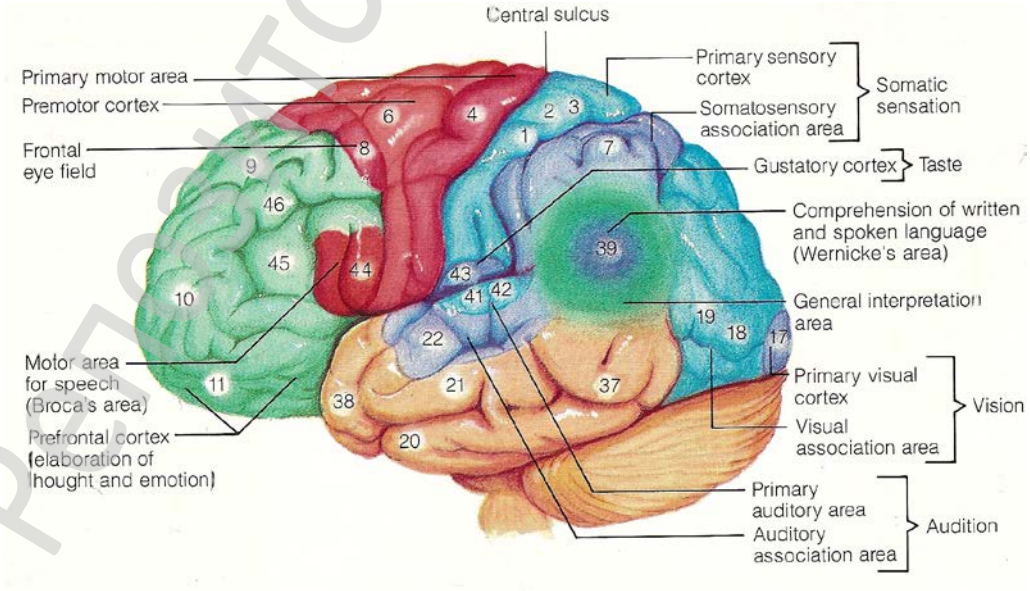


Figure 4.23 — Functional areas of the left cerebral cortex.
The numbers indicate the regions plotted by the Brodman system
(by Elaine N. Marieb, 1989)

The cortex has regions with less definite functions. A significant part of the frontal lobes, especially on the right, can be removed without visible disorders. However, removal of both the frontal lobes causes serious mental disorders.

The presence of structurally various areas in the cortex assumes their different functional value.

Sensory regions. Each hemisphere has two sensory regions:

1. ***Somatic*** (dermal, muscular, joint sensitivity).
2. ***Visceral*** (impulses from the internal organs come here).

The somatic region is located in the area of the ***postcentral gyrus***. Information from the skin and organs of the locomotor system comes here from the specific nuclei of the thalamus. The dermal receptor system is projected to the posterior central gyrus. The receptive fields of the skin of the lower extremities are projected to the superior parts of this gyrus, receptive fields of the body — to the medium parts, and those of the hand and head — to the lower fields. Removal of certain fields of this region results in a loss of sensitivity of the corresponding organ. The area of the somatic cortex which is responsible for the work of the finger muscles, facial mimic muscles, vocal apparatus occupy the larger part than that responsible for the work of the muscles of the hips, legs, and trunk since they have less receptors.

The second somatosensory region is localized in the ***zone of the sylvian sulcus***. In this region integration and critical assessment of information from the specific nuclei of the thalamus take place. For example, the visual area is localized in the occipital lobe within the area of the calcarine sulcus. The acoustic system is projected to the transverse temporal gyruses (Heschl's gyrus).

The cortex contains the ***projective regions of analyzers***. By the structure and functional value, they are divided into 3 basic groups of areas:

1. ***Primary areas*** (nuclear regions of analyzers).
2. ***Secondary areas***.
3. ***Tertiary areas***.

The primary *areas* are connected with the organs of sense and motions. They develop first. Pavlov called them the nuclear regions of analyzers. They perform the initial analysis of separate signals which come to the cortex. If the primary areas to which information comes from the organs of vision or audition are affected, there comes cortical blindness or deafness.

The secondary areas are the peripheral regions of the analyzers. They are localized near the primary areas and connected with the sense organs through the primary areas. In these areas generalization and further processing of information take place. If the secondary areas are affected, a person can see, hear, but is not able to understand the meaning of signals.

The tertiary areas are the regions where analyzers are overlapped. They are located on the borders of the parietal, temporal, and occipital regions and also in the region of the frontal lobes. In the process of ontogenesis they develop after the primary and secondary areas. The development of the tertiary areas is connected with speech. These areas ensure balanced work of both the cerebral hemispheres. Here, ***the highest analysis and synthesis of information, task and problem solution take place.*** The tertiary areas have major communications.

The primary visual area is located in the calcarine fissure area in the occipital cortex. This area is the terminus of direct visual signals from the eyes (from the lateral geniculated bodies of the thalamus).

The auditory area is located mainly in the superior gyrus of the temporal lobe (within the lateral fissure). The primary auditory cortex is directly excited by projections from the medial geniculate body of the thalamus.

The motor area of the cortex is located in the ***anterior central gyrus***. The pyramidal tract originates here. Damage to this area of the cortex results in imbalanced voluntary movements. Through the associative pathways the motor area is connected with other sensory zones of the opposite hemisphere.

All the sensory and motor areas occupy less than 20 % of the cortex surface. The rest of the cortex organizes the **associative area**. Each associative area of the cortex is connected with several projective regions. The associative area of the cortex includes some part of the parietal, frontal and temporal lobes. The borders of the associative area are not clear. Its neurons participate in integration of diverse information. The highest analysis and synthesis of stimuli take place here thus resulting in the formation of complex elements of consciousness. The parietal part of the cortex participates in the assessment of the biological value of information and space perception.

The frontal lobes (fields 9–14) along with the limbic system control motivated behavior and program behavior. Damage to the frontal lobes results in short-term memory impairment.

Speech centers of the cortex

Speech and language functions are connected with both the motor and sensory areas. The functions of the sensory and motor speech areas are usually much more highly developed in one cerebral hemisphere than in the other. In 95 % people the centers of speech are located in the left hemisphere of the brain.

Broca's area (the motor center of spoken speech) is located in the posterior part of the inferior frontal gyrus and controls the motor functions involved in speech production and language comprehension. Damage to Broca's area causes motor aphasia. In this type of aphasia a person may understand speech and know what they want to say but cannot make the vocal system emit words.

Wernicke's area (the sensory center of speech) is located in the posterior superior temporal gyrus. It provides auditory comprehension of speech. Damage to Wernicke's area causes sensory aphasia. In this type of aphasia a person has difficulty understanding language and is unable to arrange words into a coherent thought.

The angular gyrus is associated with the processing of visually perceived words (reading).

4.2.9.3. Electrical activity of the cortex of the cerebrum

Changes in the functional state of the cortex influence its biological potentials. Spontaneous electrical fluctuations which have certain periodicity are called ***electroencephalography (EEG).***

In 1924, Berger succeeded in recording the first human electroencephalogram. An electrode which registers the total activity of the cortex and subcortical structures is applied to certain points of the skin surface in the frontal, parietal, occipital fields. EEG is widely used in clinical practice, as it allows to determine the state of the cortex, ***to obtain information about the depth of narcosis and localization of a pathological process***.

There are following EEG rhythms (Figure 4.24):

Alpha-rhythm — frequency of 8–13 Hz, voltage — 50 mV. This rhythm is registered at rest and is fully present only when a person is mentally inactive, with eyes closed.

Beta-rhythm — frequency of 14–30 Hz, voltage — 25 mV. This rhythm is observed in a person upon sensory stimulation, especially with light, or when they are engaged in purposeful mental activity and indicates desynchronization of the cortex.

Figure 4.24 — The EEG rhythms (by Korobkov A. V., Chesnokova S. A., 1986)

Theta-rhythm — frequency of 4–7 Hz, voltage — 100–300 mV. It is observed during various states of light sleep or arousal.

Delta-rhythm — frequency of 3–5 Hz, voltage — 100–300 mV. It is registered during deep sleep, loss of consciousness, narcosis. In people who do not sleep the delta-rhythm is not registered, however it is typical for the hippocampus even in an active state.

EEG does not evaluate human mental capabilities.

4.2.9.4. Functional asymmetry of the cortex

The functional asymmetry of the cortex or cerebral asymmetry refers to anatomical, physiological, or behavioral differences between the two cerebral hemispheres.

There are 3 kinds of asymmetry:

1. ***Motor*** — unequal motor activity of the muscles of the right and the left halves of the body. For example, in people who tend to do everything with their left hand, the functional activity of the right hemisphere of the cortex dominates, and vice versa.

2. ***Sensory*** — unequal perception of information by the right and the left hemispheres of the cortex.

3. ***Mental***. People with the *dominant left hemisphere* are logical, analytical in nature and more academically inclined, purposeful and capable to make predictions.

People with the *dominant right hemisphere prefer* certain kinds of activity, are slow, intuitive, thoughtful, sentimental.

Recently, the concept of the mutual influence of both the hemispheres of the cortex has been accepted. It means that domination of either hemisphere can be expressed only in one kind of activity.

4.3. Autonomic (vegetative) nervous system

4.3.1. Morpho-functional characteristics of the vegetative nervous system

By the functional value, the nervous system is divided into:

Somatic —performs the motor and sensory functions.

Vegetative — regulates the activity of the internal organs and supply trophicity of skeletal muscles, skin, bone and adipous tissue.

The autonomic (vegetative) nervous system (ANS) has 4 differences from the somatic system:

1. *Focal outlet of fibers* from the head and spinal cord.

2. *Absence of segmental distribution of fibers* on the periphery.

3. *Small diameter of fibers*.

4. ***Two-neuron principle*** of the structure of the efferent part of the reflex arc (Figure 4.25), i. e. preganglionic fiber forming the axon starts from the body of the ***first efferent neuron (preganglionic neuron)*** located in the CNS.

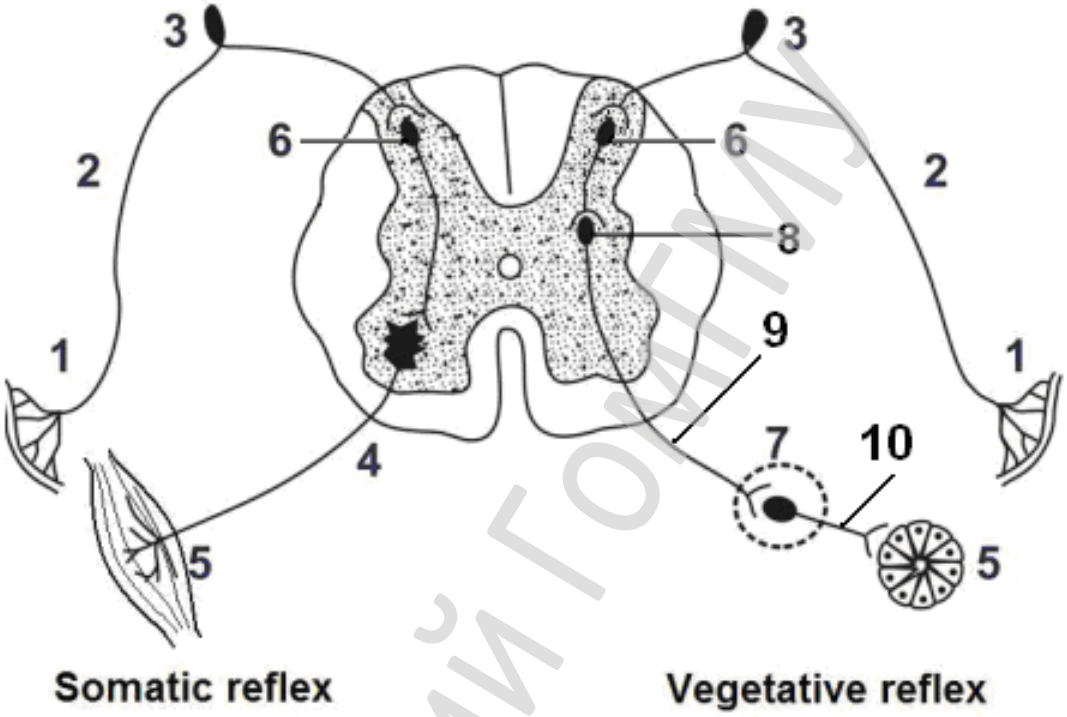


Figure 4.25 — Reflex arch

Notes: 1 — receptor; 2 — afferent fiber; 3 — sensory neuron; 4 — motor neuron; 5 — working organ (muscle, gland); 6 — interneuron; 7 — vegetative ganglia; 8 — preganglionic neuron; 9 — preganglionic fiber; 10 — postganglionic fiber

In the ***vegetative ganglia,*** excitation from this neuron is conducted to the ***second efferent neuron***, from which the postganglionic fiber goes to the executing organ. However, there exist one- and three-neuron pathways. For example, the chromophilic cells of the adrenal medulla are innervated by one preganglionic fiber, and in the gastrointestinal tract the postganglionic fiber ends on the parasympathetic ganglia of the walls of the organs.

The vegetative ganglia do not only conduct signals. These are peripherally located reflex centers capable to regulate the functions of the internal organs independently, i. e. without participation of the CNS.

As per the structurally-functional properties, the ANS can be divided into: ***sympathetic (SNS)***, ***parasympathetic (PSNS),*** and ***metasympathetic*** *(located in the microganglia of the internal organs: heart, gastrointestinal tract, etc.).*

The division of the ANS into the sympathetic and parasympathetic parts is based upon the following principles (Tabe 4.4).

Table 4.4 — Differences of the sympathetic and parasympathetic parts of the ANS

Principle of difference	Sympathetic part	Parasympathetic part
The localization of the nerve centers in the brain	Thoracal-lumbar segments of the spinal cord	Midbrain, medulla, sacral segments of the spinal cord
Location of the vegetative ganglia	Vertebral and prevertebral ganglia	Intramural plexuses
The secreted mediator	The main mediator is noradrenalin	The main mediator is acetylcholine
Influence on the functions of the organs	Ensures the power supply of an organism (influences the redistribution of the blood flow, increases the heart rate, increases metabolism, increases the blood glucose level)	Corrects changes in the organism induced by the sympathetic nervous system (restores and maintains homeostasis)

1. ***The localization of the nerve centers*** in the brain. The centers of the ***PSNS*** are localized ***in the midbrain and medulla***, and also in the ***sacral segments of the spinal cord***. The centers of the ***SNS*** are localized in ***the thoracal-lumbar segments of the spinal cord.***

2. ***Influence on the functions of the organs***. The sympathetic and parasympathetic parts of the ANS more often act as functional antagonists.

3. ***The location of the ganglia*** in which nerve pathways terminate.

4. ***The secreted mediator.***

All the parts of the ANS are controlled by the superior subcortical center of the regulation of the vegetative functions, – ***hypothalamus***. The hypothalamus is controlled by the cortex.

The efferent fibers of the ***SNS*** are accumulated in the ganglia connected to one another and forming the symmetric **paravertebral chain** (Figure 4.26).

That is why the SNS acts as a whole, its stimulation goes simultaneously with changes of the functions of various organs. The neurons of the PSNS are localized in several parts of the CNS and are not connected with one another, therefore they influence the organs selectively (Figure 4.27).

Sympathetic nerve fibers are major in the human body and innervate almost all the organs. Some organs ***have only sympathetic innervation*** (*adrenals, skeletal muscles, organs of sense, CNS*), other organs have double innervation (heart, intestinal and salivary glands). If an organ is innervated only by one part of the ANS, the regulation of its functions is ensured by weakening or intensifying of the activity of this part of the ANS. In double innervation nerves provide the inverse effect and in norm these influences are balanced.

On the whole, the SNS ensures power supply to the organism. It influences the *blood flow distribution, metabolism intensification, increase of the blood glucose level,* which is necessary for adaptation of the organism to certain conditions (work, emotions, temperature or environmental fluctuations, etc.).

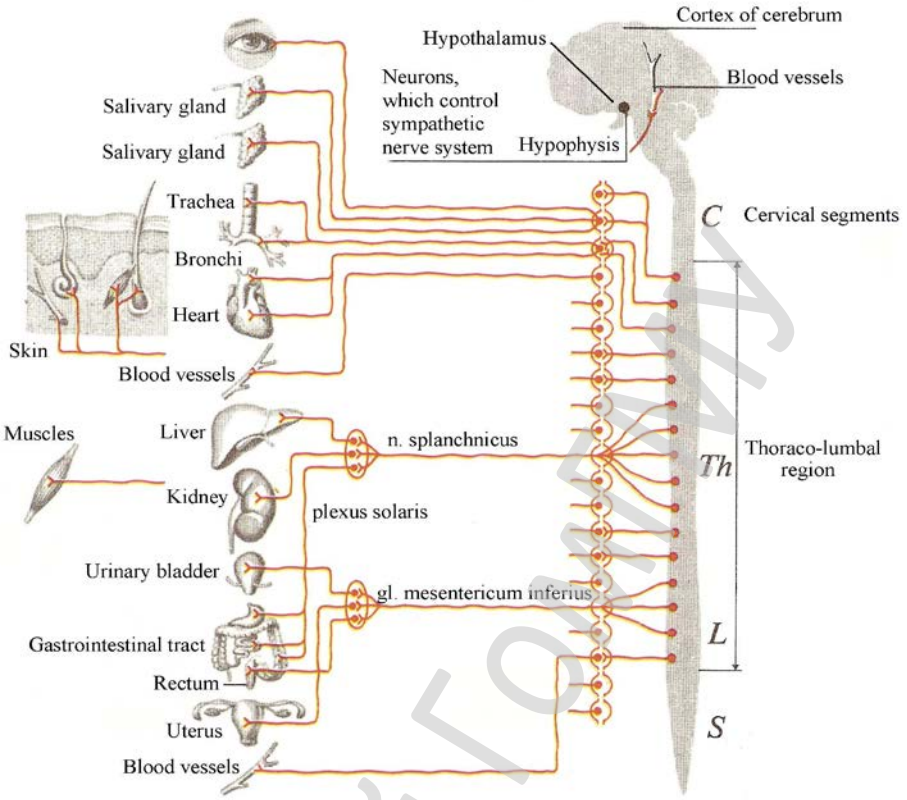


Figure 4.26 — General structure of the sympathetic nervous system (by Korobkov A. V., Chesnokova S. A., 1986)

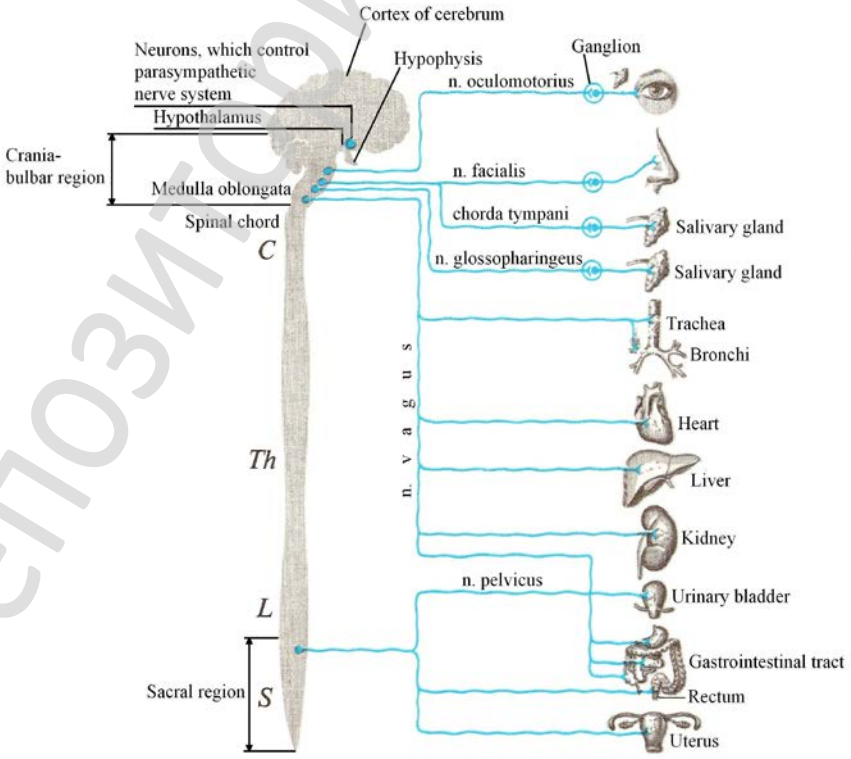


Figure 4.27 — General structure of the parasympathetic nervous system (by Korobkov A. V., Chesnokova S. A., 1986)

The PSNS constantly *corrects changes occurring in the organism induced by the SNS*, i. e. restores and maintains homeostasis (Figure 4.28).

Figure 4.28 — Changes of the functions of different organs in increased activity of the sympathetic and parasympathetic nerves (from biology.reachingfordreams.com)

Notes: 1 — vessels of the brain; 2 — periphery vessels; 3 — hair muscles; 4 — suprarenal gland; 5 — urinary blander; 7 — intestines; 8 — stomach; 9 — heart; 10 — bronchi; 11 — salivary glands; 12 — pupil

Orbeli and Genetsynsky performed an experience on the frog's gastrocnemius muscle and defined that if was stimulated for a long time, the muscle got tired. After that the tired muscle was innervated with sympathetic fiber. It resulted in increased metabolism in the skeletal muscle and reduced restoration period after tiredness. This phenomenon was called the adaptive-trophic influence of the SNS on skeletal muscles (***Orbeli-Genethsynsky's phenomenon***).

4.3.2. Classification of the vegetative ganglia

By their localization, the vegetative ganglia are divided into 3 groups:

1. ***Vertebral (paravertebral) ganglia***, related to the ***SNS*** and stretched like two marginal tubes along the *spinal column* and connected with the spinal cord

with white copulative branches (preganglionic fibers). Postganglionic fibers go to the organs either independently or within somatic nerves. The majority of sympathetic fibers terminate in the vertebral ganglia.

2. ***Prevertebral ganglia*** (*solar plexus, superior and inferior mesenteric ganglia*). They are located anterior to the vertebral column and innervate organs. Other ***sympathetic nerve fibers*** terminate in these ganglia.

3. ***Intramural plexuses***. They are localized in the internal organs or close to them. Only ***parasympathetic fibers*** terminate in these ganglia.

Metasympathetic department of the ANS

The metasympathetic department of the ANS is a complex of microganglionic structures forming nervous plexuses and located in the walls of the internal organs (for example in the stomach, intestines, urinary bladder, heart, bronchi). Thus, the metasympathetic department of the intestines includes intermuscular (Auerbah's) and submucous (Meissner's) plexuses, which consist of a set of the microganglia and accept impulses from the sympathetic and parasympathetic departments of the ANS and also from their own afferent neurons, which are situated in the microganglia, transfer information from the sensory receptors of the intestinal walls.

The postganglionic fibers of the efferent neurons of the metasympathetic system go to the myocytes and glandular cells of the intestines and control their activity. The influences of the sympathetic and parasympathetic departments have the modulating role. A loss of impulsion from these departments (for example during transplantation of the intestines) does not reduce the activity of the neurons in the replaced plexuses. This activity provides self-control of the functions of the intestines.

The metasympathetic department of the ANS possesses greater independence from the CNS in comparison with other departments of the ANS.

Besides cholinergic and adrenergic neurons in the metasympathetic department of the ANS, there are non-cholinergic and non-adrenergic neurons. As mediators there can be peptides (cholecystokinin, somatostatin), biogenic amines (serotonin, histamine, melatonin), purines (ATP), etc. Some motor neurons can contain up to five various mediators, which is, probably, necessary for better regulation of the work of effector cells (for example, regulation of intestinal motility).

<u>The basic functions of the metasympathetic department of the ANS:</u>

1. It participates in the maintenance of homeostasis.

2. It carries out the role of the peripheral nerve centers and provides constant and continuous control over the work of the internal organs.

3. It participates in the process of information transfer from the sensory receptors of the internal organs to the CNS.

The interaction of the departments of the ANS in the regulation of the vegetative functions. It is realized at two levels: peripheral and central.

The interaction at the peripheral level takes place on effector cells, which receive double (or even triple) vegetative innervation. The basis of this interaction is the antagonistic influence of the parasympathetic and sympathetic departments of the ANS on innervated cells. Thus, stimulation of sympathetic nerves causes strengthening of heart activity, inhibition of intestinal peristalsis, and stimulation of the parasympathetic fibers of the vagus nerve — suppression of the work of the heart, stimulation of intestinal motility. The antagonistic effects of the interaction take place at other levels as well. Excitation transfer in the sympathetic ganglia is inhibited by parasympathetic influences, and in the parasympathetic ganglia — by sympathetic.

The interaction of various departments of the ANS at the central level has a complex, cooperative and intercontrolling character. The functions of the preganglionic neurons of the ANS are controlled by the higher vegetative oversegmental centers located in various departments of the brain: *1) brain stem: vasomotor center, blue substance, the centre of vomiting; 2) cerebellum; 3) diencephalons: hypothalamus, thalamus; 4) telencephalon: basal ganglia, cortex of the cerebrum.*

The oversegmental formations integrate the human body functions and provide the expedient processes of adaptive activity. The oversegmental mechanisms regulating the vegetative functions have three important features:

1) there are no specific vegetative neurons;

2) damage *to the oversegmental centers* can be revealed not only in vegetative disorders, but also in somatic (mental and/or motor) dysfunctions;

3) the oversegmental centers use all the departments of the ANS for organization of adaptive interaction of the work of various departments of the ANS, which is performed by the hypothalamus.

Conduction of excitation in the synapses of the ANS

The preganglionic fibers of the ANS are group B nerve fibers (thin myelinated fibers, the rate of excitation conduction is 3–18 m/sec). The mediator in the presynaptic terminals of all the preganglionic fibers (both sympathetic and parasympathetic) is ***acetylcholine*** (Figure 4.29). On the postsynaptic membranes of all the ganglia synapses **nicotinic cholinoreceptors** are located (they are activated by nicotin, and can be blocked by curare).

Postganglionic fibers are group C fibers (unmyelinated, the rate of excitation conduction is 1–3 m/sec). The mediator released by the terminations of the parasympathetic nerves is acetylcholine, and in sympathetic fibers — noradrenaline (except for sympathetic fibers which innervate the sweat glands, and also fibers which provide dilatation of the vessels of skeletal muscles, as in these fibers the mediator is acetylcholine).

In the postsynaptic membranes innervated by postganglionic parasympathetic fibers, **muscarinic cholinoreceptors** are located (they are activated by muscarin, and can be blocked by atropine). In the postsynaptic membranes innervated by postganglionic symphathetic fibers the **adrenergic receptors** are located (α, β).

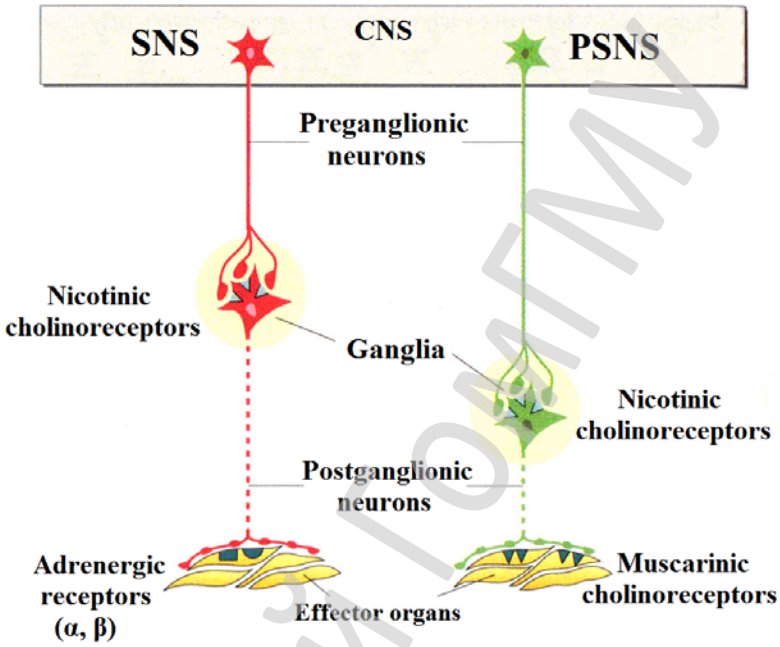


Figure 4.29 – Excitation conduction in the synapses of the ANS (from studylib.net)

There are also two major types of the adrenergic receptors: alpha receptors and beta receptors. The beta receptors in their turn are divided into beta 1, beta 2, and beta 3 receptors, because certain chemicals affect only certain beta receptors. Also, there is the division of the alpha receptors into alpha 1 and alpha 2 receptors. Table 4.5 gives the distribution of the alpha and beta receptors in some organs.

Table 4.5 — Adrenergic receptors and their functions

Alpha Receptor	Beta Receptor
Vasoconstriction	Vasodilation (β2)
Iris dilation	Cardiac acceleration (β1)
Intestinal relaxation	Increased myocardial strength (β1)
Intestinal sphincter contraction	Intestinal relaxation (β2) Uterus relaxation (β2)
Pilomotor contraction	Bronchodilation (β2)
Bladder sphincter contraction	Calorigenesis (β2)
Inhibits neurotransmitter release (α2)	Glycogenolysis (β2) Lipolysis (β1) Bladder wall relaxation (β2) Thermogenesis (β3)

When the mediator (acetylcholine or noradrenalin) binds with the receptor on the membrane of the effector cell, this causes a conformational change in the structure of the protein molecule of the receptor. In turn, the altered protein molecule excites or inhibits the cell, most often by two mechanisms:

1) causing a change in the cell membrane permeability to one or more ions;

For example, the sodium and/or calcium ion channels open and allow influx of these ions into the cell, usually depolarizing the cell membrane and exciting the cell. If the potassium channels are opened, allowing potassium ions to diffuse out of the cell, this usually inhibits the cell.

2) activating or inactivating an enzyme attached to the other end of the receptor protein, which protrudes into the cell.

For example, the binding of noradrenaline with its receptor on the outside of the cell increases the activity of the enzyme adenylylatcyclase on the inside of the cell, and this causes the formation of cyclic adenosine monophosphate (cAMP). The cAMP can initiate any of many different intracellular actions, the exact effect depending on the function of the effector cell.

The effects on different visceral functions of the body caused by stimulating either the parasympathetic nerves or the sympathetic nerves are listed in table 4.6.

Table 4.6 — Autonomic effects on various organs (by Arthur C. Guyton)

Organ	Effect of sympathetic stimulation	Effect of parasympathetic stimulation
Pupil of the eye Ciliary muscle of the eye	Dilated Slight relaxation (far vision)	Constricted Constricted (near vision)
Glands: Nasal Lacrimal Salivary Gastric Pancreatic	Vasoconstriction and slight secretion	Stimulation of copious secretion
Sweat glands	Copious sweating (cholinergic)	Sweating on palms of hands
Blood vessels	Most often constricted	Most often little or no effect
Heart muscle	Increased rate Increased force of contraction	Slowed rate Decreased force of contraction
Coronary arteries	Dilated (β2); constricted (α)	Dilated
Intestine lumen Intestine sphincter	Decreased peristalsis and tone Increased tone (most times)	Increased peristalsis and tone Relaxed (most times)
Liver	Glucose released	Slight glycogen synthesis
Gallbladder and bile ducts	Relaxed	Contracted
Kidney	Decreased urine output and increased renin secretion	None

Organ	Effect of sympathetic stimulation	Effect of parasympathetic stimulation
Bladder detrusor Bladder trigone	Relaxed (slight) Contracted	Contracted Relaxed
Abdominal visceral arterioles	Constricted	None
Muscle arterioles	Constricted (adrenergic α) Dilated (adrenergic β2) Dilated (cholinergic)	None
Skin arterioles	Constricted	None
Blood coagulation	Increased	None
Blood glucose level	Increased	None
Basal metabolism	Increased up to 100 %	None
Adrenal medullary secretion	Increased	None
Piloerector muscles	Contracted	None
Fat cells	Lipolysis	None

4.3.3. Vegetative reflexes

The vegetative reflexes are divided into:

1. ***The viscerovisceral reflex,*** which includes the ways in which excitation appears and ends in the internal organs. For example, an increase or decrease of the pressure in the aorta results in altered heart activity and tone of the blood vessels.

The axon-reflex is a variant of the viscerovisceral reflex. The axon-reflex appears if nerve fiber (axon) generates branching and therefore innervates one organ with one branch, and another organ or part of an organ with another branch. As a result, stimulation from one branch can be transferred to others thus changing the activity in several organs. The axon-reflex illustrates the mechanism of vascular reactions (vasoconstriction or vasodilatation) under stimulation of dermal pain receptors.

2. ***The viscerodermal reflex*** appears under stimulation of the internal organs and manifests itself as changes of sweating, tone of the dermal vessels, increased tactile and pain sensitivity of certain regions of the skin. This pain is called reflected, and the areas of its manifestation — ***Zakharin-Ged's zones***. For example, heart pain irradiates into the left hand, because stimulation from the affected internal organ coming to a certain segment of the spinal cord for a long time results in changes of the neural properties of this segment. Sensory nerves from the skin and muscles come to these segments thus changing the sensitivity of the skin in the regions of its innervation by the given segment.

3. ***Dermovisceral.*** Stimulation of some regions of the body surface induces vascular reactions and change the functioning of the internal organs. This determines prescription of reflexotherapy (heating, massage, acupuncture, etc.) to the patient.

For the assessment of the state and reactivity of the ANS, different methods are applied in medical practice:

1. Oculocardiac reflex.
2. Respiratory arrhythmia.
3. Orthostatic test, etc.

4.3.4. Levels of the regulation of the vegetative functions

The system regulating the vegetative functions includes several levels which interact among themselves. The influence of the superior levels on the inferior ones is also observed here.

Spinal level

There is the ***spinal ciliary center*** at the level of the last *cervical and two superior thoracal segments* of the spinal cord. Its fibers end at the eye muscles. Stimulation of these neurons results in *mydriasis, which is dilation or widening of the pupil, widening of palpebral fissure and abnormal protrusion of the eyeball (exophthalmia)*. Damage to this segment reveals in *Gornar's symptom — constriction of the pupil (miosis), constriction of palpebral fissure and retraction of the eye (endophthalmia)*.

Five superior segments of the thoracic segments of the spinal cord (***SNS***) send their signals to the heart, bronchi. Damage to separate segments of the thoracic and superior lumbar segments leads to *disappearance of the tone of the blood vessels, sweating*.

The PSNS centers are localized in the ***sacral segments*** of the spinal cord. The reflexes of the *urogenital system, defecation* are regulated with the participation of these segments. Transection of the spinal cord above the sacral segments can terminate these functions.

