MINISTRY OF HEALTH CARE REPUBLIC OF BELARUS
GOMEL STATE MEDICAL UNIVERSITY

Normal Physiology Department

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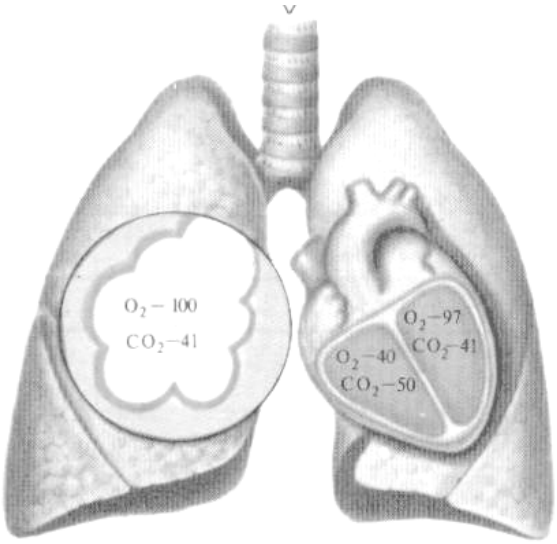
HUMAN PHYSIOLOGY

In two parts

Part I
Lectures for overseas students in English medium



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Представлен лекционный материал по нормальной физиологии, читаемый студентам факультета по подготовке специалистов для зарубежных стран, которые занимаются на английском языке.

В первой части авторами представлены современные сведения о физиологии крови, сердечно-сосудистой системы, физиологии дыхания и пищеварения. В конце представлены базовые константы физиологических систем в Международной системе физических единиц (СИ).

При составлении и переводе данного издания использовались материалы по разделу физиология жидких сред организма и физиология сердечно сосудистой системы, опубликованных ранее под редакцией профессора А.И. Киени и доцента Э.М. Заики.

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FOREWORD

The present guidance contains lectures in normal physiology read to overseas students who study in English medium. All material corresponds to Program in Normal physiology for students in higher medical schools, No. 08-14/5941 approved by the Ministry of Health of the Republic of Belarus.

The guidance contains contemporary context of the subject and methods of physiology, nervous and humoral mechanisms of functions regulation. Section in physiology of blood is describes main functions, composition and properties of blood.

The first part of the guidance also includes data on physiology of cardio-vascular system: composition and functions of the myocardium, electric manifestation of the cardiac activity, work of heart and its regulation, laws of hemodynamics, regulation of vascular tonus and the level of blood pressure.

The guidance also includes information on physiology of respiration: structural-functional characteristic of respiratory organs, gas transport with blood, regulation of respiration, peculiarities of breathing in different conditions.

Section in physiology of digestive system describes digestion properties in various regions of gastro-intestinal tract and their regulation.

Conclusion includes main constants of a healthy person.

Authors admit that the guidance has a restricted information about all aspects of physiology of blood, physiology of cardio-vascular system, physiology of respiration and digestion. Broader information can be obtained from list of literature at the end of the guidance.

Authors are grateful to anyone for comments which will be considered in further editions.

ПРЕДИСЛОВИЕ

Настоящее пособие представляет собой конспективный текст лекций по нормальной физиологии, которые читаются студентам факультета по подготовке специалистов для зарубежных стран УО «Гомельский государственный медицинский университет», обучающихся на английском языке. Материал пособия соответствует Программе по нормальной физиологии для студентов лечебно высших медицинских учебных заведений № 08-14/5941, утвержденной Министерством здравоохранения Республики Беларусь от 3 сентября 1997 г.

В пособие включены современные сведения о предмете и методах физиологии, нервных и гуморальных механизмах регуляции функций. В разделе физиология крови рассмотрены основные функции, состав, количество и свойства крови. Представлены сведения о сущности системы гемостаза и регуляции системы крови.

В первую часть пособия также включены материалы о физиологии сердечно-сосудистой системы: строении и свойства миокарда, электрических проявлениях сердечной деятельности, работе сердца и ее регуляции, изложены основные законы гемодинамики, регуляции тонуса сосудов и уровня артериального давления. Далее в пособии расположены материалы по физиологии дыхания: структурно-функциональная характеристика органов дыхания, транспорт газов кровью, регуляция дыхания, особенности дыхания в различных условиях.

В разделе физиология пищеварительной системы описаны особенности пищеварения в различных отделах желудочно-кишечного тракта и их регуляции.

В заключении представлены основные константы здорового человека.

При этом авторы осознают, что в данном пособии в связи с небольшим его объемом не представилось возможным осветить подробно все аспекты физиологии крови, физиологии сердечно-сосудистой системы, физиологии дыхания и пищеварения. Более расширенные сведения можно получить из списка литературы расположенного в конце пособия.

Авторы будут весьма благодарны всем, кто сочтет возможным высказать свои критические замечания в адрес предлагаемого пособия, которые будут восприняты как выражение желания оказать помощь в его улучшении при последующим переиздании.

INTRODUCTION

Theme: Subject and problems of physiology. General principles of physiological functions regulation.

Plan:

1. Subject and problems of physiology. Branches of modern physiology. Methods of investigation in physiology.
2. General concept of the structure and physiological properties of an organism.
3. General principles of physiological functions regulation. Nervous and humoral regulation.
4. Reflex as principle of the organization and regulation of physiological functions.
5. Brief history of the physiology development in Russia and Belarus.
6. Value of physiology in medical education.

1. Subject and problems of physiology. Branches of modern physiology. Methods of investigation in physiology

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

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

Branches of modern physiology

Physiology is divided into interrelated directions: general, special and applied physiology.

General physiology focuses on scientific data describing general aspects of vital activity: metabolism, mechanisms of regulation, property of biological membranes and separate cells, tissue, general laws of the reaction of the organism and its structures to irritation, 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 (blood circulation, respiratory, digestive).

Applied physiology studies behaviour of the human organism within particular working conditions (aviation, space physiology) or in particular climatic environment.

Physiology is divided into **normal** and **pathological**. Pathological physiology studies vital activity of an ill organism, nature, course and extent of a disease, develops methods of experimental therapy.

Methods of physiology

Physiology is an experimental science, its basic method is the experiment which allows to study main mechanisms of functions of the organ, cell, system, mechanisms of regulation and maintenance of vital activity.

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

Acute experiments are performed without following asepsis or antiseptics rules. An animal dies after such experiment.

Chronic experiments are performed for a long period of time (may last for years) to get reliable data following the above said rules. After such investigations an animal stays alive, e.g., fistula experiment.

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

a) Suppressing of functions up to its complete termination. For example, depressing of the functions of 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 a tissue from one region into another in a person.

b) Homotransplantations — transplantation of a tissue or an organ from one person to another.

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

d) Heterotransplantation - transplantation of a tissue or an organ from one species of an animal to the other.

2. Deinnervation.

a). Surgical dissection.

b). Drug action.

3. Method of vascular anastomoses (used for dysfunctioning of an organ).

4. Radiotelemetry.

5. Catheterization.

6. Method of radioactive atoms.

In its development physiology had several stages: empiric, anatomic-functional, functional; at all stages of studying of physiological processes there were two directions — analytical and synthetic.

The analytical direction is focused on study of a particular process proceeding in an organ, tissue or a cell as the independent, i.e. outside of its communication with other processes in the examined object. Such direction gives the complex representation about mechanisms of the given process.

This approach in physiology was replaced by **synthetic**, induced to a greater extent by the academician I.P. Pavlov. This period of the experimental physiology is characterized by tendency to study function of an organism in natural conditions, considering numerous factors of the interaction of an organism and the environment.

2. The general representations about structure and physiological properties of an organism

The human organism is an independent structural functional unit of the inorganic and organic nature and closely interacts with environment. The organism has a set of attributes and the properties characterizing and determining any alive system: metabolism, growth, development, reproduction, variability, heredity, reactivity, reliability. Reliability of the functioning of an organism is ensured by the superfluity of built, 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 organism. Structures of the human organism are in strict hierarchical construction directed to reach the optimal interaction of the organism and the environment. The alive organism is an open thermodynamic system exchanging energy and information with the environment. Environment provides an organism with nutrients, light, thermal energy, influences sensory systems of the organism. However, the healthy organism optimum functions till external impacts or its own internal processes do not break stability of the homeostasis, optimal condition of metabolism, physical and chemical constants of the organism.

3. The general principles of regulation physiological functions. Nervous and humoral regulation

Physiological regulation is a control over functions of the organism in order to adapt it to the environment. Regulation of functions of the organism is the main source of steady of medium of the organism and its adaptation to the changing conditions of the existence and is performed by the principle of self-regulation by the formation of functional systems.

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

Humoral regulation is performed through liquid mediums of the organism (blood, lymph, intercellular and cerebrospinal fluids) with the help of various biologically active substances excreted by specialized cells, tissues or organs. This kind of regulation can be carried out at the level of structures of organ — 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 influence metabolism, stimulate morpho-formation processes, differentiation, growth, metamorphosis of cells, etc.

Humoral way of regulation is rather slow, the speed of response depends on the period of formation and secretion of the hormone, its penetration into lymph and blood, speed of blood-flow. Period of action of the hormone depends on the speed of its destruction in the organism. In various cells of the organism including brain, neuropeptides are formed which determine behaviour of the organism and regulate secretion of hormones.

Nervous regulation is carried out via nervous system, is based on data processing by neurons and its transmission along the nerves. It has the following features:

• high speed of action development;

• precise communications;

• high specificity — only strict number of components needed at present participate in reaction.

In the process of evolution there was a uniting of nervous and humoral mechanisms of regulation.

Division of regulation mechanisms into nervous and humoral is conditional. Within organism these mechanisms are inseparable.

4. Reflex as principle of organization of regulation and physiological functions

The basis of the central nervous system (CNS) activity is the reflex principle. Reflex is a natural reaction of an organism to change of the external and internal medium. This reaction is determined by the participation of nervous system in response to irritation of receptors. Reflex sets up the balance of the activity of organs within the system, system within the organism, organism in its interrelations with the environment. The structural basis of reflex is the reflex arch. It includes the following:

1) sensory receptors receiving irritation from external or internal;

2) afferent (sensitive) nervous fiber;

3) nerve centres;

4) motor (efferent) nerve conductors;

5) effector (executing organs).

An obligatory element of reflex is the feedback between an the executing organs and CNS.

5. Brief history of physiology development in Russia and Belarus

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

The following Russian scientists contributed much into physiology: I.P. Pavlov, I.M. Sechenov, A.I. Babuhin, F.V. Ovsyannikov, V.J. Danilevsky.

Physiology of higher nervous activity received its fundamental development in scientific experiments of I.P. Pavlov. Result of his work was the most important contribution into physiology of cardiovascular system, higher nervous activity, digestion (in 1904 he was awarded a Nobel Prize for this work). I.P. Pavlov discovered the conditioned reflex.

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

The most rapid development of physiology was in the 20^{th} century. W. Kennon developed the doctrine of homeostasis, created the bases of cybernetics in biology. C. Sherrington was the first to explain the concept of synapse; the concept of receptor field was explained. R. Magnus described mechanisms of posture maintenance.

Development of physiology in Belarus is connected with creation in 1922 of the Belarussian University, in 1929 — the Republican Academy of Sciences and organization in 1936 of the Belarussian Society of Physiologists, Biochemists and Pharmacologists headed in 1936–56 by I.A.Vetokhin. In 1937 I.A.Vetokhin headed the Institute of Experimental Physiology of the Academy of Sciences of Belarus; physiology of blood circulation, digestion, and conditioned reflex was examined there. Since 1985 the Institute is headed by the Academician V.N.Gurin whose main research is connected with central mechanisms of thermoregulation and lipid metabolism.

6. Value of physiology in medical education

1. The physiology gives fundamental scientific knowledge of vital functions of healthy organism of the person.

2. The physiology sets up the **norm** of a function. The norm is a quantitative indicator of the intensity of functioning of system established on the basis of the investigation of statistically significant groups. Norm in medicine is of the diagnostic and predictive value. Deviation from the norm helps to determine the diagnosis, severity of a disease, helps to monitor the effectiveness of treatment, to prognose the outcome of the disease and to correct treatment.

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

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

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

PHYSIOLOGY OF BLOOD

Theme: Blood composition and amount and properties. Lecture 1

Plan:

1. Concept of blood system.
2. Blood basic functions.
3. Blood composition and amount (hypervolemia, hypovolemia).
4. Blood plasma.
5. Physical and chemical properties of blood (osmotic pressure, oncotic pressure, viscosity, relative density).
6. Buffer systems of blood.

1. Concept of blood system

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

System of blood, as proposed by G.F. Lang (1939), includes:

1. Blood (in vessels).
2. Organs of haemopoiesis — red bone marrow, lymph nodes, spleen, thymus gland.
3. Organs of blood destruction (liver, bone marrow, spleen).
4. Neurohumoral apparatus.

The main place of blood cells formation is the *red bone marrow*. Here, also the destruction of cells (erythrocytes), re-using of iron, synthesis of Hb, and also maturing of B-lymphocytes populations — factors of humoral immunity, takes place.

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

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

2. Blood basic functions

1. Transport (transition of various substances).
2. Respiratory (transition of oxygen from respiratory organs to tissues, and CO_2 in reverse direction).
3. Trophic or nutritional (transition of nutrients from digestive duct to cells of an organism and use of blood components by cells of tissues and organs for plastic and energy needs).

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

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

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

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

8. Protective (contains factors of humoral and cellular immunity: antibodies, phagocytes, factors of coagulation, interferon, populations T- and B-lymphocyte, etc.).

9. Correlative (blood transfers biologically active substances which provide interconnection between various organs and tissues thus ensuring the organism to function as a whole).

10. Maintenance of the constancy of base-alkaline state due to buffer system.

3. Blood composition and amount

Blood consists of plasma and uniform elements (erythrocytes, thrombocytes, leucocytes).

Between the volume of plasma and uniform elements there is a certain interrelation which is called hematocrit number. Hematocrit is a part of the volume of blood for the part of cells. In norm, the volume of erythrocytes in men compounds 44–46%, plasma 54–56%. To transform it into SU (system of units) the obtained number is multiplied by 0,01. It is in norm: in men 0,44–0,46, in women 0,41–0.43. In a newborn hematocrit is 10% higher.

Amount of blood. In adult the absolute amount of blood compounds approximately 4,5–6 liters. Its relative contents corresponds to 6–8% of the body weight (in a newborn — 15%).

The normal contents of blood is called *normovolemia*. There are simple, oligocythemic and polycythemic normovolemia (tabl. 1).

Simple normovolemia — normal interrelation between the volume of uniform elements and plasma.

Oligocythemic normovolemia — is met at anemia as result of loss of blood when the volume of blood is restored due to fluid part as result of transition of interstitial fluid into vessels and the amount of uniform elements was not yet restored.

Polycythemic normovolemia — at transfusion of small amounts of erythrocytic mass.

Increase of blood amount (*hypervolemia, plethora*).

1. At administration of big amount of blood.

2. At intensive haemopoiesis (increase of erythrocytes amount).

3. At delay of water in an organism (disease of kidneys).

4. At excessive water intake.

Decrease of amount bloods *(hypovolemia)*.

1. At acute loss of blood.
2. At anemia.
3. At loss of fluid (dehydration of an organism), for example, at profuse diarrhea, continuous vomiting.

Table 1

Changes of blood volume

Interrelation between uniform elements and plasma	Variant of volemia	Hematocrit number
	NORMOVOLEMIA	
UE 0,45% plasma 0,55%	Simple	normal
UE 0,35% plasma 0,65%	Oligocythemic	below normal
UE 0,55% plasma 0,45%	Polycythemic	above normal
	HYPOVOLEMIA	
UE 0,45% plasma 0,55%	Simple	normal
UE 0,35% plasma 0,65%	олигоцитемическая	below normal
UE 0,55% plasma 0,45%	Polycythemic	above normal
	HYPERVOLEMIA	
UE 0,45% plasma 0,55%	Simple	normal
UE 0,35% plasma 0,65%	олигоцитемическая	below normal
UE 0,55% plasma 0,45%	Polycythemic	above normal

Note: UE — uniform elements of blood.

Kinds of hypervolemias:

- *Simple* — proportional increase of uniform elements and plasma (at hemotransfusion). Hematocrit in normal.
- *Oligocythemic* — increase of blood volume due increasing its fluid part (administration of blood-substituting fluids, dysfunction of kidneys). Hematocrit is lower.
- *Polycythemic* — increase of volume of blood due to increased amount of uniform elements (compensatory character in mountains populations). Hematocrit is increased.

Kinds of hypovolemia:

1. Simple — proportional decrease of volumes of uniform elements and plasma (it is short-term at acute hemorrhages). Hematocrit is unchanged.

2. Oligocythemic — decrease of blood volume due decrease of the amount of uniform elements after loss of blood (when the volume of blood is restored due to coming of interstitial fluid into vessels). Hematocrit is decreased.

3. Polycythemic — decrease of blood volume due to decrease of fluid part of blood (clotting at dehydration, for example, at profuse diarrhea, continuous vomiting, hyperhidrosis). Hematocrit is increased.

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

Depot of blood:

- Liver. Big amount of blood is deposited (up to 20% of its general volume), but completely (opposed to spleen) is not excluded from the general blood flow.
- Spleen. In the spleen up to 500 ml (10–16%) of blood can be deposited (excluded from blood flow).
- Skin. Blood is deposited in capillars and veins (about 10%). Deposition blood in skin is connected with thermoregulation.
- Lungs. Deposition of blood due to change of the volume of arteries and veins.
- Venous system (regarded as depot of fluid part of blood containing significant amount of lymph).

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

Transfer of the deposited blood into circulation one is observed at:

1. Emotional state.
2. Physical strain.
3. Air hunger (hypoxia).
4. Hemorrhages.

Value of depot of blood. Opportunity of fast increase of mass of the circulating blood necessary in concrete conditions for maintenance of needs of an organism in oxygen (at climbing up the mountains, at physical work and other states connected with increased oxygen consumpyion).

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

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

4. Blood plasma

Plasma is a colloid-polymeric solution in which H_2O is a solvent, dissolved substances are salts and low-molecular organic compounds. Colloidal component are proteins and their complexes. Plasma - fluid part of blood (its volume is approximately 2,8–3,0 l).

Structure of plasma: H_20 (90–92%) and solid (dense) residual (8–10%) which includes inorganic and organic substances.

I. *Organic part*:

Proteins (albumins, globulins, fibrinogen) — 65–80 g/l.

1. ***Albumins*** (*45g/l*).

➢ Form 80% of colloid-osmotic pressure (high concentration, relatively small size of molecules).

➢ Participation in regulation of water-salt balance.

➢ Transport of many substances (bilirubin, fats acids, exogenous substances, including drugs — antibiotics, sulfanilamids, mercury, and others);

➢ Binding of hormones (for example, thyroxine).

➢ 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.

β-globulin – transmitting agent of lipids, lipoids and polysaccharides.

— transport of Cu, Fe (transferrin).

Y-globulins — (IgA, IgD, IgE, IgG, IgM) immune functions. Agglutinins of bloods are related to this fraction.

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

Formation of proteins:

a) Albumins, fibrinogen are formed in liver.

b) Globulins — in bone marrow, spleen, lymph nodes, cells of mononuclear phagocytic system.

Role of plasma proteins:

➢ Formation oncotic pressure (1/200 of osmotic pressures of plasma).

➢ Maintenance of pH (buffer properties).

➢ Maintenance of viscosity of blood (important for blood pressure).

➢ Prevent sedimentation of erythrocytes (stabilization).

➢ Participate in blood coagulation (fibrinogen, etc.).

➢ Factors of immunity (immunoglobulins).

➢ Transport (transmission of hormones).

➢ Nutrient (plastic).

➢ Regulators of concentration of free ions, for example, Fe^{++} (transferrin).

➢ Inhibitory in relation to some proteases (antitrypsin — inhibitor of trypsin).

➢ Regulators of functions, metabolism (proteins hormones, enzymes).

➢ Provide redistribution of water between tissues and blood (1 g of albumin binds 0,35 g of water and at swelling it can bind up to 18 ml of water. At hypoproteinemia (decrease of protein up to 55 g/l) — edemas occur. Hungry edemas, for example, at starvation.

Glucose. Concentration in adults:

➢ Whole blood — 3,30–5,55 millimole/l.

➢ Plasma — 3,88–6,10 millimole/l.

➢ In newborn — 1,70–4,20 millimole/l.

3. Not proteins, keeping nitrogen, substances (polypeptides, amino acids, urea, urinary acid, creatine, creatinine, bilirubin, etc.).

Not proteins *(residual)* nitrogen —14,3–28,5 millimole/l.

Triglycerides — 0,40–1,81 millimole/l. Cholesterin 3,64–6,76 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 cation of plasma are Na^+, K^+, Ca^{++}, which play an important role in maintenance of osmotic pressure, redistribution of water between blood and tissues, coagulation of blood, excitability and contraction of cells, etc. The basic anions of plasma are CI^-, sodium hydrogenums HCO^{3-}, phosphates playing an important role in the regulation of pH, acid-base state, excitability of cells, and other.

5. Physical and chemical properties of blood

Osmotic pressure is equal to 7,6–8,1 atm. It is formed mainly by salts in the dissociated state. The osmotic pressure has important value in maintenance of concentration of various substances dissolved in fluids of organism, and promotes distribution of water between blood, cells and tissues.

By size of osmotic pressure in comparison with osmotic pressure of blood there are isotonic, hypotonic and hypertonic solutions.

