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NORMAL PHYSIOLOGY

(SHORT LECTION COURSE FOR THE STUDENTS OF MEDICAL DEPARTMENT)

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Dear students!

In a brief course of our lectures on normal physiology for the students of medical faculty, offered to you, the basic concepts about all human organism systems functionning are stated. It is natural, that because of material statement brevity due to very much lectures amount, they can not give the complete answer to numerous questions, which can appear at their reading, all the more so there is no illustrative material in them. However, from our point of view, these lectures can be good addition to the existing textbooks and manuals. All the more so we read lectures from a position of clinical physiology, and not just from those classical performances about physiology, which are stated in the bulk of educational literature. It all does not mean, that in our lectures the knowledge of classical physiology is not used. The thing is that the knowledge is so quickly replenishes with the new items of information, that the known textbooks and manuals at any stage and in any sections obviously lag behind modernity. Lectures contain as well the data, which undoubtedly can be very useful to you at a study of internal diseases, surgery and other clinical disciplines. Believe our experience, you, being trained on the senior courses, will open these lectures time and again! We wish a success to you!

Yours faithfully, professor V.P.Mishenko and assistant E.V.Tkachenko.

Lecture 1
(Introductional)

Physiology as a science. Physiological investigations methods. Physiology chapters. Excitive tissues physiology.

Physiology as a science. ***Physiology*** is a science about functions and processes taking place in organism as well as in its compartments: systems, organs, tissues and cells.

Function – is a system or organ specific activity. For instance, blood circulation system function – is blood movement through vessels.

Process – is a phenomena and states consequent change in any action development or consequent actions integrity.

System – organs and tissues integrity connected with their general function. For example, heart-vascular system, providing nutrients, oxygen, metabolism products transport to the tissues by menas of heart and vessels.

Separate functions description is obeyed to integral organism tasks, regularities of interrelation with environment, his behavior in different existancial conditions, maturation in course of phylogenesis and onthogenesis. Physiological mechanisms study requires obligatory knowledge of anatomy, histology, biology, chemistry, physics and other sciences.

Physiology studies organism viability under norma. ***Norma –*** are limits of alive system optimal existance. The term "norma" is rather complicated, dynamic and ambiguous. Many normal indexes in medicine are described as middle-statistic sizes (for example, blood formed elements amount, pulse frequency et al.). All these ziphras depend on many factors (natural, social). These factors should be taken into account while assessment of one or other organism function. For instance, pulse frequency depends on: time, age, place of investigated person localization and many others.

Physiological investigations methods depend on aims and tasks. The simplest physiological method is observation. Power of observation is essential for any doctor. It allows him to tell about patient's problems according patient's appearence (stature, carriage, face colour and other features).

Second widely-spread physiological method is experiment. One can differentiate acute experiment - with animal section and his further death and chronic – when after operation, in some time after wound repairing one performes investigations. The term "chronic experiment" and chronic experiment itself was proposed by I.P.Pavlov (remind hid world-known experiments on dogs alimentary tract with fistules application).

Besides, different models which allow to investigate cell, tissue and organ function are used in physiology.

Physiology chapters. Though physiology is united science about organisms functions one can differentiate several chapters in it:

1. **a)** *General* - studying processes general for organisms and their separate structures.
   b) *Partial* – its task – to investigate separate organs (brain, heart, kidney et al.) and systems (alimentary, circulative, respiratory) functions.

2. a) *Comparative* – functions similarity and difference in various representatives of animal's world.

b) *Evolutional* – common biological regularities and mechanisms investigation in humans and animals in ontho- and phylogenesis.

c) *Applied* – organism functions investigation taking into account his specific activity:

- physiology of agricultural animals;
- aviational physiology;
- cosmic;
- submerged et al.

Excitory tissues physiology.
Excitive tissues functionning general features.

Human and animals' organism has the highest ability to adapt to the constantly varying conditions of external and internal medium. In the basis of adaptive organism reactions lies the universal property of alive tissue - **irritability** - the ability to respond to the irritating factors action by metabolism change. The irritability is evolutionally the ancient form tissues reaction. During evolution gradual differentiation of tissues participating in adaptive organism activity has taken place. The irritability in these tissues has reached the best expression and has received the name an excitability. The **excitability** is an ability of a tissue to respond to an irritation specializedly, singlemindedly and with the maximal velocity. **Excitation** – complex (difficult) biological process expressing by response reaction to an irritation.

A nervous, muscular, epithelial secretory tissue (excitable tissues) have an excitability. The specialized form of response reaction is an excitation process physiological display. A contraction will be a response reaction in any muscular tissue. At a nervous tissue it will be an impulse conduction. At a secretory tissue it will be a synthesis and allocation of biologically active substance.