The medulla and midbrain also have the ***PSNS*** centers. The medulla has the *vasculomotor center,* which coordinates the activity of the sympathetic nerves located in the thoracolumbar segments of the spinal cord. Also the medulla has centers *inhibiting cardiac work and activation of the gastrointestinal glands*.

The midbrain has the centers of the *pupillary light reflex and eye accommodation reflex*.

These parts of the brain are controlled by the superior structures.

The hypothalamus is the ***highest subcortical center regulating all the vegetative functions***. Its *anterior* part activates the activity of the *PSNS*, *posterior* — *SNS.* The hypothalamus regulates the activity of the endocrine glands thus controlling all the vegetative functions.

The reticular formation, cerebellum, basal ganglia participate in the regulation of the vegetative functions.

The highest level of the regulation of the ANS activity is the **cortex (frontal lobes)**. The cortex influences the ANS *through the hypothalamus*. The participation of the cortex in the regulation of the activity of the internal organs is proved by the method of conditioned reflexes (for example, salivary secretion in response to inadequate signals (light, sound). Similar effects can arise if influenced by the hypnosis. For example, a person drinks a glass of water and if it is suggested to them that he has drunk a bucket of water, the person will have intensified uropoiesis.

These examples prove the possibility of voluntary control over the vegetative functions after special trainings (Indian yogis).

Thus, the nervous mechanisms of the regulation of the vegetative functions represent a multileveled structure in which the inferior regions are controlled by the superior ones.

Review questions

1. Name the main structures of the limbic system. What are the main functions of the limbic system? Describe the functions of the amygdaloid complex and hippocampus.

2. Name the basal ganglia. How are they divided by functions and phylogenesis? What are the main functions of the basal ganglia? What are the main symptoms of Parkinson's disease?

3. Name the main structures of the cortex of the cerebrum. What are the layers of the neocortex? What is the functional unit of the cortex?

4. Name the main areas of the cortex and explain their functions. What are the speech centers of the cortex?

5. What is electroencephalography? What are the main EEG rhythms? When are they registered?

6. What is the functional asymmetry of the cortex? Name the three kinds of the asymmetry.

7.What are the differences of the autonomic nervous system from the somatic nervous system? What are the main components of the vegetative reflex arch? What are the differences of the sympathetic part of the ANS from the parasympathetic one? Name the main types of receptors providing excitation conduction in the synapses of the ANS and their localization.

8. Name the groups of the vegetative ganglia. Where they are located?

9. Name the groups of the vegetative reflexes. What is the axon-reflex? What are Zakharin-Geds's zones?

10. What are the main levels of the regulation of the vegetative functions? What are the main effects of the SNS and PSNS on various organs?

Multiple Choice Questions
PARTICULAR PHYSIOLOGY
OF THE CENTRAL NERVOUS SYSTEM

1. Which spinal roots are damaged in an animal if it has all kinds of sensitivity on both the sides of the body and no motor reactions on the right side?

Variants of answer:

a) the ventral root of the spinal nerve on the right side;
b) the dorsal root of the spinal nerve from the left side;
c) the dorsal root of the spinal nerve on the right side;
d) the dorsal root of the spinal nerve on the right and left sides;
e) the ventral root of the spinal nerve on the right and left sides.

2. The reflex arches of …reflexes are not located in the spinal cord.

Variants of answer:

a) elbow;
b) intestines;
c) conditioned;
d) urination;
e) knee.

3. Which departments of the CNS are linked to posture maintenance, mastication, swallowing, secretion of the digestive glands, respiration, heart activity, regulation of the tone of the blood vessels?

Variants of answer:

a) the mesencephalon;
b) the thalamus;
c) the afterbrain;
d) the spinal cord;
e) the cerebellum.

4. Why is normal functioning of the medulla vitally important?

Variants of answer:

a) because the centers of tonic reflexes are located there;
b) because the centers of respiratory and cardiovascular reflexes are located there;
c) because the centers of salivation and swallowing are located there;
d) because the centers of vomiting are located there;
e) because the centers of sneezing and coughing are located there.

5. How are the reflexes providing balance called if there are any changes in speed and movement directions?

Variants of answer:

a) static;

b) statokinetic;

c) vegetative;

d) food;

e) defensive.

6. Orienting visual and auditory reflexes are regulated by…

Variants of answer:

a) the afterbrain;

b) the thalamus;

c) the mesencephalon;

d) the cerebellum;

e) the spinal cord.

7. The basic function of the quadrigeminal plate of the midbrain is…

Variants of answer:

a) to regulate homeostasis of all the vegetative functions;

b) to realize the orientation reactions on acoustical and visual stimuli;

c) to regulate muscle tone;

d) to participate in the mechanisms of memory;

d) all the answers are correct.

8. The basic function of the black substance of the midbrain is…

Variants of answer:

a) to participate in the complex coordination of movements and regulation of muscle tone;

b) to participate in the mechanisms of memory;

c) to regulate biorhythms;

d) to act as the center of pain sensitivity;

d) all the answers are correct.

9. What develops in animals after transection of the brainstem below the level of the red nucleus and how this influences the tone of extensor muscles?

Variants of answer:

a) decerebrate rigidity develops, and the tone sharply rises;

b) muscle atrophy develops, and the tone sharply rises.

c) denervation develops;

d) muscle hypertrophy develops, and the tone sharply reduces;

e) ataxia develops, and the tone is disturbed.

10. The nuclei of which cranial nerves are located in the midbrain?

Variants of answer:

a) III and IV;

b) V—VIII;

c) IX—XII;

d) V—XII;

e) the midbrain contains no nuclei of cranial nerves.

11. Damages of the cerebellum do not result in …

Variants of answer:

a) disorders of movement coordination;

b) loss of consciousness;

c) changes of muscle tone;

d) vegetative disturbances;

e) all the answers are correct.

12. Damages of which department of the CNS do not cause ataxy, atony, astasia, adiadochokinesia, asynergia?

Variants of answer:

a) the thalamus;

b) the spinal cord;

c) the afterbrain;

d) the cerebellum;

e) the hypothalamus.

13. Which part of the CNS has an activation influence on the cerebral cortex?

Variants of answer:

a) the hypothalamus;

b) the reticular formation;

c) the subcortical nucleus.

d) the thalamus;

e) all the answers are correct.

14. The thalamus is …

Variants of answer:

a) a regulator of all the motor functions;

b) a regulator of muscle tone;

c) a collector of afferent pathways, the highest center of pain sensitivity;

d) a regulator of the digestive system;

e) all the answers are correct.

15. The medial geniculate bodies transfer impulses into the cortical center of…

Variants of answer:

a) the visual analyzer;
b) the acoustic analyzer;
c) the motor analyzer;
d) the pain analyzer;
e) all the answers are correct.

16. The lateral geniculate bodies transfer impulses into the cortical center of…

Variants of answer:

a) the visual analyzer;
b) the skin analyzer;
c) the acoustic analyzer;
d) the pain analyzer;
e) all the answers are correct.

17. What is the highest subcortical center of the ANS and all the major vegetative functions?

Variants of answer:

a) the cerebellum;
b) the hypothalamus;
c) the medulla;
d) the spinal cord;
e) the thalamus.

18. The functional zones of the cerebral cortex are…

Variants of answer:

a) only sensory;
b) only motor;
c) both motor and sensory;
d) motor, sensory, and associative;
e) sensory and associative.

19. If the primary projective areas of the visual analyzer in the cerebral cortex are damaged, the person …

Variants of answer:

a) loses vision;
b) sees images, but does not understand the value of signals;
c) has no impairment in the visual analyzer;
d) loses color vision;
e) cannot determine the distance to objects.

20. The functions of which part of the cerebral cortex will be affected in hemorrhage within the area of the temporal lobe?

Variants of answer:

a) the primary acoustical cortex;

b) the primary visual cortex;

c) the primary somatosensory cortex;

d) the primary motor cortex;

e) the primary visual cortex and motor cortex.

21. The functions of which zone of the cerebral cortex will be affected in extensive hemorrhage within the area of the occipital cortex?

Variants of answer:

a) the primary acoustical cortex;

b) the primary visual cortex;

c) the primary motor cortex;

d) the primary somatosensory cortex;

e) the primary associative cortex.

22. The alpha rhythm of the electroencephalogram is registered in a person …

Variants of answer:

a) during active mental work;

b) at rest and absence of external stimuli;

c) when the person is falling asleep;

d) under anesthesia;

e) has disturbed brain function.

23. The beta rhythm of the electroencephalogram is registered in a person …

Variants of answer:

a) during active mental work;

b) at rest and absence of external stimuli;

c) when the person is falling asleep;

d) under anesthesia;

e) has disturbed brain function.

24. The division of the ANS into departments is based on…

Variants of answer:

a) all the answers are correct;

b) on the localization of the brain centers;

c) on the character of the influence on the functions of the organs;
d) on the secreted mediator;
e) on the location of the vegetative ganglia.

25. The preganglionic neurons of the sympahthetic nervous system are located in…

Variants of answer:
a) the sacral department of the spinal cord, medulla, and midbrain:
b) the thoracal-lumbar segments of the spinal cord;
c) the basal nucleus;
d) the geniculate bodies;
e) the black substance.

26. Which body functions do not belong to the vegetative functions?

Variants of answer:
a) the motor functions performed by skeletal muscles;
b) blood circulation;
c) respiration;
d) excretion;
e) the motor functions performed by smooth muscles.

27. The centers of the parasympathetic nervous system are located in...

Variants of answer:
a) the department of the spinal cord and reticular formation;
b) the sacral department of the spinal cord, medulla and midbrain;
c) the basal nucleus;
d) the geniculate bodies;
e) the black substance.

28. Which organs do not have parasympathetic innervation?

Variants of answer:
a) the lungs, liver, kidneys, adrenal glands;
b) the salivary glands, stomach, small intestine, spleen;
c) the skeletal muscles, CNS, most blood vessels, uterus, sweat glands;
d) the pancreas, bronchi, heart, esophagus;
e) smooth muscles, the large intestine.

29. The metasympathetic nervous system …

Variants of answer:
a) all the answers are correct;
b) possesses a relative independence;
c) is located in the walls of the internal organs;

d) can regulate the activity of the internal organs by means of the peripheral reflex arches.

e) is a complex of the microganglionic formations forming the nervous plexus.

30. The visceродermal reflexes arise under the stimulation of the internal organs and can result in …

Variants of answer:

a) changes of sweat secretion and skin sensitivity;

b) changes of the internal organs;

c) changes of cardiac activity;

d) changes in the activity of the digestive system;

e) all the answers are correct.

31. Which of the following chemicals acts as the major neurotransmitter in the substantia nigra?

Variants of answer:

a) dopamine;

b) noradrenaline;

c) acetylcholine;

d) serotonin;

e) none of the above.

32. The nucleus of the basal ganglia includes…

Variants of answer:

a) the dentate nucleus;

b) the thalamus;

c) the caudate nucleus;

d) the red nucleus;

e) the blue nucleus.

33. The efferent fiber bundle of the substantia nigra releases dopamine to one of the following areas…

Variants of answer:

a) the thalamus;

b) the corpus striatum;

c) the pontine tegmentum;

d) the tectum of the midbrain;

e) all the answers are correct.

34. The output from the cerebellum is solely from…

Variants of answer:

a) Basket cells;

b) Granular cells;
c) oligodendrocytes;
d) Purkinje cells;
e) pyramidal cells.

35. The function of the hypothalamus is…

Variants of answer:
a) the regulation of temperature;
b) the synthesis of antidiuretic hormone;
c) the regulation of food intake;
d) hypophyseal control;
e) all the answers are correct.

36. Which of the following states of a patient do the Beta waves of the electroencephalogram reflect?

Variants of answer:
a) deep anesthesia;
b) surgical anesthesia;
c) light anesthesia, the eyes are closed, relaxed;
d) awake/alert state;
e) when a patient is at rest, there are no external stimuli, the eyes are closed.

37. The EEG waves from the hippocampus are…

Variants of answer:
a) the alpha-waves;
b) the beta-waves;
c) theta-waves;
d) the delta-waves;
e) none of the above.

38. The functions of Broca's area are linked to…

Variants of answer:
a) word formation;
b) comprehension;
c) repetition;
d) reading;
e) all the answers are correct.

39. Sympathetic stimulation causes all of the following except…

Variants of answer:
a) high heart rate;
b) high blood pressure;

c) high total peripheral resistance;
d) high venous capacitance;
e) pupillary dilatation.

40. Parasympathetic stimulation causes…

Variants of answer:

a) decreased gastrointestinal secretion;
b) bronchodilation;
c) sweat secretion;
d) pupillary constriction;
e) high heart rate.

CORRECT ANSWERS
NERVOUS REGULATION OF PHYSIOLOGICAL FUNCTIONS
GENERAL PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	a	8	c	15	a	22	a
2	a	9	a	16	c	23	a
3	c	10	a	17	c	24	c
4	a	11	c	18	c	25	b
5	b	12	b	19	b		
6	a	13	d	20	b		
7	c	14	d	21	c		

PARTICULAR PHYSIOLOGY OF THE CNS

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	a	11	b	21	b	31	a
2	c	12	d	22	b	32	c
3	c	13	b	23	a	33	b
4	b	14	c	24	a	34	d
5	b	15	b	25	b	35	e
6	c	16	a	26	a	36	d
7	b	17	b	27	b	37	c
8	a	18	d	28	c	38	a
9	a	19	a	29	a	39	d
10	a	20	a	30	a	40	d

UNIT 5
HUMORAL REGULATION OF PHYSIOLOGICAL FUNCTIONS

5.1. Properties of hormones

Endocrinology is the science which studies the development, structure, and functions of the endocrine glands (EG) and endocrine cells.

Hormones (from the Greek word *«horman» — to excite*) are biologically active substances which are secreted by EG in the blood or lymph and regulate human metabolism and body physiological functions.

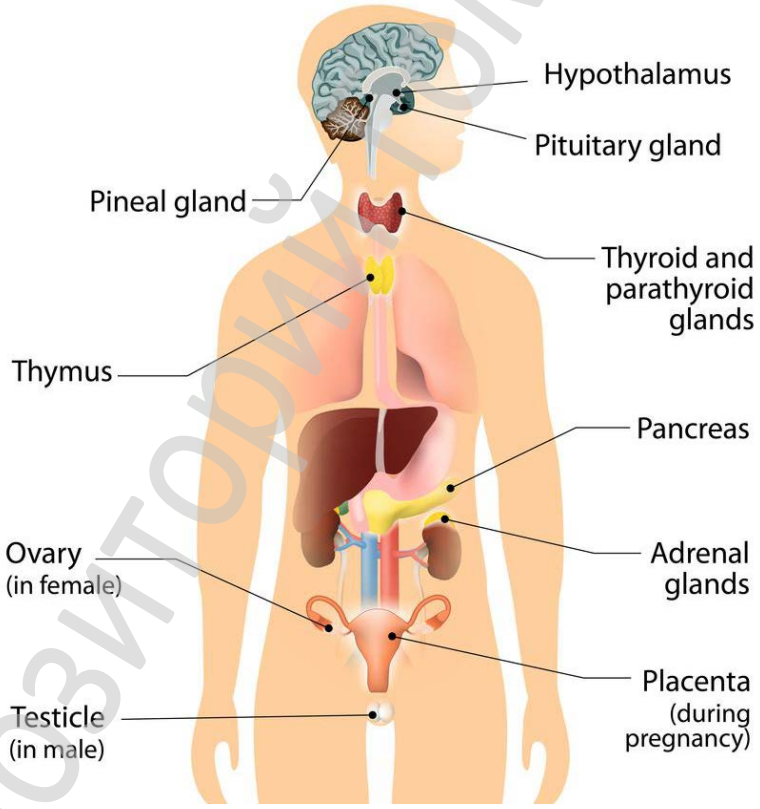


Figure 5.1 — Endocrine glands (from biology.reachingfordreams.com)

The pituitary body, thyroid gland, parathyroids, insular apparatus of the pancreas, cortical and medullary layers of the adrenal glands, sex glands, placenta, and epiphysis are related to EG (Figure 5.1). These glands release their secret directly into the bloodstream or the lymphatic system, therefore they are called EG (Table 5.1). Besides, some hormones are secreted by organs and tissues performing in the body apart from endocrine other specific functions (kidneys, gastrointestinal tract, etc.).

Table 5.1 — Hormones and their effects

Hormone	Target	Effects	Effects of hyposecretion and hypersecretion
Hormones of the anterior lobe of the hypophysis			
Growth hormone (somatotropin)	Body cells, mainly bones and muscles	Stimulates somatic growth; mobilizes fats	Hyposecretion: pituitary dwarfism (pituitary nanism) in children Hypersecretion: gigantism in children; acromegaly in adults
Thyroid-stimulating hormone (thyrotropin)	Thyroid gland	Stimulates the thyroid gland to release thyroid hormone	Hyposecretion: cretinism in children, myxedema in adults Hypersecretion: symptoms of Graves's disease (Basedow's disease)
Adrenocorticotropic hormone (corticotropin)	Adrenal cortex	Promotes the release of glucocorticoids and androgens	Hyposecretion: Rare Hypersecretion: Cushing's disease
Follice-stimulating hormone	Ovaries and testes	In females: stimulates ovarian follicle maturation and estrogen production. In males: stimulates sperm production.	Hyposecretion: failure of sexual maturation Hypersecretion: no important effects
Luteinizing hormone	Ovaries and testes	In females: triggers ovulation and stimulates ovarian production of progesterone In males: promotes testosterone production	Hyposecretion: failure of sexual maturation Hypersecretion: no important effects
Prolactin	Breast secretory tissue	Promotes lactation	Hyposecretion: decreased milk production in nursing women Hypersecretion: galactorrea; absence of menstruation in females; impotence in males
Hormones of the intermediate lobe of the hypophysis			
Melanocyte-stimulating Hormone (intermedin)	Melanocytes	Stimulates pigment production	Hyposecretion: lack of skin pigmentation Hypersecretion: hyperpigmentation

Hormone	Target	Effects	Effects of hyposecretion and hypersecretion
Posterior pituitary hormones			
Oxytocin	Uterus	Stimulates uterine contractions (especially during delivery). Initiates milk secretion	Hyposecretion: powerless delivery
Antidiuretic hormone (vasopressin)	Kidneys, Vessels	Stimulates water reabsorption in the kidneys	Hyposecretion: diabetes insipidus Hypersecretion: unknown
Hormones of the thyroid gland			
Triiodothyronine and tetraiodothyronine (thyroxin) (T3,T4)	The whole body	Accelerates metabolism and oxygen consumption by tissues	Hyposecretion: cretinism (in children), myxedema Hypersecretion: thyrotoxicosis
Thyrocalcitonin	Bones, kidneys	Decreases the calcium level in the blood	—
Hormone of the parathyroid glands			
Parathormone	Bones, kidneys, digestive tract	Increases the calcium level in the blood. Simultaneously reduces the concentration of inorganic phosphates in the blood, and increases their excretion with urine	Hyposecretion: tetany Hypersecretion: osteoporosis
Hormone of beta-cells of the pancreas			
Insulin	The whole body	Decreases the blood glucose level. Stimulates glycogen synthesis in the liver.	Hyposecretion: diabetes mellitus Hypersecretion: hypoglycemic coma
Hormone of alpha-cells of the pancreas			
Glucagon	Liver	Promotes glycogen breakdown and increases the blood glucose level.	Hyposecretion: pathological syndrome: dermatitis, anemia.

Hormone	Target	Effects	Effects of hyposecretion and hypersecretion
Hormones of the cortex of the adrenal gland			
Mineralocorticoids (aldosterone)	Kidneys	Increases the amount of Na^+ (due to the increased reabsorption of Na^+ in the kidneys) and decreased amount of K^+ in the blood. The sodium reabsorption is accompanied with water reabsorption, and due to this the blood volume and blood pressure increase	Hyposecretion: Addison's disease Hypersecretion: aldosteronism
Glucocorticoids (cortisol)	The whole body	Promote gluconeogenesis and hyperglycemia; mobilize fats for energy metabolism; stimulate protein catabolism; assist the body to resist stress factors; depress inflammatory and immune responses	Hyposecretion: Addison's disease Hypersecretion: Cushing's disease
Gonadocorticoids (mainly androgens)		May be responsible for female libido and are a source of estrogen after menopause	Hypersecretion: virilization of females
Hormones of the adrenal medulla			
Adrenaline	Myocardium, smooth muscles of arterioles, liver, skeletal mus-	Increases heart rate and blood pressure (due to vasoconstriction), stimulates lipolysis	Hypersecretion: hypertension

Hormone	Target	Effects	Effects of hyposecretion and hypersecretion
Noradrenaline	cles, fatty tissue Arterioles	and glycogenolysis. Increases blood pressure by promoting vasoconstriction	
Hormones of the ovaries			
Estrogens, Progesterone	Female genitals, mammary gland, uterus, the whole body	Stimulate the development of secondary sex characteristics; provide the cyclic process in the uterus and ovaries, mammary glands	Hyposecretion: hypogonadism
Hormones of the testes			
Testosterone	Male genitals, the whole body	Stimulates the development of secondary sex characteristics and normal function	Hyposecretion: hypogonadism
Other hormones			
Active vitamin D_3 (is produced in the skin, then activated in the liver and kidneys)	Intestines	Stimulates active transport of calcium through the intestinal cell membranes	Hypoproduction: in children — rachitis.
Atrial natriuretic hormone (is produced in heart)	Kidneys	Inhibits reabsorption of sodium ions and renin release	—
Thymosin (is produced in the thymus)	Lymphoid tissue	Participates in the regulation of lymphocyte development and immune response, stimulates antibody formation.	Hypofunction: immune deficiency
Hormones of the placenta (chorionic gonadotropin estrogen, progesterone, placental lactogen, and others)	The whole body of the mother and fetus	Regulation of pregnancy and fetus development, replacing the conforming hormones of the hypophysis and ovaries.	—

Hormones have some properties:

1. Distant character of their action**,** i. e. coming into the blood vessels, they can influence organs and tissues located distantly from the glands where they are formed.

2. Specificity of hormones, i. e. each hormone carries out a certain function and cannot be replaced with other biologically active substances. For example, growth hormone.

3. High biological activity of hormones. Hormones are active at low doses. For example, 1 gram of adrenaline can increase the heart rate of 10 million frogs, 1 gram of insulin can decrease the blood glucose level of 125 thousand rabbits.

4. The small size of the hormone molecules facilitates the transit of some hormones through the cell membranes.

5. Hormones are quickly destroyed. For example, the half-life of thyroxin is 4 days, aldosterone — 30 minutes, adrenaline — 2.5 minutes.

6. Some hormones are not species-specific, i.e. some animal hormones can influence the human body as well. For example, thyroid hormones, adrenaline.

Hormones released into the blood are transported to the organs and tissues. Only a small part of hormones is circulating in free forms. Most of them are present in the blood in the form of plasma protein complexes. The majority of transport proteins specifically bind hormones (transcortin – corticosteroids, thyroxine-binding globulin –thyroid hormones).

As they form a complex with proteins, hormones are accumulated in the blood and can not bind with receptors. Free (not bound with proteins) forms are active. A complex of proteins and hormones serves as a reserve form of hormones.

There are five types of the influence of hormones on the body:

1. Metabolic (impact on metabolism).

2. Morphogenetic (stimulation of form-building processes, differentiation, body growth, metamorphosis).

3. Kinetic (including certain activity of organs).

4. Correcting (changing of the intensity of organ and tissue functions).

5. Permissive (the presence of one hormone is required to allow a second hormone to exert its full effects on the target cell. For example, thyroid hormones increase the number of receptors available for adrenaline in the target cell, thereby increasing the effect of adrenaline on that cell).

By their chemical structure, hormones can be divided into three basic classes:

1) steroids:

— corticosteroids (cortisol, aldosterone);

— sex glands hormones (androgens, estrogens, progesterone);

2) derivatives of amino acids:

— thyroxin, adrenaline, melatonin;

3) protein-peptide compounds:

— polipeptides (vasopressin, releasing hormones);

— proteins (insulin, somatotropin, prolactin);

— glycoproteins (thyrotropin, corticotropin).

Steroid hormones and hormone derivatives of amino acids have no species specificity and usually render the same action on representatives of different species.

Protein-peptide hormones, as a rule, are species-specific.

The mechanism of hormone action on target cells

Hormones influence the target cell by changing the cell activity: they decrease or increase the rates of cellular processes.

The influence of hormones on the cell is performed basically by:

1) redistribution of substances in the cell;

2) chemical modification of cell proteins;

3) induction or suppression of the processes of protein synthesis.

These primary effects lead to changes of the number and activity of regulatory cell proteins and rate of catalytic processes and, as a result, cause the physiological response of tissues to the hormone signal.

The main two mechanisms of the action of hormones are as follows:

— formation of intracellular second messengers, which mediate the target-cell response to the hormone;

— direct gene (DNA) activation by the hormone.

The regulatory influence of protein-peptide hormones, catecholamines, and some others is performed through the system of ***second messengers*** (*cyclic AMP, GMP and others)*. The mechanism of the action of second messengers can be demonstrated on the example of cyclic AMP. When the hormone binds to the receptors coupled to the membrane bound enzyme adenylate cyclase, adenylate cyclase is activated and catalyses the conversion of intracellular ATP to cyclic AMP (cyclic adenosine 3', 5'-monophosphate). Cyclic AMP then diffuses throughout the cell and initiates a cascade of chemical reactions, as a result of which proteinkinases phosphorylate different proteins, many of which are enzymes. The process of phosphorylation activates some of these proteins and inhibits others, which causes various reactions.

Steroid, thyroid hormones after getting into the cell bind to the receptors in the cytoplasm and nucleus (Figure 5.2). Then the hormone-receptor complex is connected with the DNA and proteins of chromatin, which stimulates transcription of certain genes and, as a result, synthesis of new proteins in the cell. These proteins include enzymes which influence the metabolic activity and in some cases the synthesis of structural proteins.

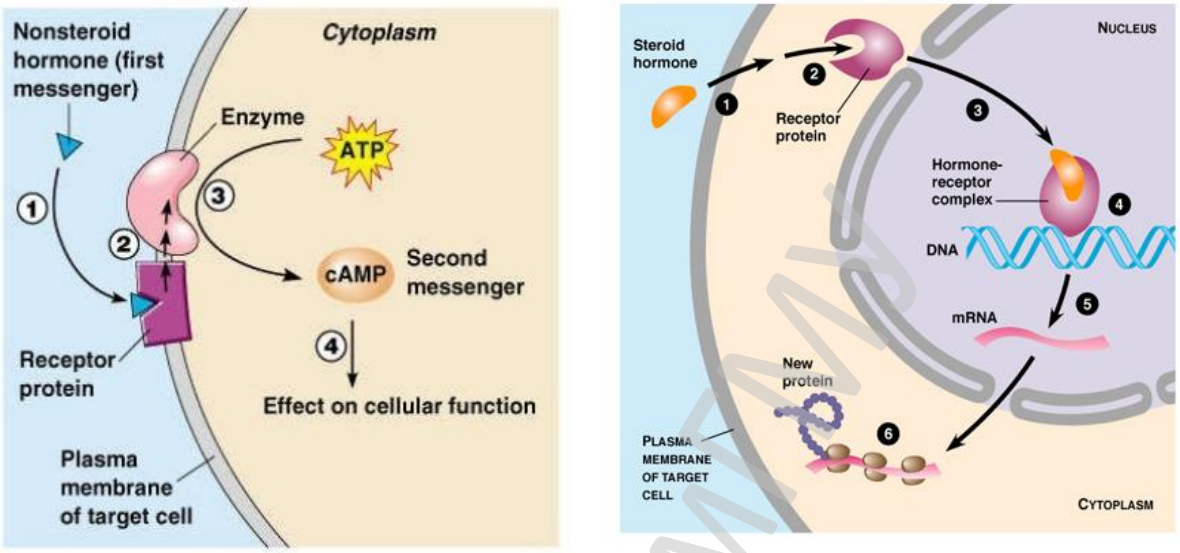


Figure 5.2 — Mechanism of the action of nonsteroid and steroid hormones (from studylib.net)

Notes: The action of nonsterioid hormones: 1 – the hormone is transported by the blood; 2-the hormone is bound to the receptor; 3 - adenylate cyclase is activated and catalyses the formation of cyclic AMP; 4 - cyclic AMP initiates a cascade of chemical reactions.
The action of steroid hormones: 1 – the hormone passes through the cell membrane; 2- the hormone binds with receptor inside the cell; 3, 4, 5- the hormone-receptor complex is connected with the DNA and stimulates transcription of genes; 6 -synthesis of new proteins in the cell.

5.2. Study methods of the activity of the endocrine glands

The following methods are usually applied to study the EG functions:

1. Removal (complete or partial) of the glands and observation over the body functions.

2. Administration of extracts received from a particular gland, to a healthy animal or an animal after the removal of the glands or transplantation of the tissue of this gland into the body.

3. Formation of common blood circulation of the two organisms, one of which has affected or removed EG.

4. Comparison of the physiological activity of the blood flowing into and out of EG.

5. Biological or chemical determination of the concentration of a certain hormone in the blood and other body fluids (blood, urine, cerebrospinal fluid, etc.) The methods of the quantitative analysis of hormones include:

- high-performance liquid chromatography
- radioimmunoassay (RIA)
- immunoradiometric assay (IRMA)

- radioreceptor analysis
- immunochromatographic analysis (test strips for express diagnostics)
- enzyme-linked immunosorbent assay (ELISA)

6. Examination of the mechanisms of hormone biosynthesis (more often with the help of the method of radioactive atoms, i. e. radioactive isotopes).

7. Determination of the chemical structure and artificial synthesis of the hormone.

8. Examination of patients with hypo- or hyperfunction of a particular EG and outcomes of surgical operations performed in these patients for medical purposes.

5.3. Incretion of the hypophysis

The hypophysis (pituitary gland) consists of three lobes — anterior, intermediate, and posterior, each of them being EG. The posterior lobe, which is connected with the hypothalamus, is called neurohypophysis, and the anterior — adenohypophysis (Table 5.1).

5.3.1. Anterior lobe of the hypophysis

The anterior lobe, or adenohypophysis, consists of the main, or chromophobic cells (55–60 % of all cells) and chromophilic cells: acidophilic (30–35 %) and basophilic (5–10 %). Chromophobic cells, apparently, do not produce hormones and are precursors of chromophilic cells. Acidophilic cells produce somatotropic hormone (STH, growth hormone) and prolactin. All the hormones of the anterior lobe are protein substances. The production of these hormones is regulated by the release and inhibition of the hormones of the hypothalamus.

Basophilic cells produce adrenocorticotropic hormone (ACTH), thyrotropic and gonadotropic (follicle-stimulating and luteinizing) hormones.

Somatotropic hormone

Somatotropic hormone (STH, somatotropin, growth hormone) stimulates the synthesis of proteins in organs and tissues and promotes body growth of young organisms.

Somatotropin increases the biosynthesis of ribonucleic acid necessary for protein synthesis. It strengthens amino acid transport from the blood into cells. There is retention of nitrogen (nitrogen balance becomes positive), phosphorus, calcium, sodium in the body.

For the somatotropin effect which intensifies protein synthesis in the cell, the presence of carbohydrates and insulin is necessary. After the removal of the pancreas in animals, and also if carbohydrates are excluded from diet, the action of growth hormone is inhibited. The administration of growth hormone

increases fat mobilization from the depot and its use in energy metabolism. It leads to increased fat metabolism, and also to the increased level of ketone bodies in the blood and their excretion with urine.

Somatotropic hormone has well-marked specific specificity. Preparations obtained from the hypophysis of a bull and a pig exert little or no influence on human growth or development, but human growth hormone influences the growth processes of lower organized animals.

Somatotropic hormone is secreted continuously during the whole human life. Its secretion is stimulated by growth hormone-releasing hormone and inhibited by growth hormone-inhibiting hormone (somatostatin). These substances are the products of hypothalamic neurosecretion. The secretion of growth hormone is intensified during night time.

Growth hormone deficiency causes a sharp growth delay in children. A lack of this hormone in early childhood leads to ***pituitary dwarfism,*** and the person remains a dwarf for the whole life. The body constitution in these individuals is rather proportional, however, their wrists, feet are little, fingers are thin, the ossification of the skeleton is delayed, their genitals and secondary sex characteristics are underdeveloped, their hair differs in terms of softness and silkiness typical of healthy children. These people bear infectious diseases and other illnesses badly and frequently die at a young age. Sexual development is often delayed or impaired into adulthood. Males with this disease often suffer from impotence, i.e. the inability to copulate or get an erection, and females suffer from sterility, i. e. the disability to procreate.

Overproduction of growth hormone in children causes ***gigantism***; the body height of such an individual can reach 240–250 cm, and body weight — 150 kg and more. If overproduction of growth hormone develops in an adult whose bone growth has stopped, the body height does not increase on the whole, but some body parts are capable to keep growing: fingers and toes, hands and feet, nose, lower jaw, tongue, organs of the thoracic and abdominal cavities. This disease is called ***acromegaly*****.** In acromegaly insulin insufficiency in the tissues of the pancreas results in diabetes and other serious health effects. The cause of acromegaly is usually tumors of the anterior lobe of the hypophysis.

Gonadotropic hormones (gonadotropins)

Gonadotropic hormones are **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)**.

The physiological effects produced by FSH and LH are caused by their action on male and female genitals, stimulation of the development of the pubertal gland and follicles (formation of sexual hormones).

The administration of gonadotropic hormones to castrates causes no typical physiological effects.

The immediate cause of puberty is the action of the hormones formed by the genitals but not of the gonadotropines of the hypophysis.

The secretion of FSH and LH by the hypophysis is stimulated by the action of hypothalamic neurosecretion (**gonadotropin-releasing hormone).** Increased androgen level (in males) or estrogen level (in females) in the blood inhibits the secretion of the above hormone, and also the secretion of the gonadotropins by the adenohypophysis. This negative feedback regulates the normal level of the sex hormones in the body.

The production of gonadotropic hormones in humans is influenced by emotional experience. Thus, during World War II the fear caused by bomb attacks sharply affected the secretion of gonadotropic hormones in women and led to the arrest of menstruation.

Prolactin (luteotropic hormone) released by the acidophilic cells of the anterior lobe of the hypophysis strengthens the production of milk in the mammary glands, and also stimulates the development of the yellow body.

If to remove the hypophysis in nursing rats, lactation, or the secretion of milk decreases. The administration of prolactin does not only stimulate milk secretion in nursing rats but also produces its low secretion in non-nursing ones if they have reached puberty and even if they are castrated. Prolactin injections may also cause lactation in males. However, for this purpose estrogens and progesterone should be administered to them for some time as males have rudimentary mammary glands and thus cannot lactate. The administration of prolactin before puberty produces the development of the maternal instinct.