Isotonic solution is the one osmotic pressure of which *is equal* to that of blood (for example, 0,85% solution of NaCl). Erythrocytes placed in such solution do not change as osmotic pressure in them and in solution is equal. This solution is called physiological. It is used as blood-substituting solution, solvent for many medications for parenteral administration. Over 60% of osmotic pressure of blood is provided by NaCl. Totally, inorganic substances provide 96% of osmotic pressure.

The hypotonic solution is a solution the osmotic pressure of which *is lower* than that of blood (for example, 0,3% solution of NaCI). Erythrocytes placed in such solution swell and burst (i.e., hemolyzed) as result of transition of water into cells, as the osmotic pressure in erythrocyte is higher, than in solution.

The hypertonic solution is solution the osmotic pressure of which *is higher* than that of blood (for example, 2% solution of NaCI). Erythrocytes placed in such solution, wince as result of output of water from cell as the osmotic pressure in erythrocytes *is lower* than in solution.

Osmotic pressure in person is rather constant. In its neurohumoral regulation participate organs of excretion (kidneys, sweat-glands). Change of the osmotic pressure is perceived by special osmoreceptors located both at periphery (in endothelium of vessels) and center (in 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 0,03–0,04 atm. which approximately makes 1/200 of all osmotic pressures of plasma.

Because of small size of molecules of albumins and their big amount (as compared with fibrinogen and globulins) more than 80% of oncotic pressure are caused by them.

Oncotic pressure is important for:

1. Formation of interstitial fluid.
2. Lymphization.
3. Formation of urine.
4. Adsorption H_2O in intestine.
5. Redistribution of H_2O between blood and tissues.

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

Viscosity of blood: — whole — 5 (viscosity of water is accepted as 1,0);
— plasma — 1,7–2,2.

Viscosity of blood increases at dehydration of an organism which reduces thickening (profuse diarrhea, continuous vomiting), increase in blood of uniform elements (polycythemia, leukosis), accumulation of CO_2, increased content of proteins, especially fibrinogen. With increased viscosity of blood the hydrodynamical peripheral resistance in vessels increases that results in difficulty of heart work and slowing down the blood-flow.

Viscosity of blood depends on the amount of erythrocytes (tabl. 2). With the increase of their number it rises.

Table 2

Dependence of blood viscosity on the erythrocytes contents in it

Number of erythrocytes	Viscosity of blood
$4{,}5\times10^{12}$/l	5,0
$6{,}7\times10^{12}$/l	6,4
$7{,}4\times10^{12}$/l	8,1
$9{,}3\times10^{12}$/l	20,9

Viscosity of blood decreases at hydration of an organism (intake of great volume of water, water delay in an organism at diseases of kidney), anemias, hypoproteinemias, decrease of blood coagulation (under the influence of the administered heparin). Decrease of blood viscosity leads to an acceleration of blood-flow.

Relative density (specific gravity) of blood depends on the contents in it of proteins, salts and erythrocytes. The relative density of the whole blood changes in rather narrow limits (1,050–1,060), plasma 1,025–1,034, and relative density of erythrocytes is higher than that of the whole blood and plasma (1,090).

Reaction of blood (acid-base state). Active reaction of blood (pH) is caused by the interrelation in it of hydrogen (H^+) and hydroxyl (OH^-) ions. It is one of the rigid parameters of homeostasis.

pH of arterial blood — 7,40;

pH of venous blood — 7,35 (it has more carbonic acid);

pH inside cells — 7,0–7,2 (acidic metabolic products).

pH limits compatible with life — 7,0–7,8. But long shift of pH in 0,1–0,2 is dangerous for life. The shift of pH, first of all, is reflected in the activity of enzymes.

Despite constant coming into blood of CO_2, lactic acid and other acidic components which can affect pH of blood, active reaction (pH) remains constant. It is provided by buffer properties of blood and activity of excretory organs (excretion of CO_2 by lungs, excretion of acidic and holding of alkaline products by kidney).

6. Buffer systems of blood

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

Buffer systems of blood:

1. Carbonate (H_2CO_3+$NaHCO_3$) and (H_2CO_3+$KHCO_3$). The acidic components which coming into blood cooperates with bicarbonate. Alkaline components coming into blood cooperate with H_2CO_3 thus forming salt and H_2O (removed by 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 — properties of alkalinity and reacts with acid components.

3. *Protein.* It is caused by amphoteric properties of plasma proteins. In acidic medium they behave like alkali, in alkaline — as acids, connectng in the first case acids, in the second-alkalis.

4. *Hemoglobin* (the most powerful). The restored Hb is a weaker acid than H_2CO_3 and gives the K^+ ion to it, attaches H^+ itself and becomes low-dissociated acid.

Buffer systems are available also in tissues (the main ones are protein and phosphatic).

During metabolism acidic products are formed more than basic, therefore the danger of pH shift to the acidic side exists. In a human organism daily the total acidity of HCl, lactic, pyruvic, coal, and other acids is equal to 20 – to 30 liters of 1,0 normality of HCl. Despite of it, the organism lives and the constant pH is maintained. Buffer systems of blood and tissues provide the big steadiness to action of acids. So, for pH shift:

to *the alkaline* side — it is necessary to add alkalis in 40–70 times more than to the same amount of water;

to *the acidic* side — it is necessary to add acids in 327 times more than to the same amount of water.

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

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

By the degree of intensity there are acidosis compensated and not compensated.

In *compensated acidosis* at acids supply into blood the changes of the latter can be limited only to decrease of alkaline reserve without changes of pH. Despite chemical and functional shifts in an organism, pH is maintained at the action of buffer systems. At exhaustion of the alkaline reserve and failure of protective mechanisms pH is shifted outside the limits and *the compensated acidosis* is developed.

By their origin there are:

1. Gaseous acidosis and gas alkalosis;
2. Nongaseous acidosis and not gas alkalosis.

Gaseous acidosis (respiratory) — at increase of H_2CO_3 in an organism. It can arise at:

1. Insufficient function of external respiration.
2. Circulatory insufficiency.
3. Inhalation of air (admixture) with the increased concentration of H_2CO_3.

Gas alkalosis (respiratory) — at lungs hyperventilation CO_2 is excreted in excess (mountain disease, excessive artificial respiration).

Non-gaseous acidosis (metabolic) — at accumulation in an organism of acidic products. Such condition can arise at:

1. Excessive formation of acidic products at dysbolism (diabetes, starvation).
2. Affected excretion of acidic products from an organism (nephrites).
3. Losses of the alkali by an organism (profuse diarrhea, fistulas of intestine).
4. Excessive administration of mineral substances into an organism (poisoning by acetic acid).

Not gas alkalosis (metabolic) — at accumulation of alkaline products in an organism. Such state can arise at:

1. Administration of big amount of alkaline products into an organism (baking soda, alkaline waters abuse).
2. Loss of big amount of gastric juice (continuous vomiting, stomachal fistula).
3. Hyperproduction of glucocorticoids or treatment by the preparations of adrenal hormones.

Lecture 2
Theme: Blood forming components

Plan:

1. Erythrocytes, their structure, properties and functions.
2. Hemoglobin, their structure, properties, varieties, compounds and functions.
3. Hemolysis and its varieties.
4. Erythrocyte sedimentation rate.
5. Leucocytes, their classification, features and functions.
6. The leucocytary formula. Changes in the quantities of leucocytes.
7. Thrombocytes, their structure, properties and functions.

1. Erythrocytes, their structure, properties and functions

Erytrological system — the physiological system including erythrocytes circulating in blood, bodies of their formation and destruction, incorporated into system of neuroendocrinology regulation.

In human and mammal, erythrocytes do not contain nucleus. Absence of nucleus presumes that erythrocytes consume oxygen for own needs in 200 times less than nuclear representatives (erythroblasts, normoblastes).

Sizes of erythrocyte: diameter — 7,7 microns, thickness — 2,2 microns.

One and important feature of erythrocytes is their form of biconcave disk.

The biconcave form erythrocytes:

- Increases in 20% common surface in comparison with the form of a sphere.
- Performs of one of the basic functions — transition of O_2 and CO_2.
- Increases ability to convertible deformations (plasticity) at passage through the narrow and bent capillaries.

At some kinds of pathologies (anemia) there are erythrocytes of various form (crescent, pear-shaped, etc.), named *poikilocytosis,* and also of various size — *anisocytosis*.

By structure, erythrocyte consists of skeleton of cell — stroma, and upper layer — membrane. Thickness of the membrane is 10 nanometers.

The membrane of erythrocyte consists of 4 layers:

- External which is formed glycoprotein.
- Average 2 layers — bi-lipid layer.
- Internal layer-protein layer.

Chemical compound of erythrocytes: 60% — H_2O, 40% — the dry sediment (almost 90% of it is hemoglobin (Hb)).

Functions of erythrocytes:

- Transition of O_2 (participation of hemoglobin).
- Transition of CO_2 (participation of hemoglobin).
- Protective (absorption of harmful substances, production of antibiotic-eritrin).
- Regulation of water-and-salt exchange.
- Transition of nutrients.
- Participation in regulation of erythrogenesis.
- Creative. It presumes transition of macromolecules ensuring information links of the organism (see «Main Functions of Blood»).
- Participation in regulation of the acidic-basic condition (hemoglobin buffer).
- Participation in blood coagulation (contain thromboplastin released at their destruction. Presence of destroyed erythrocytes in blood induces hypercoagulation and thrombus formation. Along with it, they are heparin bearers which is an anti-coagulant).

Amount of erythrocytes in blood:

in men — $4,5–5,0 \times 10^{12}$/л ;

in women — $3,8–4,5 \times 10^{12}$/л.

Increase of erythrocytes number (erytrocytosis).

Reduction of erythrocytes number (erythropenia). Erythropenia is marked at anemia (the combination to low Hb maintenance).

Life period of erythrocytes is 130 days.

Formation of erythrocytes occurs in red bone marrow (in 1 minute it is formed 160×10^6 of cells), and destruction — in spleen, liver, red bone marrow.

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

One of the major functions of blood is 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 in them of red blood pigment — hemoglobin.

Localization advantages of Hb in erythrocyte:

- Provides decrease of viscosity of blood.
- Reduces oncotic pressure, preventing loss of water by tissues.
- Prevents of Hb loss at filtration of blood in nephrones.

By the chemical nature — it is a chromoproteid consisting of protein globin (96%) and prosthetic group of heme (4%). There are 4 groups of heme. It represents protoporphyrin, Гема содержится 4 группы. Он представляет собой протопорфирин with a Fe^{++} ion in the centre.

The key role in Hb activity is played with ion Fe^{++}.

Functions of hemoglobin:

- Transport of O_2 — oxyhemoglobin ($HHbO_2$). One molecule of Hb attaches 4 molecules of oxygen. 1 g of Hb binds 1,34 ml of O_2.
- Transport of CO_2.
- Participates in maintenance of acid-alkaline state (hemoglobin buffer).

Bonds of Hb:

1. **Oxyhemoglobin** ($HHbO_2$). Hemoglobin is connected with O_2. Arterial blood contains about 98% of $HHbO_2$, and venous — about 60%. After feedback of O_2 from HHb it is called *the restored or reduced* hemoglobin. Hemoglobin has high affinity to oxygen.

2. **Carbohemoglobin** ($HHbCO_2$) — bond of hemoglobin with CO_2.

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

4. **Carboxyhemoglobin** (HHbCO) — bond of hemoglobin with carbonic oxide (CO). This bond is in 150–200 times stronger than that of $HHbO_2$. At CO 0,1% concentration in air, 80% of Hb turns into carboxyhemoglobin. At concentration of 1% of CO death occurs in a few minutes.

Physiological bonds of Hb are $HHbO_2$ and $HHbCO_2$.

Myoglobin — the respiratory pigment, or muscular hemoglobin contained in skeletal muscles and myocardium. It has the big affinity to oxygen in com-

parison with hemoglobin. It binds up to 14% of O_2 in organism. Its role consists in muscle supply with oxygen at muscles contraction when capillars are pressed and tissues do not receive blood. In this moment the main source of oxygen is myoglobin which in the phase of muscles relaxation is filled with oxygen.

Synthesis of Hb takes place in erythroblasts in bone marrow.

The state of reduced amount of Hb in one unit of blood volume (more often at decrease of the number of erythrocytes) is called *anemia.*

In males anemia is observed when Hb amount is less than 130 grams per liter, in females — less than 120 grams per liter (at pregnancy — less than 110 grams per liter).

Types of Hb:

- HbP — (primitive) – is formed at 7–12 week of intra-uterine development.
- HbF — fetus — at 9-th week of intra-uterine development.
- HbA — hemoglobin of adults-appears before birth.

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

In norm, Hb concentration in blood of male varies within 130–160 grams per liter, in female blood — 115–145 grams per liter.

3. Hemolysis and its varieties

Hemolysis — destruction of erythrocytes membrane accompanying with the release of Hb into plasma (laky blood, or pellucid blood).

Kinds of hemolysis:

1. Mechanical (in vivo at impacts on the body, in vitro at stirring blood in the vial).
2. Thermal (in vivo at burns, in vitro at freezing and de-freezing of blood)
3. Chemical (in vivo under influence of chemical materials, at aspiration of volatiles (acetone, benzene, chloroform), destruction of erythrocytes membrane in vitro under influence of acids, alkalis, heavy metals, etc.).
4. Electrical (in vivo at affection by electric current, in vitro at transit of electric current through blood in the vial). On the anode (+) is hemolysis acid, on the cathode (-) — alkaline.
5. Biological. Under influence of factors of biological nature (hemolysins, poison of snakes, fungal poison).
6. Osmotic. In hypotonic solutions in person hemolysis begins in 0,48% of NaCl solution, and in 0,32% — full hemolysis of erythrocytes.

Osmotic resistance of erythrocytes (ORE) — their stability in hypotonic solutions.

Distinguish:

Minimal ORE — concentration of NaCl solution at which the hemolysis (0,48–0,46%) begins.

Maximal ORE — concentration of NaCl solution, at which all erythrocytes are destructed (0,34–0,32%).

The osmotic resistance of erythrocytes depends on degree of their maturity and form.

The young forms of erythrocytes are formed of the bone marrow of blood and are more resistant to hypotonia.

7. Immune hemolysis — at transfusion of incompatible blood or at presence of immune antibodys to erythrocytes.

8. Physiological — hemolysis of old erythrocytes in the end of their life (in liver, spleen, a red bone marrow).

4. Erythrocyte sedimentation rate

If to prevent blood from coagulation (with the help of an anticoagulant) and to let it stand, sedimentation of erythrocytes is observed.

Erythrocyte sedimentation rate (ESR) in norm is:

in men	1–10 mm / hour;
in women	2–15 mm / hour;
in newborn	1–2 mm / hour.

ESR depends on:

Properties of plasma:

- ESR is accelerated due to increase of concentration of molecules of large globulins and fibrinogen in particular. Their concentration raise at inflammatory processes, pregnancy. They reduce the electrical charge of erythrocytes, promoting cohesion of erythrocytes and formation of monetary columns.
- ESR decreases at augmentation of amount of erythrocytes (for example, sedimentation of erythrocytes can stop completely owing to increase of blood viscosity). At anemias ESR it is accelerated.
- ESR goes down at change of the form of erythrocytes (drepancytic anemia).
- ESR it is slowed down at the decrease of pH and, vice versa, accelerated at the increase of pH.
- The erythrocytes sedimentation rate increases at the increase of hemoglobin concentration in cells.

5. Leucocytes, their classification, features and functions

Leucocytes, or white blood cells, opposite to erythrocytes, have nucleus and other structural elements peculiar to cells. The dimension from 7,5 up to 20 micrometres.

Functions of leucocytes:

- *Protective* (participation in maintenance of nonspecific and cell immunodeficiency).
- *Metabolic* (release into digestive system, seizure of nutrients and their transmission to blood. Especially, it has essential value in maintenance of immunity in a newborn in the period of breast feeding.
- Dissolution of damaged tissues;

➢ *Morphogenetic* — destruction of various malformations in embryonic period.

Functions of separate kinds of leucocytes:

1. *agranular:*

a) **монocytes** — 2–10% of all leucocytes (macrophags). They are the largest blood cells, have bactericidal activity, appear in affection spot after neutrophils. In tisues monocytes turn into tissue macrophags. In the affection spot they perform phagocytosis of:

➢ Microorganisms.
➢ died leucocytes.
➢ Damaged cells of a tissue.

They thus clear the affection area.

b) **Lymphocytes** — 20–40% from all leucocytes.

Opposite to other forms of leucocytes, after release from vessels they do not come back and their life period is from some days, as in other leucocytes, to 20 and more years.

Lymphocytes are the central part of immune system of an organism. They provide with genetic constant of an organism.

They carry out:

➢ Antibody formation.
➢ Destruction of alien cells.
➢ Provide reaction of a transplant rejection.
➢ Keep immune memory.
➢ Destruction of own mutant cells.
➢ State of sensibilization.

Distinguish between:

T-lymphocytes (provide cellular immunodeficiency):

a) T-assistants.
b) T-suppressors.
c) T-killers.
d) T-accelerators.
f) immune memory.

Bursacytes (provide non-cellular immunity).

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

Zero lymphocytes. They make 10–20% of all lymphoid cells.

2. Granular:

a) **neutrocytes** — the biggest groups of leucocytes (50–70% of all leucocytes). They possess high bactericidal activity. They are carriers of receptors to IgG, to proteins of complement. They first appear in the affection area destroy harmful agents. One neutrophil is capable to destroy 20–30 bacteria.

b) **Eosinocytes** — 1–5% of all leucocytes (stained with eosin). It stays in blood for some hours then migrate into tissues where they are destructed.

Functions of eosinocytes:

1. Phagocytosis.

2. Neutralization of toxins of the albuminous nature.

3. Destruction of alien proteins and antigen-antibody complexes.

4. Production of plasminogen, i.e. participation in fibrinolysis. Their amount increases at helminthosis. They perform effect in struggle against helminthes, their eggs.

c) **Basophils** — 0–1% of all leucocytes. They produce histamin and heparin (they are called heparinocytes). Heparin prevents coagulation of blood, histamin dilates capillars, promotes resorption and healing of wounds.

Amount of leucocytes in norm: $4–9 \times 10^9$ per litre.

The increase of amount of leucocytes is called leucocytosis. There are the following kinds of leucocytosis:

Physiological. It is caused by redistribution of leucocytes between vessels and organs.

Physiological kinds of leucocytosis are:

1. *Nutrition*. After reception of nutrition as the result of release of leucocytes into blood circulation from depot. Their accumulation in sub-mucous layer of intestine where they carry out protective function.

2. *Muscular.* Under influence of heavy muscular work the quantity of leucocytes grows in 3–5 times.

3. *Pregnant*. Leucocytes are accumulated in sub-mucose of a uterus.

4. *Newborn* (metabolic function).

5. At pains.

6. At emotions.

Pathological — connected to diseases, infection contaminations, purulent, inflammatory, septic and allergic processes.

Leucocythemia — uncontrollable formation of leucocytes. Leucocytes in these cases are poorly differentiated and do not carry out the physiological functions.

Leucocytopenia (the amount of leucocytes is lower than 4×10^9 per litre).

Lifetime of various forms of leucocytes differs (from 2–3 days till 2–3 weeks). Long-living lymphocytes (cells of immune memory) live for decades.

6. Thrombocytes, their structure, behavior and functions

Thrombocytes or blood a plate — the irregular round form the with length of 1–4 microns, and depth 0,5–0,75 microns.

Their amount in blood — $180–320\times10^9$/l. They are formed in red bone marrow by separation from the part of protoplasm of megakariocyte. One megalokariocyte forms 3–4 thousand thrombocytes. 2/3 thrombocytes circulate in blood, others are situated in spleen.

Constitution.

Range of cytoplasm directly adjoining to an environment is not structured. The central part of cytoplasm contains granules. Distinguish beads of 3 type:

α granules — contain blood-coagulation factors.

ß granules — the enzymes participating in a metabolism in a thrombocyte.

γ granules — tubules with englobed particles. Thrombocytes are capable to englobe abiological foreign bodys, viruses, cell-bound immune complexes, i.e. participate in nonspecific protective system of an organism.

Duration of their life in blood is 5–11 days, then they are destroyed in liver, lungs and spleen.

Upon destruction of thrombocytes the following materials are released:

Participate in blood coagulation.

Promote angiospasm — serotonin (F10), adrenalin, noradrenalin.

Produce adhesion and aggregation of thrombocytes.

There are daily fluctuations of thrombocytes number: in the afternoon the amount of them increases, at night – it goes down. One of the basic functions of thrombocytes is their participation in coagulation of blood.

Lecture 3
Theme: Hemostasis

Plan:

1. Blood coagulation system.
2. Vascular platelet hemostasis.
3. Coagulating hemostasis.
4. Blood anticoagulating system.
5. Fibrinolysis.
6. Blood aggregate state regulation.

1. Blood coagulation system

Maintenance of blood in a fluid state and its ability to circulate in blood vessels is a necessary condition for keeping up of an organism. It is ensured by the regulation system of liquid state of blood. This system includes:

• Coagulations system of blood (microvascular and coagulation hemostasis);

• Anticoagulating system of blood (anticoagulants and fibrinolysis).

• Mechanisms of regulation.

Disturbance of blood coagulation is the basis of many human diseases.

Hemostasis (termination of bleeding) - is caused by:

• Spasm of blood vessels;

• Coagulations of blood and formation of thrombus.

System of hemocoagulation:

•Blood and tissues which produce and secrete materials participating in the given process.

•Neuro-humoral regulating mechanism.

2. Vascular platelet hemostasis. *(initial)*

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

1. **Reflex spasm of damaged vessels** (caused by release of noradrenalin, adrenalin, serotonin at irritation of receptors). It is known as *initial angiospasm*.