The excitability of tissues is various. A measure of an excitability is the **threshold of stimulation** – minimal stimulus force, capable to cause excitation.The stimuli with a size that is less than a threshold one, are called **subliminal** ones. The stimuli, on force exceeding a threshold of stimulation are called **epiliminal** ones.

All stimuli can be divided into three groups: physical, chemical and physico-chemical. **Physical** stimuli - mechanical, temperature, light, sound and electrical ones. **Chemical** stimuli - acid, alkalis, medicines. **Physico-chemical** stimuli –osmotic pressure, pH, ion structure changing. Besides, they distinguish **biological** stimuli - hormones, vitamins and others biologically active substances. They allocate also a group of **social** stimuli - a word.

All stimuli divide on adequate and inadequate on biological value. **Adequate** stimuli are such stimuli, acting to the given biological structure under natural conditions and to perception of which it is adjusted specially (e.g., for eye retina photoreceptors the seen part of light is an adequate stimulus). **Inadequate** stimuli are such, to perception of which the given structure is not adjusted specially (e.g., for a sceletal muscle the adequate stimulus is the nervous impulse, but it can contracts at a mechanical impact too).

Characteristic attribute of exaltation is an electrical current occurrence in tissues (cells). The electrical phenomena (currents or potentials), which arise in organism cells, tissues and organs are named the **biological potentials**.

The biological potentials arise because there is a difference of potentials between the external and internal party of a cell membrane, which is in a status of rest. Potential, which is registered in a such cell status, is named a **membrane potential (resting potential)**. It is caused by the difference of a potassium, calcium, sodium, chlorine and other ions concentration between intracellular and extracellular medium. So, the potassium ions concentration in a cell exceeds in many times (about 20-40 times) their contents in extracellular medium. The of sodium ions concentration, on the contrary, is lower in intracellular medium in 10-20 times. The ions of chlorine, as well as of a sodium, are mainly concentrated outside of cell membrane, where their content is in 15-20 times more than inside. Their such non-uniform distribution till that and other membrane party provide ion pumps. Ion canals, available in a membrane, can be opened and closed, that depends on a membrane status. So, in a cell which is in a resting status, the sodic canals are closed, and the potassium ones - are opened. Therefore the permeability for different ions is various. If a potassium ions permeability to accept for 1,0, for chlorine it will make - 0,45, and sodium - 0,04. It results that the potassium ions on a concentration gradient diffuse from a cell to extracellular space. The sodium ions counter flow is a very small. In a result the potentials difference between cell internal medium and its outer surface is formed which is from 50 up to 100 mV for different tissues. This potentials difference also refers to as a resting potential or a membrane potential.

At stimulus action there is a membrane status change, ion canals open in it, through which positively charged ions available in excess behind its limits can move in a cell. The "fast" sodic canals opening occured most often. Originally ion current to cell is promoted also by a transmembrane potentials difference. Such process is called depolarization, because it results in this potentials difference reducing. If the stimulus is weaker (subliminal), ion canals are opened a little, therefore the ion current is insignificant. Depolarization occurs slowly. Such changes are named the **local depolarization** or local potential.

If the of threshold stimulus acts, the depolarization reaches a **critical (threshold)** level. As a result of it all active electroexcitable ion canals are opened. Depolarization is sharply accelerated and there is even a potential reversion (potential mark change). Thus the positively charged sodium ions flow stops, the appropriate canals are closed. Excessive potassium ions from inside direct outside, resulting to the membrane potential restoration. At first it occurs rather quickly (**fast repolarization**), and then, when the potassium ions flow decreases, the membrane potential restoration occurs in a slowed-up way (**slow repolarization**). Further potassium ions exit can proceed and cause a **hyperpolarization**. Potassium-sodic pump work adducting in initial potentials difference restoration (**to polarization**) amplifies at this time. All this process from a beginning up to the end is called as an **action potential**.

As the vital activity of all cells, tissues, organs is accompanied by their electrical activity, the registration of potentials, arising at it, allows to judge processes occurring in them. The diagnostics and control of a treatment of this or that disease is based on it. For example, in a heart such registration of its biological potentials wears the name electrocardiogram (ECG).

In physiology they determine one more property of excitable tissues, which has received the name a **lability**. It is a functional mobility of tissues, its parameter is the potentials action maximal number, which the excitable tissue is capable to generate per 1 second according to a rhythm of a submitted boring (irritation). The normal size of a lability, e.g., for a nervous tissue makes 500-1000 impulses per second, and for sceletal muscles - 150-200 impulses per second. There is a sceletal muscles lability rising with ageing. It is shown in augmentation of irritation freaquency, at which the gear (incomplete) tetanus turns in smooth. In newborn's muscles it occurs at a stimulus freaquency 4-20 per second, at adulthood - 50-100 impulses per second.