Prolactin decreases the consumption of glucose by tissues, which causes an increase of its amount in the blood, i. e. its effect is similar to somatotropin but is much weaker.

Prolactin secretion is stimulated by the reflex of the centers of the hypothalamic region. The reflex arises during the stimulation of the receptors of the nipples (during suction). This results in excitation of the hypothalamic nuclei, which influences the function of the hypophysis in the humoral way.

The reflex stimulation of prolactin secretion is carried out by the decreased production of prolactin-inhibiting factor.

Thyroid-stimulating hormone (TSH), or thyrotropin stimulates the thyroid function. The mechanisms of this stimulation are numerous. TSH intensifies the secretion of thyroxine and triiodothyronine into the blood, promotes iodine accumulation in the thyroid gland; besides, it increases the activity of its secretory cells and increases their number.

TSH administration produces the growth of the thyroid gland, and the removal of the hypophysis in young animals leads to their underdevelopment. In animals after the removal of the hypophysis, basal and protein metabolism reduce. It can be once again increased by the administration of thyroxine, trans-

plantation of the hypophysis or administration of thyrotropin. Thyroxine administration normalizes basal and protein metabolism. This is the way insufficient production of thyroxine in the atrophied thyroid gland of the animal is compensated, and the transplantation of the hypophysis or administration of TSH normalizes metabolism, ensuring growth of the thyroid gland exposed to atrophy in the absence of this hormone.

If an excessive amount of TSH is daily administered to animals for a long time, they acquire the symptoms of *Basedow's disease (Graves' disease).*

Thyrotropin is constantly secreted in small amounts. The stimulation of thyrotropin secretion is carried out by the hypothalamus whose nervous cells produce ***thyrotropin-releasing hormone*** stimulating the formation of thyrotropin in the adenohypophysis. The level of thyrotropin secretion depends on the amount of the thyroid hormones in the blood. If the amount is sufficient, thyrotropin secretion is inhibited, and vice versa.

If the body is cooled down, thyrotropin secretion intensifies and increases the formation of the thyroid hormones thus increasing heat production (thermogenesis). The cortex of cerebrum can influence the secretion of TSH.

Corticotropin, or adrenocorticotropic hormone (ACTH) produces the growth of the fascicular and reticular regions of the adrenal cortex and intensifies the synthesis of their hormones but does not influence the glomerular zone of the cortex and adrenal medulla. ACTH impacts the adrenals and increases the production of glucocorticoids (which promote higher body resistance to unfavorable factors), and, to some extent, androgens.

The ACTH release by the hypophysis is increased under the influence of all extreme stimuli producing strains (stress) in the body. These stimuli by the reflexes influence the nuclei of the hypothalamus in which the formation of adrenocorticotropin-releasing factor increases. This substance reaches the cells of the anterior lobe of the hypophysis and stimulates ACTH secretion (Figure 5.3).

5.3.2. Intermediate lobe of the hypophysis

The intermediate lobe of the hypophysis in the majority of animals and humans is separated from the anterior lobe and is adherent with the posterior one. The hormone of the intermediate lobe is **intermedin, or melanocyte-stimulating hormone.**

Intermedin is reported to cause skin dimness in amphibians (frogs, in particular) and in some fishes due to expansion of its pigment cells — melanophores — and wider distribution of pigments in their protoplasm. The value of intermedin consists of the adjustment of body integuments to the color of the environment.

In humans having skin spots which do not possess any pigment, the subcutaneous administration of intermedin on the appropriate spots results in gradual normalization of their color.

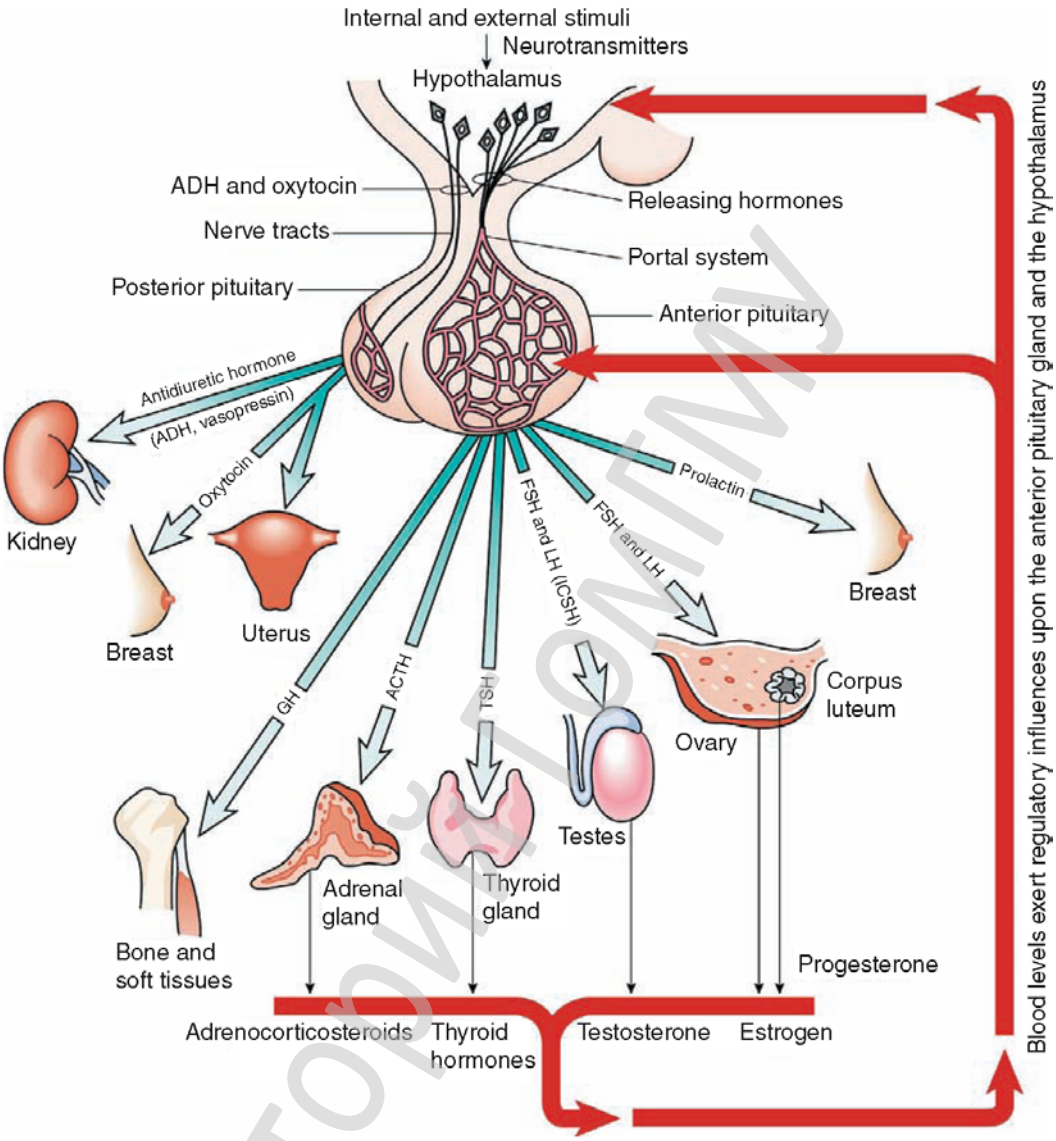


Figure 5.3 — Hypophysis (pituitary) hormones (from picgalleria.com)

Notes: GH — growth hormone; FSH — follicle-stimulating hormone; LH — luteinizing hormone; TSH — thyroid-stimulating hormone; ACTH — adrenocorticotropic hormone.

In pregnancy and adrenal cortical deficiency (changes in skin pigmentation are often observed in both the cases), the amount of intermedin in the hypophysis increases. Apparently, in humans intermedin is a regulator of dermal pigmentation as well.

Intermedin secretion is regulated by the action of light on the eye retina. In mammals and humans, intermedin is essential for the regulation of the movements of the black pigmented layer cells in the eye. Under the action of bright light, the cells of the pigmented layer release pseudopodia, due to which the excess of light rays is absorbed by the pigment, and the retina is not exposed to intensive stimulation.

5.3.3. Posterior lobe of the hypophysis

The posterior lobe of the hypophysis (neurohypophysis) consists of cells similar to those of glia, — so-called *pituicytes.* These cells are regulated by the nerve fibers which pass to the peduncle of the hypophysis and are processes of the neurons of the hypothalamus.

From the posterior lobe of the hypophysis two preparations are obtained: one sharply decreases urinary excretion and increases blood pressure, and the other one stimulates the muscle contractions of the uterus. The former is called **antidiuretic hormone, or vasopressin***,* the latter is **oxytocin***.*

The ***antidiuretic effect of vasopressin*** is based on accelerated reabsorption of water in the renal tubules. That is why the administration of this hormone to animals and humans not only leads to decreased diuresis, but also to increased relative density of urine.

Overproduction of the antidiuretic hormone is a cause of ***non-sugar diabetes (diabetes insipidus)***. In this disorder excretion of too much sugar-free urine (sometimes dozens of liters daily) and excessive thirst are observed. Damage to the posterior lobe of the hypophysis is usually revealed. The subcutaneous administration of the preparation of the posterior lobe of the hypophysis to these patients normalizes their daily urinary excretion.

Vasopressin produces contractions of smooth muscles of the blood vessels (especially of arterioles) and leads to increased blood pressure. However, the pressor effect is observed only after artificial administration of big doses of the hormone; the amount of vasopressin secreted in norm gives only the antidiuretic effect and practically does not influence the smooth musculation of the blood vessels.

Oxytocin stimulates contractions of the smooth muscles of the uterus, especially at the end of pregnancy. This hormone is essential for normal delivery. After the removal of the hypophysis in pregnant females delivery becomes more complicated. Oxytocin also influences milk secretion.

5.3.4. Regulation of incretion of the hypophysis

The incretion of the hypophysis, regulating functions of some other glands (sex, adrenal, thyroid glands), depends on the functioning of these glands. Thus, the deficiency of androgens, estrogens, glucocorticoids, and thyroxine in the blood stimulates the production of gonadotropins, ACTH and TSH of the hypophysis respectively, and vice versa. Thus, the hypophysis is included into the system of neurohumoral regulation working by the principle of negative feedback, automatically supporting the production of hormones of the corresponding glands at the necessary level.

In the hypothalamus, substances are formed and then transferred to the adenohypophysis. They are called *releasing factors (hormones)*: *corticotropin-*

releasing factor, *thyrotropin-releasing factor, gonadotropin-releasing factor, somatotropin-releasing factor.* They promote the formation and secretion of ACTH, gonadotropins, thyrotropin, somatotropin.

The substances inhibiting the secretion of some hormones by the adenohypophysis are formed in the hypothalamus. In particular, these substances are the factor inhibiting the formation of prolactin (prolactostatin) and growth hormone-inhibitory factor (somatostatin).

The evidence that the products of hypothalamic neurosecretion influence the function of the hypophysis plays an important role and is proved by the fact that the hypophysis transplanted to the neck stops secreting ACTH, gonadotropin, thyrotropin, and somatotropin.

5.4. Incretion of the thyroid gland

The thyroid gland consists of glandular follicles and parafollicular tissue. The follicles are filled with a semifluid substance of high hormonal activity called colloid (Figure 5.4). The walls of the follicles consist of the glandular epithelium. The gland has a large number of blood and lymphatic vessels. The amount of blood flowing through the thyroid gland per minute 3–7 times exceeds the mass of the gland itself.

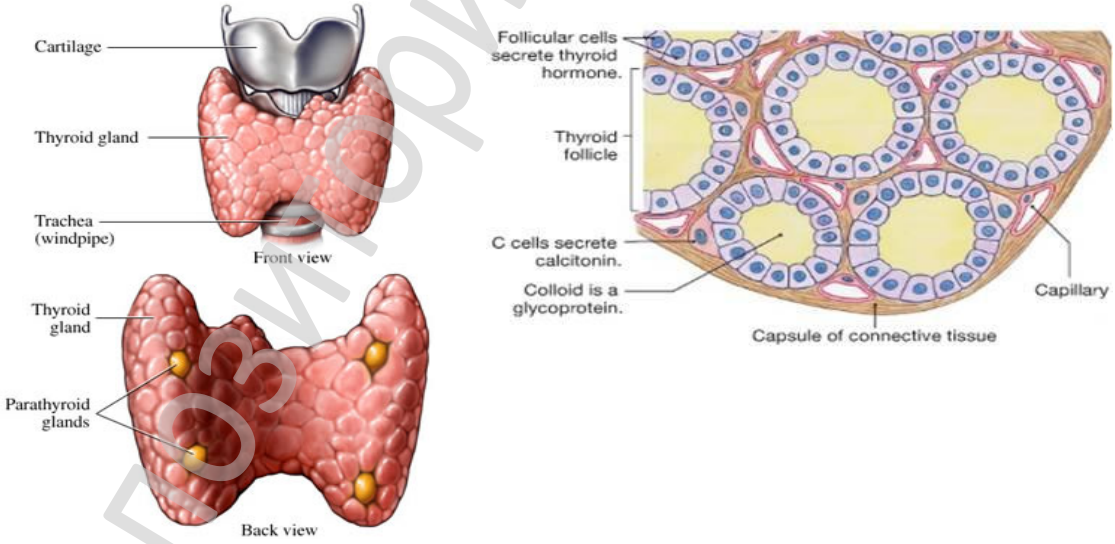


Figure 5.4 — Thyroid gland (from bianoti.com)

5.4.1. Hormones of the thyroid gland

Thyroid tissue contains iodine included into the hormones formed by the follicles of the gland. The cells of this gland have the specific ability to absorb iodine so that its amount inside cells becomes 300 times higher than in blood plasma.

The recommended daily intake of iodine is 100-150 mcg per day for most adults.The first stage in the formation of thyroid hormones is the transport of iodides from the blood into the thyroid glandular cells and follicles. The next step is the conversion of the iodide ions to an oxidized form of iodine which is capable of combining directly with the amino acid tyrosine (this oxidation of iodine is promoted by the enzyme peroxidase). The thyroid hormones are formed within the thyroglobulin molecule, which contains tyrosine amino acids. Tyrosine is first iodized to monoiodotyrosine and then to diiodotyrosine. Then iodotyrosine residues become coupled with one another. The molecule **tetraiodothyronine**, or **thyroxine** (T4) is formed, when two molecules of diiodotyrosine are joined together. The molecule **triiodothyronine** (T3) is formed, when one molecule of monoiodotyrosine couples with one molecule of diiodotyrosine. They form a complex compound with the protein thyroglobulin in the cells of the gland follicles, and it can stay in the follicles for several months. After endocytosis of the thyroglobulin-thyroid hormone complex into follicular epithelial cells it is hydrolyzed in lysosomes; and then thyroxine and triiodothyronine are released into the blood.

Triiodothyronine and thyroxine are transmitted into the blood where they bind with the proteins of blood plasma by thyroxine-binding globulin (TBG) and prealbumin transmitting hormones. In tissues these complexes decompose and release thyroxine and triiodothyronine.

The amount of free thyroxine (not bound with protein) in blood plasma is about 0.1 % of the whole amount of this hormone in the bloodstream. However, it is free thyroxine which has a physiological action. Protein-bound thyroxine is a reserve from which its new active portions are released.

Triiodothyronine is physiologically more active than thyroxine, its amount in blood plasma is 20 times less.

The main effects of thyroid hormones

1) The typical action of the hormones of the thyroid gland is intensified energy metabolism. After the administration of thyroxine, its action starts within 24 hours with its peak on 12 day. After the administration of triiodothyronine, the increase of energy metabolism starts within 6–12 hours.

2) Thyroxine, triiodothyronine, and some other iodine compounds formed by the thyroid gland, intensify oxidative processes. The oxidative processes in the mitochondria are the most active, which intensifies energy metabolism of cells.

3) Basal metabolism considerably increases. Oxygen consumption and carbonic dioxide excretion are increased. The body becomes sensitive to oxygen deficiency.

4) Thermogenesis is increased.

5) Thyroxine intensifies the consumption of carbohydrates, fats, and proteins. In hypersecretion of the thyroid hormones the consumption of glucose from the blood by tissues sharply increases. The loss of glucose from the blood is compensated by glycogen splitting in the liver and muscles. The intensive consumption of proteins results in the increased amount of nitrogen in the urine.

6) The hormones of the thyroid gland accelerate body development. The iodine hormone of the thyroid gland influences the CNS. Continuous administration of big doses of thyroxine to dogs causes their anxiety; tendinous (for example, knee-joint) reflexes intensify, tremor of extremities appears. The iodine-containing hormones of the thyroid gland are accumulated in the structures of the reticular formation in larger as compared with other regions of the CNS thus increasing its tone and activate the cortex of the cerebrum.

Thyroxine and triiodothyronine production is regulated by thyrotropin-releasing hormone (produced in the hypothalamus) and thyroid-stimulating hormone (produced in the hypophysis) (Figure 5.5).

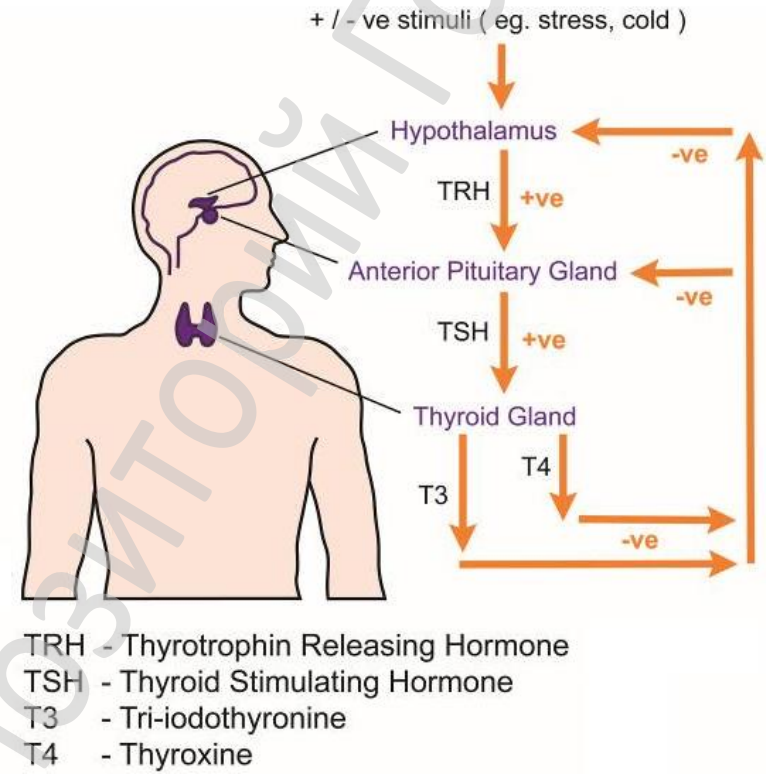


Figure 5.5 — Regulation of thyroid hormone production (hypothalamic-hypophysis-thyroid axis) (from studylib.net)

Deficient thyroid gland function (hypothyroidism) which appears in childhood results in the development of ***cretinism*** characterized by growth retardation, body proportion disorders, sexual and mental delays. Hypothyroid cretins display open mouth and the tongue hanging out because of its extremely big size, which makes it difficult for them to swallow and breathe.

In adults underactive thyroid results in ***myxedema***. Basal metabolism decreases by 30–40 %. The body weight increases due to the increased amount of intercellular fluid. The intercellular spaces of the organs and tissues have an increasing number of mucin and albumins due to protein metabolism disorders. Proteins increase the oncotic pressure of tissular fluid thus holding water in tissues, especially in subcutaneous fat, which induces the development of myxedema. An individual with myxedema may notice thinking and speech retardation, apathy, swelling in their face and body, sexual disorders (in women — termination of menstruation), low body temperature.

In areas where the soil (along with drinking water and food, both vegetable and animal) is poor in iodine, there are numerous cases of thyroid dysfunction with significant growth of its tissues forming so-called endemic goiter. The thyroid gland is hypertrophied and has an excessive number of follicles, though the hormone production is reduced. It is observed mainly in highlands.

The prevalence of endemic goiter in the regions with iodine deficiency can be considerably reduced if small amounts of potassium iodine are added into salt or drinking water.

In the 60s of the last century the typical signs of goiter were described: exophthalmus, high heart rate, extreme irritability, increased metabolism and body temperature, increased food intake with simultaneous weight loss. Tendon reflexes are strengthened, muscle tremor is sometimes observed. Patients are lively, fidgety and sometimes unaware of their behaviour. ***Graves' disease*** **(Basedow's disease)** is caused by hyperthyroidism, i. e. hyperproduction of the thyroid hormones and their elevated amounts in the blood up to the range inducing toxic phenomena. This disease is also known as thyrotoxicosis (Table 5.2).

Table 5.2— The main differences between hypo- and hyperthyroidism

Sign / Symptom	Hypothyroidism	Hyperthyroidism
Body weight	Weight gain.	Weight loss.
Mental state	Depression. Poor memory. Inability to concentrate. Sleepiness.	Anxiety. Irritability. Nervousness. Insomnia.
Temperature sensitivity	Cold intolerance	Heat intolerance
Heart rate	Bradycardia. Slow heart rate.	Tachycardia. Accelerated heart rate.
Gastrointestinal tract	Decreased appetite. Constipation.	Increased appetite. Diarrhea.
Eyes	Peri-orbital edema	Protruding eyeballs (exopthalmos) may be present.
Skin and hair	Dry, pale skin. Dry, coarse hair. Hair loss. Legs, hands, eyelid swelling, edema.	Perspiration (sweaty skin). Warm and smooth skin.
Muscles/movements	Slow relaxation of muscles.	Tremor. Muscle weakness.

Thyrocalcitonin. Except for the iodine-containing hormones, the thyroid gland forms thyrocalcitonin, which decreases the calcium level in the blood. Thyrocalcitonin is formed in the parafollicular cells located outside the glandular follicles of the thyroid gland.

Thyrocalcitonin inhibits the function of osteoclasts which destroy osteal tissue, and activate the function of osteoblasts which promote osteogenesis and Ca^{2+} absorption from the blood. Thyrocalcitonin is a hormone which stores calcium in the body.

5.5. Incretion of the parathyroid glands

Humans have four parathyroid glands, two of which are located on the posterior surface of the thyroid gland and two — at the anterior pole, and sometimes in its tissue.

The parathyroid glands produce **parathormone.** Parathormone activates the function of the osteoclasts destroying bone tissue. In the body parathormone causes destruction of bone tissue with the release of calcium ions, thus increasing their level in the blood. Parathormone intensifies calcium absorption in the intestines and the processes of its reabsorption in the renal tubules. Parathormone influences vitamin D activation. Vitamin D is required for intestinal absorption of calcium from food. Vitamin D is formed in the skin in its inactive form, then under the influence of parathormone it is activated in the liver and kidneys.

All these effects lead to a significant increase of the calcium level in the blood. At the same time, the concentration of inorganic phosphate in the blood is reduced, and its urinary excretion increases.

Normally the concentration of Ca^{2+} in blood plasma is maintained at a constant level. Decreased calcium levels in the blood perfusing the gland result in the intensified secretion of parathormone and, therefore, increased calcium release into the blood from its ostial depots, and vice versa.

Thus, there is a direct bilateral connection between the content of calcium in the blood and incretion of the parathyroid glands: a shift in the calcium concentration in the blood causes changes of the secretion of thyrocalcitonin and parathormone, the latter regulating the calcium content in the blood (Figure 5.6).

If parathormone is deficient, the amount of calcium in the blood decreases, and on the contrary increases in its excess. Simultaneously, in the former case the amount of phosphate is increased in the blood and is decreased in the urine, in the latter — vice versa.

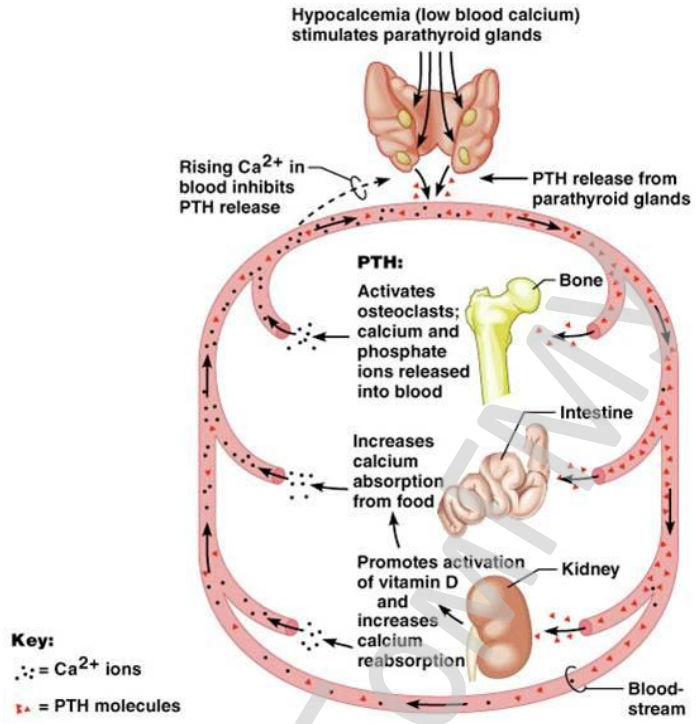


Figure 5.6 — Regulation of parathormone secretion (from slideplayer.com)

Note: PTH-parathormone

Body changes associated with hypo- and hyperfunction of the parathyroid gland

Within some days after parathyroidectomy in dogs, contractures of skeletal muscles become more intensive and occur more frequently.

The absence of the parathyroid glands results in death due to contractures of respiratory muscles. Convulsive attacks after parathyroidectomy are caused by the damage of the CNS. Once motor nerves are dissected, contractures of de-innervated muscles do not occur. The administration of calcium salts to these animals prevents the development of tetany. In tetany the functions of the liver are also affected. ***Human hypoparathyrosis*** intensifies the excitability of the CNS and causes contractures because of the decreased calcium level in the blood. Mild deficiency of the parathyroid glands causes latent tetany, which leads to the contractures of the face and hands and appears only in the pressing on the nerve innervating these muscles. In children with congenital deficiency of the parathyroid glands, the content of calcium in the blood is reduced, the growth of skeletal bones is affected, long-term contractions of muscles (forearm, thorax, pharynx, etc.) are observed.

Hyperparathyroidism of the parathyroid glands is not common, and is found, for example, in tumors of the parathyroid glands. Here, the content of calcium in the blood is increased, and the amount of inorganic phosphate is decreased. This results in the development of osteoporosis, i.e. destruction of

bone tissue, muscle weakness (making the patient lie down all the time), backache, pains in the feet and hands. The timely removal of the tumor restores normal condition.

Review questions

1. What glands are called endocrine glands? Name the main endocrine glands. What are hormones? What are the properties of hormones? Name the types of the influence of hormones on the body. How are hormones classified according to their chemical structure?

2. What is the mechanism of the action of protein-peptide hormones and catecholamines on target cells? What is the mechanism of the action of steroid and thyroid hormone on target cells? Name the study methods of the activity of the endocrine glands.

3. What hormones are secreted by the anterior lobe of the hypophysis? What is the physiological role of these hormones? How is the production of the hormones of the adenohypophysis regulated? What are the effects of hypo - and hypersecretion of the hormones of the adenohypophysis?

4. What hormones are secreted by the intermediate and posterior lobes of the hypophysis? What is their physiological role? How is the production of these hormones regulated? What are the effects of hypo — and hypersecretion of these hormones?

5. Describe the structural organization of the thyroid gland. Name the iodine-containing hormones of thyroid glands. What are the features of the biosynthesis of thyroid hormones and their transport by blood? What are the main effects of thyroid hormones? How is the production of thyroid hormones regulated? What cells produce thyrocalcitonin? What is the physiological role of thyrocalcitonin?

6. What are the effects of hypo - and hypersecretion of thyroid hormones? What are cretinism, myxedema, Grave's (Bazedow's) disease? What is endemic goiter and what are the methods of its prophylaxis?

7. What is the hormone of the parathyroid glands? What is its role in the regulation of Ca and P metabolism? How is the production of parathormone regulated? What are the effects of hypo — and hypersecretion of parathormone?

5.6. Incretion of the pancreas

The histological examination of the pancreas has revealed that apart from the secretory epithelium excreting digestive enzymes, it has specific groups of cells — white dendritic epidermocytes (islets of Langerhans). These epidermocytes do not have excretory ducts and release their secret directly into the blood (Figure 5.7).

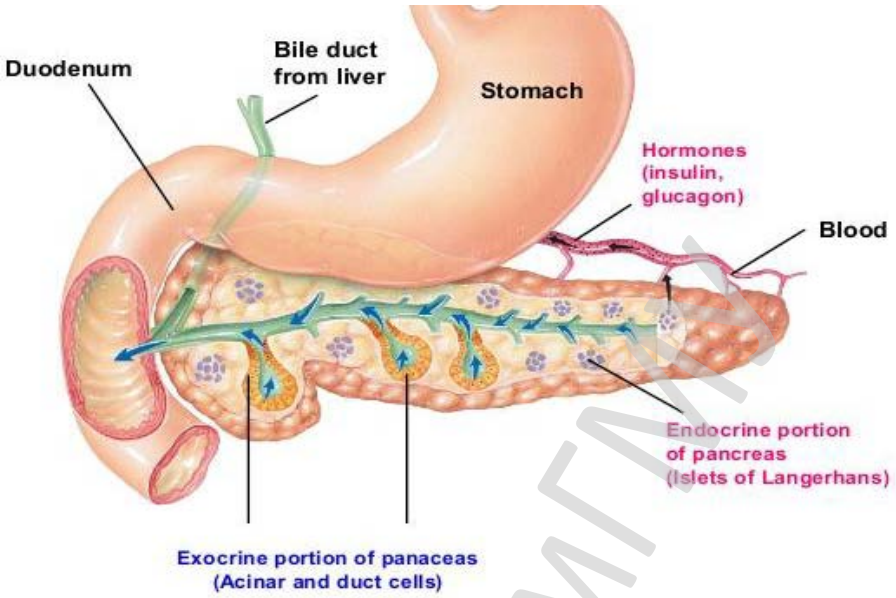


Figure 5.7 — Pancreas (from bianoti.com)

5.6.1. Hormones of the pancreas

White dendritic epidermocytes (islets of Langerhans) consist of cells of several types: ά-, β-, δ- and G-cells. β-cells are in the largest amount (in dogs about 75 %); they are of small size and have acinose protoplasm.

Beta-cells secrete insulin; alpha-cells produce glucagon.

δ-cells produce somatostatin, G-cells produce gastrin.

Somatostatin causes decreased secretion of insulin and glucagon. Gastrin stimulates the secretion of hydrochloric acid in the stomach.

The epithelia of the small ducts of the pancreas secrete lipocain. In the extracts of this gland two more hormones are found — vagotonin and enterpnein.

Insulin is the first human protein to be chemically synthesized.

Insulin molecules do not contain zinc (Zn), however are capable to bind it; thus the effect of insulin action is prolonged and extended.

Insulin increases the permeability of muscle and fat cell membranes to glucose sharply. Therefore, the velocity of glucose transition into these cells increases approximately by 20 times in comparison with the velocity of glucose transition in cells in a medium which does not have insulin, which promotes its utilization.

The increase of glucose transport through the membranes of muscle fibers under the action of insulin promotes the synthesis of glycogen and its accumulation in muscle fibers. In fatty tissue cells insulin stimulates fat formation from glucose.

Under the influence of insulin the permeability of the cellular membrane increases to amino acids from which proteins are synthesized in cells. Insulin stimulates the synthesis of the information RNA and also promotes protein synthesis.

Transition of a significant amount of glucose from blood plasma inside the cells of skeletal muscles, cardiac muscle, smooth muscles, mammary glands, and some other organs arising after the administration of big doses of insulin produces low glucose levels in the blood and, therefore, insufficient supply of glucose into the cells of the nervous system (on whose permeability insulin does not influence). That is why the brain and the spinal cord depend upon glucose, which is the basic energy source for nervous cells. When the amount of sugar in the blood reduces to 2.5 mmol/L, there is an acute disorder of brain activity — ***hypoglycemic coma***. Its symptoms are periodic attacks of muscle contractures, then poor muscle tone, low body temperature, loss of consciousness. Hypoglycemic coma can develop even under the influence of a small dose of insulin if administered on an empty stomach, when glucose from the digestive tract does not come into the blood. Intravenous infusion of a glucose solution immediately stops hypoglycemic coma.

At the end of the 19th century it was found out that the removal of the pancreas in a dog resulted in urinary excretion of sugar within 4–5 hours. The content of glucose in the blood sharply increased, and the loss of sugar with the urine resulted in weight loss, the animal drank a lot of water and became gluttonous. All the symptoms were similar to those found in diabetic patients. After the transplantation of the pancreas to any other part of the body, for example, under the skin, the signs of diabetes in the dog disappeared.

Diabetes mellitus is characterized by an abnormally high concentration of glucose in circulating blood ***(hyperglycemia), i.e. more than*** **10 mmol/L** and even higher, instead of 4.4 ± 1.1 mmol/L. It develops because in diabetes the glucose which comes into the blood is not completely utilized by tissues and does not turn into glycogen in the liver.

High glucose in the blood and, consequently, in glomerular filtrate results in the fact that the epithelium of the renal tubules does not reabsorb glucose completely and it is excreted with urine (***glucosuria***), followed by loss of sugar with the urine — diabetes mellitus.

The excretion of urine is excessive (***polyuria***). The reason of this phenomenon is that high glucose in the urine of the renal tubules increases its osmotic pressure and holds water. Water is insufficiently absorbed in the tubules and the volume of the urine excreted by the kidneys is increased. Water deficiency in the body of diabetic patients induces a strong thirst and results in an excessive fluid intake (***polydipsia***). The urinary excretion of glucose induces sharply increased breakdown of proteins and fats providing energy metabolism of the body.

The products of incomplete oxidation of fats (ketone bodies) are accumulated in the body. In severe cases intensive formation of acidic products produces a shift of blood pH to its acidic side — acidosis.

Accumulation of ketoacids and acidosis can produce a severe state which is a lethal hazard — diabetic coma, which proceeds with a loss of consciousness, respiration, and blood circulation disorder.

These abnormalities are connected with the poor hormonal function of the pancreas.

Glucagon is the second hormone of the pancreas produced by the alpha-cells of white dendritic epidermocytes. Inside the cell glucagon stimulates the transition of inactive phosphorylase (enzyme participating in glycogen splitting with the formation of glucose) into the active form and thus promotes glycogen breakdown (in the liver, not in muscles) increasing the blood sugar level. Simultaneously, glucagon stimulates glycogen synthesis in the liver from amino acids. Glucagon inhibits fatty acid synthesis in the liver but activates hepatic lipase, promoting the splitting of fats. It also stimulates lipolysis in fat tissue. Glucagon promotes the contractile function of the myocardium not influencing its excitability.