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

3. Accumulation and aggregation of thrombocytes at the damaged focus. Stimulators of the given process are adrenalin, thrombin, Ca^{++}, thromboplastin, released from thrombocytes and erythrocytes (*internal system*), and collagen released from cells of tissues of the damaged vessel (*external system*). In result, the platelet thromb is formed. Aggregation of thrombocytes in this stage has reversible character.

4. Irreversible aggregation of thrombocytes. Thrombocytes flow into uniform mass, forming a thromb not penetrable for blood plasma. Reaction is influenced by thrombin which is released from destroyed thrombocytes which results in release of physiologically active substances: adrenalin, noradrenalin, serotonin, nucleotides, blood-coagulation factors. They promote *secondary* spasm of a vessel. Excreted in such way F3-platelet thromboplastin (thrombo-plastic factor) starts the mechanism coagulating hemostasis. The small amount of fibrin is formed.

5. Compression of platelet thrombus. Compression of thrombus is ensured by protein of thrombocytes - thrombostenin (F6) and fibrin. It results in termination of bleeding.

In fine vessels the hemostasis stops at this stage. Such kind of the hemostasis refers to as initial, or microvascular.

In large vessels, with high blood pressure, platelet thrombus is not held up and washed away. In similar vessels on the basis of such mechanism stronger thrombus is formed as result of another mechanism — coagulating, or secondary hemostasis.

3. Coagulating hemostasis

Coagulating hemostasis includes the following:

- Plasma blood-coagulation factors.
- Blood-coagulation factors of uniform elements of blood.
- Tissue blood-coagulation factors.

I. Plasma factors (marked chronologically in Roman figures).

• **FI** — *fibrinogen*. Protein of plasma. Concentration in blood is 3 g/l, formed in liver. It is also a building stuff at healing wounds.

• **FII** — *thrombinogen*. Synthesized in liver with the presence of vitamin K.

•**FIII** — *thromboplastin*.

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

• **FV** — *proaccelerin*. It is formed in liver. Participates in the 1st and 2nd phases of blood coagulation.

• **FVI** — it is excluded from classification.

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

• **FVIII** — *antigemophilic globulin A*. Formed in liver, spleen and leucocytes. It activates prothrombin. It ensures optimum conditions for interaction of factors IX and X. It is necessary for adhesion of thrombocytes and activation of prothromboplastin. At absence of this factor hemophilia A occurs.

• **FIX** — *antigemophilia globulin B*. Glycoprotein. At absence of this factor hemophilia B occurs.

• **FX** — *factor Stuart -Pruyr*. Is part some tissue and blood thromboplastin.

• **FXI** — *plasma predecessor of thromboplastin*. It is necessary for activation of blood thromboplastin, activates FIX. At absence of this factor hemophilia C occurs.

• **FXII** — factor Hagemun - is activated at contact with an alien surface (for example, a place of the damaged vessel) that is why him name the contact factor. It is the initiator of formation of blood prothromboplastin and all process hemocoagulation. At absence of this factor hemophilia D occurs.

• **FXIII** — *fibrinstabilization* factor. Contains in plasma, cells and in tissue. It is necessary for formation of final or unsolvable fibrin. It is activated by thrombin and Ca^{++}. At deficiency of the given factor badly heal wounds.

Phases of coagulating hemostasis:

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

• **II phase** — activation of inactive thrombinogen into active form — **thrombin**. This process is influenced by FVI — pro-accelerin (accelerin), FVII — convertin, Ca^{++} and some factors of thrombocytes.

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

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

• 2. In result of polymerization of fibrin-monomers, the molecule of soluble fibrin — polymer «S» is formed. For polymerization presence of Calcium ions is necessary.

• 3. Under influence of fibrinstabilization factor (FXIII) the insoluble fibrin ("I") is formed.

Uniform elements of blood get stuck into fibrin nets, thus forming the blood thrombus. Such thrombus is subject to compression influenced by protein trombostenin. At compression of thrombus the periphery of the wound are closing.

Time of blood coagulation is 5–7 min.

4. Blood anticoagulating system

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

Mechanisms of maintaining of blood liquidity:

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

• Negative charges of wall of vessels and uniform elements of blood that provides their repulsion from each other.

• Wall of vessels is coated with thin layer the soluble fibrin having ability to adsorb active blood-coagulation factors.

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

• Presence of natural anticoagulants.

In the organism there are 2 groups of anticoagulants:

• 1. Initial (constantle presenting in blood).

• 2. *Secondary* (formed during coagulation or fibrinolysis).

Initial anticoagulants — antithromboplastins, antithrombins:

• Antithrombin II (heparin). It inhibits all 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.

• Tromboxane — Inhibits aggregation of thrombocytes.

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

• Antithrombin I (fibrin) is capable to absorb significant (up to 90%) amount of thrombin.

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

Anticoagulants used in laboratory clinical practice:

• 1. Heparin.

• 2. Citric acid and its 0,5% salt solutions.

Factors accelerating blood coagulation:

• Affection of wall of vessels.

• Augmentation of thromboplastin formation.

• Augmentation of vitamin K absorption in an organism.

• Augmentation of fibrinogen formation.

• Temperature increase.

• Increased contents of amino acids in blood.
• Decrease of fibrinolysis process.

Factors decreasing coagulation

• Decrease of thromboplastin formation.
• Decrease of vitamin K absorption.
• Increased development of anticoagulants.
• Decrease of fibrinogen formation.
• Type A hemophilia — terminated phase I of coagulation (disturbance of thromboplastin formation). At absence of FVIII, phases II and III are also terminated.
• Type B hemophilia — absence of FIX.
• Type C hemophilia — absence of FXI (plasma precursor of thromboplastin).
• Type D hemophilia — absence of FXII.

In men hemophilia is met more often than in women.

5. Fibrinolysis

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

Only at damage of tissue the process of formation of fibrin dominates fibrinolysis and local blood coagulation takes place. The main function of fibrinolysis — regeneration of lumen of a blood vessel.

Fibrinolysis starts immediately upon thrombus compression in 2 phases:

I phase plasminogen transformation into *plasmin*.

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

Factor providing fibrinolysis is the plasminogen which under influence of tissue and blood factors transform into the active form - plasmin.

6. Blood aggregate state regulation

In the norm there is no intravascular coagulation of blood or it occurs in very insignificant degree. The fragile regulation process of blood coagulation involves many factors and systems:

• Presence of the number of inhibitors pro-coagulants in plasma.
• Many factors are in inactive state.
• Concentration of pro-coagulants decreases due to fibrinolysis. Therefore, thrombus is not formed in vessels with the fast blood flow but appears in vessels with low blood flow.
• Pro-coagulants inactivate in blood.

On the whole, the mechanism of coagulation regulation is neuro-humoral. In the organism there are special chemoreceptors reacting to thrombin, plasmin and other factors coagulation and anticoagulation systems concentration in blood.

Stimulation **of sympathetic** nervous system increases the speed of blood coagulation (hypercoagulation). It is marked at stressful states, pains, accompanying with 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.

• Glycocorticoids, somatotropic hormone, antidiuretic hormone, Calcitonin, testosteron, progesteron primarily cause hypercoagulation but once again activate fibrinolysis.

Blood coagulation is prevented by action complex anticoagulation mechanism.

• At appearance in vessels of slowly formed thrombin it is neutralized by plasma anticoagulants antithrombins, heparin).

• Heparin:

• Prevents formation of thromboplastin and thrombin, alongside activating fibrinolysis.

Stimulation **of parasympathetic** nervous system (n. vagus) results in the same effects as stimulation of sympathetic nerves.

Lecture 4
Theme: Blood groups. Blood system regulation

Plan:

1. Blood groups. Fundamentals of blood transfusion.
2. Rhesus-factor.
3. Blood system regulation.
4. Blood substituting solution.

1. Blood groups. Fundamentals of blood transfusion

In 1901 Charles Landshtener observed that at blending of blood from different people in one case there was an agglutination of erythrocytes, in other cases it was absent. His further research and also that of J. Jansky allowed to establish blood groups which differ from each either by presence or absence of erythrocytes of antigens (agglutinogens) and antibodies (agglutinins) in plasma (tabl. 3).

Table 3

Blood groups of system AB0

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

Agglutinogens of erythrocytes (A and B). With them, γ-globulin-natured specific antibodies (agglutinins α and ß) dissolved in the plasma incorporate. They have 2 centers of linkage that provides an opportunity of formation of the bridges between two erythrocytes and thus formation of erythrocytes conglomerates.

In norm in each person agglutinins to corresponding agglutinogens are absent, i.e. each person has individual panel of erythrocytes of agglutinogens.

In blood of a neonatal there are no antibodies of system AB0 and their formation to antigens absent in the newborn, happens within the first year of life.

At blood transfusion they select blood to avoid meeting of similar agglutinogens of the donor with agglutinins of the recipient (e.g. A and α, B and ß). Agglutinins of the donor are not considered since there is their dilution in the blood of the recipient and they cannot cause agglutination of his erythrocytes (at transfusion of small amounts of blood of 200–500 ml). At transfusion of big amount (4–5 l) of blood plasma of 0 (I), a big number of agglutinins comes into the recipient's blood. Thus dilution effect is lost and therefore agglutinins of the donor may cause agglutination of erythrocytes of the recipient.

As a rule, they transfuse only identical blood (e.g. 1st group blood with the 1st group blood). With its absence in emergency cases blood transfusion is performed under scheme of blood groups compatibility (tabl. 4).

Table 4

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).

Persons with the I (0) blood group are known as universal donors, those with the IV (AB) group — universal recipients.

To avoid complications at blood transfusion:

1. They determine blood group with application of standard serum of I, II and III groups by blending of a drop from each serum kind with the drop of the examined blood. By presence or absence of agglutination in them group compatibility is determined. To avoid mistakes, examination is conducted at temperature of 15–25°C. The drop of blood brought into serum should be in 3–5 times less than serum drop volume. In case of indistinct results, examination is repeated with serum of other series. Should the doubtful result is obtained again, direct and reverse test is carried out:

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

2. Biological test is carried out. First, they perform stream intravenous introduction of 10–15 ml of donor blood and for 3–5 min the patient is watched for presence or absence of complications (heart and respiration rate increase, short-breath, heavy breathing, face hyperemia, etc.). Such introduction is repeated for *three times*. At absence of any complications the rest portion of blood is administered.

In people with I (0) blood group anti-A and anti-B immune agglutinins, i.e. ά and ß, present in plasma. Transfusion of such blood in big amounts is prohibited since in these cases agglutinins of the donor are not dissolved in plasma of the recipient and can cause agglutination of erythrocytes of the recipient. Besides, in persons with I (0) blood group **antigen H** presents on surface of erythrocytes which can interact with anti-H-antibodes frequently met in blood plasma of II (A) and IV (AB) groups and little bit less in III (B)group. In these cases blood transfusion of I (0) group to the persons having other blood groups can result in hemotransfution shock. Therefore universal donors are called *dangerous* universal donors.

Presence of the H-antigen on a surface of erythrocytes ensured name of AB0 system as ABH.

Prevalence of people with blood groups: I (0) — 40–50%, II (A) — 30–40%, III (B) — 10–20%, IV (AB) — 5%. Geography: 40% of people of Central Europe have blood group II (A), 90% of North America — I (0), more than 20% of Central Asia — III (B). I (0) blood group presents in all nationalities, II (A) — dominates at inhabitants of Europe, Mid East, China, Japan. People with III (B) blood group are the least, IV (AB) dominates in inhabitants of India, Central Asia, valley of Nile.

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, system Kell-Chellano consists of 2 agglutinogen K and k and forms 3 groups — KK, кк and Кк. The given system of blood presents in 100% of people.

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

Alongside with agglutinins, blood plasma contains *hemolysins* (marked agglutinins α and ß respectively). When met with similar agglutinogens they result in hemolysis of erythrocytes. Their action is revealed at temperature of 37–40°C and in 30–40 seconds hemolysis of erythrocytes happens.

2. Rhesus-factor

The Rh-factor (Rh) was discovered in 1940 by Landschtaner and Wiener. It presents in 85% of people blood has this factor, in 15% it is absent. People whose blood has Rh-factor are called rhesus — positive (Rh^+), those who have not are rhesus - negative (Rh^-).

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

At transfusion of Rh^+ blood to the Rh^- person the agglutinins formation in such recipient lasts slowly (within several months). That's why at single transfusion hemotransfutions complications are not observed. At the repeated transfusion, rhesus-incompatibility (rhesus-conflict) with serious hemotransfutions complications occurs: formation of conglomerates of erythrocytes and their hemolysis, intensive intravascular blood coagulation, many organs are affected, kidneys in particular.

It is important to take into account rhesus-factor of a mother at pregnancy. If the fetus inherits Rh-positive blood from the father, and the mother is Rh-negative, in this case antibodies to Rh^+ erythrocytes of fetus are formed in the mother's organism. Formation of Rh in fetus starts only from the 3rd month of antenatal period and becomes active by the end of pregnancy. During this period the organism of the mother has not time for sensibilization. Formation an antirhesus — agglutinins lasts slowly (3–5 months). Therefore, at the first pregnancy complications are almost not observed. At repeated pregnancy there is a rhesus — conflict menace at which erythrocytes of fetus are destroyed which can result in his intra-uterine death.

For depressing of antibody formation to Rh, anti-D-prevention is performed in the mother's organism, i.e. they administer immune serum to the mother instantly upon delivery. This serum contains anti-D-globulin which destroy Rh^+ erythrocytes of the fetus which got into blood of mother, i.e. the factor causing antibody formation and their accumulation is destroyed.

3. Blood system regulation

Erythrogenesis.

Neuro-humoral regulation erythrogenesis. For the normal erythrogenesis process the normal nutrition sufficient amount of *ferrous lactate* is necessary. It is a limitation factor. The lack of it results in anemia.

Erythropoietins are formed in many organs (lien, liver, bone marrow, salivary glands) but most of all in kidneys. The basic starting mechanism is hypoxia, or loss of blood.

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

Ascorbic acid — promotes absorption of ferrous lactose into intestine transmitting it from Fe^{+++} into Fe^{++}. The daily need in ferrous lactose for realization of normal erythrogenesis is 20–25 mg.

Products of erythrocytes destruction stimulate hemopoiesis (autoregulation). The amount of the destroyed erythrocytes is equal to that of newly formed erythrocytes (self-control).

Hormones. Androgens increase and estrogens decrease erythrogenesis. That is why the number of erythrocytes in men's blood is higher than in women. Erythropiesis is stimulated by adrenalin, thyroxin, somatotropic hormone.

The role of nervous system. The irritation of the nerves going to the bone marrow, enforces erythropiesis. Action of nervous and hormonal factors on red bone marrow is carried out through erythropoitetins.

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

Leukopoiesis.

Neuro-humoral regulation of leukopoiesis.

1. A stimulation of leukopoiesis *by products of leukocytes destruction* (self-control). The more destruction is, the higher is their formation.

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. *Hormones.* Adrenalin, hydrocortisone result in *leukocytosis* due to release from blood depot of neutrophils, monocytes and lymphocytes (leukocytosis at stress, emotional excitation).

The role of nervous system. The irritation of sympathetic nervous system increases the amount of neutrophils. The irritation of vagus reduces the amount of leukocytes in blood of peripheric vessels.

Thrombocytopoiesis.

Thrombocytopoietins are of short and long action. The first are formed in lien and stimulate release of thrombocytes into blood. The second are contained contain in blood plasma and stimulate formation of thrombocytes in the bone marrow.

Thrombocytopoiesis increases after loss of blood. In some hours the number of thrombocytes can increase and exceed their normal amount in twice.

4. Blood substituting solution

At hemodynamic disorders caused by loss of blood, apart from blood transfusion various blood substituting solutions are used. The latter should conform with the following demands:

- By physico-chemical properties they should be close to the basic parameters of blood (isotonic, isoionic, etc.).
- Absence of influence on basic biological properties of blood.
- Absence of toxicity.

- Long-term stay in vascular system.
- To maintain sterilization and long storage.
- Should not produce sensibilization of an organism and lead to anaphylaxis shock at repeated introduction.

Salt solutions:

- Saline solution — 0,85–0,9% NaCl.
- Ringer-Lock's solution.
- and other.

Since these solutions do not contain colloids they are quickly released from blood channel, i.e. they can fill the amount of the lost blood within short period of time.

Synthetic *colloid* blood substituting solutions (plasma substitutes).

Negative properties of colloid blood supplements are their ability to produce allergic responses.

Protein preparations: native, preserved and fresh frozen plasma (FFP).

Solution albumin 5%.

Protein is an albuminous preparation of isogenic human plasma.

At their intravenous introduction the volume of circulating blood increases. They bind toxic materials.

Transfusion of whole blood at present is applied rather seldom, they use for transfusion only those components of blood which the organism needs much: plasma, erythrocytes mass, etc.

Preparations of blood: preserved blood, plasma, erytrocytes mass, washed erythrocytes, leukocytes (fresh), thrombocytes (fresh).

PHYSIOLOGY OF CARDIOVASCULAR SYSTEM
PHYSIOLOGY OF HEART

Lecture 1

Theme: Structure, properties of myocardium. Electrical manifestation of heart activity

Plan:

1. Structurally functional characteristic of circulation system.
2. Physiology of heart. Structure, properties of myocardium. Laws of heart contraction.
3. Conducting system of heart.
4. Extrasystoles.
5. Electrical manifestation of heart activity. Electrocardiography, its diagnostic significance.

1. Structurally functional characteristic of circulation system

Blood can perform the multiple life functions only at its continuous circulation that is ensured by the activity of system of circulation organs — heart and vessels.

At circulation blood follows the complex path through the big and small circles of circulation.

The big (system) circle starts from left ventricle of heart, includes aorta, arteries, arterioles, capillars, veins and ends with hollow veins in right atrium.

The small (pulmonary) circle starts from the right ventricle, includes pulmonary artery its branching, arterioles, capillars, veins and ends in the left atrium. While passing this path blood is released from excess of CO_2 and oxygenated.

2. Physiology of heart. Structure, properties of myocardium. Laws of heart contraction

Function of heart consists in rhythmic blood supply in artery as result of contraction (systole) and relaxation (diastole) of myocardium.

In norm the systole, diastole and general pause of atriums and ventricles are in concordance among themselves and organize the *cardiac cycle* which lasts 0,75–1,0 sec (0,8 sec). This cycle is started by the auricular systole. Upon its termination the ventricular systole begins. Atriums at this time are in diastole state. The ventricular systole is followed by their diastole. In its end 0,1 before the termination the new atrium systole begins.

At quiet state of an organism heart works for 9 hrs 24 min a day and has rest for 14 hrs 36 min.

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

The myocardium differs in original constitution. The main portion of working myocardium consists of the transversely-striated irregularly organized fibers. Apart from the working myocardium there are accumulation of special cells called atypical *muscular tissue*: it contains few myofibrils, lot of sarcoplasm and weak banding. It forms the *conductive system* of heart.

Properties of myocardium

1. ***Excitability*** — ability to react to excitation. At excitation during systole the excitability is reduced and disappears — there is a refractory period (non-excitability). The refractory period helps heart to pump the blood into vessels without disturbance.

2. ***Conduction*** — provides spread of excitation along conductive system and myocardium.

3. ***Contraction*** and ***relaxation*** phenomenon.

Force of cardiac contraction depends on the initial length of muscular tissue (the Franc — Starling's law of heart). At physical exertion when more blood comes to the heart, ventricles are more stretched and their contraction become stronger.

4. ***Automaticity*** — ability of an organ (tissue) to excite under influence of impulses arising in themselves. So, the isolated heart of a frog placed into Ringer's solution can contract for a long time. The automaticity of human heart in extremely rare cases may be observed after his death.

3. Conducting system of heart

In the right auricle in the area of hollow veins opening, there situated *synoatricular* [S-A] node — pacemaker. It is the leading part of heart - pacemaker of the 1st order. It generates 60–80 impulses per minute. Excitation is spread along the myocardium of atriums and reaches *atrioventricular* (A-V) node situated in the right atrium in the area of an interatrial septum. It generates 40–50 impulses per minutes. This is a pacemaker of the 2nd order. His' bundle starts here connecting atriums with ventricles. In ventricles it is divided into right and left crus of *His' bundle*, forms pacemaker of the 3rd order, generates 30–40 impulses per minute. Final branching of conductive system under endocardium form *Purkinje's fibers* network (20 impulses/minute). Hence, the impulse is formed into S-A node, distributed along contracting myocardium, conductive system and produces systole of heart. First, the apex of ventricles is contracted, then the base.

In A-V-node at small depth of its muscular tissues and presence of synapses there is some delay in excitation conduction for 0,02–0,04 sec. Following this, excitation reaches His' bundle once atriums have pumped blood into ventricles.

The excitation spread rate in myocardium of atriums and ventricles is 1,0 m/sec;

In A-V node — 0,05 m/sec.

In His' bundle — 1,5 m/sec;

In Purkinjes fibers — 3–5 m/sec;

The high rate of excitation spread in conductive system and myocardium promotes synchronic contraction of ventricles, raises their power and pumping ability. Hence, the conductive system of heart provides rhythmic generation of impulses, sequence of contraction of atriums and ventricles, synchronic contraction of fibers of myocardium.

4. Extrasystoles

The ability to rhythmic generation of spread pulses, typical for myocardial fibers, is not revealed till the pacemaker's role is executed by S-A node. However pulses can frequently generate in other portions of myocardium both in healthy and ill people. If the myocardium is excited in the period of diastole when the excitability is recovered, there is an extra contraction — ***extrasystole***. They distinguish between extrasystoles — sinus, atrial, ventricular.

Single extrasystoles are often met in healthy people and do not have big clinical significance (emotions, pain). Repeated extrasystoles frequently arise at heart diseases.

5. Electrical manifestation of heart activity. Electrocardiography, its diagnostic significance

The excitation appeared in pacemakers is spread along the conductive system and myocardium and accompanied by formation of negative charge on surface of cells. Heart becomes the powerful generator of biological electricity. The

cumulative potential of the excited fibers is so big that it can be registered far outside the heart. Applying electrodes to certain spots of the body it is possible to write the curve reflecting potential difference during cardiac cycle. This curve of complex character is called ***electrocardiogram*** (ECG) and method of examination — ***electrocardiography***. ECG has received wide application in medicine as the diagnostic method allowing to establish character of some disorders of cardiac activity.

There are different methods of ECG leads.

1. Leads from extremities

a) Bipolar (Einthowen method)

b) Unipolar (Goldberger's method)

2. Thoracal (pre-cardiac) leads

a) Bipolar (by Nab) (small thoracal triangle)

b) Unipolar (by Wilson).

More often for ECG registration they make potential leads from extremities by method of Einthowen triangle (bipolar lead).

Three standard leads are used:

I — right hand — left hand;

II — right hand — left leg;

III — left hand — left leg.

Typical ECG consists of 5 positive and negative oscillations-waves, conforming to cycle of cardiac activity. They are marked with latin letters P, Q, R, S, T. Interspaces between waves are made by segments, the unity of wave and segment make an interval. Three waves — P, R, T — are directed upwards, two small — Q and S — downwards.

Wave P reflects excitation of an atrium (right and left). Segment P-Q — corresponds to spread of excitation along atrioventricular node. Interval P-Q reflects transmission time of excitation from atriums to ventricles.

QRS complex reflects origination and a spread of excitation in myocardium of ventricles.

Wave Q reflects excitation of interventricular septum, internal surface of ventricles, right papillary muscle, apex of heart.

Wave R, the highest one, is the period of spread of excitation in ventricular bases, external surface of ventricles.

Wave S reflects complete scope of ventricles with excitation when all their surface becomes electronegative and potential difference between separate portions of heart disappears.

Wave T — regeneration (repolarization) of myocardium. It is the most changeable since the regeneration process occurs nonsimultaneously in various areas of myocardium.

Segment T-P — quiescent period, general pause and diastole. Interval QRST is called «electrical systole» of heart, its duration is 0,36 sec.

ECG reveals the following manifestations of the activity of heart:

1. Heart rate — in norm in rest it makes 60–80 per minute. More rare rate — 40–50 contractions per minute is called *bradycardia*. It is observed at stimulation of vagus nerve, introduction of acetylcholin, in sportsmen at rest.

Frequency of 90–100 and more contractions per minute at rest (*tachycardia*) is observed at increased temperature of the environment, excitation of sympathetic nerve, introduction of adrenalin, emotions, coffee intake.

2. Localizations of the excitation focus in atriums, A-V node, ventricles.

3. Rhythm disorder. Fluctuations of tone of vagus nerve nucleus during respiration causes respiratory arrhythmia. Intervals between waves R-R change. At the end of expiration the hear rate slows down, at inspiration it raises. In norm arrhythmia can be observed in children.

4. Disorders of excitation conduction are reflected.

5. Myocardial infarctions, at complete disturbance of blood supply of heart, etc.

However, it is necessary to remember that ECG analysis for final conclusion about heart diseases is not enough.

Lecture 2

Theme: Work of heart. Regulation of heart activity

Plan:

1. Work of heart, as of force-pump.
2. Consistency of period and phases of cardiac cycle.
3. Mechanical and sound manifestations of heart activity. Heart tones.
4. Systolic and minute volumes of blood, methods of their definition.
5. Regulation of heart activity (myogenetic self-regulation, nervous, humoral).
6. Endocrine function of heart.

1. Work of heart, as of force-pump

Atriums carry out the role of reservoir. During ventricular systole they collect blood from veins. Then it flows in ventricles during their diastole. Ventricles carry out the role of a pump bringing blood under pressure into arterial system. In norm blood flow in cardiac cavities is one-side directed: from atriums into ventricles and from ventricles into vessels. Atriums contract first. In the beginning of their contraction ostiums of veins are narrowed also blood cannot come back to veins. Ventricles at this time are relaxed, pressure in them is lower than in atriums and blood comes into them. Movement of blood from ventricles in arteria is caused by presence in heart of atrioventricular and semilunar valves. Atrioventricular valves are located between atriums and ventricles:

3-clack-valve in the right half of heart;

2-clack-valve, or mitral, in the left.

They interfere the return of blood from contracted ventricles into atriums. Tendinous chord do not allow valves to be turned outside towards atriums.

Semilunar valves are located in the beginning of aorta and pulmonary artery. The aortal valve is located in the left ventricle, the pulmonic valve — in the right.

During ventricular systole pressure of blood in them grows, semilunar valves open, blood comes into artery. At relaxation of ventricles pressure in them becomes lower than in vessel and, directing back into ventricles, blood closes trigeminal valves.

In diastole ventricles are filled in 70% with blood. At atricular systole 30% added. Atriums have small pumping function, easily extended.

2. Consistency of period and phases of cardiac cycle

After atricular systole there comes ventricular systole. It is divided into some periods and phases.

Period of ***extension*** includes phases:

1. Phase of *asynchronous* contraction (0,05 sec). Excitation and contraction is distributed along myocardium of ventricles non-simultaneously, yet not all muscular fibers are covered with excitation. Pressure in ventricles is close to 0. By the end of phase at contraction of all myocardium fibers pressure quickly increases.

2. Phase of *isometric* contraction. Under pressure of blood clack-valve are closed, the 1st tone arises — SYSTOLIC. In this phase pressure in ventricles raises up to 70–80 mm Hg in the left ventricle, up to 15–20 mm Hg in the right one. Clack-valve and semilunar valves are closed. The strain of fibers (not the length) is enlarged only. The volume of blood does not vary, it is constant. Pressure in ventricles continues to increase, left ventricle becomes spherical, strikes an internal surface of thorax. It is accompanied by originating of apical thrust in the 5th intercostal gap on the left from medium clavicle lines (in men). By the end of the period pressure in ventricles becomes higher than in an aorta and pulmonary artery. Cusps of semilunar valves open and blood comes into vessels.

The next, ***expulsion*** period comes:

1. Phase of *fast expulsion* of blood.

2. Phase of *slow expulsion* of blood.

Pressure in ventricles raises up to 120–130 mm Hg in the left and up to 25 mm Hg in the right ventricle.

At the end of slow expulsion of blood there comes relaxation of ventricles. In the beginning of diastole pressure in ventricles goes down. Blood goes back into ventricles and closes semilunar valves, there is the 2nd tone — ***diastolic***.

Diastole of ventricles (0,47 sec) is divided into the following period and phases.

The ***protodiastolic*** period (0,04 sec). This is time from the beginning of relaxation of ventricles to the closing of semilunar valves.

The period of ***isometric relaxation*** (0,08 sec). Pressure in ventricles is reduced up to 0. Clack-valve valves are still closed, the volume of the residual blood and length of myocardium fibers do not change. Pressure in ventricles by the end of the period becomes lower than in atriums, clack-valves open, blood comes to ventricles. There comes the next period.

Period of ***filling*** of ventricles with blood (0,25 sec). It includes:
Phase of *fast* filling (0,08 sec).
Phase of *slow* filling (0,17 c), thus appear the 3rd and the 4th cardiac tones.
Then there comes the ***presystolic*** period (0,1 sec).

3. Mechanical and sound manifestations of cardiac activity. Cardiac tones

Apex at systole rises and presses to internal surface of thorax. In the 5th intercostals gap there is an ***apical thrust***. Work of heart is accompanied also by sound phenomena.

Cardiac tones

At an auscultation of heart two tones are determined: the first — systolic, second — diastolic.

I. ***Systolic*** tones is low, prolonged (0,12 sec).

Characteristic of the 1st tone is determined by strain of clack-valves, strain of tendinous fibers, papillary muscles, walls of ventricles myocardium.

The 1st tone is well auscultateted in the 5th left intercostals gap.

The 2nd tone — ***diastolic*** (high, short — 0,08 sec). It arises at strain of the closed semilunar valves. The higher is the pressure in aorta and pulmonary artery, the higher is the tone. It is well auscultated in the 2nd intercostal gap on the right and on the left of sternum.

The 3rd tone is formed by fluctuations of walls of ventricles at their fast filling with blood, the 4th tone is formed at additional filling ventricles at atricular systole.

Cardiac tones are auscultated to with help of stethoscope at application of ear to thorax.

At incomplete closing of valves due to turbulent blood flow, cardiac murmurs occur. Their detection has an important diagnostic value.

4. Systolic and minute volumes of blood, methods of their definition

The amount of blood released by the ventricle into an artery in one minute is the important parameter of functional state of cardiovascular system (CVS) and is called the ***minute volume of blood*** (MVB). It is identical for both ventricles and at rest is 4,5–5,0 l. If divide MVB by heart rate in one minute, we receive ***systolic*** volume (SV) of blood flow. At heart rate of 75 beat per minute it is equal to 65–70 ml, at work it is enlarged to 125 ml. It sportsmen at rest it makes 100 ml, at work — 180 ml.

All complex of cardiac activity is registered by means of various physiological techniques — *cardiographies*: ECG, electrokymography, ballistocardiography, dynamocardiography, apical cardiography, ultrasonic cardiography, etc.

5. Regulation of heart activity (myogenetic self-regulation, nervous, humoral)

Extra-cardiac nervous regulation. The highest level of adaptation of activity of cardiovascular system is ensured by neurohumoral regulation. Nervous regulation is carried out by central nervous system (CNS) through sympathetic and vagus nerves.

The influence of vagus nerve.

At strong excitation of peripheric end of cut vagus nerve the following changes were detected:

1. Negative chronotropic effect (decrease of contraction rhythm).
2. Negative inotropic effect — decrease of contraction amplitude.
3. Negative bathmotropic effect — decrease of excitability of myocardium.
4. Negative dromotropic effect — decrease of rate of excitation conduction cardiomyocites.

Influences of sympathetic nerve.

The Inverse influence of sympathetic nerve on activity of heart was determined:

1. Positive chronotropic effect (acceleration of heart contraction).
2. Positive inotropic effect (increase in contraction amplitude).
3. Positive bathmotropic effect (increase of excitability of myocardium).
4. Positive dromotropic effect (increase of excitation conduction rate).

Despite inverse influences of sympathetic and vagus nerves they are functional synergists. Dependening on the degree of filling of heart and coronary vessels with blood vagus nerve can have inverse influence, i.e. not only to inhibit but also to enhance activity of heart.

Transfer of excitation from the terminals of sympathetic nerve onto heart is carried out with the help of mediator of noradrenalin. It is destroyed slowly and acts longer. In the terminals of vagus nerve acetylcholin is formed. It is quickly destroyed by choline esterase, thus having only local action. The regulation of cardiac activity is executed by hypothalamus, limbic system, cortex of cerebrum.

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

The most significant are: aortal, sinocarotid zone, pulmonary arteria, of heart itself, etc. Included into these zones mechano- and chemo-receptors participate in stimulation or retardation of heart activity which results in increase or decrease of blood pressure.

Danini-Achner's ***ocular-cardiac*** reflex. At pressing of an eyeball the heart rate decreases in 10–20 in one minute.

Acceleration and intensifying of heart rate is observed at pain, muscular work, emotions. Participation of cortex of cerebrum in regulation of heart is proved by method of conditioned reflexes. If repeatedly to combine the conditioned excitator (sound) with pressing on eyeballs that results in heart rate de-

crease, in some time only the conditioned excitator (sound) will produce the same reaction. This phenomenon is called the Danini-Achner's conditional ocular-cardiac reflex.

Humoral regulation. It is carried out by hormons and ionic structure of intercellular liquid. Adrenalin and noradrenalin increase force and rhythm of contractions.

The contraction force is also influenced by glucagon, corticosteroids (aldosteron), angiotensin, serotonin, thyroxine. Ca^{++} raises an excitability and conduction of excitation in myocardium.

Acetylcholin, anemic hypoxemia, hypercapnia, acidosis, increased amount of K^+, HCO_3^-, H^+ suppress cardiac activity.

6. Endocrine function of heart

In myocytes of atriums natriuretic hormon is formed. It increases excretion of Na^+ and Cl^- by kidneys, glomerular filtration, lowers secretion of renin, effect of influence of angiotensin II, aldosteron, relaxes smooth myocytes of fine vessels which promotes decrease of blood pressure.

PHYSIOLOGY OF VASCULAR SYSTEM

Lecture 3

Theme: Fundamentals of hemodynamics. Blood pressure. Arterial pulse

Plan:

1. Fundamentals of hemodynamics.
2. Volumetric and linear rates of blood flow in various areas of blood channel.
3. Factors ensuring blood circulation in vessels of high pressure.
4. Blood pressure, its kinds and its determining factors. Measuring methods.
5. Morphological and functional classification of vessels.
6. Arterial pulse, its nature and characteristic.

1. Fundamentals of hemodynamics

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

1. Pressure (P) under which it flows, i.e. difference of pressure in the beginning and the end of tube. This force promotes circulation.

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

Relation of difference of pressure to resistance determines volumetric rate of fluid flow.

Peripheral resistance is formed by the resistance of each vessel. At rest only small part of capillars is open. Big amount of them is included into blood

flow in parallel. Therefore, their traction resistance will be much less than in arteries. Viscosity of blood determines resistance but it is changeable in different areas of vascular channel. The lesser the diameter of a vessel is, the lesser is viscosity. Basic vessels of resistance, or resistive vessels, are arteries and arterioles. They have small diameter (15–70 microns), thick layer of ring unstriped musculation which, at contraction, can considerably decrease the diameter and raise the blood-flow resistance. Arterial pressure in them thus raises. Decrease of arterioles tonus promotes blood outflow from arteries and decrease of arterial pressure in them. Hence, change of arterioles diameter is the main regulator of the general arterial pressure level. In working organs the tonus of arterioles walls goes down, blood supply is improved. In non-working organs it does not happen. It supports the necessary arterial pressure level.

Heart, pushing blood into vessels, forms pressure in them necessary for blood-flow. Pressure determines rate of blood-flow and promotes overcoming of resistance. The higher resistance is, the more force is necessary for blood-flow ensuring. In large and average arteries pressure is reduced only by 10%. In arterioles and capillars — by 85%.

The important condition for normal blood circulation is its interrelation in arteries and veins:

Arteries contain 27% of blood,

Veins — 73%.

The basic parameters of hemodynamics are:

1. Volumetric rate of blood-flow.
2. Linear rate (rate of bloods circulation).
3. Pressure in different areas of vascular channel.

2. Volumetric and linear rates of blood flow in various areas of blood channel

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

Linear rate is the blood-flow rate along the vessel. It varies in different areas of vascular channel and depends on total sum of the area of lumens of concrete department of vessels.

In aorta, the cross-section is 8 cm^2, rate of blood-flow is 50–70 cm/sec. In capillars the total section of all vessels is 8000 cm^2, the rate of blood-flow is 0,05 cm /sec.

In arteries the blood-flow rate is 20–40 cm/sec, in arterioles — 0,5–10 cm/sec, in hollow vein — 20 cm/sec.

Due to output of blood from heart in vessels in the separate portions, the blood-flow in arteries is of pulsating character.

Continuity of flow in all system of vessels is connected with elastic properties of aorta and arteries. During systole heart produces basic kinetic energy necessary for blood-flow. Part of this energy goes for pushing of blood, another turns into potential energy of distension of wall of aorta and arteries during systole. During diastole this energy turns into kinetic energy of blood-flow.

3. Factors ensuring blood circulation in vessels of high pressure

All vessels inside are covered with epithelium forming smooth surface. It interferes blood coagulation in norm. Besides, except capillars, vessels contain elastic, collagen, unstriped muscular fibers.

Elastic fibers are easily stretched, produce elastic strain counteracting blood pressure.

Collagen fibers resist distention, form folds and counteract pressure when the vessel is strongly stretched.

Unstriped muscular fibers create tonus of walls of vessels and change lumen of the vessel if necessary. Some unstriped muscular cells have ability to contract spontaneously (regardless nervous system) which sustains constant tonus of walls of vessels.

4. Blood pressure, its kinds and its determining factors. Measuring methods

Level of blood pressure is determined by set of different factors:

1. Pumping force of heart;
2. Peripheral resistance of vessels;
3. Volume of circulating blood.

It is measured in mm Hg.

Major factor of maintenance of arterial pressure level is the work of heart. Blood pressure in arteries constantly changes. Its rise at systole determines the ***maximal (systolic)*** pressure. In middle-aged person in brachial artery (and in aorta) it is 110–120 mm Hg. Pressure decrease at diastole corresponds to the ***minimal (diastolic)*** pressure which is equal to 80 mm Hg on average. It depends on peripheral resistance of vessels and heart rate. The difference between systolic and diastolic pressure compounds ***pulse pressure*** (40–50 mm Hg). It is proportional to the volume of the pumped out blood. These values are the main parameters of functional state of all cardiovascular system.

The increase of the arterial pressure is called *hypertension* (140–160 mm Hg), the decrease — *hypotension* (90–100 mm Hg). Influenced by various factors the arterial pressure can considerably variate. Thus, at emotions reactive rise of arterial pressure (at examinations, sport competitions) is observed. Daily fluctuations of arterial pressure are observed, it is higher in the day-time, at quiet sleep it is a little bit lower (20 mm Hg). Pain is accompanied with rise of the arterial pressure but at long influence of pain irritant the decrease of arterial pressure is possible.

Hypertension arises:
— at rising of cardiac release;
— at rising of peripheral resistance;
— at combination of both factors.

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

The third factor — amount of circulating blood and its viscosity. At transfusion of large amount of blood arterial pressure raises, at loss of blood it is reduced. Arterial pressure depends on venous return (for example, at muscular work).

Methods of hemodynamometry

Two methods of arterial pressure measuring are used.

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

Indirect. In 1905 I.S.Korotkov offered *auscultation* method by auscultation of sounds (Korotkov's tones) in brachial artery below cuff with the help of stethoscope. At opening of the valve the blood pressure in the cuff goes down and when it becomes lower than systolic, short, clear tones (systolic pressure) appear in the artery. Systolic pressure is marked on the manometer. Then tones become louder and further fade, thus determining diastolic pressure.

5. Morphological and functional classification of vessels

Amortizing vessels — aorta, pulmonary artery, other large vessels. They contain elastic elements and reduce arterial pressure at systole.

Resistive — arteries and arterioles. Thick unstriped muscular walls of these vessels are capable to variate considerably the diameter of vessel, they regulate blood supply of organs.

Vessels ***sphincters*** are the last area of pre-capillary arterioles. Changing the arterioles diameter, they determine the number of functioning capillars.

Metabolic vessels — capillars. Their thin walls are characterized by permeability, promote metabolism between blood and tissues.

Capacitor vessels — venulas, veins. Their walls are more thin than arterial, easy stretched; large veins contain valves. They contain lot of blood (especially veins of liver).

Shunt vessels (anastomosis) - bind arteries with veins by-passing capillars. They participate in regulation of peripheral blood-flow, temperature of parts of body. These are vessels of ear, nose, foot, etc.

6. Arterial pulse, its nature and characteristic

Pulse is rhythmic fluctuations of walls of vessels connected with the dynamics of their filling with blood and pressure in them during one cardiac cycle. The amount of blood pumped out into aorta at systole produces increase of pressure

and stretches its walls. Due to elasticity walls of aorta tend to reduce their capacity and push blood forward where also walls are extended, «compensatory chamber» appear. Such processes occur in the next areas of vessels, gradually weaken and fade in arterioles and capillars. Accordingly, blood-flow has pulsating character.

These pulse variation of blood-flow, pressure, volume of blood are distributed as pulse-wave (wave of rised pressure) with certain rate. With years, the rate increases. At rising of the arterial pressure walls of vessels are strained and their distensibility is reduced, rate of pulse wave distribution is enlarged. Hence, rate of pulse-wave distribution reflects elasticity of walls of vessels.

Characteristics of pulse.

Pulse can be investigated by means of a simple palpation. They distinguish:

1. ***Heart rate***: slow, rapid, normal. In children at rest pulse is more rapid. In newborns on average pulse is 140 beat per minute, influenced only by sympathetic nerve. In sportsmen — athletes pulse at rest is slower considering predominance of influence of vagus nerve and augmentation of systolic volume of blood.

2. ***Rhythm***: rhythmic, arrhythmic. It is determined by duration of R-R interval. Respiration (respiratory arrhythmia) influences the rhythm. At inspiration the pulse raises, at expiration it slows down.

3. ***Filling*** (height): good, satisfactory, weak, thready pulse. Filling depends on systolic volume and volumetric rate of blood-flow in diastole, on elasticity of walls of vessels.

4. ***Rate***: normal, rapid, slow pulse. Rapid pulse can reflect failure of the aortal valve. The enlarged amount of blood is pumped out, part of blood returns into ventricle. Slow pulse can be observed at narrowing of an aortal opening when blood comes to aorta slower.

5. ***Strain***: moderate, firm, mild pulse. It is determined by effort of squeezing of an artery before pulse disappearance.

With the help of sphygmograph it is possible to register the form of pulse wave — ***sphygmogram***. They distinguish some components in it:

Anacrotism. This initial sharp rise of a curve is connected with the opening of semilunar valve and blood outflow into aorta. Pressure raises, walls of aorta are stretched.