5.6.2. Regulation of pancreatic secretion

Insulin secretion by white dendritic epidermocytes proceeds continuously but the intensity of its formation is not always identical.

Insulin release (and also glucagon release) is regulated by the blood glucose level. The increased content of glucose in the blood after its large intake, and also in hyperglycemia associated with intense physical work and emotions, increases insulin secretion. Vice versa, a low glucose level in the blood inhibits insulin secretion but increases glucagon secretion. Glucagon works to counterbalance the actions of insulin. Glucose influences the alpha- and β-cells of the pancreas directly. This influence was observed on the de-innervated or isolated pancreas: high glucose in the blood results in intensified secretion of insulin, and low glucose — in secretion of glucagon.

Insulin synthesis increases during digestion and decreases if a person is hungry. The increased secretion of insulin during digestion provides intensified formation of glycogen in the liver and muscles from glucose which comes at this time into the blood from the intestines. The concentration of insulin in the blood depends not only on the intensity of the formation of this hormone, but also on the speed of its destruction.

Insulin is split up by *insulinase,* contained in the liver and skeletal muscles. Liver insulinase is the most active.

The level of glucose in the blood, apart from insulin and glucagon, is regulated by the somatotropic hormone of the pituitary gland, and also by the hormones of the adrenal glands, TSH, ACTH, T3, and T4.

5.7. Incretion of the epiphysis

The epiphysis forms a substance called melatonin. This substance has an active influence on melanophores (melanin-containing cells especially of fishes, amphibians, and reptiles). The action of **melatonin** is opposite to that of intermedin, as it lightens the skin.

The main effect of melatonin can be divided into three groups:

1) Participation in biorhythm regulation

There is a pronounced circadian rhythm of melatonin secretion.

The epiphysis also contains large amounts of *serotonin,* which is the precursor of melatonin. The formation of serotonin in the epiphysis is increased in the period of the highest illumination. During the day time, the secretion of serotonin increases, and melatonin secretion decreases. Incretion of the epiphysis is regulated by the sympathetic nervous system. The cyclic activity of the epiphysis represents the biological clock of the organism.

Melatonin is involved in the regulation of seasonal rhythms. Increased melatonin production in autumn and winter may be accompanied by apathy, foul mood, loss of strength, lack of attention.

2) Modulating effect on adenohypophysis hormone secretion

Melatonin suppresses the secretion of adenohypophysis hormones, especially gonadotropins. Melatonin slows down the development of the secondary sexual signs, participates in the regulation of sexual cycles and sexual behavior.

In mammals melatonin influences the sex glands inducing delayed sexual development in immature animals and decreasing the size of the ovaries and inhibiting the estrous cycles in adult females. Epiphyseal injuries in children lead to their earlier puberty. Under the influence of light, melatonin formation in the epiphysis decreases, that is why there are seasonal patterns of sexual behavior of some animals showing sexual activity in spring and in summer when due to longer days the formation of melatonin decreases.

3) Antioxidant activity

As a powerful antioxidant, melatonin protects the mitochondrial and nuclear DNA from damage, serves as a trap of free radicals and has a radioprotective and antitumor activity.

5.8. Tissue hormones

Biologically active substances are formed not only by the cells of EG but also by special cells located in various organs. Thus, the groups of polypeptide structure hormones are formed in the gastrointestinal tract; they play an important role in motor control, secretion, and the processes of adsorption in the gastrointestinal tract. These hormones include: *secretin, cholecystokinin, vaso-*

active interstitial polypeptide, gastrin, somatostatin, enkephalin, neurotensin, etc. A number of these peptides are found in the CNS.

The recent studies have revealed that musclular tissue (as well as adipose tissue) can also pruduce regulatory substances, which have both paracrine and endocrine effects. *Adipokines* are a family of hormones and cytokines with both pro- and anti-inflammatory effects that are secreted by adipose tissue. Adipose tissue produce *leptin* — a hormone that helps to regulate energy balance by inhibiting hunger. Myokines, a group of skeletal muscle derived peptides, are produced, expressed and released by muscle fibers under contraction. It is assumed that contraction-regulated myokines play a role in the communication between muscle and other tissues such as adipose tissue, liver, and pancreatic cells. They are involved in exercise-associated metabolic changes, as well as in the metabolic changes following training adaptation, and also participate in tissue regeneration and immunomodulation.

5.9. Incretion of the adrenal glands

The adrenal gland is composed of two parts — the adrenal cortex and the adrenal medulla — each of which is responsible for producing different hormones.

5.9.1. Physiological value of adrenaline and noradrenaline

The hormone of the adrenal medulla — ***epinephrine*** (also called ***adrenaline)*** — is a derivative of the tyrosine amino acid. The adrenal medulla also secretes norepinephrine (or noradrenaline), which is a direct precursor of adrenaline in its synthesis in the cells of chromophilic tissue. Noradrenaline is a mediator released by the terminals of sympathetic fibers.

Adrenaline and noradrenaline are united under the name of catecholamines. They are also called sympathomimetic amines since the action of adrenaline and noradrenaline on organs and tissues is similar to that of sympathetic nerves.

Adrenaline influences many body functions, including intracellular metabolic processes. It intensifies the breakdown of glycogen and decreases its reserve in the liver and muscles, being in this respect the antagonist of insulin, which strengthens glycogen synthesis.

Under the influence of adrenaline, glycogenolysis is intensified in muscles. In the liver, glucose is formed from glycogen and passes into the bloodstream; following this, the amount of glucose in the blood increases (adrenal hyperglycemia). Thus, the action of adrenaline causes firstly, the use of the glycogen reserve of muscles as an energy source for their work, secondly, elevated glucose supply from the liver into the blood, which can also be used by muscles during their active work.

Adrenaline produces intense heart contractions and accelerated heart rate, improves signal conduction in the heart. (At the same time it increases the tonus of the vagus nerve nuclei and, consequently, can produce HR retardation). Adrenaline produces an especially sharp positive chrono- and inotropic action on the heart when cardiac muscle tissue is weakened. Adrenaline constricts the arterioles of the skin, organs of the abdominal cavity and those skeletal muscles which are at rest. Adrenaline dilates the blood vessels of working muscles.

Adrenaline relaxes contractions of the stomach and small intestine. Peristaltic and pendulum contractions decrease or stop at all. The tone of the smooth muscles of the stomach and intestines decreases. Bronchial muscles under the action of adrenaline are relaxed, owing to which the lumen of the bronchi and bronchioles dilates. Adrenaline produces contractions of the radial muscle of the eye iris resulting in pupil dilatation. Due to the contractions of the smooth muscles of the skin, the skin hairs erect (pilomotor reflex) and so-called goose-flesh or goose bumps appears.

The administration of adrenaline increases the working capacity of skeletal muscles (especially in muscle fatigue). Influenced by adrenaline, the excitability of receptors increases, in particular those of the retina, acoustic and vestibular apparatus. It improves the perception of exogenous stimuli by the organism.

Thus, adrenaline is able to activate the functions which are directed at enhancing the interaction of the organism with the environment, increasing working capacity when the body needs additional resources and energy to endure unusual strains.

The action of ***noradrenaline*** on the body functions is similar to that of adrenaline, but is not always identical. Thus, noradrenaline produces contractions of the smooth muscles of the uterus in rats, and adrenaline relaxes them. In humans noradrenaline increases peripheral vascular resistance and also systolic and diastolic pressure to a greater extent than adrenaline, which results in increased systolic pressure. Adrenaline stimulates the secretion of the anterior pituitary hormones, but noradrenaline does not produce such an effect.

Nervous control of the intrasecretory function of the chromophilic tissues of the adrenal gland. In 1910 M. N. Cheboksarov found that the release of adrenaline is regulated by the sympathetic nervous system, the fibers of which are a part of the celiac nerve. The nerve centers regulating the secretory function of the chromophilic tissue of the adrenal glands are located in the hypothalamus.

The effects arising under the action of adrenaline resemble the shifts produced by excitation of the sympathetic nervous system. This system mobilizes energy resources so that the organism could bear big strains and overcome urgent situations. In all situations which are accompanied by excessive activity of

the organism and intensified metabolism, for example, in emotional excitement, muscle work, hypothermia, etc., the secretion of adrenaline increases.

The increased secretion of adrenaline explains the mechanism of appearance of some physiological changes caused by emotional states of a person. Thus, high blood glucose level and glucose excretion with the urine in students during examinations and in racers before the start are caused by more intense secretion of adrenaline by the adrenal gland.

5.9.2. Hormones of the cortex of the adrenal glands

In the adrenal cortex there are three zones, or layers: external — *glomerular* (zona glomerulosa), middle — *fascicular* (zona fasciculata) and internal — *reticular* (zona reticularis) (Figure 5.8). From the adrenal cortex about *50* corticosteroids are identified, however, only 8 of them are physiologically active.

Adrenal hormones

There are three groups of adrenal hormones: 1) mineralocorticoids — *aldosterone* and *deoxycorticosterone* secreted by the glomerular layer and regulating mineral metabolism; 2) glucocorticoids — *cortisol, cortisone, and corticosterone* (the last is also a mineralocorticoid), secreted by the fascicular layer and influencing carbohydrate, protein, and lipid metabolism; 3) sex hormones — *androgens, estrogens, progesterone,* secreted by the reticular layer.

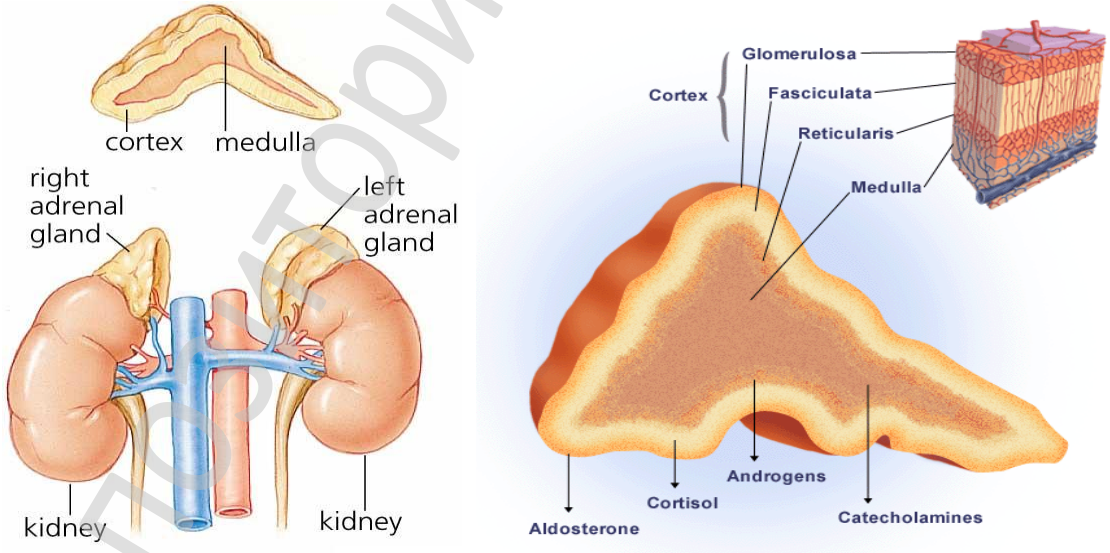


Figure 5.8 — Adrenal glands (from biology.reachingfordreams.com)

Mineralocorticoids. Mineralocorticoids participate in the regulation of mineral metabolism of the organism, first of all of the sodium and potassium levels in blood plasma.

Aldosterone is the most active of all mineralocorticoids. In the epithelium cells of the renal tubules it activates the synthesis of enzymes which increase

the energy effect of the sodium pump. Therefore, sodium and chlorine reabsorption in the renal tubules increases, which leads to increased sodium amount in the blood, lymph, and intercellular fluid. Simultaneously, it reduces potassium reabsorption in the renal tubules, and this results in the loss of potassium and reduces its content in the organism. These changes develop in the cells of the epithelium of the stomach and intestines, salivary and sweat glands. In this way aldosterone can prevent the loss of sodium in hyperhidrosis.

Increased concentrations of sodium in the blood and intercellular fluid under the influence of aldosterone increase their osmotic pressure, which results in water retention in the body and promotes elevated blood pressure. As a result, the development of renin by the kidneys is inhibited. Increased sodium reabsorption can result in the development of hypertension.

In mineralocorticoid deficiency the reabsorption of sodium in the renal tubules decreases, and the organism loses enormous amounts of sodium, which results in changes of the internal medium incompatible with life, and within a few days after the removal of the cortical layer of the adrenal gland leads to death. The administration of mineralocorticoids or big doses of sodium chloride may sustain life of an animal whose adrenal gland has been removed. Therefore, mineralocorticoids are called life-saving hormones.

Regulation of the mineralocorticoid level in the blood (Figure 5.9). The amount of mineralocorticoids secreted by the adrenal glands is in a direct relationship on the sodium and potassium content in the organism. Increased amount of sodium in the blood which perfuses the adrenal gland, inhibits the secretion of aldosterone, and vice versa.

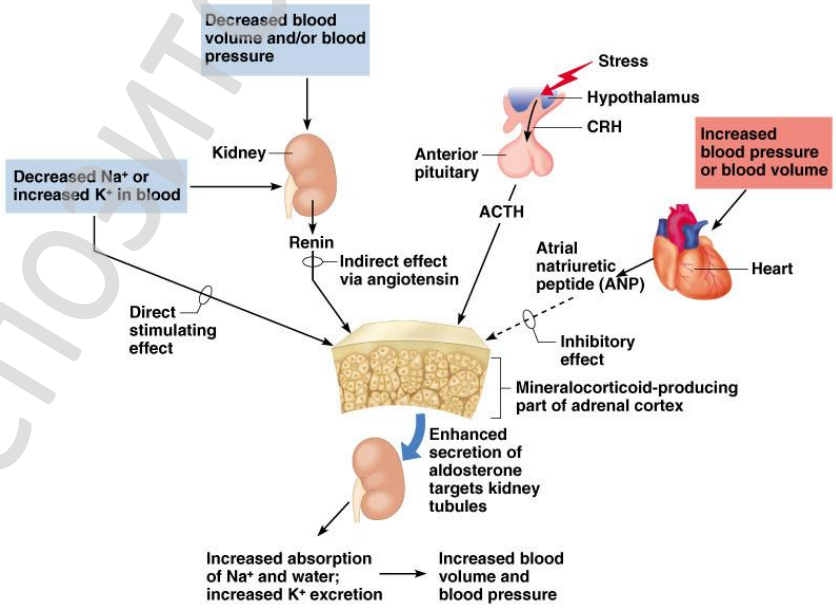


Figure 5.9 — Regulation of aldosterone production (from studylib.net)

Notes: CRH-corticotropin-releasing hormone; ACTH-adrenocorticotropic hormone.

The amount of secreted aldosterone depends not only on the content of sodium in blood plasma and intercellular fluid but also on the interrelation between the concentrations of sodium and potassium ions. The proof of this lies in the fact that intensified aldosterone secretion arises not only in sodium ion deficiency but also in the excessive content of potassium ions in the blood, and inhibited aldosterone secretion is observed not only after the administration of sodium in the blood, but also if the content of potassium in the blood is insufficient.

Changes of the volume of circulating blood are registered with the volume-receptors of the right atrium of the heart. Impulses arising in them influence the functions of the hypothalamus, the development of adrenocorticotropic hormone and secretion of aldosterone. The increased volume of circulating blood in this way inhibits aldosterone secretion. It results in the excretion of Na^+ (and water at the same time) with the urine, and, hence, in normalization of the volume of circulating blood and amount of fluids in the body. Decreased volume of circulating blood in the same way produces inverse alterations, i. e. increased secretion of aldosterone. It results in Na^+ and water retention in the organism.

Glucocorticoids (cortisol, cortisone, corticosterone) influence carbohydrate, protein and lipid metabolism. Cortisol is the most active among them. Glucocorticoids received their name because of their ability to increase the glucose level in the blood due to the stimulation of glucose formation in the liver.

The administration of glucocorticoids, cortisol in particular, even in sufficient protein nutrition the negative nitrogen balance occurs, which indicates the dominance of protein breakdown over protein synthesis. The expression of glucocorticoids leads to increased excretion of nitrogen metabolic products with the urine. The changes of protein metabolism under the influence of cortisol in different tissues are various: in lymphoid tissue — intensified disintegration of proteins occurs; in muscles — their synthesis is depressed; in the liver — the synthesis of proteins and especially enzymes is accelerated.

Glucocorticoids also influence fat metabolism. They intensify fat mobilization from the fat depot and its use during energy metabolism. Thus, these hormones influence metabolism in many ways, changing both energy and plastic processes.

Glucocorticoids stimulate the CNS, lead to insomnia, euphoria, general excitement.

In hypersecretion glucocorticoids promote the development of muscle weakness and atrophy of skeletal muscles, which is connected with the intensified disintegration of muscle proteins, and also with the decreased calcium level in the blood. They inhibit the body growth, development and regeneration of skeletal bones. Cortisol inhibits the production of hyaluronic acid and collagen, proliferation and activity of fibroblasts. All this results in dystrophy and loose skin, appearance of wrinkles.

Cortisol increases the sensitivity of the blood vessels of muscles to the action of vasoconstrictive agents and decreases the permeability of the endothelium. In large doses glucocorticoids increase cardiac output.

Glucocorticoids decrease inflammatory and allergic reactions. This forms the basis for the clinical application of glucocorticoids in chronic pneumonia, rheumatic disease, and other diseases. As glucocorticoids suppress the development of inflammation, they are called anti-inflammatory hormones.

Factors influencing the intensity of glucocorticoid formation. Such conditions as pain, trauma, blood loss, overheating, overcooling, some intoxications, infectious diseases, serious emotional experience intensify glucocorticoid secretion. The above states trigger increased secretion of adrenaline by the adrenal medulla. Adrenaline coming into the blood influences the hypothalamus and in its several cells induces intense formation of polypeptide — corticotropin-releasing factor, which promotes ACTH formation in the anterior lobe of the hypophysis (Figure 5.10). This hormone is the factor stimulating glucocorticoid formation in the adrenal gland. The removal of the hypophysis results in atrophy of the fascicular region of the adrenal cortex, and reduced secretion of glucocorticoids.

There are also daily fluctuations of glucocorticoid levels. The secretory rates of ACTH and cortisol are high in the early morning but low in the late evening.

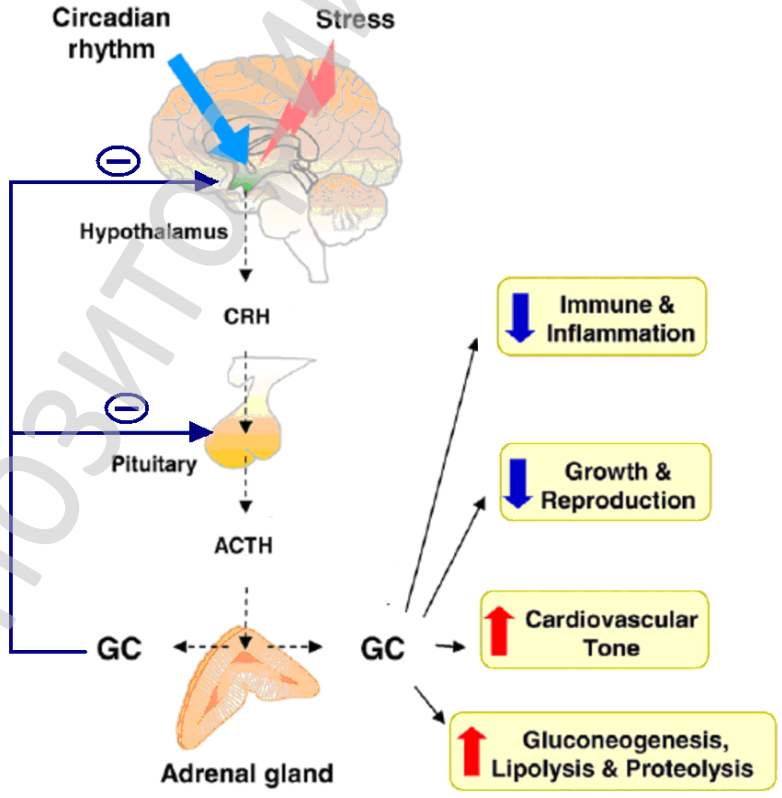


Figure 5.10 — Regulation of glucocorticoid production (from slideplayer.com)

Notes: GRH-corticotrophin-releasing hormone; ACTH-adrenocorticotropic hormone; GC-glucocorticoids.

Sex hormones of the cortex of the adrenal glands play an important role in the development of the genitals in childhood, i.e. at the stage of ontogenesis when the endocrine function of the sex glands is weak.

The role of these hormones after puberty is insignificant. However, at the old age, after the endocrine function of the sex glands is stopped, the cortical layer of the adrenal gland again becomes the only source of the secretion of sex hormones.

In hyperproduction of glucocorticoids, ***Cushing's disease*** or syndrome occurs, which is also known as hypercortisolism. The most common symptoms of this condition are: obesity and fatty tissue deposits, particularly around the midsection and upper back, in the face (moon face), and between the shoulders (buffalo hump); pink or purple stretch marks (striae) on the skin of the abdomen, thighs, breasts and arms; thinning, fragile skin; glucose intolerance; high blood pressure; cognitive dysfunction; anxiety; irritability; depression.

Hypoproduction of adrenal hormones is observed in patients suffering from the serious disease which was first described by Addison in 1855 and received the name of ***Addison's disease***. Its early signs are: darkening of the skin (hyperpigmentation) which is sometimes referred to as "bronzing" and usually develops in the areas of the skin that are exposed to direct sunlight (hands, neck, face); weakened cardiac muscle; asthenia (extreme fatigue caused by muscular or mental work); weight loss and decreased appetite; low blood sugar (hypoglycemia). The patient becomes sensitive to cold and pain stimulations, more susceptible to infections.

In tumors of the adrenal gland (hypernephroma) the production of hormones is increased and qualitatively changed: mainly two sex hormones are produced — male and female — which in norm are formed in small amounts. Therefore patients with hypernephroma have more or less well-marked changes of their sexual development. There are cases of hypernephroma in 3–4 year-old boys with early puberty who observed growing of facial and pubic hair. Hypernephroma in women was also described and was characterized by ischomenia, appearance of a beard and raspy male voice. The removal of the tumor liquidates these symptoms.

Role of the adrenal hormones in stress reaction and adaptation

Adaptation is a complex of physiological reactions which provide adjustment of the organism to the changing conditions of the environment. **Stress** is a non-specific reaction of the organism to the action of any important stimulus. When a stress response is triggered, it sends signals to the structures of the hypothalamus, hypophysis, adrenal glands, and vegetative nervous system. The stressor activates the secretion of adrenaline and noradrenaline, the hypothalamus stimulates the pituitary gland and it secretes adrenocorticotropic hormone, which

stimulates the secretion of glucocorticoids. The functional and metabolic effects of catecholamines, ACTH, and glucocorticoids increase the organism`s resistance.

Stressor is an external or internal environment stimulus that causes stress.

Stressors are subdivided into:

Physical - mechanical effects (injuries), various types of radiation (radioactive, electromagnetic, etc.), overheating, hypothermia, etc.;

Chemical -acids, alkalis, toxic substances;

Biological - microorganisms, viruses, toxins;

Psychical - strong positive and negative emotions, long-term negative emotions, pain, intense receiving of information.

Depending on duration, stress can be:

- acute stress;
- chronic stress.

Stages of stress reaction.

The alarm stage is an initial, short-term stage of stress characterized by emergency mobilization of the organism`s resources and uneconomical energy expenditure. The main hormones that provide the anxiety response are catecholamines.

The resistance stage is a long stage of stress when the organism gets adapted to stress conditions and is economically using energy and plastic resources. The basic hormones providing the stage of increased resistance are glucocorticoids.

The exhaustion stage occurs when the factors that caused the stress exceed the protective forces of the organism.

The hormones involved in stress reaction (catecholamines, glucocorticoids, thyroid hormones, somatopropin and others) provide adaptation reactions: activation of the nervous, muscular, cardiovascular and respiratory systems, mobilization of energy and structural resources of the organism. However, an intensive and prolonged stress reaction can contribute to the development of pathological processes (such as hypertension, gastrointestinal disorders, immune deficiency, endocrine dysfunction and others).

5.10. Incretion of the sex glands

The sex glands or reproductive glands are glands which produce the gametes (sex cells) — spermatozoa and ova — and perform the intrasecretory function, secreting sex hormones into the blood. These are of the two groups: male sex hormones — androgens (from Greek ***andros*** — man) and female sex hormones — estrogens (from Greek ***oestrus*** — estrus). Both are formed in the male and female sex glands, but not in identical amounts.

The physiological role of the sex hormones is to perform sex functions. These hormones are necessary for puberty, i. e. the stage of reproductive and

sexual development of the organism during which the secondary sex characteristics (features of pubertal organism that are not connected directly with sex activity but are typical distinction between male and female organisms) begin to develop and the capability of sexual reproduction is attained. In females the sex hormones play an essential role in the appearance of menstruation (Figure 5.11), normal pregnancy, and breast-feeding.

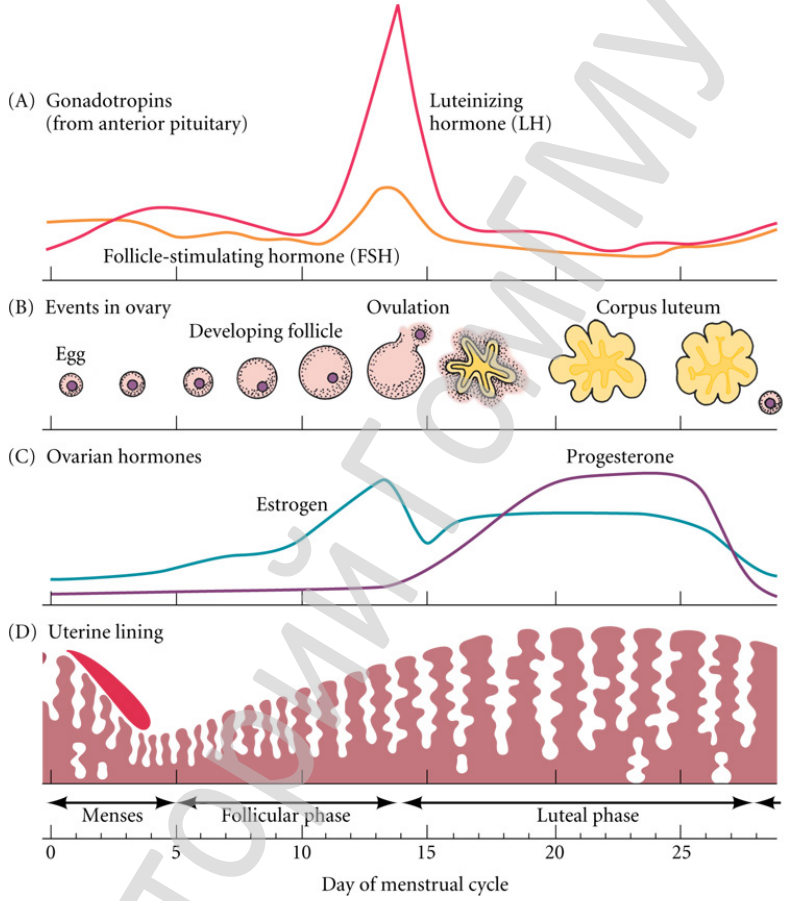


Figure 5.11 — Hormonal regulation of the menstrual cycle (from bianoti.com)

Changes in the organism caused by the insufficient secretory function of the sex glands. The removal of the sex glands is called castration. It is performed not only in animals, but sometimes in humans based on medical indications in some diseases. In some oriental countries there has been a tradition to castrate males for their employment as eunuchs (keepers of harems). In Western Europe castration of boys who sang in church choirs before their puberty was a means to keep their voice at a higher pitch.

After castration the formation of sex hormones in the organism does not stop completely. Androgens and estrogens continue to come into the blood and urine from the cortical layer of the adrenal gland, yet in much smaller amounts than with the presence of the sex glands. It implies a number of characteristic changes. If castration is performed long before puberty, it ends: the

penis, prostate gland, vagina, uterus do not reach a mature state and even regress (exposed to involution), and the secondary sex characteristics do not develop. If castration is done after puberty, the sex apparatus regresses to a lesser degree, and the secondary sex characteristics are partially present. The secondary sex characteristics which are present after castration of a person who has reached puberty are called independent sex characteristics, and those which are lost, — dependent.

The human skeleton is an independent sex characteristic since after the castration of pubertal males and females their typical features remain. The male dependent sex characteristics are: growth of facial and body hair, including underarm, abdominal, chest hair and pubic hair; enlargement of larynx (Adam's apple) and deepening of voice; increased stature, muscle mass, and strength; lower body fat percentage, in females — enlargement of breasts and erection of nipples; growth of body hair, most prominently underarm and pubic hair; changed distribution in weight and fat, i.e. more subcutaneous fat and fat deposits, mainly around the buttocks, thighs, and hips. After castration of males and females who have reached puberty, these characteristics regress till they are completely lost. If castration is done at an early age, the organism acquires asexual characteristics. In men this is expressed in the absence of facial hair, high-pitched voice, more expressed subcutaneous fatty layer. However, these characteristics should not be mixed with female secondary sex characteristics. Asexual characteristics do not depend on the incretion of the sex glands. To the list of human asexual characteristics longer extremities caused by late calcification of the cartilaginous regions of the tubular bones can also be related. This is absent in those people who are subjected to castration after the end of their growth period, but it is sharply marked if castration is performed at an early age, and also in eunuchoidism.

5.10.1. Regulation of the activity of the sex glands

The activity of the sex glands is regulated by the nervous system and the hormones of the hypophysis and epiphysis.

The central nervous system plays an important role in the maintenance of normal menstrual periods. The absence of menstrual periods is called amenorrhea. Primary amenorrhea is the failure to start having menstruation by the age of 16. Secondary amenorrhea is more common and refers to either temporary or permanent end of menstrual periods in a female who has menstruated normally before. Some of the causes of primary amenorrhea can also cause secondary amenorrhea—strenuous physical activity, excessive weight loss, use of antidepressants or tranquilizers, in particular. Missed periods are usually caused in adolescents by stress (emotional amenorrhea) and changes in the environment.

The neural regulation of the sex glands is carried out by the reflex changing the incretion of the hypophysis (gonadotropic hormones). Their administration into a growing organism accelerates and intensifies the development of the reproductive organs and secondary sex characteristics due to the stimulation of the endocrine function of the sex glands.

There are three gonadotropins: follicle-stimulating hormone (FSH), luteinizing hormone, and prolactin. FSH in females accelerates the development of *follicles* in the ovaries and their transformation into vesicular ovarian follicles; in males it accelerates the development of the spermatogenic tubules in the testicles (tubulae seminiferae) and spermatogenesis (Figure 5.12), i. e. the formation *of spermatozoa*, and also the development of *prostate*. Luteinizing hormone stimulates the development of intrasecretory elements in the testicles and ovaries and thus leads to the intensified formation *of the sex hormones* (androgens and estrogens). It stimulates ovulation in the ovaries and *progesterone* production, which is produced by corpus luteum, the yellow endocrine hormone-secreting body formed in the ovary at the site of a ruptured ovarian follicle. Prolactin, or the luteotropic hormone of the hypophysis stimulates progesterone formation and lactation.

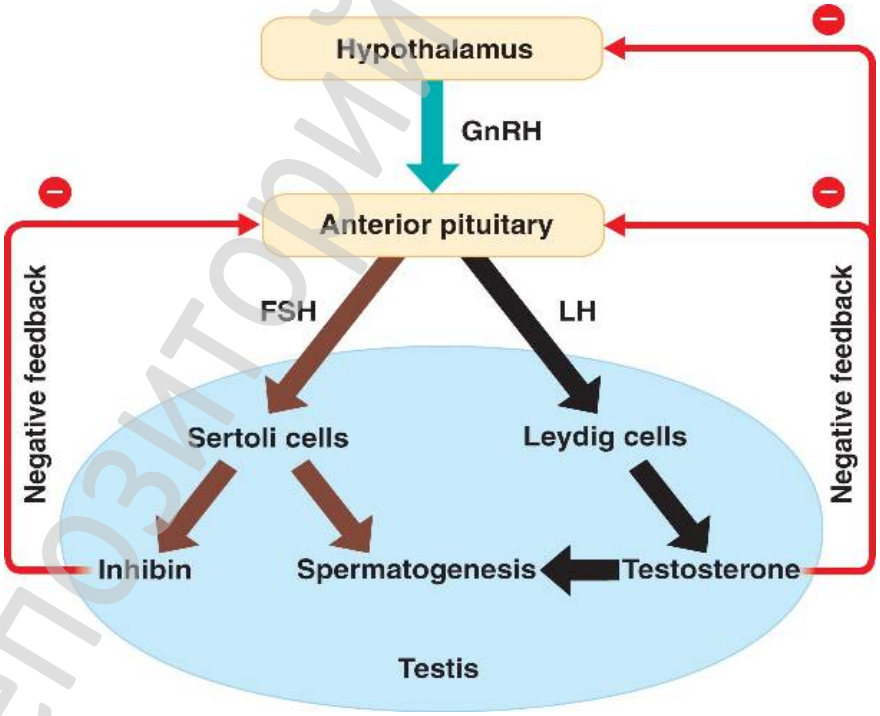


Figure 5.12 — Regulation of testosterone production and spermatogenesis (from studylib.net)

Notes: GnRH - Gonadotripin relasing hormone; FSH -follicle-stimulating hormone; LH- luteinazing hormone

After the removal of the hypophysis in immature animals, the development of the sex glands is slowed down and remains unfinished. The development of the

sex apparatus — penis, prostate gland, vagina, uterus and oviduct — is not completed either: the testicles do not produce spermatozoa, and in the ovaries follicles does not reach maturity and do not turn into vesicular ovarian follicles.

Opposite to the hypophysis, *melatonin* (epiphysis hormone) inhibits the development of the sex glands and their activity.

5.11. Hormones of the placenta

The placenta also participates in the hormonal regulation of pregnancy. It secretes *estrogen, progesterone,* and *chorionic gonadotropin.* Due to this, the surgical removal of the pituitary body or an ovary, if it is performed in an animal in the second half of pregnancy (i. e. when the placenta is well developed and produces a big amount of the above hormones), does not stimulate abortion. Placental hormones can replace the conforming hormones of the hypophysis and ovaries in this situation. By its action chorionic gonadotropin is close to the luteinizing hormone of the pituitary body. In pregnant women its high doses are excreted with the urine.