Catacrotism. It is the recession of the curve. Ventricle is relaxed, pressure in it becomes lower than in aorta, blood directs in ventricle, pressure in aorta is sharply reduced, walls of aorta return into initial state.

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

Smoothed dicrotism testifies the affection of the aortal valve.

PHYSIOLOGY OF VASCULAR SYSTEM

Lecture 4

Theme: Microcirculation. Regulation of blood flow in vessels.

Plan:

1. Blood flow in low pressure vessels. Venous pulse.
2. Microcirculation. Capillary blood flow and its features. Factors influencing processes of microcirculation.
3. Regulation of blood flow in vessels.

1. Blood flow in low pressure vessels. Venous pulse

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

Veins determine the value of blood return to heart, systolic volume, minute volume of blood. In veins blood flow from the region of higher pressure to the region of lower pressure. In venula blood pressure is 12–18 mm Hg. In veins outside thorax it is 5–9 mm Hg. At flowing into the right atrium it is almost equal to the atmospheric pressure and changes depending on phases of respiration: at inspiration — below atmospheric and at expiration — higher in 2–5 mm Hg. Very dangerous is the affection of veins located close to thoracic cavity (for example, jugular vein). At inspiration, when pressure in veins becomes negative, atmospheric air, penetrating into veins cavity, can cause the air embolism. Air bubbles in blood cause occlusion of arterioles and capillars and can lead to death.

Pressure in the right atrium forms *central venous pressure*. In norm it varies synchronically with respiratory and cardiac rhythm.

Increase of venous pressure up to 20–35 cm of water column is a sign of cardiovascular failure. It is observed at low activity of the right ventricle, failure of tricuspid valve.

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

1. Suction action of thorax. At inspiration atmospheric pressure in thorax is decreased which promotes veins distention, thus inducing the effect of blood sucking from adjacent vessels. The diaphragm, moving down, increases intra-abdominal pressure that promotes venous inflow to heart from the vessels of abdominal cavity.
2. «Muscular pump». At contraction skeletal muscles squeeze veins which pushes blood to heart. Presence of valves on internal surface of some veins prevents inverse blood flow. These mechanisms act at movement of a man.
3. Suction action of heart. Atrioventricular septum at systole of ventricle is shifted downwards and creates suction effect of blood to heart from veins.
4. Peristaltic contraction of walls of some veins is 2–3 times a minute.

In small and middle veins pulse fluctuation of blood pressure are not present. In large vessels close to heart blood flow in veins is of pulse character.

Venous pulse. Pulse wave in veins is of other origin, than in arteries. It is formed at increase of pressure in veins stretching vascular wall, at termination of blood outflow from veins at systole of heart.

The curve of venous pulse, ***phlebogram***, distinguishes 3 waves:

a-wave reflects increase of pressure in hollow vein at systole of atrium when blood outflow from veins is terminated;

c-wave is ensured by the increase of pressure in hollow vein at contraction of ventricle. Atrioventricular valve is stuck out into the right atrium increasing pressure in it, which complicates blood outflow from veins. Then, at expulsion of blood the valve is displaced to the apex of ventricles, the fast decrease of pressure in vein follows.

v-wave is ensured by increase of pressure in vein in connection with the termination of blood outflow from vein at the end of auricular diastole, after their filling with blood. Changes of venous pulse curve are the important parameters in diagnostics since it reflects tricuspid valve insufficiency.

The total circulation time through systemic and pulmonary circulation in man is 23 sec at heart rate of 70–80 bpm.

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

The most important, in functional feature, region of vascular system are capillars which are related to metabolic vessels. They participate in supply of cells with nutrient, plastic substances and excretion of metabolism products. This process also presents in venulas.

At rest blood circulates only in 25–35% of all capillars. Arterioles, metarterioles, venulas participate in regulation of capillary blood flow. Set of vessels from arterioles to venulas is called terminal (microcirculation) channel. They compound general functional unit.

Density of capillars in different organs considerably varies. Big number of them is contained in myocardium, brain, liver, kidneys (up to 2500–3000 capillars in 1 mm^2). This number is less in osteal, adipose, conective tissues. Blood in capillars contacts very big surface at rather long time.

Diameter of capillars is 5–30 μm.

General surface of all capillars is about 1000 m^2.

Wall of capillars represents the semipermeable membrane closely connected functionally and morphologically with surrounding connective tissue, that is, capillars are inseparable from organs, they are component of organs. There are squamous, loop capillars, they are easily stretched corresponding to diameter of erythrocytes.

Walls of capillars consist of 2 membranes: internal-endothelial and external-basal. Depending on ultrastructure of capillars walls they can be divided into 3 types:

1. ***Somatic*** type — has continuous endothelial and basal envelope, big number of the smallest pores (4–5 nm in diameter). They easily transmit water and

mineral substances, present in sceletal and unstriped musculation, adipose and connective tissue, lungs, cerebral cortex.

2. ***Visceral*** type — has fenestration (holes) with diameter — 0.1 μm. Fenestrations are frequently covered with the thinnest membrane. They present in kidney, digestive canal, endocrine glands.

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

For the function of capillars, the blood-flow rate in them, permeability of walls, value of hydrostatic and oncotic pressure, the number of perfusing capillars have high significance. The average linear rate in capillars is 0,5–1 mm/s. Each blood cell remains in a capillar approximately for 1,0 s.

Hydrostatic pressure in capillars depends on resistance in arteries and arterioles. In capillars it continues to decrease and compounds in arterial end 30–35 mm Hg, in venules end — 15–20 mm Hg.

Flow of fluid and various substances through wall of capillars is carried out by *diffusion, filtration* and *osmosis*.

Diffusion is of double nature, its rate is very high. Passing through capillar, fluid of plasma 40 times completely exchanges with intercellular fluid. Through the general metabolic surface of an organism the diffusion rate is approximately equal to 60 l/min, in 24 hours it makes 85,000 l on average.

Filtration rate in norm is practically equal to reabsorption rate. Only small part of intercellular fluid gets into lymphatic vessels. Filtration rate compounds 20 l/day, reabsorption rate — 18 l/day, 2 l of fluids a day gets into lymphatic vessels.

In arterial end of capillars the effective filtration pressure is 9 mm Hg. At venous end the effective reabsorption pressure is 6 mm Hg. Filtration is ensured by passing of erythrocyte through capillar.

3. Regulation of blood flow in vessels

Mechanisms of regulation of blood flow in vessels can be divided into two constituent parts:

1. Central, determining the value of arterial pressure and systemic circulation;
2. Local, regulating blood flow in separate organ and tissues.

Substances formed during metabolism are capable to dilate arterioles and to enlarge the number of functioning capillars. The decrease of unstriped muscles tonus leading to vasodilatation, happens under influence of the increase of concentration of H^+, CO_2, decrease of O_2 presence.

Unstriped muscles of vessels constantly keep some strain — muscle tonus. In its maintenance the leading role belongs to myogenic regulation. Tonus is preserved even at complete absence of nervous and humoral influences and received the name of *basal* or *peripheric*.

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

Neuro-humoral regulation of blood-flow.

Mechanisms of this regulation include some parts:

1. Afferent (receptor) part
2. Central part
3. Efferent part

Afferent part is represented by baro- and chemoreceptors situated in walls of vessels (angioreceptors).

Baroreceptors respond to the rate and degree of distention of walls of vessels. By the mechanism of action they are mechanoreceptors.

Chemoreceptors are sensitive to chemical structure of blood.

Angioreceptors are situated in vessels of all system of circulation forming uniform receptive field, its structure includes reflexogenic zones. From them, the most significant are aortal, sinocarotid, zone of pulmonary circle vessels, and others.

Aortal zone is located in the wall of aortic arch. At increase of arterial pressure walls of aorta are stretched, baroreceptors are excited, excitation by fibers of aortal nerve reaches vasomotor center of medulla. It promotes the increase of nucleus vagus tonus, tonus of vasoconstrictor center is reduced, arterial pressure is decreased.

At decrease of arterial pressure frequency of pulses in depressor decreases, center of vagus nerve is tinned, sympathetic department is activated. Vessels are narrowed, activity of heart strengthens, arterial pressure raises. So, self-regulation of constant level of arterial pressure maintenance is carried out.

Synocarotid zone is located in the place of branching of general carotid artery into internal and external, is connected with the vasomotor center of a sinus nerve.

At increase of arterial pressure in carotid artery baroreceptors are excited that by reflex reduces tonus of the vasomotor center and raises tonus of vagus nerve. Arterial pressure in vessels is reduced owing to dilation of blood vessels and slowering of heart rate (vasocardial reflex of Bainbridge).

Once the blood pressure in the carotid artery has decreased, excitation intensiveness from the baroreceptor also decreases. The tonus of vascular walls increases, peripheral resistance grows up, and blood pressure becomes normal. Both zones can have both depressing and pressing effects.

Aortal and sinocarotid zones contain chemoreceptors sensitive to O_2, CO_2, H^+ presence in blood. Hypoxia, hypercapnia lead to cardiovascular, respiratory reflexes normalizing homeostasis.

Central part. It carries out regulation by totality of nervous frames which make vasomotor center. It includes various levels of CNS.

The main center of maintenance of vessels tonus and regulation of the arterial pressure is the vasomotor center of medulla.

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

The influence of cortex of cerebrum on changes of vascular tonus and, consequently, on blood-flow, is examined more deeply by method of conditioned reflexes. If repeatedly to combine warming or cooling of a part of skin changing of a lumen of vessels, with sound or light, in some time one indifferent conditioned excitator (sound) produces the same vascular reaction as unconditional excitation (warmth, cold).

Efferent part.

Efferent regulation is carried out by nervous and humoral mechanisms.

The nervous mechanism is realized through sympathetic and parasympathetic nerve fibrils. Sympathetic fibers are the main vasoconstrictors, sustain tonus of vessels and constant level of blood pressure.

Parasympathetic nerves produce strong dilation (vasodilatation) of vessels. But not everywhere parasympathetic nerves produce identical effect. Influenced by them, constriction of vessels is observed in heart. Sympathetic nerves dilate vessels of heart and skeletal muscles.

Humoral regulation

The important role in humoral regulation of tone of vessels is played by hormons of paranephroses, neurohypophysis, uxtaglomerular apparatus of kidneys.

Adrenalin renders strong influence on vessels. It constricts arteries and arterioles of skin, digestive system, kidneys, lungs. It relaxes vessels of skeletal muscles, unstriped muscles of bronchis. Noradrenalin produces constricting effect. It cooperates basically with α-receptors, excitation of which promotes constriction of vessels. In extreme conditions adrenalin mobilizes functions and induces reserve forces of the organism.

Aldosteron changes sensitivity of walls of vessels to action of adrenalin and noradrenalin.

Vasopressin (hormon of neurohypophysis) constricts arteries of abdominal cavity, lungs, dilates cerebral and cardiac vessels.

Renin turns into an Angiotensin II — vasoconstrictor.

Biologically-active substances and local hormons participate in regulation of blood flow. Histamin dilates vessels. Intensive formation and action of histamin produces reaction of skin redness.

The bradykinin dilates vessels.

Prostaglandins act in multiple way.

PHYSIOLOGY OF RESPIRATION

Lecture 1

Theme: External respiration

Plan:

1. External respiration.
2. Respiratory movements.
3. Pressure in pleural cavity and its change at respiration.
4. Ventilation of lungs. Pulmonary volumes.
5. Dead space.
6. Alveolar ventilation.
7. Gas exchange in lungs.

1. External respiration

Set of the processes providing receipt of O_2 by the organism, its delivery and consumption by tissues and excretion of the respiration end-product CO_2 into environment, is called **respiration**.

Complex process of gas exchange with environment is formed by the number of consecutive processes.

External respiration (pulmonary):

1. Gas exchange between pulmonary air and atmospheric (ventilation of lungs).
2. Gas exchange between pulmonary air and blood of small circulation circle capillaries.

Internal:

3. O_2 and CO_2 transport with blood.
4. Gas exchange between blood and cells (tissue respiration) i.e. consumption of O_2 and excretion of CO_2 at metabolism.

In man, the function of external respiration and refreshing of gas structure of blood is performed by respiratory ways (nasal and oral cavity, larynx, trachea, bronchi, bronchioles, alveolar ways) and lungs.

For realization of gas exchange processes lung structure contains the number of adaptive features:

1. Presence of air and blood channel, separated by the thinnest (0,004 mm) membrane consisting of double layer — alveole itself and a capillary. Through this aerohematic barrier gases diffusion occurs.
2. The extensive respiratory area of lungs is 50–90 m^2.
3. Presence special — small circle of blood circulation.
4. Presence of elastic tissue in lungs ensuring expanding and falling of lungs at inspiration and expiration. Lungs are in condition of elastic tension.
5. Presence of support cartilage tissues as of cartilage bronchi in respiratory ways. It prevents falling of respiratory ways and promotes fast and easy passage of air.

2. Respiratory movements

Ventilation of alveoles necessary for gas exchange is carried out due to alternation of inspiration and expiration. At inspiration air saturated with O_2 gets into alveoles. At expiration, air poor with O_2 but rich in CO_2 is released from the alveoles. The phase of inspiration and the following phase of expiration make *respiratory cycle*.

Movement of air is caused by alternate increase and reduction of thorax volume.

The mechanism of inspiration. Inspiration is *an active* process.

Increase of thoracic cavity happens in vertical, sagital, frontal planes. It is provided by: raising of ribs and lowering of the diaphragm.

Movement of ribs. Ribs form mobile connections with bodies and cross processes of vertebras. At raising of ribs the size of thorax increases in anteroposterior and lateral directions. Raising of ribs is caused by the contraction of inspiration muscles. They include: external intercostal, internal intercartilaginous muscles.

Movement of inferior ribs has big influence on the volume of thorax, that id why inferior lobes of lungs are ventilated better than superior.

In a healthy young man the difference between circumference of thorax at inspiration and expiration is 7–10 cm, in women — 5–8 cm. Forced respiration involve auxiliary inspiration muscles:

- greater and smaller pectoral muscles;
- scalene muscle;
- sternocleidomastoid;
- trapezius muscle, etc.

Movement of diaphragm. The diaphragm has the form of the dome protruding into thoracic cavity. At expiration it adjoins the internal wall of thorax. At inspiration diaphragm flattens as result of reduction of its muscular fibers.

The mechanism of expiration is ensured by:

- weight of thorax.
- elasticity of costal cartilages.
- Elasticity of lungs.
- Pressure of organs of abdominal cavity on the diaphragm.

At rest expiration is *passive*.

In forced respiration *expiration* muscles take part: internal intercostal muscles and auxiliary *expiration* muscles: backbone flexors, abdominal muscles.

Types of respiration. There are 3 types of respiration depending on which component raising (ribs or diaphragm) causes the increase in thoracic volume:

- thoracic;
- abdominal;
- mixed.

To the greater extent the type of respiration depends on age (mobility of thorax increases), clothes, profession. Abdominal respiration becomes difficult at last months of pregnancy, then thoracic respiration is involved.

The abdominal type of respiration is most effective:

- ventilation of lung is more deep;
- return of venous blood to heart is ensured.

The abdominal respiration prevails at physical workers, opera singers, etc. After birth a child has the abdominal respiration, to the age of 7 it is changed into thoracic.

3. Pressure in pleural cavity and its change at respiration

Lungs are covered with visceral pleura and membrane of thoracic cavity with parietal pleura. Between them there is serous liquid. They are closely connected (gap of 5–10 μm) and slide relating each other.

If to insert a needle into the pleural cavity and connect it with water manometer, the pressure in it will be:

at inspiration — 6–8 cm H_2O

at expiration — 3–5 cm H_2O lower of atmospheric.

This difference between intrapleural and atmospheric pressure is usually called pleural cavity pressure.

Negative pressure in pleural cavity is caused by elastic traction of lungs, i.e. tendency of lung to fall.

At inspiration the increase in thoracic cavity leads to increase of negative pressure in pleural cavity.

The accumulation of liquid in pleural cavity is interfered by lower oncotic pressure of pleural liquid (less protein) than in plasma.

Elastic traction of lungs is caused by 3 factors:

1. Surface tension of membrane of the liquid covering the internal surface of alveoles.
2. Elasticity of alveoles walls (contain elastic fibres).
3. Tonus of bronchial muscles.

At any gap surface between air and liquid there are forces of intermolecular link (forces of surface tension). Influenced by these forces alveoles tend to fall. Forces of surface tension make 2/3 of elastic traction of lungs.

If the internal surface of alveolus were covered with water solution, surface tension would have to be in 5–8 times more. In these conditions the fall of alveoles would be observed.

On the internal surface of alveoles there are substances reducing surface tension called surface active substances whose role is carried out by surfactant.

At reduction of alveoles size molecules of surfactant become closer and the surface tension is reduced — alveole does not fall.

At expansion of the alveoles their surface tension increases which strengthens elastic traction of lung.

Infringement of surfactant formation results in fall of big number of alveoles — atelectasis, or absence of ventilation of big portions of lungs.

In newborns surfactant are necessary for extension of lungs at the respiratory movements.

Receipt of air into pleural cavity is called pneumothorax (through a damaged thorax or lung). Due to their elasticity lungs fall into 1/3 of their volume.

4. Ventilation of lungs. Pulmonary volumes

1. Respiratory volume (RV) — amount of air inspired and expired by the person at quiet respiration (0,3–0,9 l, average 500 ml).

2. Reserve inspiration volume (RVin) — the amount of air which can be inspired after quiet inspiration (1,5–2,0 l).

3. Reserve volume of expiration (RVex) — the amount of air which can be expired after quiet expiration (1,0–1,5 l).

4. Residual volume — volume of air remaining in lung after maximal expiration (1,0–1,5 l).

5. Vital capacity of lung (VC) = RV + RVin + RVex (0,5 + 1,5 + 1,5) = 3,5 l. Reflects force of respiratory muscles, extensibility of lungs, the area of respiratory membrane.

6. Functional residual capacity (FRC), or alveolar air — the amount of air remaining in lungs after quiet expiration (2,5 l).

7. General capacity of lung — the amount of air contained in lungs at the maximal inspiration limit (4,5–6,0 l).

8. Inspiratory capacity includes respiratory volume + reserve volume of inspiration (2,0 l).

Thus, there are 4 initial respiratory volumes and 4 capacities of lungs:

Volumes	Capacities
Respiratory volume	Inspiratory capacity
Reserve volume of inspiration	Vital capacity
Reserve volume of expiration	General capacity of lung
Residual volume	Functional residual capacity

VC determines the maximal volume of air which can come or go out of lungs during one inspiration or expiration. This is the indicator of mobility of lungs and the thorax.

Factors influencing VC:

- Age. After 40 years VC goes down (decrease of elasticity of lung and mobility of thorax).
- Sex. In women VC on the average is in 25% lower than in men.
- Body size.
- Position of body. In vertical position it is higher than in horizontal (the greater filling of vessels of lungs).
- Degree of training. In trained people VC increases (especially in swimmers where endurance is necessary).

5. Dead space

There are:

- Anatomic;
- Functional (physiological).

Anatomic dead space — the volume of respiratory tracts in which there is no gas exchange (nasal and oral cavity, larynx, trachea, bronchi, bronchioles, alveolar ways).

Its physiological role is in:

1. Refreshing of air (mucous membrane catches fine particles of dust, bacteria).
2. Humidifying of air (secret of glandular cells of an epithelium).
3. Warming of air (temperature of expired air is approximately 37°C).

The volume of anatomic dead space is on the average 150 ml (140–170 ml).

Therefore, from 500 ml of respiratory volume only 350ml will get into alveoles. The volume of alveolar air is 2500 ml. The pulmonary ventilation coefficient thus is 350 : 2500 = 1/7, i.e. in the result of 1 respiratory cycle only 1/7 part of air of FRC is refreshed, or its complete refreshing occurs in the result of not less than 7 respiratory cycles.

Functional dead space — portions of respiratory system in which there is no gas exchange, i.e. to anatomic dead space such alveoles are added which are ventilated but not supplied with blood.

In norm such alveoles are few, therefore in norm the volume of anatomic and functional dead space coincides.

6. Alveolar ventilation

In man breath rate on average is 14 (12–18) in one minute.

In children it is more frequent: in babies — 30–40 in min., in newborns — 40–55 in min.

The minute volume of respiration (MVB) = 500 ml × 14 = 7 l.

At physical exertion MVB is 120 l/min.

Deep and infrequent respiration is more effective than surface and frequent respiration.

The size of ventilation is regulated so that to provide constant gas structure of alveolar air.

If MVB in norm is 7 l/min but respiration is frequent (35 in min) and surface (RV = 0, 2 l), mainly the dead space will be ventilated and inspired air will almost not rich alveoles. Such condition is dangerous.

One of the indicators of reserves of respiratory system is *the maximal ventilation of lungs* (MVL) — volume of air passing through lungs within certain time interval at respiration with maximal possible frequency and depth.

In norm MVL varies within 120–170 l/min.

Its size depends on age, sex, size of body.

7. Gas exchange in lungs

The exchange of gases occurs in alveoles where diffusion of O_2 takes place from alveolar air into blood, and CO_2 from blood into the alveolar air. In a day approximately 500 l of O_2 comes into blood from alveolar air, and in reverse direction — 450 l of CO_2.

1. For gas exchange in lung the partial pressure of gases has the main importance.

Structure of air (in %)

Air	O_2	CO_2
Inhaled	21.0	0.02–0.03
Exhaled	16.0	4.5
Alveolar	14.0	5.5

Diffusion of gases occurs due to difference of partial pressure of these gases in alveolar air and their pressure in blood.

In blood gases are in dissolved and chemically connected conditions. Force with which molecule of gas tends to go into gas environment is called *voltage* of gas in a liquid.

The amount of gas dissolved in liquid depends on:

- composition of the liquid;
- volume and pressure of gas over liquid;
- temperature of liquid;
- nature of gas.

The constancy of gas structure of alveolar air is the necessary condition of normal gas exchange. In maintenance of the given constancy the essential role is played by the dead space, it carries out the function of a buffer smoothing fluctuations of structure of alveolar air during respiratory cycle.

Ventilation-perfusion relations, i.e. conformity of minute volume of respiration to minute volume of blood flow in small circle of blood circulation. Ventilation-perfusion coefficient in norm is 0,8–0,9.

In vessels of big circle of blood circulation the unstriped muscles of the majority of vessels at lack of O_2 relaxes. In vessels of small circle, on the contrary, it is reduced, which causes narrowing of vessels in poorly ventilated portions of lungs and reduction of blood-flow in them.

The human need in O_2 is 350 ml/min (at physical exertion — 5000 ml).

2. Comparatively thin aerohematic barrier (0,4–1,5 μm) between air- and blood channels including:

1) surfactant layer (surfactant is one of the factors promoting O_2 diffusion);
2) alveolar epithelium;
3) two basal membranes;
4) endothelium of capillaries.

Apart from this barrier, during diffusion O_2 comes through:

- layer of plasma of blood;
- membrane of erythrocytes.

3. High diffusion ability of lung. It is defined by the amount of gas penetrating through the lung membrane for one minute in 1 mm Hg of gradient of pressure.

For O_2 it is 25 ml / min. x mm Hg in norm.

For CO_2 diffusion ability is in 24 times more (CO_2 has the increased solubility).

4. Big general surface of alveoles (approximately 90 m^2).

PHYSIOLOGY OF RESPIRATION

Lecture 2

Theme: Transport of gases by blood. Regulation of respiration

Plan:

1. Transport of gases by blood.
2. Regulation of respiration.

a) Localization and structural organization of respiratory center.

b) Role of gas structure in regulation of respiratory center activity.

c) Role of chemoreceptors in regulation of respiration.

d) Role of mechanoreceptors of lungs in regulation of respiration.

1. Transport of gases by blood

O_2 and O_2 are transferred by blood in two forms:

a) In free (dissolved) form;

b) In bound form;

As a simple physical solution they present in comparatively small volume (O_2 — 0,3%, CO_2 — 3,0%). Actually from blood they can be extracted: O_2 — in 60 times and CO_2 — in 18 times more, i.e. it testifies that the basic form of their transmission is bound.

However, 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 and CO_2 is dissolved for a while before it gets erythrocytes.

O_2 transport. The large part of O_2 is transported by blood as chemical compound with hemoglobin (Hb) — *oxyhemoglobin*. 1g of hemoglobin can bind 1,34–1,36 ml of O_2.

However, the degree of Hb oxygenation first of all depends on partial pressure of O_2 in the medium with which blood contacts. This dependence is expressed by the so-called oxyhemoglobin dissociation curve.

During O_2 absorption in lungs O_2 strain in blood is close to pO_2 conforming in alveoles making 96 mm Hg. At such strain approximately 97% of HbO_2 is formed.

Then even at the decrease of pO_2 in arterial blood up to 60 mm Hg Hb oxygenation is to small and HbO_2 is 90%. It has an important physiological value: with age or at 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 O_2 strains typical for tissues (35 mm Hg and lower). It creates favorable situation for return of O_2 to tissues.

HbO_2 dissociation in tissues depends on intensity of oxidative processes in them: in intensively working tissues and organ dissociation of HbO_2 increases, in less intensively working tissues and organs it decreases. Why? Which factors influence this process?

1. Temperature. The temperature increasing, slope of HbO_2 dissociation curve descends and it shifts to the right, i.e. dissociation of HbO_2 is increased.

2. At pH shift towards its decrease, i.e. increase of H^+ the curve of HbO_2 dissociation shifts to the right, i.e. dissociation is increased.

3. pCO_2 in blood. The higher is pCO_2, the higher is dissociation of HbO_2 (the curve shifts to the right).

These factors reduce affinity of O_2 to Hb.

Changes of the given factors have the important value for tissues provision with oxygen, mainly those functioning more intensively at the moment.

E.g.: in a working muscle t° and CO_2 raise and pH decreases, i.e. factors promoting dissociations of HbO_2 and providing optimal oxygen nutrition of such muscle, appear.

At hypoxia (at decrease of pO_2 in tissues) synthesis of 2,3-diphosphat glycerate which reduces Hb affinity to O_2 raises in erythrocytes. This will result in dissociation and O_2 return to tissues.

The curve of HbF (fetus) dissociation, due to its higher affinity to the oxygen is shifted leftwards as compared with HbA (adults).

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 blood of capillaries. In erythrocytes:

$$CO_2 + H_20 \rightarrow H_2CO_3$$

Process is enlarged in 20.000 times by carbonic anhydrase. This process proceeds only in erythrocytes (there is no carbonic anhydrase in plasma). In capillaries of lungs this enzyme, on the contrary, catalyzes splitting of H_2CO_3.

In erythrocytes part of CO_2 + Hb → Carbohemoglobin

Since in the result of these processes CO_2 stress in erythrocytes does not increase, all new portions of CO_2 diffuse into erythrocytes. At same time, concentration of HCO_3^- ions in erythrocytes increase, part of which goes into 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 — $KHCO_3$. Oxyhemoglobin is stronger acid than carbonic acid, therefore, HbO_2 expels K^+ from bicarbonates and is transported as $KHbO_2$ salt.

In capillars $KHbO_2$ releases O_2 and transforms into KHb. Carbonic acid, as stronger one, expels K^+ from it: $KHBO_2 + H_2CO_3 \rightarrow HHb + O_2 + KHCO_3$

Therefore, transformation of HbO_2 into hemoglobin is accompanied by the increased ability of blood to bind CO_2. In such state CO_2 is transferred to lungs.

In lungs. From carbohemoglobin CO_2 is detached. Oxyhemoglobin is simultaneously formed. It expels K^+ from bicarbonate which results in formation of H_2CO_3 in erythrocytes (carbonic anhydrase).

Ions of HCO_3^- enter into erythrocytes and Cl^- — into plasma where the volume of Na^+ bicarbonate decreases. CO_2 diffuses into alveoli.

Gas exchange in tissues.

	Tissues	tissular liquid	arterial blood
pO_2	0	20–40	100 (96)
pCO_2	60–70	46	36–40

2. Regulation of respiration

a) Localization and structural organization of respiratory center.

Somatic nerve fibers innervate respiratory muscles. Their denervation results in an apnea. Motoneurons of intercostal muscles and stomach are located in thoracic segments of spinal cord. Motoneurons innervating diaphragm are located in III–IV cervical segments. After dissection of spinal cord at the level of superior cervical segments respiratory movements stop. Dissection at the level of inferior cervical segments (below III–IV) — movements of diaphragm continue, those of intercostal muscles stop.

Therefore, centers of brain participate in regulation of respiration.

The dissection between midbrain and medulla does not change respiration at rest. It testifies the location of respiratory center (RS) in medulla and pons varolii. Dissection of brain between medulla and pons varolii does not stop respiration but it differs from normal. It means that major structure of RS are located in medulla. These structures form **bulbar RS** damage of which results in the arrest of respiration.

There are 2 basic group of respiratory neurons:

1. *Inspiratory*.
2. *Expiratory*.

Localization of respiratory neurons. In both halves (left and right) of medulla 2 groups of respiratory neurons are situated: dorsal and ventral respiratory nuclei.

1. *Dorsal respiratory nucleus* contains mainly inspiratory neurons axons of which are directed to diaphragm nuclei of cervical part of spinal cord. Collaterals from them go to ventral respiratory nucleus where they form excitant synapses on expiratory neurons and inhibit their activity.

As for expiratory neurons, their volume in dorsal respiratory nucleus is insignificant. This part, i.e. dorsal respiratory nucleus where mainly inspiratory neurons are located is called **«inspiration center»**.

2. *The ventral respiratory nucleus* contains inspiratory and expiratory neurons. This part is called «expiration center». Expiratory neurons send pulses:

1) to motoneurons of intercostal and abdominal muscles situated in thoracal and lumbar parts of spinal cord;

2) partially to motoneurons of diaphragm.

At same time, respiratory neurons are met both in reticular formation of medulla and in pons varolii.

b) Role of gas structure in regulation of respiratory center activity.

Functional activity of RS is determined by strain of gases and pH in blood. Leading role here is played by partial pressure of CO_2.

In general conditions human organism is supplied with sufficient volume of O_2. Even in conditions when pO_2 in alveolar air can decrease to 60–70 mm Hg significant disorders in the organism do not happen. pCO_2 is maintained at relatively constant level providing functional activity of RS.

Change of gases strain in blood influences the activity of RS, signs of which is the change of:

1. Respiration rate.
2. Depths of respiration.
3. Ventilations of lung.

It can result in:

1) maintenance of normal CO_2 volume in blood (normocapnia);

2) increase of CO_2 (hypercapnia);

3) decrease CO_2 (hypocapnia);

4) normal O_2 volume (normoxia);

5) deficiency of O_2 in tissues (hypoxia);

6) deficiency of O_2 in blood (hypoxemia).

In norm, there is no increased volume O_2 in blood.

Normocapnia is accompanied by the normal respiration (eupnea). Simultaneous hypoxia and hypercapnia cause asphyxia (dyspnea). At hypercapnia or decrease of pH (acidosis) — the ventilation of lungs is increased due to the depth of respiration (basically) and its frequent rate (hyperpnea). Hypocapnia or increase of pH (alkalosis) result in decrease of ventilation of lungs and then to apnea.

The hypoxia is marked at ascend to altitude, blood circulation and structure of blood disorders, hard physical work.

At asphyxia respiration becomes very deep (with participation of auxiliary muscles) with unpleasant sensation of asphyxia. Such state is called dyspnea.

c) Role of chemoreceptors in regulation of respiration.

The strain in arterial blood of O_2, CO_2 and pH depends on ventilation of lungs.

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. In two dogs carotid arteries were cross-connected with jugular vein, vertebral artery being ligated. In the result the head of the first dog was supplied with blood of the second dog, and vice versa. If to pinch trachea in the first dog (to cause asphyxia) hyperpnoea appears in the second dog. In the first dog apnea happens despite the increase of pCO_2 and decrease of pO_2.

Cause: into the carotid artery of the first dog blood came from the second dog in which, in the result of hyperventilation, pCO_2 in blood decreased. This influence is carried out through special chemoreceptors situated:

1. In central structures (bulbar chemoreceptors).
2. In periphery (arterial chemoreceptors).

From these receptors signals about gas structure of blood come to respiratory center.

Role of central chemoreceptors. The central chemoreceptors are located in medulla. Perfusion of medulla portion in the location of the given receptors with solution of lower pH results in rapid intensifying of respiration, and vice versa.

In natural conditions central chemoreceptors are constantly stimulated by H^+. Concentration of H^+ in blood depends on CO_2 strain in arterial blood. Decrease of pH in 0,01 induces increase of lungs ventilation in 4 l/min.

At the same time, central chemoreceptors respond also to changes of pCO_2 but to a lesser degree than to changes of pH. It is presumed that the basic chemical factor influencing central chemoreceptors is H^+ volume in intercellular fluid of brain stem and action of CO_2 is connected with formation of these ions.

Role of arterial chemoceptors. O_2, CO_2 and H^+ can influence the structure of nervous system not only centrally but also by means of excitation of peripheral chemoreceptors.

The most important of them are:

1. Carotid bodies located at division place of the general carotid artery into internal and external;
2. Aortal bodies.

Chemoreceptors of the indicated zones are excited at the increase of pCO_2 and decrease of pO_2 and pH. The influence of O_2 on respiratory center is mediated only by peripheric chemoreceptors.

Thus, neurons of RS are maintained in the state of activity by the pulses coming from central (bulbar) and peripheral (arterial) chemoreceptors reacting to the change of 3 parameters of arterial blood:

1. Decrease of pO_2 (hypoxemia).
2. Increase of pCO_2 (hypercapnia).
3. Decrease of pH (acidosis).

The main stimulant of respiration is the hypercapnia. The higher is pCO_2 (pH is also connected with it), the higher is ventilation of lung.

But especially strong stimulant of the central respiratory mechanism is combined action of hypoxemia and hypercapnia (and acidosis connected with it).

d) Role of mechanoreceptors of lungs in regulation of respiration.

In the change of respiratory phases, i.e. periodic activity of RS the essential role is played with mechanoreceptors (stretch receptors), located in unstriped muscles of walls of trachea, bronchi, bronchioles. For them the various degree of excitability is typical. One of them (approximately 1/2) is *low-threshold*. They are intensively excited at inspiration. Impulsation from them is strengthened at inspiration and reduced at expiration; others are *high-threshold,* they are excited only at inspiration.

At inspiration, in the result of lungs expanding there is an excitation of stretch receptors. Afferent fibers from these receptors go in the structure of n. vagus into dorsal respiratory nucleus of medulla (inspiratory center) and inhibit the activity of inspiratory neurons. Act of inspiration is inhibited.

This reflex provides change of respiratory cycle phases and is called inspiration-inhibit reflex. For the first time it was described by Hering and Breuer and received the name as Hering-Breuer reflex.

Physiologic value of this reflex is in limitation of respiratory movements. Due to this, the conformity of depth and frequency of respiration to the conditions of functioning of an organism at the present moment is reached and receptors interfere overdistension of lungs.

In state of relative rest in the person the role of Hering-Breuer reflex is relatively small. Their value is extremely great at hyperpnea.

Lecture 3

Theme: Regulation of respiration. Features of respiration in different conditions

Plan:

1. Influence of irritant receptors on respiratory center.
2. Participation of proprioreceptors of respiratory muscles in regulation of respiration.
3. Role of pneumotoxic center in regulation of respiration.
4. Value of receptors of upper airways in activations of respiratory center.
5. Role of cerebral cortex in regulation of respiration.
6. Influence of nonspecific factors on respiration.

7. Coordination of respiration and circulation.
8. First inspiration of newborn.
9. Features of respiration in different conditions.

1. Influence of irritant receptors on respiratory center

In the epithelium and subepithelial layer of airways there are receptors which are called irritant. They are especially numerous in the region of roots of lungs.

For them the following properties are typical:

a) as mechanoreceptors;

b) as chemoreceptors.

They are excited at very strong changes (increase or decrease) of lung volume. The excitation threshold in them is higher than in all other receptors. Pulses in afferent fibers of irritant receptors arise in packs only within short period of time during change of the lung volume but part of them is excited also at general inspiration and expiration.

As stimulators of irritant receptors there can be:

- Dust particles.
- Mucus.
- Gases of caustics (tobacco smoke, ammonia, etc.).
- Biologically active substance formed in walls of airways (histamine).
- They can be strongly excited at number of diseases (pulmonary edema, pheumothorax, bronchial asthma, etc.).

Stimulation of irritant receptors results in:

- Cough.
- Unpleasant sensations like burning or scratching.
- Intensifying of inspiratory activity.
- Shortening of expiratory phases.
- Hyperpnoe.
- Reflex bronchoconstriction.

Irritants receptors take part in appearance of an original reflex, so-called «deep sigh» reflex. At rest a person makes deep sigh approximately 3 times per hour. The sigh results from infringement of balanced ventilation of lungs and their compliance. It results in excitation of irritant receptors. «Sigh» is accumulated on one of the next inspirations which results in expanding of lungs and regeneration of their ventilation.

2. Participation of proprioreceptors of respiratory muscles in regulation of respiration

Receptors of respiratory muscles take part in regulation of respiration (proprioreceptors), in particular, stretch receptors — muscular spindles.

In case of heavy breathing (of inspiration or expiration) receptors are excited that results in increased contraction of respiratory muscles (proprioceptive reflex). In the result, the conformity of mechanical parameters of respiration to resistance of respiratory system is reached.

3. Role of pneumotoxic center in regulation of respiration

If to dissect brain stem below pons varolii, breathing does not stop but its rhythm is irregular, there can appear respiration at which the long expiration may be interrupted with short inspirations. This respiration type is called *gasping*.

If, after brain dissection on the border between pneumotoxic center and medulla, to perform vagotomy, apnoea will occur at inspiratory phase. Sometimes such condition is interrupted with expiratory movements. Such breathing is called apneusis. In these conditions braking influences on inspiration are eliminated. It means that pneumotoxic center takes part in change of inspiration-expiration phases.

Pneumotoxic center:

- Raises activity of inspiration standstill mechanism;
- Activates the expiration center;
- Provides smooth transition of inspiration-expiration phases.

Thus, in pons varolii there is a central mechanism promoting change of respiration phases, that is periodic activity of respiratory center.

4. Value of receptors of upper airways in activations of respiratory center

Inspiratory stream of air stimulate receptors of nasal mucous membrane (mainly, cold receptors). Pulses from receptor of nasal mucous membrane go to brain by fibers of trigeminus and influence respiratory center (weak inhibiting).

At irritation of receptors of the upper airways the number of protective reflex appear:

- *Sneezing* — (at stimulation of receptors of nasal mucous membrane). Strong expiration through the nose.
- *Cough* — (at stimulate of receptors of larynx, trachea). Cough starts at inspiration, then closing of vocal cords follows, contraction of expiratory muscles and divergence of vocal cords-cough.

Plunger reflex — action of water on receptors of the inferior nasal ways causes apnea preventing ingress of water into airways.

Respiration is inhibited during swallowing, ingress of caustics (gases of ammonium) into nasal cavity.

5. Role of cerebral cortex in regulation of respiration

Considering mechanisms of regulation of respiration, it is necessary to outline two groups of processes:

1. Maintenance of constant gas structure of arterial blood. It is assured basically by respiratory center (*homeostatic* reaction).

2. Processes adjusting respiration to changing conditions of the environment and vital activity of the organism (*behavioral* regulation).

Respiration changes under different conditions: speech, singing, comprehension, attention, emotions, during sleep, influence of the environment, etc.

In the processes of adaptation of respiration to conditions of existence of organism the special role is played by cerebral cortex.

Changes of respiration differ at excitation of cortex regions. Removal of cerebral cortex results in increase in frequency and ventilation of lungs.

Participation of cerebral cortex in regulation of breathing is proved my the method of conditional reflex (pre-start state of sportsmen), opportunity of voluntary breath-holding and intensifying of respiration.

6. Influence of nonspecific factors on respiration

These are factors which directly do not participate in regulation of respiration but influence ventilation of lungs.

1. Cold and thermal influences on skin result in excitation of respiratory center (in a newborn breathing may be stimulated by contrast baths). Change of body temperature: fever and moderate hypothermia increase ventilation of lungs. Deep hypothermia, on the contrary, suppresses activity of respiratory center.

2. Pain. Ventilation of lungs at first moment of pain influence can lead to apnoea (at inspiration). Then respiration becomes more frequent and deep.

3. Hormones. Adrenalin (at physical activity) — increases ventilation of lungs.

7. Coordination of respiration and blood circulation

Normal exchange of gases in lungs and tissues and its adaptation to needs of an organism are provided by change of not only lung ventilation but blood circulation as well.

1. The reflex influences proceeding from reflexogenic regions (aortal and carotid) are reflected in the work of cardiovascular and respiratory systems.

2. Respiratory arrhythmia of cardiac activity and blood pressure.

3. At physical work and emotional load - increase of minute volume of blood (MVB) and increase of lung ventilation and rising of minute volume of respiration (MVR).

4. At loss of blood the blood pressure is reduced and is accompanied by increase of lung ventilation, etc.

Such coordination is assured by close interaction of neurohumoral mechanisms of regulation of cardiovascular and respiratory systems.

This coordination is carried out at level of cerebral cortex and underlying structures among which the important role is played with hypothalamus.

8. First inspiration of newborn

After umbilical ligation and development of hypoxia there is an inhibition of intra-uterine respiratory movement, and then in 1–1,5 minute there appear first respiratory movement.

During the first inspiration the thorax expands, ribs rise, their heads are fixed in intervertebral fossae and they do not return in initial position.

During the first respiratory movement the negative pressure is developed in thoracic cavity which is in 10–15 times is higher than at subsequent quiet breathing.

Such significant increased negative pressure provides overcoming of elasticity of pulmonary tissue and expanding of lungs. Active inspiration is followed with active expiration.

At subsequent respiratory movement distension of lungs is increased, their elasticity is reduced, the work for respiratory movement is reduced.

After three respiratory movements the 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. Decrease in blood of O_2 increases excitability of respiratory center and its sensitivity to CO_2.

2. Accumulation of CO_2 — irritant capable to activate respiratory center.

3. Metabolic acidosis developing after removal of afterbirth when extraction of acidic products is stopped and alkaline reserves are reduced (decrease of pH).

4. Along with it, stimuli for appearance of respiration are various thermal, mechanical irritants imposing the newborn who gets during birth to completely different environment.

5. Besides, there is an opinion that after transit of fetus through birth canal the constrained thorax, due to its elasticity, sharply extends, significant negative pressure is accumulated in thoracic cavity promoting entry of air into airways.

9. Features of respiration in different conditions

1. *Respiration at muscular work.* At rest the person consumes 250–300 ml of oxygen per 1 min, at fast walking — up to 2,5 l, at hard physical work — up to 4 l in 1 min. Simultaneously, formation of CO_2 and acidic products increase.

Ventilation of lungs increases proportionally to energy expenses (can reach 120–150 l in 1 min).