Review questions

1. What hormones are produced by the pancreas? What is the role of these hormones in the regulation of carbohydrate, fat, and protein metabolism? How is the secretion of pancreatic hormones regulated? What are hypo — and hyperglycemia states? What are their causes? What are the main symptoms of diabetes mellitus?

2. What hormone is produced by the epiphysis? What is its physiological role?

3. What are the hormones of the adrenal medulla? What is their physiological role? How is the secretion of the hormones of the adrenal medulla regulated?

4. What are the hormones of the adrenal cortex? What are the main effects of mineralocorticoids and glucocorticoids? How is the secretion of the hormone of the adrenal cortex regulated? What are the characteristic manifestations of hypo- and hypersecretion of the hormones of the cortex?

5. What is the physiological role of androgens? What are the mechanisms of the regulation of androgen secretion? What are the characteristic manifestations of insufficient secretion of androgens?

6. What is the physiological role of estrogens and progesterone? What are the mechanisms of the regulation of estrogen and progesterone secretion? What hormones does the placenta produce? What is their physiological role?

Multiple Choice Questions
PHYSIOLOGY OF THE ENDOCRINE SYSTEM

1. What kinds of action can hormones provide?
Variants of answer:
a) metabolic;
b) all the answers correct;
c) morphogenetic;
d) kinetic;
e) correcting.

2. Hormone receptors are localized …
Variants of answer:
a) in blood hemoglobin;
b) in the cells of target organs;
c) in the endothelial cells of the blood vessels;
d) in blood plasma;
e) within the surface layers of the skin.

3. Where are tropic hormones produced?
Variants of answer:
a) in the hypothalamus;
b) in the hypophysis;
c) in the adrenal glands;
d) in the pancreas;
e) in the thyroid gland.

4. Which hormones are produced in the anterior lode of the hypophysis?
Variants of answer:
a) oxytocin, vasopressin, melanotropin;
b) somatotropin, corticotropin, follicle-stimulating hormone;
c) prolactin, luteinizing hormone, lipotropin;
d) antidiuretic hormone, adrenaline, parathormone;
e) thyrotropin, glucocorticoids, mineralocorticoids.

5. Which hormone stimulates protein synthesis in muscles?
Variants of answer:
a) parathormone;
b) somatotropin;
c) antidiuretic hormone;

d) thyrotropin;
e) adrenaline.

6. Which hormone stimulates bone tissue growth?
Variants of answer:
a) somatotropin;
b) parathormone;
c) adrenaline;
d) thyrotropin;
e) glucocorticoids.

7. How does somatotropin activate the plastic processes in the organism?
Variants of answer:
a) it increases amino acid transport in cells;
b) it increases the synthesis of protein in ribosomes;
c) it activates the synthesis of the DNA, RNA;
d) it retains nitrogen in the body;
e) all the answers are correct.

8. During sleep the level of somatotropin secretion …
Variants of answer:
a) decreases;
b) increases;
c) does not change;
d) at first decreases, then increases;
e) at first increases, then decreases.

9. Which hormone stimulates estrogen synthesis?
Variants of answer:
a) thyrotropin;
b) somatotropin;
c) follicle-stimulating hormone;
d) aldosterone;
e) melanotropin.

10. Which hormone stimulates progesterone synthesis?
Variants of answer:
a) prolactin;
b) luteinizing hormone;
c) thyrotropin;
d) aldosterone;
e) melanotropin.

11. The production of which hormones does luteinizing hormone regulate?
Variants of answer:
a) prolactin, progesterone;
b) glucocorticoids;
c) mineralocorticoids;
d) thyroxin, calcitonin;
e) insulin, glucagon.

12. Which hormone stimulates the synthesis of glucocorticoids?
Variants of answer:
a) luteinizing hormone;
b) corticotropin;
c) antidiuretic hormone;
d) thyrotropin;
e) melanotropin.

13. Which hormone stimulates lactation?
Variants of answer:
a) parathormone;
b) aldosterone;
c) prolactin;
d) thyroxin;
e) calcitonin.

14. Which hormone influences skin pigmentation?
Variants of answer:
a) thyrotropin;
b) prolactin;
c) melanotropin;
d) thyroxin;
e) calcitonin.

15. Which hormone stimulates uterine contractions?
Variants of answer:
a) oxytocin;
b) progesterone;
c) somatotropin;
d) thyrotropin;
e) melanotropin.

16. Where is oxytocin synthesized?

Variants of answer:

a) in the neurohypophysis;
b) in the adrenal glands;
c) in the hypothalamus;
d) in the thyroid gland;
e) in the pancreas.

17. Where is oxytocin deposited?

Variants of answer:

a) in the adrenal glands;
b) in the thyroid gland;
c) in the adenohypophysis;
d) in the neurohypophysis;
e) in the pancreas.

18. What are the effects of oxytocin action?

Variants of answer:

a) stimulation of uterine contractions;
b) all the answers are correct;
c) contractions of the smooth muscles of the ducts of mammary glands;
d) regulation of the water-salt exchange;
e) regulation of drinking behavior.

19. The basic action of vasopressin is the stimulation of…

Variants of answer:

a) water reabsorption;
b) potassium reabsorption;
c) H^+ ion reabsorption;
d) protein reabsorption;
e) glucose reabsorption.

20. How does antidiuretic hormone influence the permeability of the collective tubules of the nephrons to water?

Variants of answer:

a) it decreases;
b) it increases;
c) it does not change;
d) at first it decreases, then increases;
e) at first it increases, then decreases.

21. How does antidiuretic hormone influence diuresis?

Variants of answer:

a) it decreases;
b) it increases;
c) it does not change;
d) at first it decreases, then increases;
e) at first it increases, then decreases.

22. What hormones are produced by the thyroid gland?

Variants of answer:

a) somatotropin, thyrotropin;
b) estriol, progesterone;
c) thyroxin, calcitonin;
d) glucocorticoids;
e) mineralocorticoids.

23. How does thyroxin influence metabolism?

Variants of answer:

a) it increases basal metabolism;
b) it decreases basal metabolism;
c) it does not influence metabolism;
d) at first it decreases basal metabolism, then increases it;
e) at first it increases basal metabolism, then decreases it.

24. Underactive thyroid function in adults causes the development of…

Variants of answer:

a) Addison's disease;
b) Basedow's disease;
c) myxedema;
d) Cushing's disease;
e) acromegaly.

25. Overactive thyroid function in adults causes the development of…

Variants of answer:

a) Addison's disease;
b) Basedow's disease;
c) myxedema;
d) Cushing's disease;
e) acromegaly.

26. The lack of which hormone in children causes inhibited growth without disproportionate constitution or any delay of intellectual development?

Variants of answer:

a) thyroxin, triiodthyronine;
b) somatotropin;
c) parathormone;
d) aldosterone;
e) insulin.

27. If a patient`s basal metabolism is increased by 45 %, then most likely this patient has the increased function of…

Variants of answer:

a) the epiphysis;
b) the beta cell of the pancreas;
c) the cortex of the adrenal glands;
d) the thyroid gland;
e) the pancreas.

28. Which hormone decreases the Ca^{2+} level in the blood?

Variants of answer:

a) parathormone;
b) thyroxin;
c) thyrocalcitonin;
d) adrenaline;
e) thyrotropin.

29. Which endocrine gland is the integrator of the immune and endocrine systems of the organism?

Variants of answer:

a) adenohypophysis;
b) neurohypophysis;
c) thymus;
d) adrenal glands;
e) thyroid gland.

30. Which endocrine gland produces hormones which influence the blood glucose level?

Variants of answer:

a) parathyroid gland;
b) pancreas;
c) parotid gland;

d) adrenal glands;
e) thyroid gland.

31. Which hormone decreases the blood glucose level?
Variants of answer:
a) thyroxin;
b) estradiol;
c) insulin;
d) aldosterone;
e) parathormone.

32. Which endocrine gland produces hormones which influence mineral exchange?
Variants of answer:
a) thymus;
b) ovary;
c) adrenal glands;
d) pancreas;
e) all the answers are correct.

33. How does aldosterone influence the formation of urine?
Variants of answer:
a) it decreases the reabsorption of Na + into the blood;
b) increases the reabsorption of Ca^{2+} into the blood;
c) increases the reabsorption of Na + into the blood;
d) increases the reabsorption of protein into the blood;
e) decreases the reabsorption of glucose into the blood.

34. Which hormone stimulates the synthesis of proteins in the liver?
Variants of answer:
a) follicle-stimulating hormone;
b) adrenaline;
c) cortisol;
d) adrenaline;
e) parathormone.

35. Which hormone has the anti-inflammatory effect?
Variants of answer:
a) hydrocortisone;
b) aldosterone;
c) thyroxin;
d) adrenaline;
e) glucagon.

36. Which hormone stimulates gluconeogenesis?

Variants of answer:

a) cortisol;
b) aldosterone;
c) oxytocin;
d) adrenaline;
e) calcitonin.

37. The atrophy of the cortex of the adrenal glands causes the development of…

Variants of answer:

a) Addison's diseases;
b) Basedow's diseases;
c) myxedema;
d) Cuching's diseases;
e) diabetes mellitus.

38. Which hormone regulates the production of glucocorticoids?

Variants of answer:

a) oxytocin;
b) somatotropin;
c) adrenocorticotropic hormone;
d) prolactin;
e) aldosterone.

39. How do big dozes of adrenaline influence the formation of urine?

Variants of answer:

a) it decreases;
b) it increases;
c) it does not change;
d) at first it decreases, then it increases;
e) at first it increases, then it decreases.

40. How does adrenaline influence the eye pupil?

Variants of answer:

a) adrenaline narrows it;
b) adrenaline enlarges it;
c) adrenaline does not influence the eye pupil;
d) at first adrenaline narrows and then enlarges it;
e) at first adrenaline enlarges and then narrows it.

41. Which hormone decreases the secretion of gastric juice?

Variants of answer:

a) prolactin;
b) noradrenalin;
c) thyroxin;
d) calcitonin;
e) melanotropin.

42. Which hormone decreases the motor activity of the intestines?

Variants of answer:

a) luteinizing hormone;
b) noradrenalin;
c) glucagons;
d) prolactin;
e) aldosterone.

43. Which hormone regulates male sexual behavior?

Variants of answer:

a) aldosterone;
b) testosterone;
c) insulin;
d) prolactin;
e) calcitonin.

44. Which hormones are produced by the ovaries?

Variants of answer:

a) somatotropin, thyrotropin;
b) estriol, progesterone;
c) thyroxin, calcitonin;
d) glucocorticoids;
e) mineralocorticoids.

45. Which hormones increase the blood glucose level?

Variants of answer:

a) parathormone, prolactin;
b) thyroxin, cortisol, adrenaline, glucagon;
c) aldosterone, insulin, calcitonin;
d) oxytocin, antidiuretic hormone;
e) luteinizing hormone, follice-stimulating hormone.

46. Which hormones play an important role in the adaptation of the organism to stressful factors?

Variants of answer:

a) glucagon, mineralocorticoids;
b) catecholamines, glucocorticoids;
c) glucocorticoids, testosterone, estrogens;
d) parathormone, prolactin;
e) luteinizing hormone, follicle-stimulating hormone.

47. Which hormones participate in the regulation of protein metabolism?

Variants of answer:

a) adrenocorticotropic hormone, antidiuretic hormone, parathormone;
b) aldosterone, glucagon, prolactin;
c) testosteron, insulin, somatotropin, estrogens, thyroid hormones;
d) follice-stimulating hormone, luteinizing hormone, insulin
e) all the answers are correct.

48. The elevated glucocorticoid level leads to decreased production of adrenocorticotropic hormone by the adenohypophysis, which is an example of…

Variants of answer:

a) positive feedback;
b) negative feedback;
c) starting action;
d) Addison's diseases;
e) Graves's disease.

49. The elevated estrogen level in the blood causes increased secretion of oxytocin, which is an example of…

Variants of answer:

a) positive feedback;
b) negative feedback;
c) morphogenetic effect;
d) metabolic effect;
e) Addison's disease.

50. Where is natriuretic hormone produced?

Variants of answer:

a) in the posterior lode of the hypophysis;
b) in the right atrium of the heart;
c) in the hypothalamus;

d) in the placenta;
e) in the pancreas.

51. Acromegaly is caused by excessive amounts of…
Variants of answer:
a) somatostatin;
b) growth hormone;
c) aldosterone;
d) insulin;
e) thyroxin.

52. The posterior pituitary gland secretes…
Variants of answer:
a) oxytocin;
b) prolactin;
c) thyroid-stimulating hormone;
d) melanocyte-stimulating hormone;
e) follicle-stimulating hormone.

53. The greatest stimulator for the secretion of antidiuretic hormone is …
Variants of answer:
a) hyperosmolarity;
b) hyponatremia;
c) hypotension;
d) hypovolemia;
e) hypervolemia.

54. Iodine uptake is found in the following organ …
Variants of answer:
a) ovary;
b) thyroid gland;
c) parathyroid gland;.
d) salivary gland;
e) mammary gland.

55. Calcitonin is secreted by…
Variants of answer:
a) the thyroid gland;
b) the parathyroid gland;
c) the adrenal glands;
d) the ovaries;
e) the adenohypophysis.

56. Which of the following hormones is a peptide hormone?
Variants of answer:
a) parathormone;
b) adrenaline;
c) cortisol;
d) thyroxine;
e) estrogen.

57. A true fact about the action of insulin is that it …
Variants of answer:
a) causes gluconeogenesis;
b) is not useful for growth and development;
c) is required for the transport of glucose, amino acids;
d) it is a catabolic hormone;
e) all the answers are correct.

58. Aldosterone synthesis is inhibited by …
Variants of answer:
a) renin;
b) endothelin;
c) dopamine;
d) endorphin;
e) hypernatremia**.**

59. The hormone secreted by the adrenal medulla is:
Variants of answer:
a) glucagon;
b) cortisol;
c) noradrenaline;
d) insulin;
e) aldosterone.

60. Melatonin is secreted by …
Variants of answer:
a) the hypothalamus;
b) the adrenal cortex;
c) the pineal gland;
d) the melanocytes;
e) the adrenal medulla.

CORRECT ANSWERS
HUMORAL REGULATION OF PHYSIOLOGICAL FUNCTIONS

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

UNIT 6
PHYSIOLOGY OF RESPIRATION

6.1. External respiration

A set of processes providing the O_2 intake by the organism, its delivery and consumption by tissues and excretion of the respiration end-product CO_2 into the environment, is called **respiration**.

The complex process of gas exchange with the environment is formed by a number of consecutive processes (Figure 6.1).

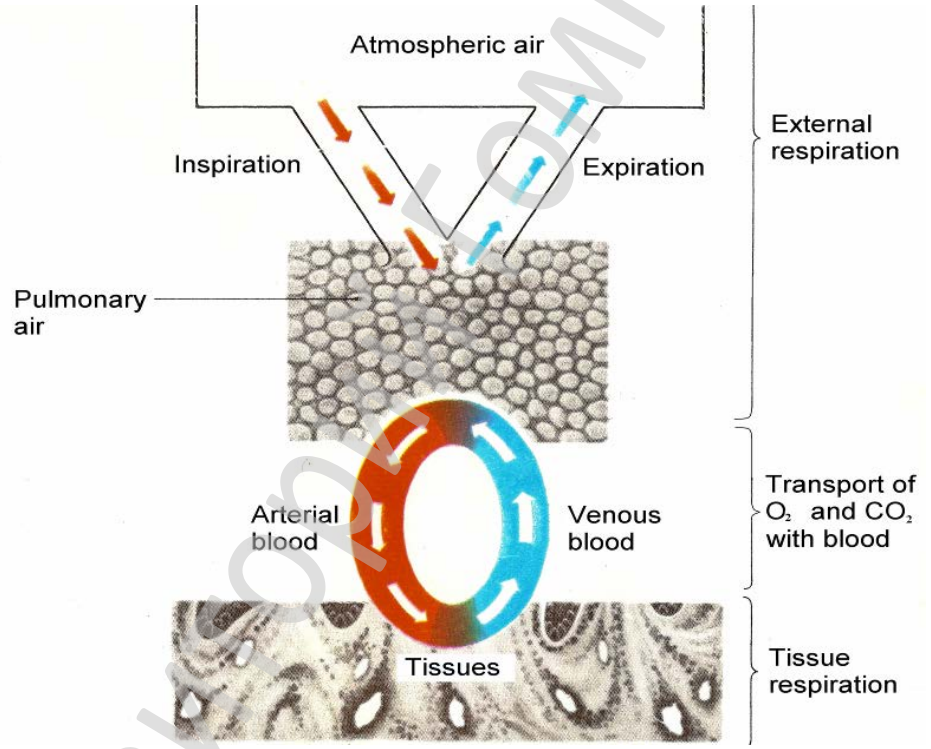


Figure 6.1 — Process of gas exchange between the environment and the organism (by Korobkov A. V., Chesnokova S. A., 1986)

***External respiration (pulmonary)*:**

1. Gas exchange between pulmonary air and atmospheric air (lung ventilation).

2. Gas exchange between pulmonary air and the capillary blood of pulmonary circulation.

Internal respiration:

3. O_2 and CO_2 transport in the blood.

4. Gas exchange between blood and cells.

5. Tissue respiration i. e. O_2 consumption and CO_2 excretion during metabolism (in mitochondria).

In humans the function of external respiration and renewal of the gas composition of blood is performed by the the respiratory passageways or ***respiratory tract*** and the ***lungs***.(Figure 6.2).The respiratory passageways include *the upper respiratory tract* (nasal cavity, pharynx and the portion of the larynx above the vocal cords) and *the lower respiratory tract* (the portion of the larynx below the vocal cords, the trachea, bronchi and bronchioles).

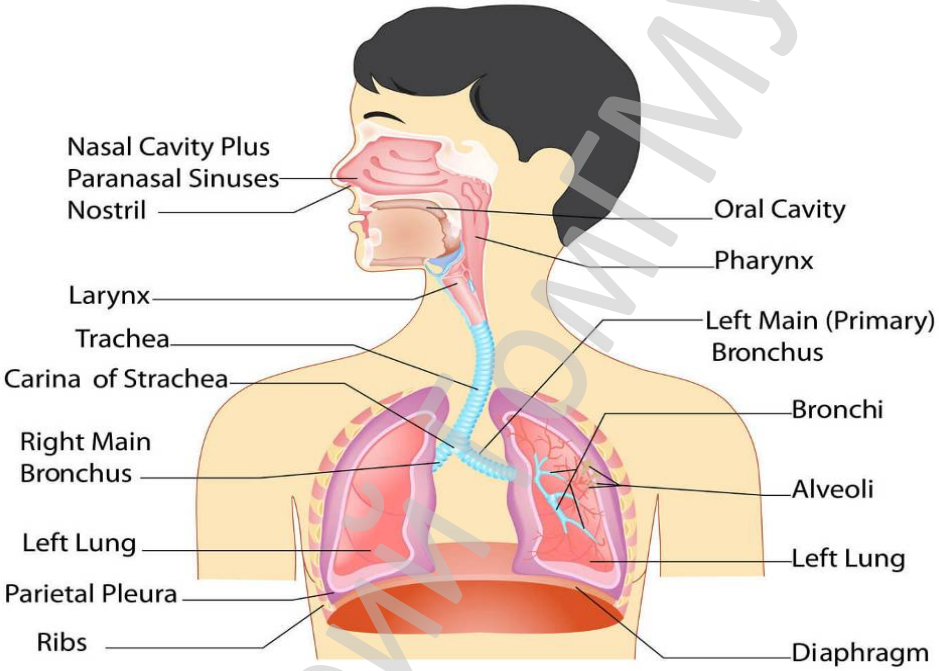


Figure 6.2 — Anatomy of the respiratory system (from studylib.net)

The trachea is divided into the right and left main bronchi (tracheal bifurcation). From tracheal bifurcation the respiratory, or tracheobronchial tree originates. At each division point (generation) one airway branches into two or more smaller airways. The human respiratory tree may consist on average of 23 generations.

The trachea, bronchi, bronchioles, and terminal bronchioles form the *conductive zone* (conducts gases into and out of the lungs and includes the respiratory passageways up to the 16th generation).

The transitory zone includes the respiratory bronchioles (from the 17th to 19th generations). The respiratory bronchioles have few alveoli, but these alveoli make only 2% of their general amount).

The respiratory zone is formed by the alveolar ducts and alveolar sacs (from the 20th to 23th generations), which includes the main number of alveoli and where the gas exchange between air and the blood takes place.

The total number of alveoli is about 300 millions, their average diameter is 0.33 mm.

A number of adaptive features of the lung structure allow to realize the gas exchange processes:

1. Presence of the ***air and blood channel***, separated by the thinnest (0.004 mm) membrane consisting of a double layer — an alveolar itself and a capillary. Through this aerohematic barrier gases diffusion occurs.

2. The ***extensive respiratory area of the lungs is 50–90 m²***.

3. Presence of the special ***small (pulmonary) circle of blood circulation***.

4. Presence of ***elastic tissue*** in the lungs ensuring lung expansion and compression during inspiration and expiration. The lungs have the property of elastic recoil, i. e. the rebound of the lungs after their stretching by inhalation.

5. **Presence of support cartilage tissues** as of the cartilage bronchi in the airways. It prevents collapse of the airways and promotes fast and easy passage of air.

Non-respiratory functions of the lungs

The primary function of the lungs is gas exchange. However, the lungs perform several important *non-respiratory functions*.

1. Protective function. The lungs are a barrier between the internal and external environment. In the lungs many immune factors are produced (interferon, lysozyme, immunoglobulins, lactoferrin) which protect the organism from infections.

2. Excretory. During respiration not only carbon dioxide, but also other substances are excreted (acetone, ethanol). Besides, about 500 mL of water is removed due to evaporation from the alveolar surface per day.

3. Blood deposition. The lungs are the physiological depot of blood.

4. Regulation of the aggregate state of blood. When blood passes through the small (pulmonary) circle of circulation, small clots and emboli are removed. The lungs contain a large number of basophils containing heparin. Also, some coagulation and anticoagulation factors are synthesized in the lungs (thromboplastin, factors II, VIII, etc.).

5. Production of biologically active substances. This function is provided by the cells of the diffuse endocrine system which are present in the lungs.

6. Metabolic. In the endothelial cells of the pulmonary capillaries the transformation of biologically active substances takes place. Such substances as serotonin, bradykinin, noradrenaline are exposed to absorption and ferment transformation in the lungs. On the internal surface of the pulmonary capillaries a large amount of angiotensin-converting enzyme is localized, which catalyzes the process of the transformation of angiotensin I into angiotensin II.

7. The lungs participate in thermoregulation (due to water evaporation from the alveolar surface).

8. The lungs play a role in the regulation of the acid-base balance of blood (mainly due to CO_2 excretion).

6.2. Respiratory movements

Alveolar ventilation necessary for gas exchange is carried out due to the constant alternation of inspiration and expiration. During inspiration the air saturated with O_2 gets into the alveoli. During expiration, the air poor in O_2 but rich in CO_2 is released from the alveoli. The phase of inspiration and the following phase of expiration make the ***respiratory cycle*.**

Air movements are caused by the alternate increase and decrease of the volume of the thorax.

The mechanism of inspiration. Inspiration is ***an active* process**.

During inspiration, the diaphragm contracts and pulls downward while the muscles between the ribs contract and pull upward. This increases the size of the thoracic cavity in the vertical, sagital, frontal planes and decreases the pressure inside. As a result, air rushes in and fills the lungs. During expiration, the diaphragm relaxes, and the volume of the thoracic cavity decreases, while the pressure within it increases. As a result, the lungs contract and the air is forced out.

Rib movement. The ribs form mobile connections with the vertebral bodies and transverse processes of vertebras. As the ribs go upward, the size of the thorax increases in the anteroposterior and lateral dimensions. The elevation of the ribs is caused by contractions of ***inspiration muscles***. They include: ***external intercostal, internal intercartilaginous muscles*** (Figure 6.3).

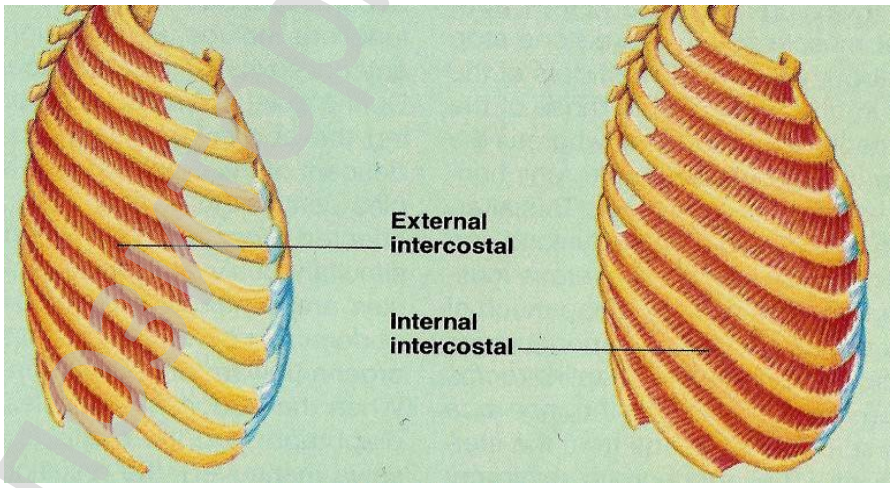


Figure 6.3 — Intercostal muscles (by Elaine N. Marieb, 1989)

The movement of the inferior ribs has a big influence on the volume of the thorax, that is why the inferior lobes of the lungs are ventilated better than the superior ones.

In a healthy young ***male*** the difference between the circumference of the thorax during inspiration and expiration ***(thoracic excursion) is 7–10 cm***, ***in a***

healthy young female — 5–8 cm. Forced respiration involve *auxiliary inspiration muscles:*

- greater and smaller pectoral muscles;
- scalene muscle;
- sternocleidomastoid muscle;
- trapezius muscle, etc.

Movement of the diaphragm. The diaphragm has the form of a dome protruding into the thoracic cavity. During expiration it adjoins the internal wall of the thorax. During inspiration the diaphragm flattens as a result of ***contractions of its muscle fibers*** (Figure 6.4).

In a person at rest expiration is *passive*.

The mechanism of expiration is ensured by:

- weight of the thorax;
- elasticity of the costal cartilages;
- elasticity of the lungs;
- pressure of the organs of the abdominal cavity on the diaphragm.

The following expiration muscles take part in forced respiration: internal ***intercostal muscles*** and *auxiliary expiration muscles* (*backbone flexors, abdominal muscles).*

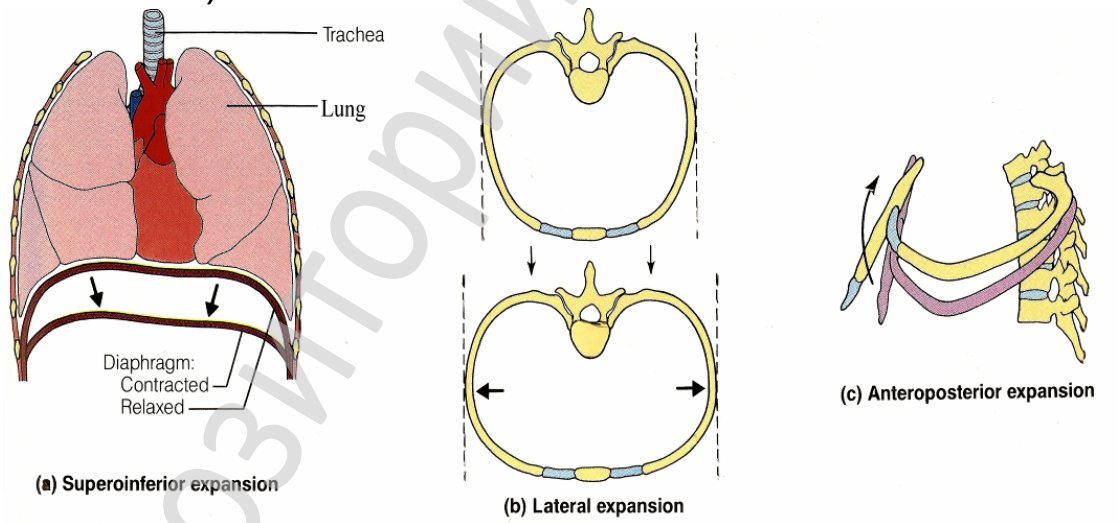


Figure 6.4 — Changes in the thoracic volume during breathing (by Elaine N. Marieb, 1989)
Notes: (a-c) Ways in which the volume of the thorax is increased during inspiration. The diaphragm descends as it contracts, increasing the superiorinferior dimension (a). Due to the contraction of the external intercostal muscles the ribs are elevated, the thorax expands laterally (b) and in the anteriorposterior plane (c).

Types of respiration. There are 3 types of respiration depending on which component (elevation of the ribs or lowering of the diaphragm) causes an increase in the thoracic volume:

- Thoracic (the main mechanism is *rib movements*).

- Abdominal (the m*ovement of the diaphragm*).
- Mixed.

To a greater extent the type of respiration depends on age (the mobility of the thorax increases), clothes, profession. As abdominal respiration becomes difficult during the last months of pregnancy, at this period thoracic respiration is involved.

The abdominal type of respiration is the most effective:

- lung ventilation is the deepest.
- return of venous blood to the heart is ensured.

Abdominal respiration prevails in physical workers, opera singers, etc. After birth a baby has abdominal respiration, by the age of 7 it is changed into thoracic. There are also gender differences in the types of respiration. In men the abdominal type prevails, and in women – thoracic.

6.3. Intrapleural pressure and its change during respiration

The lungs are covered with the *visceral pleura, a*nd the internal surface of the thoracic cavity is covered with the *parietal pleura*. A thin film of serous fluid fills the space between the two pleurae. The narrow gap (5–10 μm) between the parietal and the visceral pleura is known as the pleural cavity or space.

If to insert a needle into the pleural cavity and connect it with a water manometer, the pressure there will be:

- *during inspiration — 6–8 cm H_2O (4–5 mm Hg);*
- *during expiration — 3–5 cm H_2O (2–3 mm Hg)* ***lower than atmospheric pressure***.

This difference between the pressure in the pleural cavity and atmospheric pressure is usually called ***intrapleural pressure (also called intrathoracic pressure).***

Negative intrapleural pressure is caused by the ***elastic recoil*** of the lungs***, i. e. a tendency of the lungs to collapse.***

During inspiration an increase of the negative pressure in the thoracic cavity leads to an increase of negative intrapleural pressure (Figure 6.5).

The accumulation of liquid in the pleural cavity is interfered by the lower oncotic pressure of pleural liquid (it has less amount of protein) than in plasma.

The elastic recoil of the lungs is caused by 3 factors:

1. Surface tension of the liquid covering the internal surface of the alveoli.
2. Elasticity of the alveolar walls (contain elastic fibers).
3. Tone of bronchial muscles.

At liquid–air interfaces there are ***intermolecular forces (forces of surface tension)***. Influenced by these forces the alveoli tend to collapse. The forces of surface tension make 2/3 of the elastic recoil of the lungs.

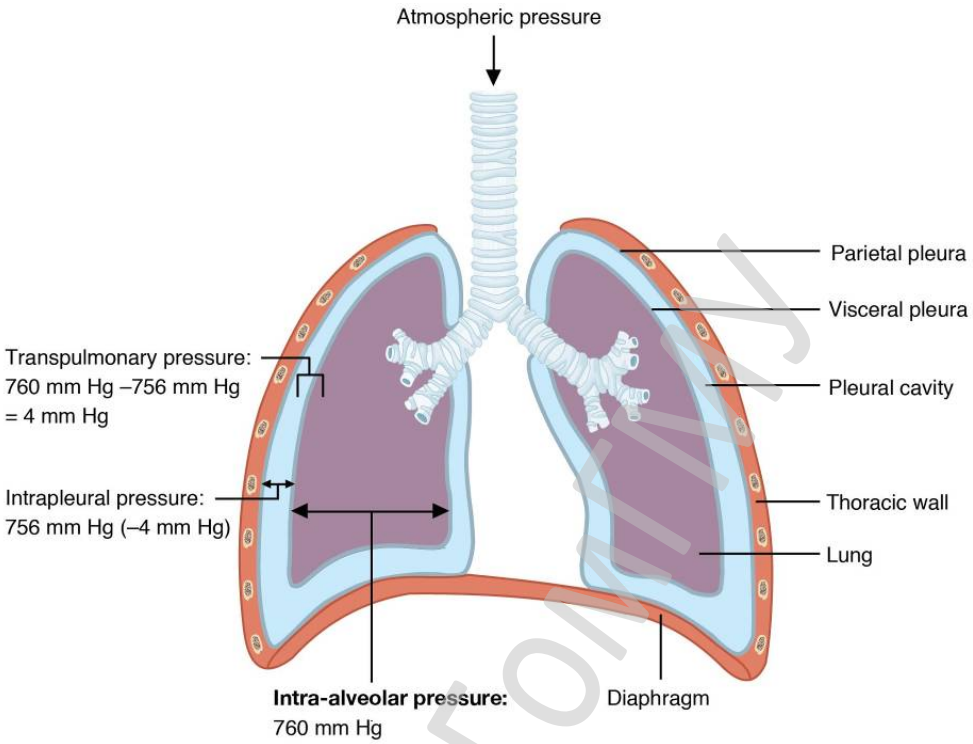


Figure 6.5 — Intrapleural and transpulmonary pressures (from picgalleria.com)

If the internal surface of the alveoli was covered with a water solution, the surface tension would have to be 5–8 times higher. In these conditions alveolar collapse would be observed.

A strong influence on the volume of pulmonary compliance and elastic recoil is performed by **surfactant** — a substance composed of phospholipids and proteins, which are formed by the pneumocytes of the 2^{-nd} type. The surfactant is located on the internal surface of the alveoli.

The role of the surfactant:

1) it reduces superficial tension in the alveoli and thus increases lung compliance;

2) it stabilizes the alveoli, interferes adhesion of their walls (interfering atelectasis);

3) it reduces resistance to gas diffusion through the wall of the alveolus;

4) it interferes pulmonary edema by decreasing the force of superficial tension in the alveoli;

5) it facilitates the lung widening in the first inspiration of a newborn;

6) it promotes activation of phagocytosis by alveolar macrophages.

If the size of the alveolus is reduced, the molecules of the surfactant become closer and the surface tension is reduced — the alveolus does not collapse (Figure 6.6).

The expansion of the alveoli leads to an increase of their surface tension, which strengthens the elastic recoil of the lungs.