The beginning of work is accompanied by rising of pCO_2 and decrease of pH of blood. Ventilation of lungs is increased when gas structure of blood is not changed yet. It means, in the beginning of work hyperpnea is induced by nervous factors. Cerebral cortex, producing voluntary movements, activates respiratory center directly through hypothalamus also. Besides, the essential role in the given process is played by pulses from proprioreceptors (mechanoreceptors) of contracting muscles.

Then during work there is slow increase of ventilation of lungs up to establishment of steady state.

Lactic acid formed in the beginning of work cannot be oxidized completely up to H_2O and CO_2. It is accumulated in muscles and comes into blood. This is an oxygen debt. Respiration strengthens and there comes state when respiration and blood circulation achieve the certain level when the short-breathing stops (dead point in a sportsman). Then hyperpnoea leads to removal of excess of CO_2 and rising of pH-balance between arrival and consumption of O_2 (second wind in sportsmen) is established.

In this phase chemoreceptors are initiated. Ascending of CO_2 formation at risen ventilation of lungs provides CO_2 volume in blood unchangeable.

Irritation of chemoreceptors is strengthened by the action of the lactic acid lowering pH of blood. Rise of body temperature is also significant since it enlarges respiration rate through hypothalamus.

After end of work ventilation of lungs is reduced but not to initial level. It remains increased for some minutes under influence of lactic acid and other suboxides.

There is gradual «repayment» of the oxygen debt.

Along with rising of ventilation of lungs at physical work there increase:

1) heart rate (from 70 up to 150–200 in 1 minute);

2) systolic volume (from 70 ml up to 200 ml);

3) minute volume of blood (from 4–5 l to 20–30 l);

4) blood flow in working muscles;

5) oxygen capacity of blood due to release of depot blood. Besides, water loss at work in the result of sweat results in clotting and rising of erythrocytes and Hb concentration.

6) dissociation of HHbO2 (decrease of pH, rising of pCO2, temperature).

7) O_2 usage coefficient (O_2 utilization coefficient) from 30–40% to 50–60%.

2. *Respiration at the lowered atmospheric pressure* (climbers, depressurization cabins of the pilot, parachutists, artificial pressure chamber). The consequence is *the hypoxia* as result of decrease of pO_2.

At rise to altitude from 2 km there is risen ventilation of lungs (stimulation of carotid and aortal chemoreceptors).

Rising of blood pressure, rise of heart rate is directed to intensified supply of tissues with O_2.

But increased ventilation of lungs has also a negative value — it can decrease pCO_2 (hypocapnia) thus limiting ventilation of lungs.

At the altitude of 4–5 km mountain disease is developed. To signs of mountain disease they relate drowse, decrease of appetite, apathy or euphoria, short-breathing, tachycardia, giddiness, vomiting, headache. Slowly developing hypoxia is especially dangerous because of possible loss of consciousness before appearance of signs serving as signals of danger.

At the altitude of 7 km there can occur loss of consciousness and breathlessness and violation of blood circulation dangerous for life. In the result of hypoxia there are no unpleasant sensations, there is no sense of alarm and danger and loss of consciousness can come suddenly.

At high altitudes life is possible provided that oxygen devices are used or in pressurized cabins, space suits in which high atmospheric pressure is maintained.

Long stay in conditions of low atmospheric pressure is accompanied with acclimatization. With this:

1. Amount of erythrocytes in blood (erythrogenesis strengthens) is increased.

2. Amount of Hb is increased that results in augmentation of oxygen capacity of blood.

3. Ventilation of lungs increases.

4. Dissociation of $HHbO_2$ increases (due to augmentation in erythrocytes of 2,3-glycerophosphate).

5. The length and tortuosity of capillars increases.

6. Resistance of cells (especially nervous) to hypoxia increases.

A person can hold up breathing for 1–2 minutes. After prior hyperventilation a trained person can not breath for 3–4 minutes. This is his limit of stay under water. But the danger is that rapid decrease of blood oxygenation can result in loss of consciousness, in this condition under influence of the increased pCO_2 of blood the breath will occur, and the diver will be breathless with water.

All variety of effects of hypoxia can be divided into 4 zones separated from each by effective thresholds:

1. Neutral zone (up to 2000 m) — physiological functions practically do not suffer.

2. Zone of complete compensation (2000–4000 m). Even at rest heart rate, systolic volume, MVB and MVR increase. Physical and mental work capacity is reduced a bit.

3. Zone of incomplete compensation or zone of danger (4000–7000 m). The threshold of safety (4000 m) is reached. Muscular twitchings appear, blood pressure decreases, consciousness is fogged. Work capacity is reduced, ability to decision-making and reactions is affected.

4. Critical zone (>7000 m) pO_2 in alveolar air becomes lower than critical threshold (30–35 mm Hg). Loss of consciousness, cramps. This is reversible if not long. If long — CNS affection and death.

7–8 km — dangerous for most of the people.

8,5–9 km — limit above which a man can not ascend without inspiration of O_2.

9–12 km — with application of the oxygen device.

12 km — space suits in which high pressure is maintained.

3. *Respiration at the increased atmospheric pressure* (works under water (divers)). At diving for each 10 m pressure upon body of the person is increased in 1 atm. At depth of 100 m person should inhale gas mixture under pressure exceeding atmospheric in 10 times. Therefore, oxygen in gas mixture is added in the amount so that its pO_2 at depth was close to that in usual conditions.

At depth under influence of pressure gases are solved in blood. At fast decompression gases pass from the dissolved state into gas state, vesicles are formed that results in gas embolism (caisson disease). Symptoms: pains in muscles, giddiness, vomiting, short-breathing, loss of consciousness. In these cases it is necessary to place the person quickly into compression chamber, to create the pressure in it conforming the pressure at depth from which the person has been lifted that again will lead to solution of air vesicles in blood, and then gradually to decrease pressure (decompression). Transition of gases from dissolved state in gas-like will happen slowly and vesicles will be removed from the organism without causing gas embolism menace.

PHYSIOLOGY OF DIGESTION

Lecture 1

Theme: Digestion in oral cavity and stomach

Plan:

1. Physiological bases of hunger and satiation.
2. Digestion in oral cavity.
   a) Salivation.
   b) Structure and properties of saliva.
   c) Regulation of salivation.
3. Digestion in stomach.
   a) Secretory activity of stomach.
   b) Structure and properties of gastric juice.

Human organism during vital activity spends various materials and great deal of energy. Substances recovering plastic and energy demands of an organism should come from an outer .environment. Obviously insufficient supply with nutrients affects homeostasis and is incompatible with life. At the same time human organism is not capable to assimilate proteins, fats, carbohydrates and number of other substances from food without pretreatment. This major function in an organism is carried out by digestive system.

Digestion is the physical and chemical processing of food.

1. Physiological bases of hunger and satiation

Hunger as physiological state (as opposite to starvation as pathological process) is an expression of needs of the organism in nutrients which it has been deprived for some time that resulted in decrease of the amount of these substances in depot and circulating blood.

Subjective manifestation of hunger are unpleasant sensations: «burning sensations», sinking sensation in the pit of the stomach, nausea, sometimes-giddiness, a headache, sense of general weakness.

External objective manifestation of hunger is the behavioral reaction of search for food directed to elimination of the reason caused hunger.

Subjective and objective manifestations of hunger are caused by excitation of neurons of various departments and levels of CNS. Academician I.P. Pavlov named the whole of these neurons the food center. Its functions are formation of food behavior directed to search and intake of food, and also regulation and functional integration of organs of digestive system.

Food center is a compound hypothalamolimbic-reticulocortical complex. The leading part which activates all food center are lateral nuclei of hypothalamus. At destruction of this nucleus there appears denial of food (aphagia), their stimulation leads to strengthened consumption of food (hyperphagia). The specified part of food center is the center of hunger.

Destruction of ventromedial nuclei of hypothalamus leads to hyperphagia and their stimulation — to aphagia. This part of food center is the center of satiation.

Hypothalamic nuclei of the food center are excited or inhibited depending on structure of blood and also entering of various signals from various peripheral receptors.

Theories of originating of sense of hunger:

- Glucostatic theory according to which the sensation of hunger is connected with the decrease of glucose volume in blood.
- Aminoacidostatic theory according to which excitability of neurons of food center is determined by the amino acids volume in blood.
- Lipostatic theory considers that the irritant of hypothalamic nuclei is insufficiency of metabolites formed at mobilization of fat.
- Thermostatic theory assumes suppression of food center due to rise in temperature of blood washing it which happens during eating.
- Hydrostatic theory binds sense of hunger with water resources of the organism: decrease of water deposit in organism reduces consumption of food.
- Metabolic theory unites all mentioned.

Eating produces state of satiation opposite to hunger. It precedes coming of nutrients digestion products into blood. Such satiation is called sensory (initial) satiation. It consists in inhibition of food center and has the complex reflex nature. The sensory satiation is replaced with metabolic (secondary, or true) satiation whose basic mechanism is coming of nutrients digestion products into blood.

However, for nutrients to come into blood to be utilized by the organism, food should pass through the complex mechanical and chemical process in gastrointestinal tract.

2. Digestion in oral cavity

Processing of food begins in the oral cavity. Here happens its grinding, wetting by saliva, analysis of gustatory properties, initial hydrolysis of some nutrients and formation of food lump. Average duration of stay of food in the oral cavity is 15–18 sec.

In the mouth food stimulates gustatory, tactile and temperature receptors. Signals from these receptors by centripetal nerve fibers of trigeminal, facial and glossopharyngeal nerves reach nerve centers of several reflexes. Centrifugal impulses from these centers excite secretion of salivary, stomach and pancreas glands, release of a bile into duodenum, change motor activity of stomach. Thus, despite short stay of food in the mouth, this part of digestive tract influences all stages of processing of food.

a) Salivation

At initial stage of digestion the role of saliva is great. It is produced by three pairs of large salivary gland: admaxillary, submandibular, sublingual gland and the number of smaller glands on surface of the tongue, in mucous membrane of

palate and cheeks. From glands by excretory ducts saliva comes into the oral cavity. Depending on the produced secret salivary glands are of three types: *serous* (produce fluid secret without mucus-mucin); *mixed* (produce serous-mucous secret) and *mucous* (produce saliva rich in mucin). Outside of food reception in person saliva is secreted on the average 0,24 ml / min for humidification of the oral cavity, at mastication — 3–3,5 ml / min (about 200 ml / h) depending on the kind of food. Responding to coming of citric acid salivation can reach 7,4 ml / minute. In a day 0,5–2,0 l of saliva is produced.

b) Structure and properties of saliva

Saliva is viscous fluid with density 1,001–1,017. The structure of saliva depends on the rate of its secretion, pH of mixed saliva is 5,8–7,4.

The mixed saliva contains 99,4–99,5% of water, the rest is dry residual. Inorganic components of saliva: chlorides and carbonates, phosphates and other salts of sodium, potassium, calcium, magnesium, etc.

The saliva contains organic substances which are in 2–3 times more than mineral salts. Organic substances are products of secretory activity of salivary gland. In structure of saliva there are various proteins, free amino acids, some carbohydrates, ammonia, creatinine and other substances. Saliva contains mucin which gives viscosity to it. Due to presence of mucin, saliva-saturated food lump is easily swallowed.

The saliva is rich enough in enzymes though the amount of some of them is insignificant. The human saliva has an ability of active hydrolysis of carbohydrates. It is carried out by *alpha-amylase* splitting polysaccharides (starches, glycogen) with formation of dextrines and then disaccharide (maltose) and partially glucose.

Amylase of salivas starts its activity in the oral cavity but it is insignificant due to short-period stay of food here. The hydrolysis of carbohydrates with enzymes of saliva continues in stomach till acidic gastric juice gets into deep layers of food contents. Gastric juice transforms action of carbohydrases and inactivates enzymes of saliva. The saliva contains the number of other enzymes: *proteinases* (cathepsines, salivain, glandulain), *lipases,* alkaline and acidic *phosphatases.* They take part in digestion but their activity is insignificant. The saliva has bactericidal property due to the enzyme *of lysozyme* presence in it. Saliva contains callecrein which dilates blood vessels and increases blood supply of salivary gland.

Physiological role of saliva:

1. Moistens and dilutes food;
2. Promotes gustatory approbation of food;
3. Enzymes of saliva provide hydrolysis of carbohydrates;
4. Protects mucous membrane;
5. Due to mucin food lump is formed;
6. The lysozyme carries out bacteriostatic action (factor of nonspecific protection);
7. The saliva neutralizes partially acidic products getting into oral cavity;

8. Contact of proteins with saliva provides their best digestion;

9. The saliva contains biologically active substances — callecrein, parotin.

Enzymic structure and properties of saliva change with age of a person, depend on diet and kind of food. The dryer is food, the more viscous is saliva. Acids, bitter taste demand significant amount of more fluid saliva. The amount and structure of saliva due to reception of food are defined by regulation influence on salivary glands.

c) Regulation of salivation

Reception of food stimulates salivation. The salivation proceeds all period of eating and stops once it's finished.

From receptors of the oral cavity signals are sent to CNS by afferent fibers of trigeminal, facial, glossopharyngeal and vagus nerves. The basic salivation center is situated in medulla. Here, and also into lateral horns of superior thoracal segments of spinal cord signals come from the oral cavity. From here influences by efferent parasympathetic and sympathetic nerve fibers go to salivary glands.

Parasympathetic innervation of salivary gland begins from nuclei of medulla. Under the influence of parasympathetic nerve big amount of fluid saliva is excreted. The sympathetic innervation of salivary gland is carried out from lateral horns of II–IV thoracal segments of spinal cord. Under its influence small amount of viscous saliva is excreted.

The salivation *begins by the type of conditioned reflexes* — in respond to the kind and smell of food.

Reflex influences can also inhibit salivation, to the moment of its termination. Such inhibition can be caused by pain stimulation, negative emotions, mental stress, dehydration of the organism. All these influences reduce activity of food center and its part — center of salivation. Inducers of the latter can be some humoral substances. For example, excessive salivation is observed at asphyxia due to irritation of salivation center by carbonic acid.

3. Digestion in stomach

The stomach performs the number of digestive and not digestive functions.

Not digestive functions of the stomach:

1. Participates in regulation of processes of erythrogenesis (Castle's intrinsic factor).
2. Participates in metabolism.
3. Carries out excretory function.
4. Carries out endocrine function (there is number of endocrine cells which form peptides of digestive system).
5. Protective (excreted HCl is unfavorable medium for microorganisms).

Digestive functions:

1. Deposition of food.
2. Mixing of food (machining).
3. Food is exposed to chemical (enzymatic) processing.

4. Portion evacuation into duodenum.

5. Adsorption of hydrolysates.

Enzymes of acidic gastric juice influence food proteins in relatively narrow zone of food contents which is in direct contact with mucous membrane of the stomach and in small distance from it where gastric juice has diffused and was not neutralized due to buffer properties of food. All mass of food in the stomach is not mixed with juice. As food is fluidified and chemically processed, its layer adjacent to mucous membrane, by motions of the stomach is moved to its antral part and further evacuated into intestine.

a) Secretory activity of stomach

The gastric juice is produced by gastric glands located in mucous membrane. In the region of fornix of the stomach glands contain main *glandulocytes (main cells)* producing pepsinogens; *parietal glandulocytes (coating cells)* which synthesize and excrete hydrochloric acid and *mucocytes (additional cells),* excreting mucoid secret. In pyloric parts of the stomach there is no parietal glandulocytes. Due to difference in the structure of fundus and pyloric glands they produce juice of different structure. The leading role in gastric digestion is played by fundus gastric juice.

In the human stomach it is excreted 2,0–2,5 l of gastric juice a day. It represents pellucid fluid containing hydrochloric acid (0,3–0,5%) and therefore has acidic reaction (pH 1,5–1,8). pH of the stomach chymus is much higher as juice of fundus glands is partially neutralized by the accepted food. The faster the gastric juice is excreted, the lesser it is neutralized and the higher its acidity is.

HCl carries out following functions:

1. Activation of pepsinogen into pepsin.

2. Denaturation and swelling of proteins (promotes hydrolysis of proteins).

3. Antibacterial.

4. Decalcification of bones.

5. Enhances gastric motor activity.

6. Stimulates formation of hormones (HCl comes into duodenum, produces hormone of secretin and pancreozymin. These hormones are absorbed into blood, approach pancreas and stimulate it).

7. Evacuation of chymus (performing of obturator pyloric reflex).

b) Structure and properties of gastric juice

In gastric juice there are many inorganic substances: chlorides, sulphates, bicarbonate of natrium, potassium, calcium and magnesium, ammonia. The osmotic pressure of gastric juice is higher than that of blood plasma.

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

Main *glandulocytes* of stomachal glands of person synthesize and excrete **pepsinogens of two groups.** Pepsinogens of the first group (5 of them) are formed in fornix of stomach, the second bunch (2 of them) — in pyloric part of the stomach and at initial part of the duodenum. Actually, pepsins are considered to be enzymes hydrolyzing proteins with maximal rate at pH 1,5–2,0. Their other fraction hydrolyzes proteins at optimum pH 3,2–3,5 and is called *gastricsin.* Pepsin and gastricsin impse different kinds of proteins. Pepsins posses the expressed property to coagulate milk. The ability of pepsins in wide range of pH is of great importance in stomachal proteolysis which occurs at different pH depending on the volume and acidity of gastric juice, buffer properties and amount of accepted food. Proteases of gastric juice split proteins up to large polypeptides. Proteins subject to preliminary action of stomachal proteases and formed at it fragments of protein molecules are then more easily split by proteases of juice of pancreas and small intestine.

The gastric juice of an adult person has small *lipolytic* activity. This lipolytic activity has important value for a child in period of its breast feeding (splitting of emulsificated fat of milk).

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

Glands of pyloric parts of stomach excrete small amount of juice of alkalescent reaction with big content of mucus. The secret of pyloric glands has small proteolytic, lipolytic and amylolytic activity. Alkaline pyloric secret partially neutralizes acidic contents of stomach evacuated from the stomach into the duodenum.

Lecture 2

Theme: Regulation of stomachal secretion. Digestion in small intestine.

Plan:

1. Regulation of stomachal secretion.
2. Phases of stomachal secretion.
3. Motor function of the stomach. Transition of food from stomach into intestine.
4. Vomiting.
5. Digestion in small intestine.
6. Secretory activity of pancreas. Structure and properties of pancreatic juice.
7. Regulation of pancreatic secretion.
8. Bile, its structure and participation in digestion.

1. Regulation of stomachal secretion

Outside digestion glands of human stomach secrete small amount of gastric juice. Reception of food sharply enlarges its secretion by glands of the body of stomach (but not pyloric) as the result of stimulation of stomachal glands by nervous and humoral mechanisms.

The main and parietal *glandulocytes, mucocytes* of stomach glands are stimulated by secretory fibers included into the structure of *vagus nerve*. Terminals of these fibers secrete acetylcholin which stimulates stomachal glands. Dissection of vagus nerves results in decrease fo stomachal secretion (this operation is sometimes performed in order to normalize secretion at its augmentation). *Sympathetic nerves* render inhibiting influence on glands of stomach reducing volume of secretion. However, at combination of sympathetic influences with other factors stimulating glands of stomach, juice with high amount of pepsin is secreted since sympathetic fibers in main glandulocytes strengthen synthesis of pepsinogen.

Potent stimulator of stomachal glands is gastrin. It is liberated from G-cells the main amount of which is in mucous membrane of pyloric parts of stomach. Liberation of gastrin is strengthened by the influence of vagus nerve and also by local mechanical and chemical irritants of this part of stomach. If pH in pyloric part of the stomach goes down (at rising secretion of hydrochloric acid by glands of stomach), release of gastrin decreases and at pH 1,0 it stops. Thus, gastrin takes part in self-regulation of stomachal secretion depending on the size of pH contents of pyloric parts of stomach.

Stimulators of stomachal glands is histamine formed in mucous membrane of the stomach. It stimulates secretion of large amount of highly acidic juice.

The secretin and cholecystokinin-pancreozymin inhibit secretion of hydrochloric acid stimulated by gastrin (less by histamine) but strengthen a little secretion of pepsins.

Inhibition of secretion of hydrochloric acid in the stomach produce others intestinal hormones *(neurotensin, somatostatin, serotonin)*. The acidity of duodenal contents is of reflex nature and through duodenal hormones inhibit searection of hydrochloric acid by glands of the stomach (self-regulation).

The secretion of gastric juice can be divided into three phases.

2. Phases of stomachal secretion

The initial secretion of gastric juice is connected with reception of food. Excitation come to glands as conditioned reflexes in response to irritation of distant receptors of the eye, ear and nose stimulated by the view and an smell of food, sounds of the whole surroundings related to food reception. They are joined with unconditioned reflexes arising at irritation of receptors of oral cavity and gullet. Nervous influences carry out starting effects. This stomachal secretion is called **the first,** or **«cerebral» phase of secretion.**

The proof of presence of the first phase of secretion of stomach is experience of the so-called imaginary feeding of esophagotomy dogs with fistula of stomach. At feeding of such dog food drops out of the esophagus and does not get into the stomach, however, in 5–10 min after beginning of imaginary feeding secretion of gastric juice begins.

Juice produced in the stomach at smell and view of food, chewing and swallowing was called «appetizing» by the Academician I.P.Pavlov. Owing to its secretion stomach is prepared to reception of food.

Conditioned-reflectory secretion of gastric juice is induced by the view of food, sounds accompanying eating (sounds of plates and forks), etc. Reflex influences on stomachal glands are transferred through vagus nerves.

The secretion into «cerebral» phase is easily inhibited at influence of external (bad table layout, unpleasant smell) and internal factors.