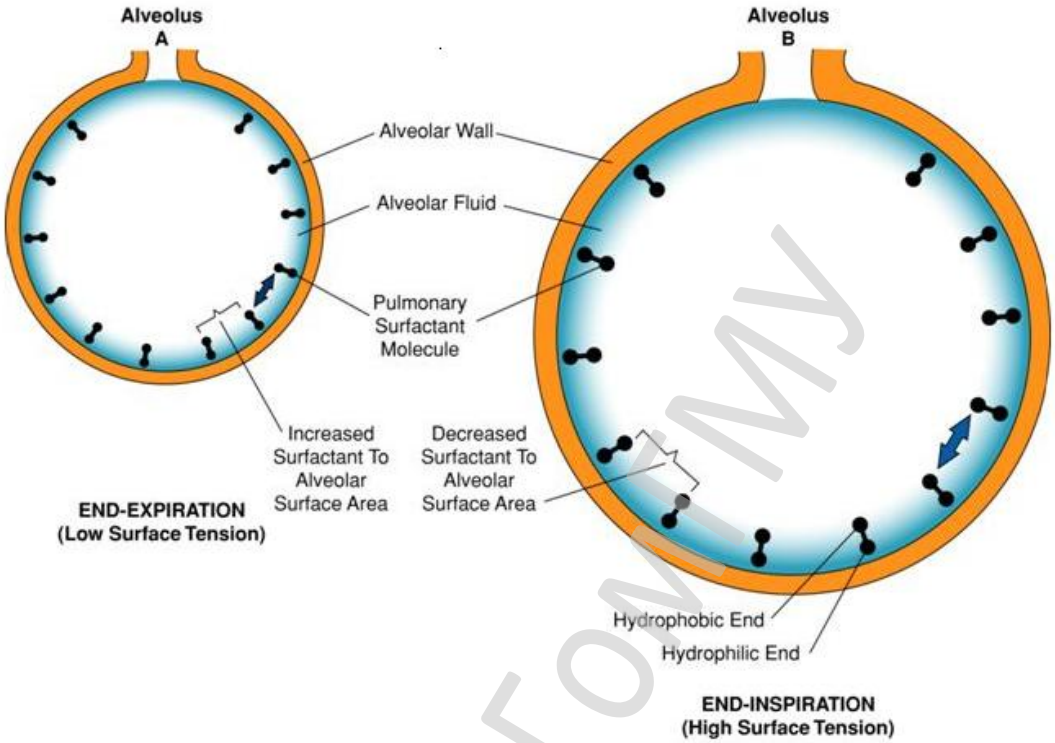


Figure 6.6 — Pulmonary surfactant regulates alveolar surface tension (from studylib.net)

Surfactant deficiency results in collapse of a great number of alveoli — atelectasis, or absence of ventilation of large portions of the lungs , i. e. incomplete expansion of the lungs.

In newborns the surfactant is necessary for the lungs to expand during respiration.

The abnormal presence of air in the pleural cavity (through the damaged thorax or lung occurring as a result of disease or injury) is called ***pneumothorax***. Due to their elasticity the lungs collapse into 1/3 of their volume.

6.4. Lung ventilation. Pulmonary volumes

Thus, there are 4 initial respiratory volumes and 4 capacities of the lungs (Figure 6.7):

1. ***Tidal (respiratory) volume (TV)*** — the amount of air inspired and expired by a person when extra effort is not applied (quiet respiration) (***0.3–0.9 L, approximately 500 mL***).

2. ***Inspiratory reserve volume (IRV)*** — the amount of air which can be inspired after quiet inspiration (***1.5–2.0 L***).

3. ***Expiratory reserve volume (ERV)*** — the amount of air which can be expired after quiet expiration (***1.0–1.5 L***).

4. ***Residual volume*** — the amount of air remaining in the lung after maximal expiration (***1.0–1.5 L***).

5. ***Vital capacity of the lungs (VCL)*** = TV + IRV + ERV (0.5 + 1.5 + 1.5) = 3.5 L (***3.5–5 L***). It indicates the force of respiratory muscles, lung compliance, the area of the respiratory membrane.

6. ***Functional residual capacity (FRC)***, or alveolar air — the amount of air remaining in the lungs after quiet expiration (***2.5 L***).

7.***Total lung capacity (TLC)*** — the amount of air contained within the lungs in the maximal inhalation (***4.5–6.0 L***).

8. ***Inspiratory capacity (IC)*** includes the tidal volume + inspiratory reserve volume (***2.0 L***).

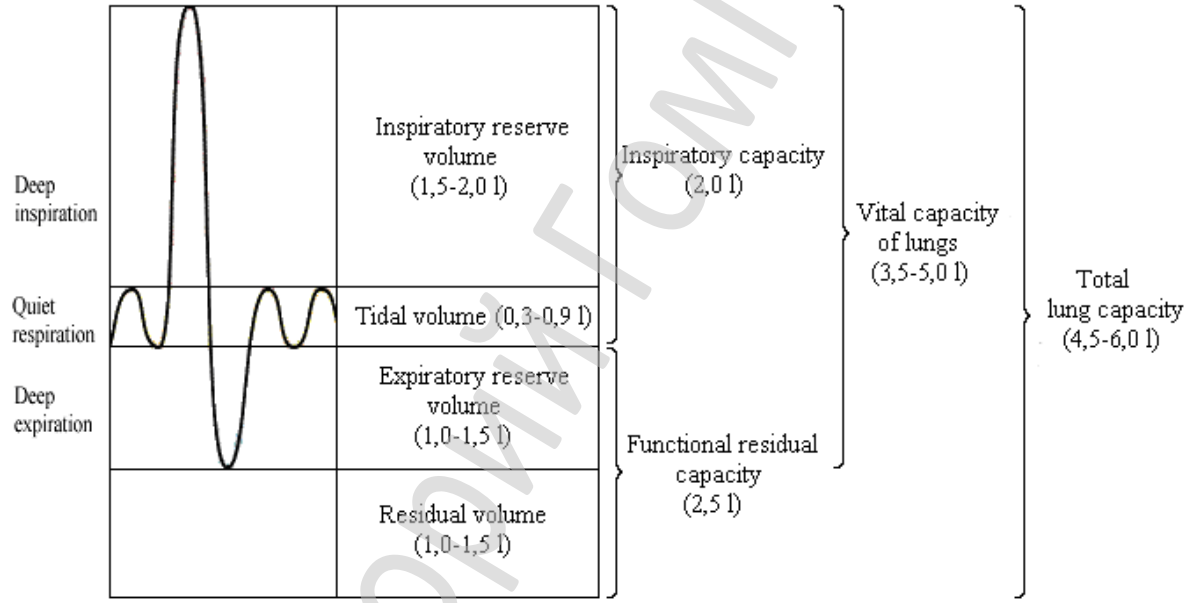


Figure 6.7 — Spirographic record. Pulmonary volumes and capacities

VCL determines the maximal volume of air which can come or go out of the lungs during one inspiration or expiration. This is the indicator of the mobility of the lungs and the thorax.

Factors influencing VCL:

- ***Age***. VCL declines after 40 (due to decreased lung elasticity and thoracic mobility).
- ***Sex***. In women VCL on average is in 25 % lower than in men.
- ***Body size***.
- ***Body position***. In the vertical position it is higher than in horizontal (due to the greater filling of the pulmonary blood vessels).
- ***Degree of physical activity***. In physically fit people VCL increases (especially in swimmers).

6.5. Dead space

There are two types of dead space:

- Anatomic dead space.
- Functional (physiological) dead space.

Dead space refers to the space in which oxygen (O2) and carbon dioxide (CO2) gasses are not exchanged in the respiratory tract. ***Anatomic dead space*** specifically refers to the volume of air located in the segments of the respiratory tract that are responsible for air conduction to the alveoli and respiratory bronchioles but do not take part in the process of gas exchange itself (nasal and oral cavities, larynx, trachea, bronchi, bronchioles, alveolar ways).

Its physiological roles are:

1. Air cleaning (the mucous membrane catches fine particles of dust, bacteria).
2. Air humidifying (secret of the epithelial glandular cells).
3. Air warming (the temperature of expired air is approximately 37 °C).

The ***volume of anatomic dead space*** is on average 150 ml (***140–170 mL***).

Therefore, out of 500 mL of the respiratory volume only 350 mL will get into the alveoli. The volume of alveolar air is 2,500 mL. ***The pulmonary ventilation coefficient thus is 350: 2,500 = 1/7***, i. e. as a result of 1 respiratory cycle only 1/7 part of air of FRC is refreshed, or its complete refreshing occurs of not less than 7 respiratory cycles.

Physiologic (functional) **dead space** is the sum of anatomic and alveolar dead spaces. *Alveolar dead space* refers to the volume of air in the alveoli that are ventilated but not perfused, and thus gas exchange does not take place. Usually such alveoli are few, therefore the volume of anatomic dead space is almost equal to functional dead space.

6.6. Alveolar ventilation

The average normal respiratory rate in an adult is 14 ***(12–18) breaths per minute***.

In children it is more frequent: in infants — 30–40 breaths per minute, ***in newborns — 40–55 per minute***.

The respiratory minute volume (RMV), or minute ventilation – the minute volume of breathing, i. e. the total volume of gas inhaled (inhaled minute volume) or exhaled (exhaled minute volume) from the lungs per minute.

The respiratory minute volume can be calculated by the following formula:

$$RMV = TV \times RR;$$

where TV is the tidal volume and RR is the respiratory rate per minute.

For example,

$$\textbf{RMV} = 500\ mL \times 14 = \textbf{7 L}.$$

Respiratory minute volume at rest is 6–8 L/min. During physical activity RMV can increase up to 120 L/min.

Deep and infrequent respiration is more effective than superficial and frequent respiration.

Minute ventilation is regulated so that it can provide constant gas composition of alveolar air.

If normal RMV is 7 L/min, but the respiratory rate is too frequent (35 breaths per minute) and superficial (TV = 0.2 L), mainly the dead space will be ventilated and inspired air will not reach the alveoli. Such a condition is dangerous for life.

Alveolar ventilation is the total volume of new air reaching the alveoli during a breath per minute. It can be calculated by the formula:

$$V_A = RR \times (TV\text{-}V_D);$$

where V_A is alveolar ventilation per minute, RR — respiratory rate per minute; TV — tidal volume; V_D — dead space volume.

Normally, alveolar ventilation is 4.2–5.6 L/min.

One of the indicators of the respiratory system reserves ***is the maximal ventilation of lungs (MVL) or maximal voluntary ventilation*** — volume of air passing through the lungs within a certain time interval during respiration with the maximal possible frequency and depth.

MVL varies within 120–170 L/min and depends on age, sex, body size.

Alongside with the respiratory volumes and capacities, some additional parameters are determined for the evaluation of pulmonary function.

Forced vital capacity (FVC) is defined as the amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible (which depends on height, weight, and other factors). *The normal difference between VCL and FVC is 100–300 mL.* In bronchial obstruction FVC is increased.

Forced expiratory volume (FEV1) refers to the maximal volume of air that can be exhaled during a forced breath per second. It averages around three liters, which makes 70–80 % of VCL (the parameter FEV1/FVC or FEV1 %, Tiffeneau index). This parameter is decreased in bronchial obstruction.

Peak expiratory flow (PEF) or peak expiratory flow rate is the maximal flow rate of air achieved during a forced expiration. It is usually measured with a peak flow meter.

In clinical practice pneumotachometers are widely used. They allow to perform continuous registration of the flow rate of expired air during expiration of forced vital capacity. Due to this it is possible to evaluate the parameters of **forced expiratory flow (FEF)** — the flow rate of air coming out of the lungs during the middle portions of forced expiration which is determined at the moments of expiration of the deferent fractions of the forced vital capacity. The usual intervals are 25, 50, and 75 % of FVC (FEF 25 %, FEF 50 %, and FEF 75 %).

The «flow — volume» curve reflects the change of the expiratory flow during the process of forced expiration (Figure 6.8). The form of the curve has a certain diagnostic value. The part of the curve corresponding to 0–25 % of FVC depends on the passage of air through the large bronchi, trachea, and upper airways. The part from 50 to 85 % of FVC reflects the passage through the distal bronchi and bronchioles.

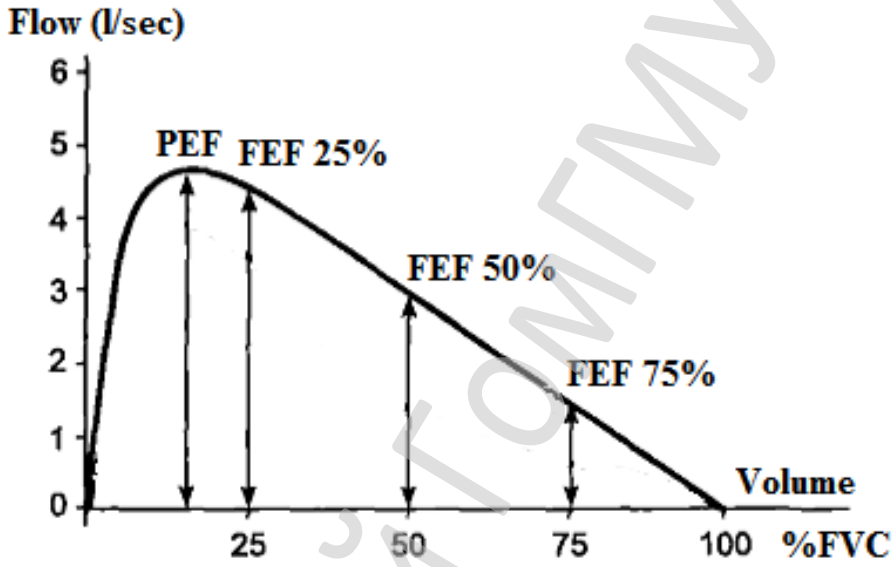


Figure 6.8 — The «flow–volume» curve in a healthy person

Note: PEF — peak expiratory flow; FEF 25 % — forced expiratory flow during expiration of 25 % of FVC; FEF 50 % — forced expiratory flow during expiration of 50 % of FVC; FEF 75 % — forced expiratory flow during expiration of 75 % of FVC

The determination of all the above listed parameters is used for the evaluation of the function of external respiration.

There are two basic types of disorders of external respiration.

1) Obstructive type is characterized by the increased resistance of the respiratory passageways for air flow. They can be caused by the increased tone of the smooth muscles of the bronchioles, hypertrophy of the mucous membrane, mucus accumulation, tumors, and other factors. Obstructive type is characterized by decreased PEF, FEV1, FEF 25 %, FEF 50 %, FEF 75 %, Tiffeneau and MVL indices. Also, in obstructive disorders the residual volume, functional residual capacity, and total lung capacity are increased.

2) Restrictive type usually occurs due to decreased lung compliance and lung expansion during inspiration. The causes are pulmonary fibrosis, accumulation of fluid in the pleural cavity and others. The main sign of restrictive disorders is decreased VCL (by 20 % and more from the due vital capacity), total lung capacity, functional residual capacity, and residual volume.

The mixed type of external respiratory failure is also observed.

Review questions

1. What is the value of respiration for living organisms? What are the external and internal types of respiration? Name the adaptive features of the lungs for respiration. What are the non-respiratory functions of the lungs?

2. What is the respiratory cycle? Explain the mechanism of inspiration. Name the main and auxiliary inspiration muscles. What is the role of the diaphragm in inspiration? Explain the mechanisms of expiration. Name the main and auxiliary expiration muscles. What are the types of respiration? What type of respiration is the most effective ?

3. What is intrapleural pressure? What are the values of intrapleural pressure during inspiration and expiration? What is the elastic recoil of the lungs? What factors cause the elastic recoil? What is the surfactant? Explain the role of the surfactant. What is pneumothorax?

4. Name the respiratory volumes and capacities and their normal values. What is the spirographic record? What factors influence the vital capacity of the lungs?

5. What is dead space? Explain the physiological role of anatomic dead space. What is the pulmonary ventilation coefficient? What is functional dead space?

6. What are the normal values of the respiratory rate in adults and newborns? What are the respiratory minute volume and maximal ventilation of lungs? What is alveolar ventilation? Give the normal values of these parameters.

6.7. Gas exchange in the lungs

Gas exchange is the delivery of oxygen from the lungs to the bloodstream, and the elimination of carbon dioxide from the bloodstream back to the lungs. The exchange of gases occurs between the alveoli and capillaries by O2 diffusing from the air of the alveoli into the blood (approximately 500 L of O2) and CO2 diffusing from the blood into the alveolar air (450 L of CO_2).

Diffusion is the process of passive transport of gases at the levels of aerohematic and histohematic barriers and it is described by Fick's equation

$$\frac{\Delta \nu O_2}{\Delta t} = -D \times S \times \frac{\Delta pO_2}{\Delta l}$$

where $\frac{\Delta \nu O_2}{\Delta t}$ — the rate of diffusion,

D — the constant of diffusion, $mLO_2/m \cdot min \cdot mm\ Hg$;

S — the surface of diffustion, m^2;

ΔpO_2 — the gradient of pressure of O_2, mm Hg;

Δl — the distance of diffusion ,m.

Thus, the factors which determine the rate of gas diffusion are :

- the gradient of partial gas pressure;
- the membrane thickness;
- the coefficient of gas diffusion;
- the surface of diffusion.

1. The **partial pressure of gases** is a measure of great importance for pulmonary gas exchange.

Atmospheric air inhaled during respiration has a relatively constant composition (Table 6.1).

Table 6.1 — Composition of air

Air	**O_2, %**	**CO_2, %**
Inhaled	21.0	0.02–0.03
Exhaled	16.0	4.5
Alveolar	14.0	5.5

Partial pressure is the pressure of gas in gas mixture. It is proportional to the concentration of gas (%) and general pressure of gas mixture.

The example of the calculation of pO_2 и pCO_2 in atmospheric air:

$$pO_2 = \frac{760 \text{ mm Hg} \times 21{,}0}{100} = 159 \text{ mm Hg.}$$

$$pCO_2 = \frac{760 \text{ mm Hg} \times 0.03}{100} = 0.23 \text{ mm Hg.}$$

To calculate the partial pressure of gases in alveolar air, the vapor pressure of water (47 mm Hg) should be taken into account:

$$pO_2 = \frac{(760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 14}{100} = 100 \text{ mm Hg}$$

$$pCO_2 = \frac{(760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 5.5}{100} = 40 \text{ mm Hg}$$

The partial pressure of each gas in the alveolar gas mixture tends to force the molecules of this gas into the blood of the alveolar capillaries.

Gas diffusion occurs due to the difference of the partial pressure of these gases in alveolar air and their pressure in the blood (partial pressure of gas in a liquid) (Figure 6.9).

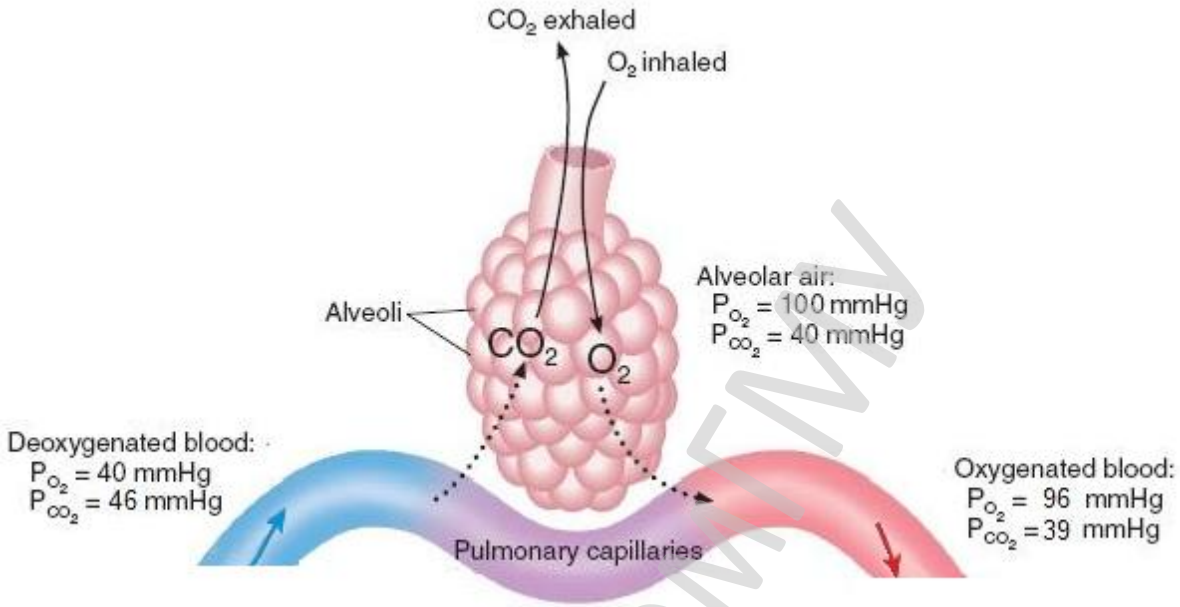


Figure 6.9— Gas exchange in the lungs between the alveolus and capillary (from biology.reachingfordreams.com)

In the blood gases are in dissolved and chemically bound conditions. The force with which a molecule of gas tends to enter a gas environment is called **the partial pressure of gas in a liquid**.

The amount of gas dissolved in a liquid depends on:

- the composition of the liquid;
- the volume and pressure of the gas over the liquid;
- the temperature of the liquid;
- the nature of the gas.

If the partial pressure of gas is *greater in the gas phase* in the alveoli, (which is normally true for oxygen), more *gas molecules diffuse into the blood.* Alternatively, if the pressure of gas is greater *in the dissolved state* in the blood, (which is normally true for CO_2), the *diffusion occurs towards the gas phase in the alveoli.*

The diffusion of O_2 is provided by the difference of its partial pressures equal to 60 mm Hg (p O_2 in alveolar air is 100 mm Hg and pO_2 in venous blood is 40 mm Hg, table 6.2). The diifference of partial pressures for CO_2 is 6 mm Hg (pCO_2 in venous blood is 46 mm Hg and pCO_2 in alveolar air is 40 mm Hg). CO_2 diffusion into alveolar air occuring at the relatively low difference of the pressures is explained by the high diffusion capacity of this gas.

Table 6.2. Partial pressure of gases (mmHg)

Gas	Venous blood	Alveolar air	Arterial blood
O_2	40	100	96
CO_2	46	40	39

The constancy of the gas composition of alveolar air is a necessary condition of normal gas exchange. Dead space, which carries out the function of a buffer smoothing fluctuations of the composition of alveolar air during the respiratory cycle, plays an essential role in the maintenance of the given constancy.

The diffusion of oxygen and carbon dioxide occurs passively, according to their concentration differences across the alveolar-capillary barrier. These concentration differences must be maintained by ventilation of the alveoli and perfusion of the pulmonary capillaries. ***Ventilation-perfusion relationships*** reflect the conformity of the respiratory minute volume to cardiac output during the pulmonary circle of blood circulation. The normal ventilation-perfusion coefficient is ***0.8–1.0***.

$$\textbf{Ventilation-perfusion coefficient} = \frac{\textbf{RMV (L/min)}}{\textbf{CO}_2\textbf{ (L/min)}} = \textbf{0.8-1.0}$$

Smooth muscles of the majority of the vessels of the systemic circle of blood circulation dilate if there is low O_2. On the contrary, smooth muscles in the vessels of the pulmonary circulation constrict, which causes the narrowing of the vessels in poorly ventilated parts of the lungs and reduction of the blood flow.

The human requirement for O_2 is 250–300 mL/min (in physical exertion — up to 5000 mL).

2. A comparatively thin **aerohematic barrier (0.4–1.5 μm)** (Figure 6.10) **between the air and blood vessels** including:

1) the surfactant layer (surfactant is one of the factors promoting O_2 diffusion);
2) the alveolar epithelium;
3) two basal membranes;
4) the endothelium of capillaries.

Apart from this barrier, during diffusion O_2 goes through:

- the layer of blood plasma;
- the membrane of erythrocytes.

3. High **diffusion capacity of the lungs**. It is defined by the amount of gas penetrating through the lung membrane per minute for 1 mm Hg of gradient of pressure.

For O_2 it is 25 mL/min. x mm Hg.

For CO_2 the diffusion ***capacity is 24 times more*** (CO_2 has high solubility).

4. **Great total alveolar surface (approximately 90 m^2)**.

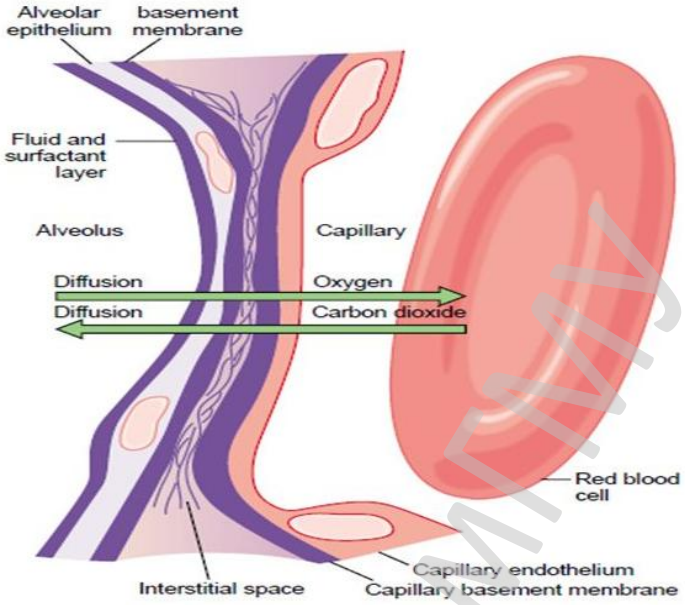


Figure 6.10 — Structure of the aerohematic barrier (from studylib.net)

6.8. Gas transport by blood

O_2 and CO_2 are transferred by blood in two forms:

a) In a free (dissolved) form;

b) In a bound form;

As simple physical solutions O_2 and CO_2 are present in a comparatively small volume (O_2 — 0.3 %, CO_2 — 3.0 %). Actually from blood they can be extracted: O_2 — 60 times and CO_2 — 18 times more, i.e. it testifies to the fact that the basic form of their transmission is the bound one.

However, the state of physical dissolution of O_2 and CO_2 is of high significance. To contact these or those substances, gases should be first dissolved in blood plasma, i.e. each molecule of O_2 or CO_2 is dissolved for a while before it reaches erythrocytes.

The law of Henry-Dalton describes gas solubility in liquids:

$$m = \frac{\alpha}{760} \times P;$$

where

m — the amount of dissolved gas, g;

α — the coefficient of Bunsen: mL O_2 /mL atm;

P — barometric pressure, mm Hg.

The coefficient of Bunsen is the parameter of gas solubility in a fluid, it depends on temperature, gas pressure, other dissolved substances.

O_2 transport. A large amount of O_2 is transported by blood as a chemical compound with hemoglobin (Hb) — ***oxyhemoglobin*. *1g of hemoglobin can bind 1.34–1.36 mL of O_2***.

The maximum amount of oxygen which can combine chemically with a given amount of hemoglobin in the blood is named the ***oxygen capacity of blood*** and does not include oxygen dissolved in plasma. It is equal to 18-22 vol. % (percent by volume).

The values of the oxygen capacity of blood depends on the Hb concentration.

The oxygen capacity of blood can be calculated by the formula:

$$\text{Oxygen capacity} = Hb \times H \ ;$$

where Hb — hemoglobin concentration, g/L.;

H — Hüfner's constant, mL O_2/g.

For example, if the concentration of Hb is 140 g/L, the oxygen capacity of blood is:

1.34 mL O_2 × 140 g/L = 187.6 mL ≈19 vol. % (1 liter of blood contains 190 mL of oxygen).

However, the degree of Hb oxygenation first of all depends on the partial pressure of O_2 in a medium in which blood contacts. This dependence is expressed by the so-called ***oxyhemoglobin dissociation curve*** (Figure 6.11).

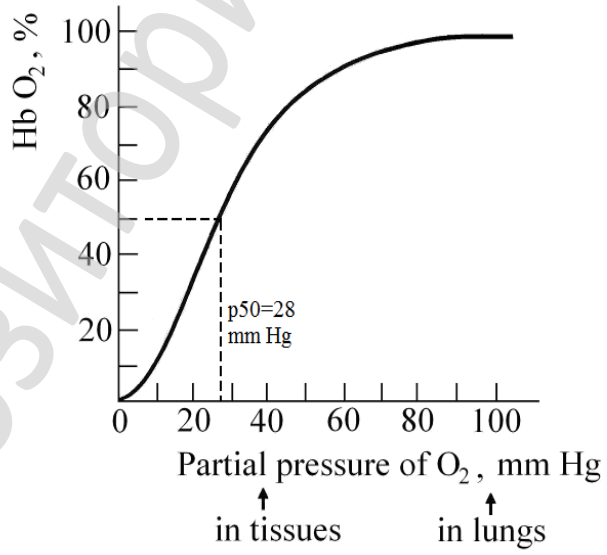


Figure 6.11 — Oxyhemoglobin dissociation curve

The oxyhemoglobin dissociation curve shows the percentage of Hb bound with O_2 at different partial pressures of O_2. There are 3 parts on the curve: $pO_2$from 0 to 10mm Hg. — directly proportional dependence, from 10 to 60 mm Hg — saturation is very fast, from 60 to 90 mm Hg — saturation is almost not changed.

During O_2 diffusion in the lungs, the partial pressure of O_2 in the blood is close to pO_2 in the alveoli making 96 mm Hg. Under this partial pressure approximately 97 % of HbO_2 is formed.

Even if pO_2 in arterial blood decreases to 60 mm Hg, Hb oxygenation drops down insignificantly and HbO_2 is 90 %. It has an important physiological value: with age or in pulmonary diseases pO_2 in alveolar air can decrease and if its level does not decrease below 60 mm Hg, oxygenation is reduced insignificantly and tissues are sufficiently supplied with O_2.

The abrupt part of the curve corresponds to the partial pressure of O_2 typical for tissues (35 mm Hg and lower). It creates a favorable situation for the return of O_2 to tissues.

The physiological role of the S-shape configuration of the oxyhemoglobin dissociation curve consists in the fact that blood oxygenation in the lungs is maintained at a high level even at relatively low alveolar pO_2, and deoxygenation changes significantly even if there are small changes of the capillary-tissue gradient of pO_2.

The parameter of Hb affinity to O_2 is the partial pressure of O_2 in which half of Hb is bound with O_2 (p50). Normally, it is equal to 26–28 mm Hg. Increased affinity of Hb to O_2 results in a decrease of p50, and vice versa.

HbO_2 dissociation in tissues depends on the intensity of oxidative processes: in intensively working tissues and organs HbO_2 dissociation increases, in less intensively working tissues and organs it decreases.

The factors which influence the ***HbO_2 dissociation curve (the affinity of Hb to O_2).***

1.**Temperature**. If the temperature goes up, the slope of the HbO_2 dissociation curve descends and ***shifts to the right***, i. e. HbO_2 dissociation is increased (Figure 6.12).

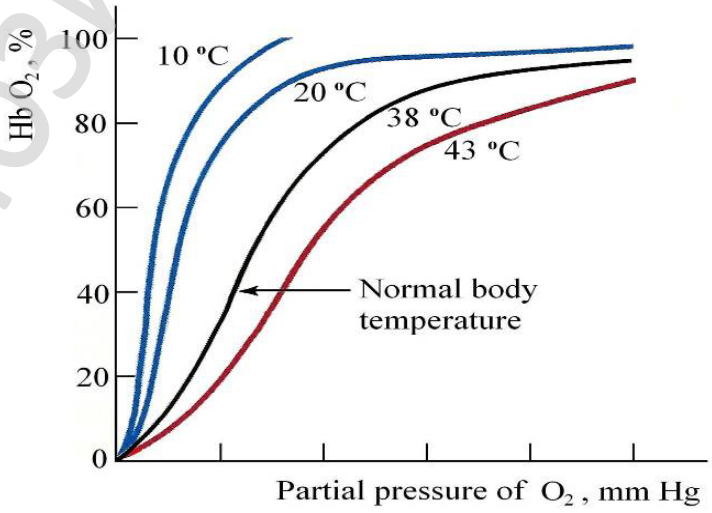


Figure 6.12 — Effects of temperature on the hemoglobin dissociation curve

2. **In a pH** shift towards its decrease, i. e. H^+ increase, the curve of HbO_2 dissociation ***shifts to the right***, i. e. HbO_2 dissociation is increased (Figure 6.13).

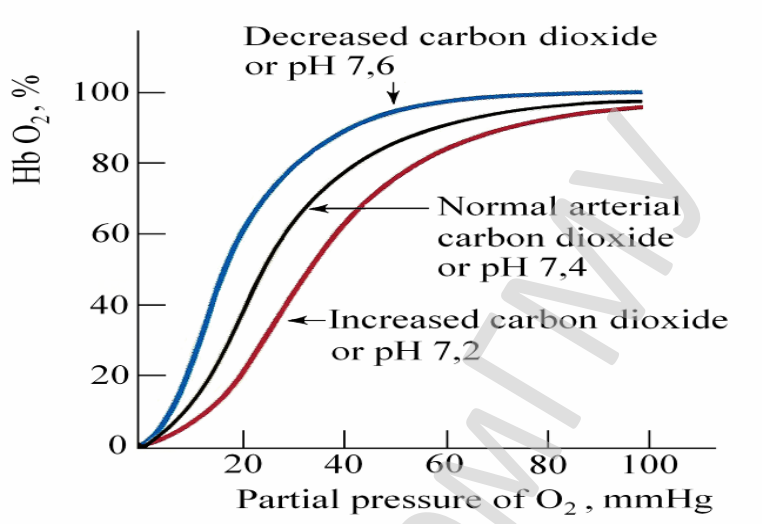


Figure 6.13 — Effects of partial pressure of CO_2 and blood pH on the hemoglobin dissociation curve

The dependence of hemoglobin affinity to oxygen from pH is named the the Bohr effect (the oxygen affinity of haemoglobin decreases in the presence of low pH or high CO2 and vice vera).

3. **pCO_2** in the blood. The higher pCO_2 is, the higher HbO_2 dissociation is (***the curve shifts to the right***).

These factors reduce Hb affinity to O_2.

Any changes of the given factors have an important value for tissue provision with oxygen, mainly those functioning more intensively at the moment.

E. g.: in a working muscle t° and CO_2 rise and pH decreases, i. e. factors promoting HbO_2dissociation and providing the optimal oxygen nutrition of the muscle, appear.

In hypoxia (low pO_2 in tissues) the synthesis of ***2,3-diphosphoglycerate,*** which reduces Hb affinity to O_2 increased in erythrocytes. This results in HbO_2 dissociation and O_2 return to tissues.

The curve of ***HbF (fetus)*** dissociation, due to its higher affinity to oxygen is ***shifted leftwards*** as compared with HbA (adults).

Arterial blood contains approximately 20 vol. % of O_2, and venous blood — 12 vol. %. For the evaluation of O_2 utilization by tissues **the oxygen utilization coefficient** is used.

$$O_2 \text{ utilization coefficient} = \frac{(O_2 \text{ vol. \%. in arterial blood} - O_2 \text{ vol. \%. in venous blood}) \times 100}{O_2 \text{ vol. \%. in arterial blood}}$$

The oxygen utilization coefficient in a person at rest is **30–40 %.** In physical activity it increases up to 50–60 %.

CO_2 transport by blood

It is transported:

1) In physically dissolved state.
2) In the form of chemical compounds:
   a) of acidic salts of carbonic acid;
   b) of carbohemoglobin.

In tissues. CO_2 formed in tissues passes to capillary blood (Figure 6.14**)**.

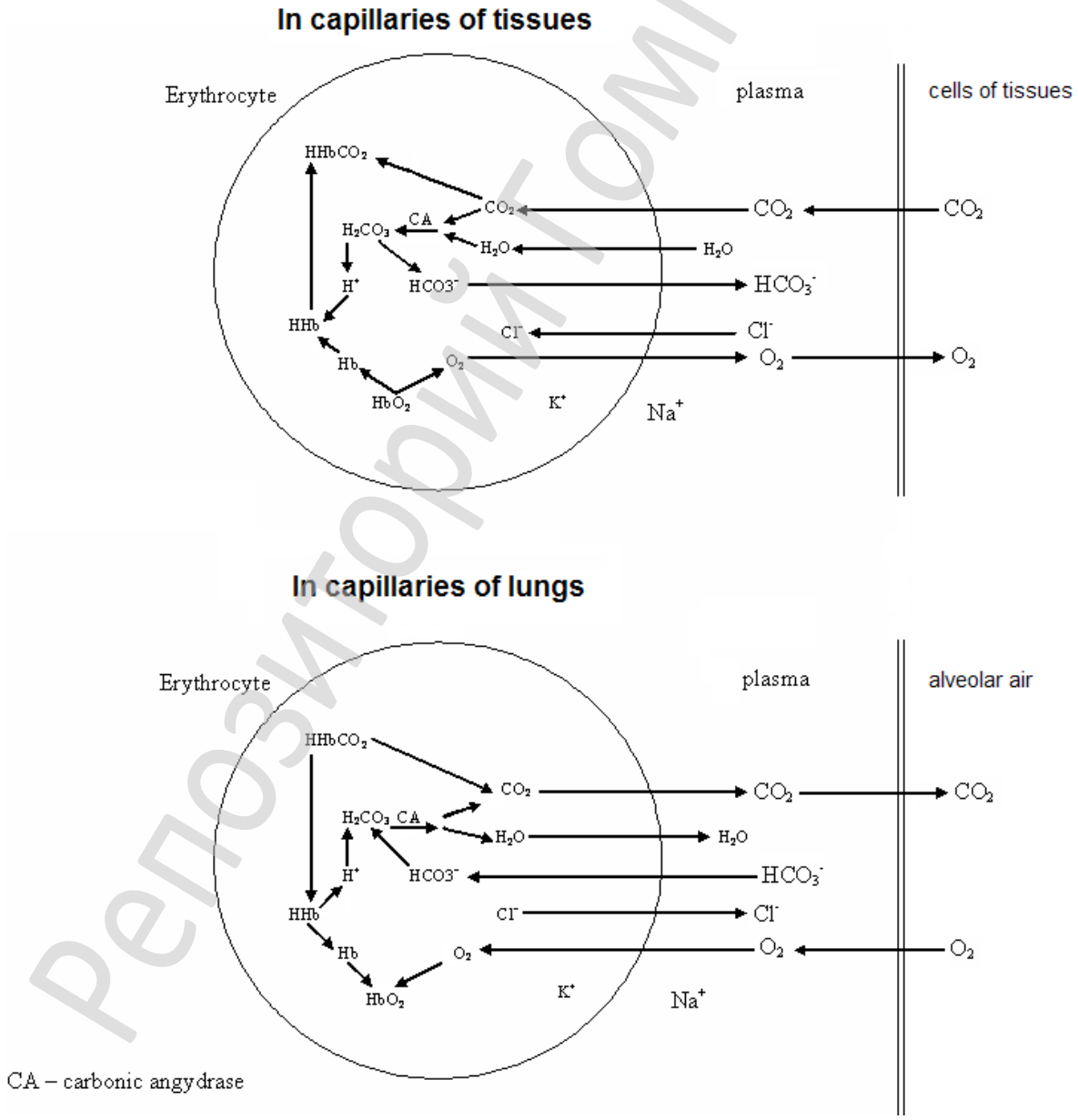


Figure 6.14 — CO_2 transport (scheme)

In erythrocytes:

$$CO_2 + H_20 \rightarrow H_2CO_3$$

The process is accelerated by 20,000 times by ***carbonic anhydrase***. This process proceeds only in erythrocytes (there is no carbonic anhydrase in plasma). In the capillaries of the lungs this enzyme, on the contrary, catalyzes the breakdown of H_2CO_3.

In erythrocytes part of CO_2 is connected with hemoglobin:

$$CO_2 + Hb \rightarrow Carbohemoglobin$$

Since as a result of these processes the partial pressure of CO_2 in erythrocytes does not increase, all new portions of CO_2 diffuse into erythrocytes. At the same time, the concentration of HCO_3^- ions in erythrocytes increases, some part of which go to blood plasma. Their place in erythrocytes is taken by Cl^- ions whose negative charges are equalized by positive K^+ ions. In plasma the volume of bicarbonate ($NaHCO_3$) increases; in erythrocytes — $KHCO_3$.

In pulmonary capillaries $KHbO_2$ releases O_2 and transforms into KHb. Carbonic acid, being a stronger acid, expels K^+ from it:

$$KHbO_2 + H_2CO_3 \rightarrow HHb + O_2 + KHCO_3.$$

Therefore, the transformation of HbO_2 into hemoglobin is accompanied by the increased ability of blood to bind CO_2. In such a state CO_2 is transferred to the lungs.

In the lungs. From carbohemoglobin CO_2 is detached, and simultaneously oxyhemoglobin is formed. Oxyhemoglobin is a stronger acid than carbonic acid, therefore, HbO_2 expels K^+ from bicarbonates and is transported as a $KHbO_2$ salt. This results in the formation of H_2CO_3 in erythrocytes (***carbonic anhydrase***).

HCO_3^- ions enter erythrocytes and Cl^- ions enter blood plasma where the volume of Na^+ bicarbonate decreases, and CO_2 diffuses into the alveoli.

Review questions

1. What factors provide gas exchange in the lungs? What are the amounts of O_2 and CO_2 (in %) in inhaled, exhaled, and alveolar air? What is the partial pressure and how is it measured? What are the partial pressures of O_2 and CO_2 in arterial and venous blood and alveolar air? What factors influence the process of O_2 and CO_2 diffusion between alveolar air and blood? What is the ventilation-perfusion coefficient? What is the diffusion ability of the lungs for gases? Describe the structure of the aerohematic barrier.

2. Name the forms of O_2 transport by blood. What is the oxygen capacity of blood? What does the oxyhemoglobin dissociation curve express? Name the factors influencing the affinity of hemoglobin to oxygen and their physiological value. What is the coefficient of O_2 utilization?

3. Name the forms of CO_2 transport by blood. What factors provide CO2 diffusion from tissues into blood? How does the formation of transport forms of CO_2 occur in the erythrocytes of tissue capillaries? What is the role of carbonic anhydrase? What factors provide CO_2 diffusion from erythrocytes into plasma and alveolar air?

6.9. Regulation of respiration

6.9.1. Localization and structural organization of the respiratory center

Somatic nerve fibers innervate respiratory muscles. Their deinnervation results in apnea. The motoneurons of intercostal and abdominal muscles are located in the ***thoracic segments of the spinal cord.*** The motoneurons innervating the diaphragm are located in ***III–IV cervical segments***. After dissection of the spinal cord at the level of the superior cervical segments respiratory movements stop. If the spinal cord is dissected at the level of the inferior cervical segments (below III–IV) — the movements of the diaphragm continue, those of intercostal muscles stop (Figure 6.15).

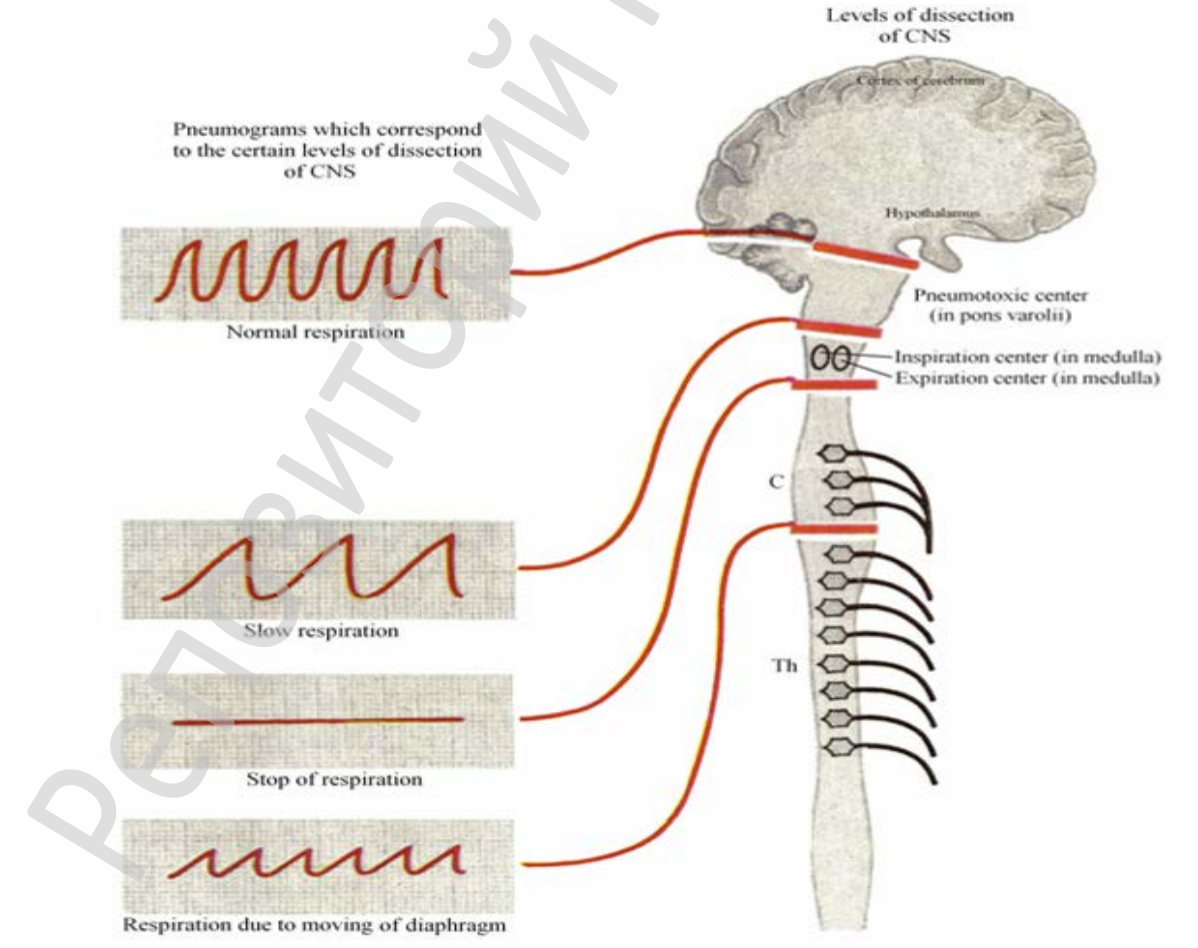


Figure 6.15 — Influence of dissection of different levels of the central nervous system on respiration (by Korobkov A. V., Chesnokova S. A., 1986)

Dissection of the brain between the midbrain and medulla does not change respiration in a person at rest. It is indicative of the location of the ***respiratory center*** in the medulla and pons varolii. Dissection of the brain between the medulla and pons varolii does not stop respiration but it differs from normal. It means that the major structures of the respiratory center are located in the medulla. These structures form **the bulbar respiratory center**, the damage of which results in arrested respiration.

Therefore, the centers of the brain participating in the regulation of respiration are located in the **medulla**.

There are 2 basic groups of respiratory neurons:

1. *Inspiratory*.
2. *Expiratory*.

Localization of respiratory neurons. In both the halves (left and right) of the medulla 2 groups of respiratory neurons are situated: dorsal and ventral respiratory nuclei.

1. ***The dorsal respiratory nucleus*** contains mainly inspiratory neurons, whose axons are directed to the diaphragm nuclei of the cervical part of the spinal cord. Collaterals from them go to the ventral respiratory nucleus where they form excitant synapses on expiratory neurons and inhibit their activity.

As for expiratory neurons, their number in the dorsal respiratory nucleus is insignificant. This part, i. e. the dorsal respiratory nucleus where mainly the inspiratory neurons are located is called the **«inspiration center»** (Figure 6.16).

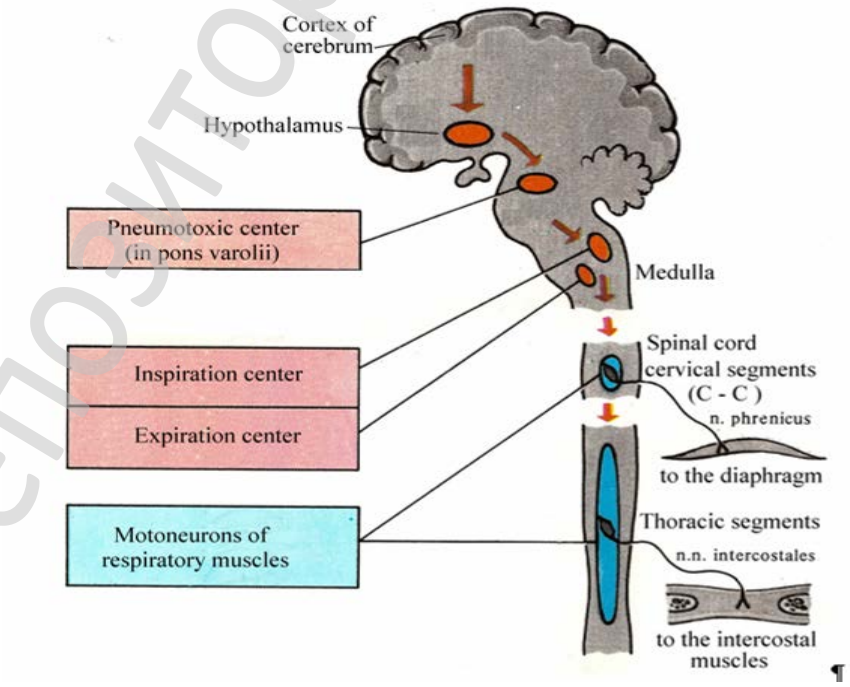


Figure 6.16 — Respiratory center (its components) and efferent nerves (by Korobkov A. V., Chesnokova S. A., 1986)

2. ***The ventral respiratory nucleus*** contains inspiratory and expiratory neurons. This part is called the «expiration center». The expiratory neurons send impulses:

1) to the motoneurons of the intercostal and abdominal muscles situated in the thoracic and lumbar parts of the spinal cord;

2) partially to the motoneurons of the diaphragm.

At the same time, the respiratory neurons are located both in the reticular formation of the medulla and in the pons varolii.

Near the ventral nucleus the Bötzinger complex and the pre-Bötzinger complex are located. The Bötzinger complex is a group of expiratory neurons which form connections between other neurons of the respiratory center and play a role in the synchronization of the right and left parts of the respiratory center. The pre — Bötzinger complex is located in the ventrolateral part of the medulla and contains neurons with potential-depended pacemaker properties, which play a role in the generation of the respiratory rhythm.

6.9.2. Role of gas composition in the regulation of the respiratory center activity

The functional activity of the respiratory center is determined by the partial pressure of gases and pH in the blood. The leading role here is played by the partial pressure of CO_2.

In general conditions the human body is supplied with sufficient volume of O_2. Even in conditions when pO_2 in alveolar air can decrease to 60–70 mm Hg, the organism does not develop significant disorders. pCO_2 is maintained at a relatively constant level providing the functional activity of the respiratory center.

Changes of gas strain in the blood influences the activity of the respiratory center, the signs of which are changes of:

1. Respiration rate.
2. Respiration depth.
3. Lung ventilation.

It can result in:

1) maintenance of normal CO_2 volume in the blood (***normocapnia***);

2) increase of CO_2 in the organism (***hypercapnia***);

3) decrease of CO_2 in the organism (***hypocapnia***);

4) normal O_2 volume (***normoxia***);

5) deficiency of O_2 in tissues (**hypoxia**);

6) deficiency of O_2 in blood (***hypoxemia***).

As a rule, there is no increased amount of O_2 in the blood.

Normocapnia is accompanied by normal respiration (***eupnea***). Simultaneous hypoxia and hypercapnia cause ***asphyxia (dyspnea)***. In hypercapnia or low

pH level (acidosis) — lung ventilation is increased due to the depth of respiration (basically) and its frequent rate ***(hyperpnea)***. Hypocapnia or high pH level (alkalosis) results in decreased lung ventilation and ***apnea***.

Hypoxia develops in individuals who ascend to high altitudes, have blood circulation or blood composition disorders, or do hard physical work.

6.9.3. Role of chemoreceptors in the regulation of respiration

In arterial blood the partial pressure of O_2, CO_2, and pH depends on lung ventilation.

But, in its turn, they are factors influencing the intensity of this ventilation, i. e. they influence the activity of RS.

The Frederico test with cross-circulation (Figure 6.17). In two dogs the carotid arteries and jugular veins were cross-connected, the vertebral artery being ligated. As a result of the experiment, the head of the first dog was supplied with the bloodstream of the second dog, and vice versa. The tracheal pinching in the first dog causing asphyxia resulted in hyperpnoea in the second dog. In the first dog apnea occurred despite the increase of pCO_2 and decrease of pO_2.

Such changes of respiration were observed because the carotid artery of the first dog received the blood from the second dog in which, pCO_2 in the blood was decreased due to hyperventilation. This influence is carried out through special ***chemoreceptors***. There are two kinds of chemoreceptors according to their localization:

1. Central (bulbar) — they are located in the *central nervous system, in the medulla*.

2. Peripheral (arterial) — they are located *in the blood vessels*.

From these receptors signals about the gas composition of blood come to the respiratory center.

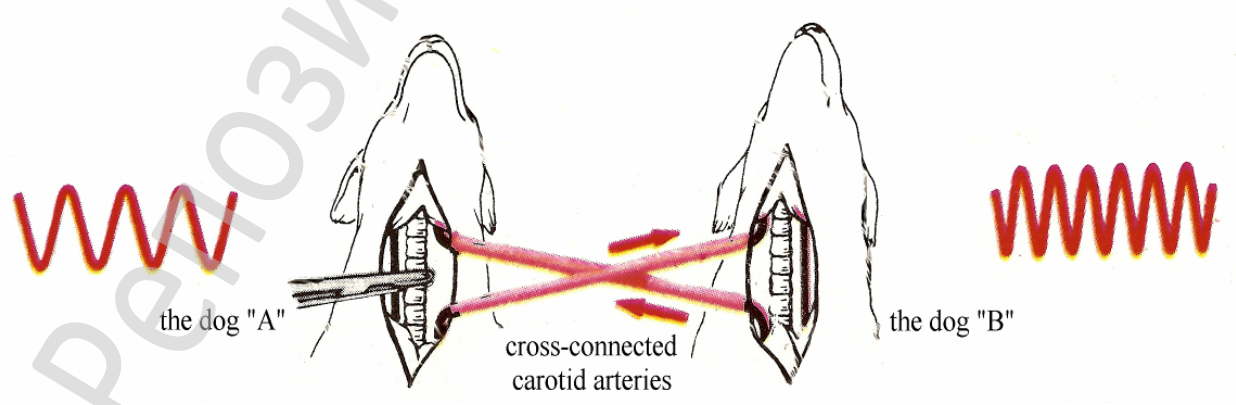


Figure 6.17 — The Frederico test with cross-circulation
(by Korobkov A. V., Chesnokova S. A., 1986)

Notes: Pinching of the trachea of the dog «A» courses hyperpnoea in the dog «B»; hyperpnoea of the dog «B» courses decreasing of ventilation rate in the dog «A».

The role of the central chemoreceptors. The central chemoreceptors are located in the medulla and detect the pH changes of nearby cerebrospinal fluid that are indicative of altered oxygen or carbon dioxide concentrations. Perfusion of the medulla portion within the area of the given receptors with ***solution of lower pH*** results in rapid intensification of respiration, and vice versa.

In natural conditions the central chemoreceptors are constantly stimulated by H^+. The concentration of H^+ in the blood depends on CO_2 strain in arterial blood. Decreased pH level by 0.01 induces increased lung ventilation by 4 L/min.

At the same time, the central chemoreceptors respond to the changes of pCO_2 but to a lesser degree than to the changes of pH. It is presumed that the basic chemical factor influencing the central chemoreceptors is the H^+ amount in the intercellular fluid of the brain stem and the action of CO_2 is mediated by the formation of these ions.

The role of arterial (*peripheral)* chemoreceptors*.*** O_2, CO_2, and H^+ can influence the central nervous system not only centrally but also by exciting the peripheral chemoreceptors.

The most important of them are:

1. ***The carotid bodies*** located in the vicinity of the division of the common carotid artery into internal and external carotid arteries.

2. ***Aortal bodies***.

The chemoreceptors of the indicated zones are excited in ***increased pCO_2 and decreased pO_2 and pH levels.*** The influence of O_2 on the respiratory center is mediated only by the peripheral chemoreceptors.

Thus, the neurons of the respiratory center remain activated by the impulses coming from the central (bulbar) and peripheral (arterial) chemoreceptors reacting to changes of the three parameters of arterial blood:

1. Low pO_2 (***hypoxemia***).
2. High pCO_2 (***hypercapnia***).
3. Low pH (***acidosis***).

The main stimulant of respiration is *hypercapnia*. The higher pCO_2 is (pH is also connected with it), the more frequent lung ventilation is.

However, the strongest stimulant of the central respiratory mechanism is the combined action of hypoxemia and hypercapnia (and acidosis connected with it).

6.9.4. Role of respiratory mechanoreceptors in the regulation of respiration

In changes of the respiratory phases, i.e. periodic activity of the respiratory center the essential role is played by the ***mechanoreceptors (stretch receptors)*** (Figure 6.18), located in the smooth muscles of the walls of the trachea, bronchi, bronchioles, for which various degree of excitability is typical. Some of them (approximately 1/2) are *low-threshold*.

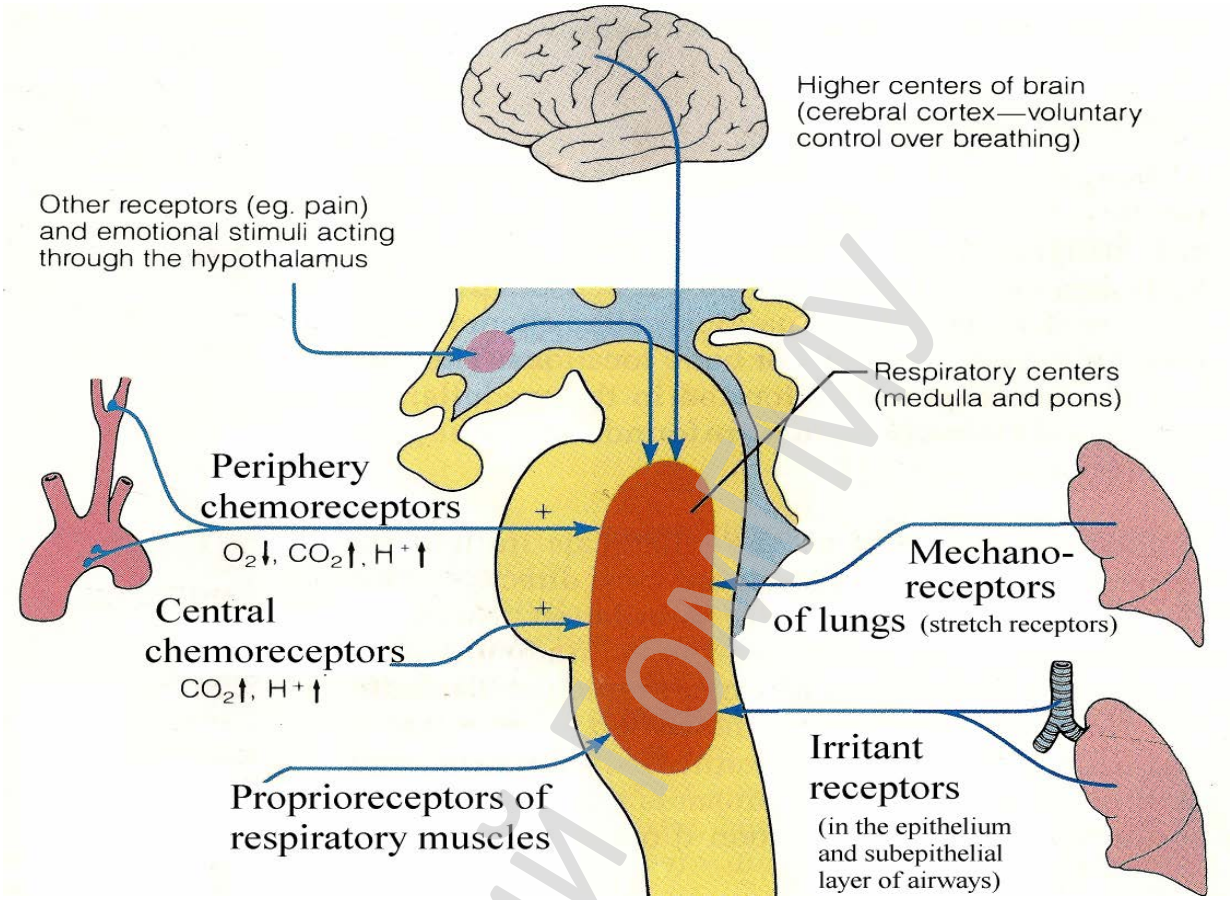


Figure 6.18 — Neural and chemical influences on the respiratory center in the medulla (by Elaine N. Marieb, 1989)

They are intensively excited during breathing. Impulsion from them is strengthened in inspiration and reduced in expiration. The other muscles are *high-threshold,* they are excited only in inspiration.

During inhalation, as a result of lung expansion stretch receptors get excited. Afferent fibers from these receptors go in the structure of *n. vagus* into the dorsal respiratory nucleus of te medulla (inspiratory center) and inhibit the activity of inspiratory neurons. ***The act of inspiration is inhibited***.

This reflex provides a change of the phases of the respiratory cycle and is called the ***inspiration-inhibitory reflex***. For the first time it was described by Hering and Breuer and received the name ***of the Hering-Breuer reflex***.

The physiologic value of this reflex is the limitation of the respiratory movements. Due to this, the conformity of the depth and frequency of respiration to the conditions of the body functions at the present moment is reached and receptors interfere lung overdistension.

The role of the Hering-Breuer reflex is relatively insignificant in a person being at a state of relative rest. The value of this reflex is extremely great in hyperpnea.

6.9.5. Influence of irritant receptors on the respiratory center

In the epithelium and subepithelial layer of the airways, there are receptors that are called ***irritant receptors***. They are especially numerous in the region of the lung roots.

They have the properties of:

a) mechanoreceptors;

b) chemoreceptors.

They are excited in dramatic changes (increase or decrease) of the lung volume. The excitation threshold in them is higher than in all other receptors. Impulses in the afferent fibers of the irritant receptors arise in groups only within a short period of time during the change of the lung volume but some of them are excited also during general inspiration and expiration.

As stimulators of the irritant receptors there can be:

- dust particles;
- mucus;
- gases of caustics (tobacco smoke, ammonia, etc.);
- biologically active substance formed in the walls of the airways (histamine);
- they can be strongly excited in a number of diseases (pulmonary edema, pneumothorax, bronchial asthma, etc.).

Stimulation of the irritant receptors results in:

- cough;
- unpleasant sensations like burning or scratching;
- intensifying of inspiratory activity;
- shortening of expiratory phases;
- hyperpnoea;
- reflex of bronchoconstriction.

The irritant receptors take part in appearance of an original reflex, the so-called ***«deep sigh»*** reflex. At rest a person makes deep sighs approximately 3 times per hour. A sigh results from an intermittent inflation of the lungs with a large volume, i. e. this is essentially a deep breath that is incorporated into the ventilation cycle and results in excitation of irritant receptors. The sigh is accumulated on one of the next inspirations, which results in lung expansion and regeneration of their ventilation.

6.9.6. Participation of the proprioreceptors of respiratory muscles in the regulation of respiration

The receptors of respiratory muscles take part in the regulation of respiration (***proprioreceptors***), in particular, stretch receptors — ***muscular spindles.***

Due to heavy breathing (inspiration or expiration) the receptors are excited, which results in increased contractions of respiratory muscles (proprioceptive reflex). Thus, the conformity of the mechanical parameters of respiration to the resistance of the respiratory system is reached.

6.9.7. Role of the pneumotaxic center in the regulation of respiration

The pneumotaxic center is located in the pons varolii. If to dissect the brain stem below the *pons varolii*, breathing does not stop, but its rhythm is irregular, which leads to respiration at which long expiration may be interrupted with short inspirations. This respiration type is called ***gasping*****.**

If, after the brain dissection on the border between the pneumotaxic center and medulla, to perform vagotomy, apnoea will occur at the inspiratory phase. Sometimes this condition is interrupted with the expiratory movements. Such sustained, gasping inhalation followed by short, inefficient exhalation is called ***apneusis***. In these conditions braking influences on inspiration are eliminated. It means that the pneumotaxic center takes part in the changing the inspiration-expiration phases.

The pneumotaxic center:

- raises the activity of the inspiration standstill mechanism.
- activates the expiration center.
- provides smooth transition of the inspiration-expiration phases.

Thus, in the pons varolii there is a central mechanism promoting the change of the respiration phases, that is the periodic activity of the respiratory center.

6.9.8. Role of the upper airway receptors in the activation of the respiratory center

An inspiratory stream of air stimulates the receptors of the nasal mucous membrane (mainly, cold receptors). Impulses from the receptors of the nasal mucous membrane go to the brain along the fibers of the trigeminal nerve and influence the respiratory center (weak inhibiting).

Stimulation of the receptors of the upper airways causes a number of protective reflexes:

- ***Sneezing*** — strong expiration through the nose (stimulation of the receptors of the nasal mucous membrane).
- ***Cough***. It develops under the stimulation of the receptors of the larynx, trachea. A cough begins with a deep breath in, at which point the opening between the vocal cords at the upper part of the larynx shuts, allowing additional air to pass through into the lungs. As the diaphragm and expiratory muscles press against the lungs, the pressure in the airways increase, and the larynx and the vocal cords open, producing an explosive outflow of air and a rushing

sound as the air moves very quickly past the vocal cords at a speed greater than 160 km per hour.

Plunger reflex. The action of water on the receptors of the inferior nasal ways causes apnea, preventing water into the airways.

Respiration is inhibited during swallowing, ingress of caustics (gases of ammonium) into the nasal cavity.

6.9.9. Role of the cerebral cortex in the regulation of respiration

Considering the mechanisms of the regulation of respiration, it is necessary to outline two groups of processes:

1. ***Maintenance of constant gas*** pressures of arterial blood. It is provided basically by the respiratory center (***homeostatic*** **reaction**).

2. ***Processes of adjusting respiration to changing conditions of the environment and vital activity of the organism*** (***behavioral*** **regulation**).

Changes of respiration under different conditions: *speech, singing, attention, emotions, during sleep, influence of the environment, etc*.

In the processes of respiratory adaptation to the demands of organism`s physical exertion a special role is played by the **cerebral cortex**.

The changes of respiration differ during excitation of the cortex regions. The removal of the cerebral cortex results in increased lung ventilation.

The participation of the cerebral cortex in the regulation of breathing is proved by the method of conditioned reflexes (*pre-start state of sportsmen*), opportunity of voluntary breath-holding and intensified respiration.

6.9.10. Influence of nonspecific factors on respiration

These are factors which directly do not participate in the regulation of respiration but influence lung ventilation.

1. **Cold** and **warmth** influence the skin, which results in excitation of the respiratory center (in a newborn breathing may be stimulated by contrast baths). Body temperature changes: fever and moderate hypothermia increase lung ventilation. Deep hypothermia, on the contrary, suppresses the activity of the respiratory center.

2. **Pain**. Lung ventilation at the first moment of a pain effect can lead to apnoea (in inspiration). Then respiration becomes deeper and more frequent.

3. **Hormones**. During physical exercise *adrenaline* increases lung ventilation.

6.10. Coordination of respiration and blood circulation

Normal gas exchange in the lungs and tissues and its adaptation to the demands of an organism are provided by the changes of not only lung ventilation but also blood circulation.

1. The reflex influences proceeding from the reflexogenic regions (aortal and carotid) affect the functioning of the cardiovascular and respiratory systems.

2. Respiratory arrhythmia of cardiac activity and blood pressure (the change of heart rate according to the phases of respiration).

3. During physical work and under emotional stress — cardiac output and lung ventilation increase raising the respiratory minute volume.

4. A hemorrhage is accompanied by reduced blood pressure and increased lung ventilation, etc.

This coordination is provided by a close interaction of the neurohumoral mechanisms of the regulation of the cardiovascular and respiratory systems and is carried out mainly by the cerebral cortex and underlying structures among which the most important role is played by the hypothalamus.

6.11. Regulation of the tone of the smooth muscles of the bronchi and bronchioles

The tone of the bronchial smooth muscles is regulated by nervous and humoral factors.

The influence of the **parasympathetic nervous system** on the tone of the smooth muscles of the bronchi is exerted by the nerve fibers of the vagus nerve. The increased tone of the parasympathetic nervous system increases the tone of the bronchial smooth muscles and leads to the narrowing of the bronchi. The mediator of the vagus nerve fibers innervating the smooth muscles of the bronchi is acetylcholine. It causes contractions of these muscles through the activation of muscarinic **cholinoreceptors.**

The narrowing of the bronchi can be caused also by activating local reflexes in the vegetative ganglions of the airways.

The sympathetic nervous system causes bronchodilation. The bronchial tree is very much exposed to adrenaline and noradrenalin released into the blood by the sympathetic stimulation of the adrenal gland medulla. Both these hormones, especially adrenaline because of its greater stimulation of **beta-adrenergic receptors**, cause dilation of the bronchial tree.