The first phase of secretion is overlaid by **the second phase** called **stomachal** as it is produced by the action of digestive contents on mucous membrane of the stomach. Presence of given phase of secretion is proved that insertion of food into stomach through fistula, introduction through it or probe of some solutions into stomach, and, finally, irritention of mechanoreceptors of stomach produce secretion of gastric juice. The volume of secret thus is in 2–3 times less than at natural reception of food. Intensifying of stomachal secretion in the second phase is produced by reflexes arising at action of stomachal contents on receptors of stomach and also by neurohumoral way.

Some kinds of food (meat bouillon, cabbage juice, hydrolysates of proteins) when administered into small intestine, produce secretion of gastric juice. Afferent influences from the intestine on glands of stomach stimulate their secretion in **the third phase** called **intestinal.** Stimulating and inhibiting influences from duodenal and jejunum on glands of stomach are carried out by nervous and humoral mechanisms. Nervous influences are transferred with mechano- and chemoreceptors of the intestine which is the result of coming into intestine of insufficiently digested contents of the stomach.

3. Motor function of the stomach

Contractions of unstriped muscles of wall of stomach carry out motor function of stomach. It provides *deposition* of accepted food in stomach by *mixing* it with gastric juice, *transporting of stomachal contents* exit to the intestine and, finally, *portion evacuation* of stomachal contents into duodenum.

During reception of food and soon after it the stomach is relaxed — *digestive receptive relaxation*. After a while, in dependence on the kind of accepted food, contractions increase.

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

The influences going by sympathetic nerves reduce rhythm and force of contractions and also rate of peristaltic wave.

Gastrointestinal hormones have big importance in regulation of gastric motor activity. Motility of stomach is forced by gastrin, motilin, serotonin and insulin. Inhibition of gastric motor activity is caused by secretin, cholecystokinin-pancreozymin.

Transition of food from stomach into intestine. Time of stay of mixed food in the stomach of an adult person compounds 6–10 hours. Food rich in carbohydrates stays in stomach less than that rich in proteins. Fatty food is evacuated from the stomach with the smallest rate. Fluids start to pass into intestine immediately after their entering in the stomach.

4. Vomiting

Vomiting — complex-reflex motor act beginning from contraction of small intestine. As the result of these contractions part of contents of intestine is pushed out into stomach. In 10–20 with there is a contraction of the stomach, entrance into stomach is opened, muscles of an abdominal wall and diaphragm are strongly contracted owing to which contents of stomach at the moment of expiration is expelled through the esophagus into the oral cavity.

The vomiting has protective value and *arises reflexly* as result of irritation of receptors of root of tongue, pharynx, mucous membrane of the stomach, intestine, vestibular apparatus (when travel-sickness or sea-sickness). Vomiting may be caused by olfactory and gustatory irritations producing sense of disgust (conditioned reflex vomiting). Vomiting is caused by some substances (for example, alkaloid apomorphin) which react *through blood to nerve center of vomiting* situated in medulla.

5. Digestion in small intestine

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

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

6. Secretory activity of pancreas. Structure and properties of pancreatic juice

The human pancreas secretes 1,5–2,0 l juice a day. This juice is a product of activity of excretory pancreacytes. It represents colorless pellucid fluid, its pH is 7,8–8,4. The alkalinity of juice is caused by the presence of sodium hydrogens. Juice contains also chlorides of sodium and potassium. Pancreatic juice is rich in enzymes which digest proteins, fats and carbohydrates. *Amylase, lipase* and *nuclease* are secreted by pancreas in active state and proteases are formed by zymogen-like cells which are activated by the action of other enzymes.

Trypsinogen of pancreatic juice in the duodenum, under action of its enzyme *enterokinase* turns into *trypsin.* Process is accelerated by ions Ca^{2+}.

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

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

7. Regulation of pancreatic secretion

Secretion of pancreas is regulated by nervous and humoral mechanisms.

The initial secretion of pancreas is produced by the view, smell of food and others irritants *(conditioned stimulus)* and also chewing and swallowing *(unconditioned stimulus)*. Nervous signals formed in receptors of oral cavity and pharynx, reach medulla and then efferent influences by fibers of vagus nerve come to the gland and produce its secretion.

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

Inhibition of pancreatic secretion is observed at pain reactions, during sleep, at intense physical and brainwork.

In stimulation of pancreatic secretion the humoral regulation has the leading value.

In I.P.Pavlov's laboratory it was discovered that introduction of hydrochloric acid into the duodenum produces excessive secretion of pancreatic juice. Under the influence of hydrochloric acid in the duodenum a substance is formed which is called hormon *secretin.*

Secretin produces secretion of big amount of pancreatic juice, rich in bicarbonates but poor with enzymes.

The second hormone intensifying secretion of pancreas is *the cholecystokinin-pancreozymin* which stimulates secretion of pancreas and release of bile into duodenum.

Nervous influences at reception of food provide *only starting influences on gland,* in the correction of pancreatic secretion the big role is played by the humoral mechanisms. The action of hormons on gland is more expressed at its unaffected innervation.

Phases of pancreatic secretion at its stimulation by food reception are similar to those for stomachal secretion, however, hormonal influences on pancreas, especially at intestinal phase are more expressed.

8. Bile, its structure and participation in digestion

Bile is the product of liver activity. Its participation in digestion is diverse. The arrest of entering of bile into intestine (at obstruction of the general cholic duct) essentially variates the process of digestion and results in severe affection of metabolism in the organism.

Functions of bile:

1. Emulsification of fats promoting their hydrolysis.
2. Strengthens action of lipolytic and amylolytic enzymes.
3. Strengthens motility of intestine.
4. Participates in neutralization of acidic products which have come from the stomach.

5. Promotes adsorption of fatty acids, liposoluble vitamins, cholesterin, amino acids and salts of calcium.

6. Inhibits decay process in the intestine

7. Protective function (has bacteriostatic action)

8. Stimulates biligenesis (the more of biliary acids, the less of biligenesis)

In human about 500–1500 ml of bile a day is produced. The process of biligenesis goes continuously, entering of bile into the duodenum — *biliary excretion* — periodically, basically in connection with reception of food. On an empty stomach bile almost does not come into intestine, it goes to the gall-bladder where it concentrates and variates is the structure a little. Therefore, there are two kinds of bile - hepatic and vesical.

Bile contains proteins, amino acids, vitamins and other substances. Bile has small catalytic activity; pH of hepatic bile is 7,3–8,0.

In human liver *cholic* and *chenodeoxycholic acids* (initial) are formed which in the intestine under influence of enzymes are be transformed into some secondary cholic acids. The basic amount of cholic acids and their salts is contained in the bile as compounds with glycocol and taurine. In person glycochilic acids are about 80%. Cholic acids and their salts determine the basic properties of bile as of alimentary secret.

From small intestine about 85–90% of cholic acids are soaked up into blood excreted into intestine within structure of bile. The cholic acids soaked up into blood are brought to the liver and included into structure of bile. Other 10–15% of cholic acids are deduced from the organism basically in structure of excrements. This loss of cholic acids is supplied with their synthesis in liver.

Cholic pigments are liver-excreted finite products of hemoglobin disintegration and of other derivative porphyrins. The basic cholic pigment — *bilirubin* is of red-yellow color assigning typical color to hepatic bile. The other pigment - *biliverdin* — in the bile of a person is contained in insignificant amounts (it is of green color).

Cholesterin in bile is in dissolved state, mainly due to salts of cholic acids.

Biligenesis happens by means of active secretion of its components (cholic acids) by hepatocytes, active and passive transport of some substances from blood (water, glucose, creatinine, electrolytes, vitamins, hormones, etc.) and readsorption of water and of some substances from cholic capillars, ducts and gall-bladder. Biligenesis is strengthened by eating and various kinds of food.

Bile itself relates to the number of humoral stimulators of biligenesis. The more of cholic acids comes from small intestine into blood of portal vein, the more of them it is deduced in the structure of bile and the less of cholic acids is synthesized by hepatocytes. If less cholic acids enter blood, their deficiency is refilled by intensifying of synthesis of cholic acids in liver. Secretin increases biliary secretion; biligenesis is weaker stimulated by glucagon, gastrin and cholecystokinin — pancreozymin.

The stimulation of vagus nerves, introduction of cholic acids and high contents appropriate proteins in food strengthen not only biligenesis but also excretion of organic components with it.

PHYSIOLOGY OF DIGESTION

Lecture 3

Theme: Digestion in large intestine

Plan:

1. Intestinal secretion.
2. Motor activity of small intestine.
3. Digestion in large intestine.
   a) The value of microflora of large intestine.
   b) Motor activity of large intestine.
4. Adsorption.

1. Intestinal secretion

Intestinal juice represents turbid, viscous enough fluid. It is the product of activity of all mucous membrane of small intestine. Intestinal glands are situated in mucous membrane of the duodenum and all small intestine.

In mucous membrane of superior part of the duodenum there is a big number of duodenal glands. By structure and function they are similar to glands of pyloric part of the stomach. Juice of duodenal glands is stiff colorless fluid of alkalescent reaction, has small proteolytic, amylolytic and lipolytic activity.

At centrifugation of intestinal juice it is divided into fluid and dense parts. Fluid part of juice is formed by aqueous solutions of inorganic and organic substances transported from blood, and by partially destroyed cells of intestinal epithelium. Among inorganic substances there are chlorides, bicarbonates and phosphates of sodium, potassium, calcium; pH of secret is 7,2–7,5. Organic substances of fluid part of juice include mucus, proteins, amino acids, urea and other metabolic products of organism. The dense part of juice — yellow-grey mass, looks like mucous lumps, consists of non-destructed epithelial cells, their fragments and mucus, or secret of goblet cells. In mucous membrane of small intestine there is continuous change of layer of cells of superficial epithelium.

The dense part of juice has much greater catalytic activity than fluid. The basic part of enzymes is synthesized in mucous membrane of intestine but some of them are transported from blood. *In intestinal juice there are more than 20 various enzymes* participating in digestion. The basic among them are: *enterokinase,* some *peptidases, alkaline phosphatase, nuclease, lipase, amilaza, lactase, saccharase.* In natural conditions they are fixed in region of brush border and carry out parietal digestion. The secretion of intestinal glands is intensified while eating, at local mechanical and chemical irritation of intestine and under influence of some intestinal hormons.

The leading value belongs to local mechanisms. The mechanical irritation of mucous membrane of small intestine sharply enlarges excretion of fluid part of juice. Chemical stimulators of small intestine are products of digestion of protein, fats, pancreatic juice, hydrochloric acid (and other acids). Products of digestion of nutrients at their local action produce excretion intestinal juice, rich in enzymes.

2. Motor activity of small intestine

Motor activity of small intestine provides *mixing of alimentary contents with* alimentary secrets, *passing of chyme* in intestine, change of layer of chyme and its mucous membrane, *rising of intraintestinal pressure* promoting filtration of some components of chyme from cavity of intestine into blood and lymph.

Contraction of small intestine occurs in the result of coordinated movements of longitudinal (external) and transversal (circulatory, i.e. internal) layers of unstriped muscles. By functional principle, all contractions are divided into two groups:

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

2) directed to removal of contents of intestine.

There are some types of contractions:

1. Rhythmic segmentation.

2. Pendulum.

3. Peristaltic (very slow, slow, fast, prompt*).*

4. Tonic.

5. Antiperistaltic (in norm are not observed).

Rhythmic segmentation is provided mainly by contraction of circulatory layer of muscles. Intestinal contents is separated into parts. The following contraction forms new segment of intestine which contains of parts of former segment. This causes chyme mixing.

Pendulum contraction are provided with contraction of longitudinal layer of muscles with participation of circulatory. These contraction induce back-and-forth movement of chyme and weak forward movement.

Peristalsis is that above chyme due to contraction of circular *layer* of muscles an intercepting is formed; below the chyme in the result of contraction of longitudinal muscles-dilating of intestinal cavity is formed. These intercepting and dilations move along the intestine and move the chyme portion before intercepting. Along the intestine several peristaltic waves move simultaneously.

Tonic contractions can have very small rate and sometimes are not be distributed at all, considerably narrowing intestinal lumen at big distance.

At antiperistaltic contraction the wave goes in inverse (oral) direction. In norm small intestine does not contract *antiperistaltically* (e.g. at vomiting).

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

Parasympathetic nerve fibrils mainly provoke, and sympathetic — inhibit contraction of small intestine. These fibers are conductors of reflex regulation of motility of small intestine. Food intake conditionally and unconditionally-reflextory first inhibits for a while, then strengthen motility.

The important role of cerebral cortex and of the second signaling system in the regulation of intestinal motility is proved that at talking or even thinking of delicious food the motility *of intestine* strengthens, at the negative attitude to food the motility is inhibited. At anger, fear and pain it is also inhibited. Some-

times at some strong emotions, for example fear, the rough peristalsis of intestine («nervous diarrhea») is observed.

Motor activity of intestine depends on physical and chemical properties of chyme. Rough food and fats raise its activity (black bread, vegetables, etc.).

3. Digestion in large intestine

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

Outside digestion the ileocecal sphincter is closed. In 1–4 mines after food intake everyone half minutes the valve opens and chyme in small portions (up to 0,015 l) passes from the small intestine into the blind gut. The valve opens reflextory. The peristaltic wave of the small intestine raising pressure in it, opens the valve. The increase of pressure in the large intestine raises tone of muscles of ileocecal sphincter and inhibits entering of small intestine contents into large intestine. During digestion the large intestine plays small role as food almost completely is digested and soaked up in the small intestine, except for some substances, for example vegetal tissue. A small amount of food and digestive juices is exposed to hydrolysis in the large intestine under influence of enzymes which have come from the small intestine, and also juice of the large intestine.

Juice of large intestine is secreted outside of its mechanical irritation in very small amount. It contains fluid and dense parts, the juice has alkali reaction (pH 8,5–9,0). The dense part looks like mucous lumps and consists of rejected epithelial cells and mucus which is produced by goblet cells.

The basic amount of enzymes is contained in dense part of juice. Enterokinase and saccharase in juice of large intestine are absent. Concentration of the alkaline phosphatase is in 15–20 times smaller than in small intestine. In small amount there are cathepsine, peptidases, lipase, amylase and nucleases.

Juice-excretion in large intestine is caused by local mechanisms. At mechanical irritation secretion is enlarged in 8–10 times.

In human, about 400 g of chyme comes from small intestine into the large intestine a day. In its proximal part there is digestion of some substances. In large intestine there is intense adsorption of water which to a greater extent is provided by the motility of large intestine. The chyme gradually turns into excrements, 150–250 g of which is produced daily excreted. With vegetative food they are more in number than with mixed or meat food.

a) The value of microflora of large intestine

The bacterial flora of gastrointestinal path is a necessary condition of normal existence of the organism. The amount of microorganisms in stomach is minimal, in small intestine they are much more in number (especially in its distal portion). The amount of microorganisms in large intestine is rather high — up to tens billions per 1 kg of contents.

90% of all flora of the human large intestine consists of sporeless anaerobe bacteria of Bifidum bacterium, Bacteroides. The rest 10% are lactobacilluses, colon bacillus, streptococci, and others.

Physiological role of microflora of the large intestine:

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

2. Building of immune barrier (inhibition of pathogenic microbes). Normal microflora *depresses pathogenic microorganism,* prevents infection of macroorganism. Affection of normal microflora at diseases or as result of long introduction of antibacterial preparations often followed by complications caused by rough breeding of yeast, staphylococci and other microorganisms in the intestine.

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

4. Participation in metabolism of organism. With participation of microflora of intestine in the organism there is an exchange of proteins, phosphotides, cholic and adipose acids, bilirubin, cholesterin.

b) Motor activity of large intestine

Process of digestion lasts in a person for about 1–3 days from which greatest time falls onto removal of food residuals in large intestine. The motility of large intestine provides:

1. Reservoir function.
2. Accumulation of intestinal contents.
3. Adsorption of the number of substances (basically water) from the intestine.
4. Formation of excrements masses and their removal from the intestine.

There are some kinds of contractions of large intestine:

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

2. Peristaltic and antiperistaltic contraction carry out the same functions.

3. Strong propulsive contraction advancing contents in caudal direction (3–4 times a day).

The large intestine possesses automaticity but it is expressed more weakly than in small intestine.

Sympathetic nerve fibers inhibit, and parasympathetic irritations stimulate motility of the large intestine. The motility strengthens during meal at participation of the conditioned reflex and also of unconditional reflex at irritations of esophagus, stomach and duodenum. Local mechanical and chemical irritations have big value in stimulation of motility of the large intestine.

4. Adsorption

Adsorption is transport into blood and lymph of various substances from the surface from cavities or hollow organs of the body through cells, their membranes or intercellular ducts. Cellular membranes have unequal permeability for various substances.

There is transport of macro- and micro molecules. Transport of macromolecules is carried out by phagocytosis and pinocytosis called *endocytosis.* Some substances can be transported by intercellular spaces — *persorbtion.*

From the cavity of gastrointestinal path into internal environment of the organism micromoleculas are transported basically: monomers of nutrients and ions. This transport is divided into passive, facilitated diffusion and active transport. Passive transport includes *diffusion, filtration* and *osmosis.* It is carried out by concentration, osmotic and electrochemical gradients. The facilitated diffusion is possible by means of special membranous transmitting agents. Active transport is transmission of substances through membranes against concentration, osmotic and electrochemical gradients with energy consumption.

BASIC PHYSIOLOGIC CONSTANT

Constant of blood system	
Amount of blood in adults (6–8% of body weight)	4,5–6 l
Hematocrit (m)	0,44–0,46
(f)	0,41–0,43
Blood: deposited	45–50%
circulating	50–55%
Volume of blood plasma	approx. 3 l
Structure of blood plasma:	
Water	90–92%
Solid residual	8–10%
General protein	65–80 g/l
Albumins	45 g/l
Globulins	20–35 g/l
Fibrinogen	3 g/l
Residual nitrogen	14,3–28,5 millimole/l
Glucose (whole blood)	3,30–5,55 millimole/l
(plasma)	3,88–6,10 millimole/l
Triglycerides	0,40–1,81 millimole/l
Inorganic substances	0,9%
Viscosity of blood in adults	5
Relative density	1,050–1,060
pH of arterial bloods:	7,40
venous	7,35
pH borders compatible with life	7,0–7,8
Amount of erythrocytes: (m)	$4,5–5,0\times10^{12}$ /l (tera per litre)
(f)	$3,8–4,5\times10^{12}$ /l (tera per litre)
Amount of hemoglobin: (m)	130–160 g/l
(f)	115–145 g/l
Color parameter: adults	0,8–1,0
Osmotic resistance of erythrocytes: Min	0,46–0,48% solution of NaCI
Max	0,32–0,34% solution of NaCI
Erythrocyte sedimentation rate (m)	1–10 mm / hr
(f)	2–15 mm / hr
Neonatal	1–2 mm / hr
Leucocytes: amount in adults	$4–9\times10^{9}$ /l (giga per litre)
in newborns	$15–20\times10^{9}$ /l (giga per litre)
The leukocytic formula (%): Neutrophils:	
Myelocytes	0
Metamyelocytes	0–1
stab neutrophil	1–5
segmentonuclear	45–70
Eosinocytes	1–5
Basophils	0–1
Lymphocytes	20–40
Monocytes	2–10
Index of regeneration (shift to the left)	0,05–0,1
Amount of thrombocytes	$180–320\times10^{9}$/l (giga per litre)
Blood coagulation time (by Lee-White)	5–7 min

Constant of cardiovascular system	
heart rate: in adults	60–80 / min
in neonatals	135–140 /min
Systolic volume of blood	65–70 ml
Minute volume of blood: at rest	4,5–5 l
at physical work	Up to 30 l
Time of cardiac cycle	0.75–1,0 sec
Arterial pressure: Max (systolic)	110–125 mm Hg
Min (diastolic)	60–85 mm Hg
Constant of respiratory system	
Respiration rate: in adults	12–18 / minute
in neonatal	40–55 / minute
Excursion of thorax: (m)	7–10 cm
(f)	5–8 cm
Interrelation of duration inspiration-expiration	1:1.2
Respiratory volume	0,3–0,9 l
Reserve volume of inspiration	1,5–2,0 l
Reserve volume of expiration	1,0–1,5 l
Vital capacity of lung	3,5–5,0 l
Residual volume	1,0–1,5 l
Functional residual capacity	2,5 l
Capacity of inspiration	2,0 l
Dead space	140–170 ml
Coefficient of lung ventilation	1/7
Minute volume of respiration: at rest	Up to 7 l
at physical activity	Up to 120 l/minute
Alveolar ventilation	4,2–5,6 l/minute
Maximal ventilation lung	120–170 l/minute
pO_2 in alveolar air	110 mm Hg
pCO_2 in alveolar air	40 mm Hg
pO_2 in arterial blood	100 mm Hg
pCO_2 in arterial blood	39 mm Hg
pO_2 in venous blood	40 mm Hg
pCO_2 in venous blood	46 mm Hg
Volume of forced expiration	3 l
Oxygen capacity of blood	19 percent by volume
Ventilation-perfusion coefficient	0,8–0,9
Consumption of oxygen at rest	350 ml/min
Coefficient of use O_2 at rest	40%
Constant of digestive system	
Saliva: amount of excreted saliva daily	1,5 l/day
pH	7,4–8,0
Gastric juice: daily volume	2,0–2,5 l
pH	1,5–1,8
Intestinal juice: pH juice of small intestines	5,05–7,07
Pancreas juice: daily volume	1,5–2,0 l
pH	7,8–8,4
Bile: daily volume	500–1500 ml

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