Several substances can cause bronchoconstriction. The most important are **histamine and leukotrienes**. They are released in the lung tissues by leukocytes and mast cells and can cause airway obstruction (for example, in allergic reactions).

6.12. First inspiration of newborns

Umbilical ligation and development of hypoxia are followed by inhibition of the intra-uterine respiratory movements, and then within 1–1.5 minute the first respiratory movements appear.

During the first inspiration the thorax expands, ribs rise, their heads are fixed in the intervertebral fossae and they do not return to their initial position.

During the first respiratory movement negative pressure develops in the thoracic cavity which is 10–15 times higher than during a subsequent quiet breath.

Such a significant increase of negative pressure provides overcoming of the elastic recoil of pulmonary tissue and lung expansion. Active inspiration is followed by active expiration.

During subsequent respiratory movements lung distension is increased, their elastic recoil is reduced, the work of the respiratory movements is reduced.

After three respiratory movements pulmonary tissue becomes regularly pellucid, therefore, stretched. That is why the first inspiration is the heaviest, the most difficult.

Factors causing the first inspiration:

1. Umbilical ligation — ***anoxia***. Decreased O_2 level in the blood increases the excitability of the respiratory center and its sensitivity to CO_2.

2. ***Accumulation of CO_2*** — irritant capable to activate the respiratory center.

3. ***Metabolic acidosis*** developing after the removal of the placenta when extraction of acidic products is stopped and the alkaline reserves are reduced (decrease of pH).

4. Along with it, the stimuli for the appearance of respiration are ***various thermal, mechanical, thermal, and sensory irritants*** influencing the newborn who upon birth gets into a completely different environment.

5. Besides, there is an opinion that after the transit of a fetus through the ***birth canal, the constrained thorax*** due to its elasticity sharply extends, and significant negative pressure is accumulated in the thoracic cavity promoting the entry of air into the airways.

6.13. Features of respiration in different conditions

1. Respiration in muscle work. A person at rest consumes 250–300 mL of oxygen per 1 min, in fast walking — up to 2.5 L per minute, in hard physical work — up to 4 L per minute. Simultaneously, the formation of CO_2 and acidic products increases.

Lung ventilation increases proportionally to energy expenses (can reach up to 120–150 L per minute).

As muscle work starts, pCO_2 rises and blood pH goes down. Lung ventilation increases when the gas composition of blood is not changed yet. It means that at the beginning of muscle work***, hyperpnea*** is induced by nervous factors. The cerebral cortex, producing voluntary movements, activates the respiratory

center directly and through the hypothalamus. Besides, the essential role in the given process is played by impulses from the proprioreceptors (mechanoreceptors) of contracting muscles.

Then during muscle work there is a slow increase of lung ventilation up to a steady state.

Lactic acid formed during muscle work cannot be oxidized completely to H_2O and CO_2. It is accumulated in muscles and comes into the blood. This is an oxygen debt. Respiration strengthens and there comes a state when respiration and blood circulation achieve a certain level when short-breathing stops (dead point in sportsmen). Then hyperpnoea leads to the removal of CO_2 excess and rising of pH. The balance between the arrival and consumption of O_2 (a second wind phenomenon in sportsmen) is established.

At this phase the chemoreceptors are stimulated. Increased CO_2 formation in increased lung ventilation provides constant CO_2 volume in the blood.

Stimulation of the chemoreceptors is strengthened by the action of the lactic acid lowering the pH level of blood. A rise of the body temperature is also significant since it increases the respiration rate through the hypothalamus.

After the end of the work, lung ventilation is reduced but not to the initial level. It remains increased for some minutes under the influence of lactic acid and other suboxides.

There is gradual «repayment» of the ***oxygen debt***.

Along with increased lung ventilation in physical work there are increased values of:

1) heart rate (from 70 up to 150–200 beats per minute);

2) stroke volume (from 70 mL up to 200 mL);

3) cardiac output (from 4–5 L to 20–30 L);

4) blood flow in working muscles;

5) dissociation of HbO_2 (decrease of pH, rising of pCO_2, temperature);

6) oxygen utilization coefficient increases from 30–40 % to 50–60 %;

7) oxygen capacity of blood due to the release of depot blood. Besides, water loss occurring during the work due to sweating results in increased erythrocyte and Hb concentrations.

2. Respiration in the conditions of low atmospheric pressure (*climbers, depressurization cabins of pilots, parachutists, artificial pressure chamber*). The consequence is ***hypoxia as a result of decreased*** $\boldsymbol{pO_2}$.

At high altitudes (higher than **2 km)** lung ventilation increases due to the stimulation of the carotid and aortal chemoreceptors.

Elevated blood pressure and heart rate are directed to intensify the supply of tissues with O_2.

But increased lung ventilation causes a decreased pCO_2 level (*hypocapnia*). Hypocapnia inhibits the respiratory center thus limiting lung ventilation.

At an altitude of **4–5 km** mountain illness develops. The ***signs of mountain or altitude illness are*** drowsiness, decrease of appetite, apathy or euphoria, short-breathing, tachycardia, giddiness, vomiting, headache. Slowly developing hypoxia is especially dangerous because a person can lose consciousness before realizing the signs serving as signals of danger.

At an altitude of **7 km** loss of consciousness, breathlessness and blood circulation disorders hazardous for life can occur. As a result of hypoxia there are no unpleasant sensations, there is no feeling of anxiety or awareness of danger, and loss of consciousness can occur suddenly.

At high altitudes life is possible only if oxygen devices are used or in pressurized cabins, space suits in which high atmospheric pressure is maintained.

A long stay in the conditions of low atmospheric pressure is accompanied with ***acclimatization***, such as:

1. The erythrocyte count in the blood (erythrogenesis strengthens) is increased.

2. The amount of Hb is increased, which results in augmentation of the oxygen capacity of blood.

3. Lung ventilation increases.

4. Dissociation of HbO_2 increases (due to augmentation in erythrocytes of 2,3-glycerophosphate).

5. The length and density of capillaries increase.

6. Cell resistance (especially nervous ones) to hypoxia increases.

All effects of hypoxia can be divided into 4 zones separated from each other by effective thresholds (Table 6.3):

1. ***Neutral zone*** (***up to 2,000 m***) — physiological functions practically do not suffer.

2. ***Zone of complete compensation*** (**2,000–4,000 m**). Even in a person at rest heart rate, stroke volume, CO and MLV increase. Physical and mental working capacity is a little reduced.

3. ***Zone of incomplete compensation*** or zone of danger (***4,000–7,000 m***). The threshold of safety (4,000 m) is reached. Muscular twitching appears, blood pressure decreases, consciousness is dimmed (foggy brain). Work capacity is reduced, the ability to decision-making and reactions is affected.

4. ***Critical zone (>7,000 m)*** pO_2 in alveolar air becomes lower than the critical threshold (30–35 mm Hg). Loss of consciousness, cramps occur. This process is reversible if the duration of the stay is not long. If a person stays at this altitude for a long time, the CNS is damaged, which may lead to death.

7–8 km — life-hazardous for most people.

8.5–9 km — the limit above which a human cannot ascend without O_2.

9–12 km — a human must apply an oxygen device.

12 km — a human must wear a space suit in which high pressure is maintained.

A person can hold breath for 1–2 minutes. After prior hyperventilation a trained person can hold breath for 3–4 minutes. This is the limit of human stay under water. But the danger is that a rapid decrease of blood oxygenation can result in loss of consciousness, and under the influence of the increased pCO_2 level of blood breath will occur, and the diver will be breathless having water in the lungs.

Table 6.3 — Critical zones of hypoxia (in respiration at the lowered atmospheric pressure)

Name of a zone	**Altitude**	**Changes in the functioning of the organism**
Neutral zone	up to 2,000 m	Physiological functions practically do not suffer
Zone of complete compensation	2,000–4,000 m	• Lung ventilation increases (due to the stimulation of carotid and aortal chemoreceptors). • Heart rate increases. • Systolic and minute volume of blood increase. • Blood pressure increases. • Physical and mental work capacity is a little reduced
Zone of incomplete compensation (zone of danger)	4,000–7,000 m	• Signs of mountain illness develop: apathy or euphoria, shortbreathing, tachycardia, giddiness, vomiting, headache. • Muscular twitching appears. • Blood pressure decreases. • Working capacity is reduced, the ability to decision-making and reactions is affected. • Consciousness is dimmed
Critical zone	>7000 m	• pO_2 in alveolar air becomes lower than the critical threshold (30–35 mm Hg). • Cramps, loss of consciousness, breathlessness, and blood circulation disorders dangerous for life can occur. If such a state lasts for a long period of time, the central nervous system is damaged, which may cause death

3. Respiration in the conditions of high atmospheric pressure (*work under water, diving)*. The pressure in water increases by about 1 atm for each 10 m increase in depth. At a depth of 100 m a person should inhale a gas mixture under a pressure exceeding atmospheric pressure by 10 times. Therefore, oxygen in the gas mixture is added at an amount so that its pO_2 at the depth was close to that in usual conditions.

At depths under the influence of pressure gases are dissolved in the blood. Due to fast decompression gases pass from the dissolved state into gas state, and air vesicles are formed, which results in gas embolism (**C*aisson disease***). If a diver does not fully exhale upon ascent, the air in the lungs expands as the pressure decreases, overinflating the lungs and forcing air vesicles (emboli) into the bloodstream. When the gas emboli reach the arteries to the brain, the blood blockage causes unconsciousness. Other symptoms are: muscle pain, giddiness, vomiting, shortbreathing. In this case it is necessary to place the person into a compression chamber, to create the pressure in it conforming the pressure at the depth from which the person has been lifted; which again will lead to dissolution of the air vesicles in the blood, and then gradually to decreased pressure (decompression). Gas transition from its dissolved state into gas will happen slowly and the vesicles will be removed from the organism without causing gas embolism.

Review questions

1. Where are the motoneurons of the incercostal and abdominal muscles and diaphragm located? Where is the respiratory center located? Name the two groups of respiratory neurons. What are the functions of the dorsal and ventral respiratory nuclei?

2. What is the role of the gas composition of blood in the regulation of the activity of the respiratory center? What are normocapnia, hypercapnia, and hypocapnia? What are normoxia, hypoxemia and hypoxia? How does the respiration change in hypoxia, hypercapnia, and hypocapnia?

3. What is the role of the chemoreceptors in the regulation of respiration? Where are the chemoreceptors located? What factors cause excitation of the central and peripheral chemorereceptors?

4. What is the role of the mechanoreceptors of the lungs in the regulation of respiration? Where are the mechanoreceptors of the lungs located? What factors cause their excitation? What is the inspiration-inhibiting reflex?

5. Where are the irritant receptors located? What factors cause excitation of the irritant mechanoreceptors? What are the results of the stimulation of the irritant receptors? What is the «deep sigh» reflex?

6. What is the role of the proprioreceptors of respiratory muscles in the regulation of respiration?

7. Where is the pneumotaxic center located? What is the role of the pneumotoxic center in the regulation of respiration?

8. What protective reflexes appear during the stimulation of the receptors of the upper airways ? Describe them.

9. What is the role of the cerebral cortex in the regulation of respiration? How is respiration changed under the influence of the nonspecific factors: cold and warmth influences, pain, hormones? Describe the features of the coordination of respiration and blood circulation.

10. Describe the mechanism of the first inspiration of newborns. What are the main factors causing the first breath?

11. What are the features of respiration during muscle work? What are the features of respiration in the conditions of low atmospheric pressure? What are the main signs of mountain illness? Name the critical zones of hypoxia and describe them. What are the features of respiration in the conditions of high atmospheric pressure? What is Caisson disease? What are the mechanisms of its development and symptoms?

Multiple Choice Questions
PHYSIOLOGY OF RESPIRATORY SYSTEM

1. Give the correct sequence of the stages of respiration.

Variants of answer:

a) lung ventilation, gas exchange in the lungs, gas transport by blood, biological oxidation, gas exchange between blood and tissues;

b) gas exchange in the lungs, lung ventilation, gas transport by blood, gas exchange between blood and tissues, biological oxidation;

c) lung ventilation, gas exchange in the lungs, gas transport by blood, gas exchange between blood and tissues, biological oxidation;

d) gas exchange between blood and tissues, gas transport by blood, lung ventilation, gas exchange in the lungs, biological oxidation;

e) lung ventilation, gas exchange in the lungs, biological oxidation, gas transport by blood, gas exchange between blood and tissues.

2. As a result of lung ventilation …

Variants of answer:

a) air exchange within the gas-exchange zone occurs;

b) air cleaning occurs;

c) all the answers are correct;

d) the constancy of the composition of alveolar air is maintained;

e) air warming and humidifying occur.

3. How does the lumen of the airways change during inspiration?

Variants of answer:

a) it decreases;

b) it increases;

c) at the beginning it increases, and then it decreases;

d) it does not change;

e) at the beginning it decreases, and then it increases.

4. Internal respiratory intercostal muscles participate in …

Variants of answer:

a) quiet inspiration;

b) forced inspiration;

c) forced expiration;

d) quiet expiration;

e) all the answers are correct.

5. The lungs of an adult are stretched ...

Variants of answer:

a) constantly;
b) during quiet inspiration;
c) during quiet expiration;
d) during forced inspiration;
e) during forced expiration.

6. The elastic recoil of the lungs is…

Variants of answer:

a) the force aimed at increased lung volume;
b) the passive strain of elastic lung tissue fibers;
c) the tone of bronchial muscles;
d) the force aimed at decreased lung volume.
e) elasticity of the costal cartilages.

7. Which factor provides about 2/3 of the elastic recoil of the lungs?

Variants of answer:

a) elasticity of lung tissues;
b) the tone of bronchial muscles;
c) elasticity of the costal cartilages;
d) surface tension of alveolar liquid;
e) surfactant.

8. Which factor promotes decreased surface tension of the alveoli?

Variants of answer:

a) surfactant;
b) Fletcher's factor;
c) bradykinin;
d) lysozyme;
e) histamine.

9. Negative pressure in the pleural cavity is provided mainly by...

Variants of answer:

a) the decreased tone of the bronchioles;
b) the presence of dead space;
c) the elastic recoil of the lungs;
d) the aerohematic barrier;
e) all the answers are correct.

10. What is the name of the condition under which air penetrates into the pleural cavity?

Variants of answer:

a) hemothorax;
b) pneumothorax;
c) hydrothorax;
d) plevritis;
e) hypercapnia.

11. The maximal volume of air which can be present in the lungs is called…

a) vital capacity of the lungs;
b) functional residual capacity;
c) total capacity of the lungs;
d) reserve volume of the lungs;
e) inspiratory capacity.

12. Physiologic dead space is the sum of...

Variants of answer:

a) anatomic dead space and respiratory volume;
b) anatomic and alveolar dead spaces;
c) anatomic dead space and residual volume;
d) alveolar dead space and reserve volume of inspiration;
e) alveolar dead space and respiratory volume.

13. The partial pressure of gas in liquid is a force, exerted by...

Variants of answer:

a) gas molecules which tend to be dissolved in the liquid;
b) gas molecules cooperating among themselves;
c) gas molecules which tend to leave the liquid;
d) gas molecules cooperating with hemoglobin;
e) all the answers are correct.

14. If the partial pressure of gas above liquid is higher than its pressure in the liquid, ...

Variants of answer:

a) the gas leaves the liquid;
b) the gas is not dissolved in the liquid;
c) the gas is dissolved in the liquid;
d) the gas is accumulated in the lungs;
e) the gas leaves the lungs.

15. The permeability of the alveolar membrane to gases is characterized by the parameter...

Variants of answer:

a) diffusion capacity of the lungs;
b) elastic resistance of the lungs;
c) size of dead space;
d) size of vital capacity of the lungs;
e) superficial tension of the alveoli.

16. In which form is oxygen transported by blood?

Variants of answer:

a) only in dissolved state;
b) only in connection with hemoglobin;
c) in dissolved state and in connection with hemoglobin;
d) in connection with blood plasma proteins;
e) in dissolved state and in connection with blood plasma proteins.

17. Can the amount of oxygen transported in physically dissolved blood (not bound with Hb), provide the oxygen demands of an organism in usual conditions?

Variants of answer:

a) yes, it can;
b) yes, it can in conditions of rest;
c) no, it can`t;
d) yes, it can, in conditions of basal metabolism;
e) yes, it can, in conditions of low atmospheric pressure.

18. What valence does iron have if it binds to a hemoglobin molecule?

Variants of answer:

a) 3;
b) 4;
c) 2;
d) 1;
e) 6.

19. In which hemoglobin compounds is iron trivalent?

Variants of answer:

a) in oxyhemoglobin;
b) in carbohemoglobin;
c) in methhemoglobin;
d) in carboxyhemoglobin;
e) in oxyhemoglobin and carbohemoglobin.

20. How much oxygen can one gram of hemoglobin bind?

Variants of answer:

a) 0.8 milliliters;

b) 2.5 milliliters;

c) 1.34 milliliters;

d) 1.8 milliliters;

e) 3.14 milliliters.

21. The maximum amount of oxygen which can be bound by hemoglobin in full saturation by oxygen is named...

Variants of answer:

a) the oxygen capacity of blood;

b) the color index;

c) the parameter of saturation;

d) the hematocrit;

e) the vital capacity of blood.

22. How does the oxygen capacity of blood change if the concentration of hemoglobin decreases?

Variants of answer:

a) it increases;

b) it does not change;

c) it decreases;

d) it can change in different ways;

e) at the beginning it increases, and then it decreases.

23. Give the comparative description of the affinity of hemoglobin and myoglobin to oxygen.

Variants of answer:

a) the affinity of hemoglobin is higher than that of myoglobin;

b) hemoglobin and myoglobin possess the same affinity to oxygen;

c) the affinity of myoglobin is higher than that of hemoglobin;

d) myoglobin is not capable of oxygen binding;

e) hemoglobin is not capable of oxygen binding.

24. In normal conditions arterial oxygen saturation makes approximately...

Variants of answer:

a) 98–100 %;

b) 96–98 %;

c) 100–105 %;

d) 60–75 %;

e) 75–85 %.

25. How does the affinity of hemoglobin to oxygen change if the dissociation curve shifts to the right?

Variants of answer:

a) it decreases;

b) it increases;

c) it does not change;

d) it can change in different ways;

e) at the beginning it increases, and then it decreases.

26. A shift of the dissociation curve of oxyhemoglobin to the right promotes...

Variants of answer:

a) decreased oxygen supply of tissues;

b) increased oxygen supply of tissues;

c) development of oxygen starvation of tissues;

d) tissue oxygenation does not change;

e) at the beginning tissue oxygen saturation increases and then it sharply decreases.

27. How does oxyhemoglobin dissociation change if the dissociation curve shifts to the left?

Variants of answer:

a) it increases;

b) it does not change;

c) it decreases;

d) it can change in different ways;

e) at the beginning it increases, and then it decreases.

28. How does the affinity of hemoglobin to oxygen change if the body temperature of a patient increases up to 39 °C?

Variants of answer:

a) it increases;

b) it does not change;

c) it decreases;

d) it increases greatly;

e) at the beginning it increases, and then it decreases.

29. How does the affinity of hemoglobin to oxygen change if the concentration of hydrogen ions and CO_2 in the blood increases?

Variants of answer:

a) it increases;

b) it decreases;

c) it does not change;
d) it can change in different ways;
e) at the beginning it increases, and then it decreases.

30. How does oxygen supply of muscles change, if during physical exercise an acid medium is created, and the CO_2 concentration and temperature rise?

Variants of answer:
a) it increases;
b) it decreases;
c) it does not change;
d) it can change in different ways;
e) at the beginning it increases, and then it decreases.

31. Transition of tissues from rest into an active state creates conditions for...

Variants of answer:
a) increased dissociation of oxyhemoglobin;
b) decreased dissociation of oxyhemoglobin;
c) decreased dissociation of carbohemoglobin;
d) increased dissociation of carbohemoglobin;
e) decreased dissociation of methhemoglobin.

32. How will the affinity of hemoglobin to oxygen change if the concentration of 2,3-diphosphat glycerate in erythrocytes increases?

Variants of answer:
a) it will increase;
b) it will decrease;
c) it will not change;
d) it can change in different ways;
e) at the beginning it increases, and then it decreases.

33. Compare the affinity of hemoglobin to oxygen in a fetus (HbF) and in an adult (HbA):

Variants of answer:
a) the affinity of HbA is higher than that of HbF;
b) both the kinds of Hb possess identical affinity;
c) the affinity of HbF is higher than that of HbA.
d) Hb F is not capable of oxygen binding;
e) HbA is not capable of oxygen binding.

34. In a fetus the dissociation curve of oxyhemoglobin is shifted to…

Variants of answer:
a) to the left;

b) to the right;
c) the dissociation curves of oxyhemoglobin of fetus and mother are identical;
d) it can be shifted in different directions;
e) at the beginning it is shifted to the left, and then to the right.

35. The oxygen utilization coefficient in a person doing physical exercise increases up to …

Variants of answer:
a) 20–40 %;
b) 90–100 %;
c) 50–60 %;
d) 70–80 %;
e) 80–90 %.

36. In which form is carbonic gas transported in the blood?

Variants of answer:
a) as $NaHCO_3$;
b) as $KHCO_3$;
c) bound to hemoglobin;
d) in dissolved state;
e) all the answers are correct.

37. Where is carbonic anhydrase mainly contained in the blood?

Variants of answer:
a) in plasma;
b) in leukocytes;
c) in erythrocytes;
d) in thrombocytes;
e) all the answers are correct.

38. The exchange of oxygen and carbonic gas between blood and tissues is carried out by ….

Variants of answer:
a) active transport;
b) participation of transmitting membrane proteins;
c) osmosis;
d) simple diffusion;
e) all the answers are correct.

39. Dissection of the spinal cord between the cervical and thoracic regions...

Variants of answer:
a) results in respiratory arrest;

b) preserves diaphragmatic respiration;
c) preserves costal respiration;
d) does not lead to any changes of respiration;
e) results in irregular respiration.

40. Automaticity is a property of the neurons of the respiratory center which are located in...

Variants of answer:
a) the cortex of the cerebrum;
b) the spinal cord;
c) the medulla oblongata;
d) the pons varolii;
e) the thalamus.

41. How does respiration change after dissection of the vagus nerves?

Variants of answer:
a) it becomes frequent and superficial;
b) it becomes frequent and deep;
c) it becomes rare and superficial;
d) it becomes rare and deep;
e) it does not change.

42. The activity of the respiratory center mainly depends on...

Variants of answer:
a) the pCO_2, pO_2, pH values of arterial blood;
b) the amount of the formed elements of blood;
c) the hematocrit;
d) the amount of blood;
e) the vital capacity of lungs.

43. Insufficient oxygen supply of tissues is named...

Variants of answer:
a) hypercapnia;
b) asphyxia;
c) acidosis;
d) hypoxia;
e) hypocapnia.

44. Hypercapnia and low blood pH level (acidosis) are accompanied by the development of...

Variants of answer:
a) eupnea;

b) hyperpnea;
c) apnea;
d) periodic respiration;
e) asphyxia.

45. Hypocapnia and high blood pH level (alkalosis) are accompanied by the development of...

Variants of answer:
a) hyperpnea;
b) eupnea;
c) hypopnea;
d) asphyxia;
e) periodic respiration.

46. The peripheral chemoreceptors, which participate in the regulation of respiration, are located mainly...

Variants of answer:
a) in the pleura;
b) in the carotid sinus and arch of aorta;
c) in respiratory muscles;
d) in the trachea;
e) in the bronchi.

47. Which receptors participate in the regulation of respiration?

Variants of answer:
a) central and peripheral chemoreceptors;
b) stretch receptors;
c) irritant receptors;
d) upper airway receptors;
e) all answers are correct.

48. Which receptors of the lungs react to the action of tobacco smoke, dust, mucus, gases of caustic substances?

Variants of answer:
a) stretch receptors;
b) J-receptors;
c) irritant receptors;
d) central chemoreceptors;
e) all the above-named receptors.

49. Caisson disease develops in fast transition from the zone of ...

Variants of answer:

a) high barometric pressure into the zone of lower barometric pressure;
b) low barometric pressure into the zone of higher barometric pressure;
c) atmospheric pressure of 760 mm Hg into the zone with the same pressure;
d) incomplete compensation into the critical zone;
e) complete compensation into the zone of incomplete compensation.

50. Mountain illness starts to develop at an altitude of...

Variants of answer:

a) 100 m;
b) 1,000 m;
c) 4,000 m;
d) 7,000 m;
e) 8,000 m.

51. Which is true: during inspiration intrapleural pressure becomes…

Variants of answer:

a) more negative;
b) more positive;
c) it stays the same;
d) initially positive, then negative;
e) there is no relation between inspiration and intrapleural pressure.

52. The volume of air taken in and given out during normal respiration is referred to as…

Variants of answer:

a) the inspiratory reserve volume;
b) the tidal volume;
c) the expiratory reserve volume;
d) the vital capacity;
e) the residual volume**.**

53. The tidal volume is calculated by…

Variants of answer:

a) the inspiratory capacity minus the inspiratory reserve volume;
b) the total lung capacity minus the inspiratory reserve volume;
c) the functional residual capacity minus the residual volume;
d) the vital capacity minus the expiratory reserve volume;
e) the total lung capacity minus the expiratory reserve volume.

54. The functional residual capacity is…

Variants of answer:

a) the air volume remaining after forced expiration;
b) the tidal volume plus the volume inspired forcefully;
c) the air volume expired after normal expiration;
d) the tidal volume plus the volume expired by forced expiration;
e) the air volume remaining after normal expiration.

55. The most economical way of breathing in a person having normal lung compliance and increased airway resistance is…

Variants of answer:

a) rapid and deep;
b) rapid and shallow;
c) slow and deep;
d) slow and shallow;
e) none of the above-mentioned.

56. Spirometry can demonstrate and measure all of the following except:

Variants of answer:

a) the tidal volume;
b) the residual volume;
c) the vital capacity;
d) the inspiratory reserve volume;
e) the expiratory reserve volume.

57. The total alveolar ventilation volume (in L/min) is …

Variants of answer:

a) 1.5;
b) 3.5;
c) 4.2;
d) 7.0;
e) 10.

58. Name the main inspiration muscles which participate in quiet inspiration…

Variants of answer:

a) abdominal muscles and the diaphragm;
b) external intercostal muscles and the diaphragm;
c) internal intercostal muscles and the diaphragm;
d) external and internal intercostal muscles;
e) internal intercostal muscles and abdominal muscles.

59. Pulmonary surfactant is secreted by…

Variants of answer:

a) type-I pneumocytes;
b) type-II pneumocytes;
c) bronchial goblet cells;
d) the endothelium of pulmonary vasculature;
e) macrophages.

60. Pulmonary surfactant is formed by…

Variants of answer:

a) fibrin;
b) mucoprotein;
c) phospholipids;
d) fibrinogen;
e) plasmin.

61. The ratio of ventilation to perfusion is maximal at…

Variants of answer:

a) the hilum of the lungs;
b) the base of the lungs;
c) the apex of the lungs;
d) the middle zone of the lungs;
e) it is identical in all the parts of lungs.

62. The factor responsible for the left shift of the HbO_2 dissociation curve is…

Variants of answer:

a) increase of 2,3-diphosphat glycerate in erythrocytes;
b) fall in temperature;
c) fall in pH;
d) increased level of CO_2 in the blood;
e) all the answers are correct**.**

63. Which compound shifts the HbO_2 dissociation curve to the right…

Variants of answer:

a) 1-phosphoglycerate;
b) 2,3-diphosphoglycerate;
c) 1,3-diphosphoglycerate;
d) glyceraldehydes;
e) all the answers are correct.

64. Which is true about the HbO_2 dissociation curve?

Variants of answer:

a) acidosis shifts the HbO_2 dissociation curve to the right;

b) increased CO_2 level shifts the curve to the left;

c) hypoxia shifts the curve to the left;

d) 2,3-diphosphoglycerate has no effect on the curve;

e) alkalosis shifts the curve to the right.

65. The HbO_2 dissociation curve shifts to the left in…

Variants of answer:

a) acidosis;

b) high pH;

c) high CO_2;

d) high temperature;

e) increased amount of 2,3-diphosphoglycerate in erythrocytes.

66. All of the following factors influence the hemoglobin dissociation curve, except…

Variants of answer:

a) chloride ion concentration;

b) CO_2 tension;

c) temperature;

d) 2-3-diphosphat glycerate levels;

e) pH.

67. ***The HbO_2 dissociation curve shifts to the right in all the below cases except for…***

Variants of answer:

a) hypercapnea;

b) rise in temperature;

c) increased 2, 3-diphosphoglycerate level;

d) metabolic alkalosis;

e) acidosis.

68. Apnoea is defined as….

Variants of answer:

a) cessation of heart beat;

b) cessation of respiration;

c) irregular respiration;

d) respiratory rate;

e) respiratory cycle.

69. The stimulation of … receptors causes the reflex of Hering-Breuer.

Variants of answer:

a) arterial chemoreceptors;

b) central chemoreceptors;

c) mechanoreceptors of lungs;

d) irritant receptors;

e) all the answers are correct.

70. Which of the following does not stimulate the peripheral chemoreceptors?

Variants of answer:

a) hypoxia;

b) hypocapnia;

c) acidosis;

d) hypercapnia;

e) all the answers are correct.

CORRECT ANSWERS
PHYSIOLOGY OF THE RESPIRATORY SYSTEM

№ question	Correct answers	№ question	Correct answers	№ question	Correct answers	№ question	Correct answers
1	c	19	c	37	c	55	c
2	c	20	c	38	d	56	b
3	b	21	a	39	b	57	c
4	c	22	c	40	c	58	b
5	a	23	c	41	d	59	b
6	d	24	b	42	a	60	c
7	d	25	a	43	d	61	c
8	a	26	b	44	b	62	b
9	c	27	c	45	c	63	b
10	b	28	c	46	b	64	a
11	c	29	b	47	e	65	b
12	b	30	a	48	c	66	a
13	c	31	a	49	a	67	d
14	c	32	b	50	c	68	b
15	a	33	c	51	a	69	c
16	c	34	a	52	b	70	b
17	c	35	c	53	a		
18	c	36	e	54	e		

BASIC PHYSIOLOGICAL CONSTANTS

Constants of the blood system	
Amount of blood in adults	4.5–6.0 L (6–8 % of body weight)
Hematocrit in males	0.42–0.52
Hematocrit in females	0.37–0.47
Deposited blood	45–50 %
Circulating blood	50–55 %
Volume of blood plasma	approx. 3.0 L
Composition of blood plasma:	
Water	90–92 %
Solid residue	8–10 %
Total protein	65–85 g/L
Albumins	35–55 g/L
Globulins	20–35 g/L
Fibrinogen	2–4 g/L
Urea	2.5–8.3 mmol/L
Total bilirubin	3.4–20.5 mmol/L
Glucose (whole blood)	3.30–5.55 mmol/L
Glucose (plasma)	3.30–6.10 mmol/L
Cholesterol	3.0–6.2 mmol/L
Triglycerides	0.55–1.65 mmol/L
Inorganic substances	0.9 %
Viscosity of blood in adults	4.5–5.0
Relative density	1.050–1.060
pH of arterial blood:	7.37-7.45
pH of venous blood	7.34-7.43
pH values compatible with life	7.0–7.8
Osmotic pressure of blood	290± 10 mosm/L
Oncotic pressure of blood	25-35 mm Hg
Erythrocytes in males	$4.5–5.1 \times 10^{12}$/L (tera per litre)
Erythrocytes in females	$3.7–4.7 \times 10^{12}$/L (tera per litre)
Normal amount of hemoglobin in males	130–160 g/L
Normal amount of hemoglobin in females	120–140 g/L
Color index in adults	0.85–1.05
Osmotic resistance of erythrocytes: min	0.46–0.48% solution of NaCl
Osmotic resistance of erythrocytes: max	0.32–0.34% solution of NaCl

Erythrocyte sedimentation rate in males	1–10 mm / hour
Erythrocyte sedimentation rate in females	2–15 mm / hour
Erythrocyte sedimentation rate in new-borns	1–2 mm / hour
Leucocytes in adults	$4–9 \times 10^9$ /L (giga per litre)
Leucocytes in newborns	$15–20 \times 10^9$ /L (giga per litre)
Leukocyte formula (%): neutrophils:	
Myelocytes	0
Metamyelocytes	0–1.0
Stab neutrophils	1–6
Segmentonuclear neutrophils	47–72
Eosinocytes	0.5–5.0
Basophils	0–1.0
Lymphocytes	19–37
Monocytes	2–11
Regeneration index (shift to the left)	0.05–0.1
Thrombocytes	$150–450 \times 10^9$/L (giga per litre)
Blood coagulation time (by Lee-White)	5–7 min
Constants of the respiratory system	
Respiratory rate in adults	12–18 breaths / minute
Respiratory rate in newborns	40–55 breaths / minute
Excursion of the thorax in males	7–10 cm
Excursion of the thorax in females	5–8 cm
Normal inspiration-expiration ratio	1:1.2
Tidal volume	0.3–0.9 L
Inspiratory reserve volume	1.5–2.0 L
Expiratory reserve volume	1.0–1.5 L
Vital capacity of the lungs	3.5–5.0 L
Residual volume	1.0–1.5 L
Functional residual capacity	2.5 L
Inspiratory capacity	2.0 L
Dead space voume	140–170 mL
Coefficient of lung ventilation	1/7
Respiratory minute volume for a person at rest	6-8 L/min
Respiratory minute volume for a person during physical exercise	up to 120 L/minute
Alveolar ventilation	4.2–5.6 L/minute

Maximal ventilation of the lungs	120–170 L/minute
pO_2 of alveolar air	100 mm Hg
pCO_2 of alveolar air	40 mm Hg
pO_2 of arterial blood	96 mm Hg
pCO_2 of arterial blood	39 mm Hg
pO_2 of venous blood	40 mm Hg
pCO_2 of venous blood	46 mm Hg
Forced expiratory volume	approximately 3.0 L (70-80 % of VCL)
Blood oxygen capacity	18-22 % mL/dL
Ventilation-perfusion coefficient	0.8–1.0
Oxygen consumption by a person at rest	250–300 mL/min
O_2 utilization coefficient in a person at rest	30-40 %

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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 1

Редактор ***Т. М. Кожемякина***
Компьютерная верстка ***Ж. И. Цырыкова***

Подписано в печать 05.02.2021.
Формат 60×84 1/8. Бумага офсетная 80 г/м². Гарнитура «Calibri».
Усл. печ. л. 35,34. Уч.-изд. л. 38,64. Тираж 100 экз. Заказ № 283.

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.
Ул. Ланге, 5, 246000, Гомель.