The general laws of tissues functionning. Between the irritation character and the answer-back reaction of an alive tissue there are close mutual relations, which find expression in the irritation laws.

Irritation force law: the more force of an irritation, the more strong answer-back reaction (up to known limits). The further stimulus force augmentation any more does not lead to the answer-back reaction increasing, and even can cause return reaction, down to its disappearance. It is explained by that each functional unit of tissues (for example, muscular) has its exaltation threshold. That's why while working the threshold stimulus, those fibers, for which this stimulus is of a such size are only involved in the answer. Others do not react.

At stimulus force augmentation the new fibers are involved, for which the given stimulus is a threshold etc. Further, when the stimulus force will exceed the opportunities of all fibers of the given tissue, its answer-back reaction to the force augmentation will not change (the resources are settled!). Such stimuli, which cause the maximal answer-back reaction, are named in physiology **maximal** or **optimum**. At the even greater stimulus force augmentation the answer-back reaction even will decrease, as at such a stinulus force the separate functional fibers of excitable tissues can even be injured. In a result, the answer-back reaction decreases and this phenomenon in physiology is named **pessimum**, and the stimuli causing it - **pessimal**.

The **law "all" or "anything"** is shown, first of all, at the cardiac muscle work analysis. According to this law, subliminal stimuli, acting to a cardiac muscle, do not cause an answer in it (it is "anything"), and threshold and epiliminal stimuli cause answer-back reaction of the same size (it is named "all"). Under the same law the functional unit of any excitable tissue works. Let's take, for example, a muscular fiber and we shall imagine, that threshold stimulus at it is 2B (electrical current strain or voltage). If we act the stimulus of 1V to it, we naturally shall not receive any reaction ("anything"), and if we take the stimulus of 4V, the muscle will give the same answer-back reaction, as well as on 2V ("all"). Naturally, "all" and "anything" are relative concepts, as at the subliminal stimulus action there is a local answer (local potential), therefore it already cannot be treated as "anything".

The law of force-time – with the augmentation of a stimulus force it is required less time of its influence to tissue for answer-back reaction reception. The relation between the duration and force can be expressed by hyperbolic curve, the both branches of which go at any stage in parallel to axes of coordinates. This last circumstance forms the basis that the stimuli of a very small size (less than the threshold) can not cause the answer-back reaction. Threshold stimulus causes answer reaction after several time. This time is called ***useful time.*** Each excitatory tissue has its own useful time. But under real conditions it is

very hard to be estimated because one can make mistakes while irritation threshold determining (it is connected with the fact that its assessment is based on subjective signs – patients sensations, his skin thickness et al.). And at wrong ziphra of threshold, it leads to strong reducing of real useful time level. That's why under real conditions one determines not useful time but ***chronaxy*** – minimal time necessary for answer reaction receiving if tissue is acted by irritator in 2 thresholds or 2 ***rheobases***. Under such conditions the determination mistake is practically equal to zero (see the curve "force-time").

Chronaxymetry is widely used in neurology, traumatology and other branches of medicine for nerves and muscles excitability determining. The chronaxy is less, the excitability is bigger and on the contrary. In clinics one assesses these indexes on muscles on extremities: their rheobase is equal to 60-70 V, chronaxy - 0,1-0,7 sec.

Lecture 2
Muscular tissue physiology: skeletal, smooth and cardiac muscles activity distinguishing features.

As it is known, muscle is the contractile unit of body. Nearly 40% of the body is skeletal muscle. There are **2 muscles types**:

1. Striated muscles:
   - Skeletal muscle
   - Cardiac muscle
2. Unstriated muscle - smooth muscle of inner organs, skin and vessels.

Skeletal muscles – are transversal-striped muscles, they transform chemical energy in mechanical and thermal. Sceletal muscle consists of fibres of cells stretched into length - muscular fibres possessing 3 features: excitability, conductance and contractility. Myocytes distinguishing feature (comparatively to cells which don't possess contractility) is sarcoplasmic reticulum.

They need in energy for their contraction. It is connected with ATP in muscles and provides definite reactions cycle performance: irritation→action potential occurence→calcium ions releasing from sarcoplasmic reticulum→calcium diffusion to myofibrilles→actine and myosine fibres interaction (sliding) →myofibrille shortage→calcium pump activation→calcium ions concentration decreasing→myofibrille relaxation.

One can differentiate muscular contractions regimes and types.

Muscular contractions regimes.

At a muscle irritation by single stimulus the single muscular contraction arises. One can distinguish the **latent** period (from irritation beginning to answer-back reaction beginning), **shortnening** period (actually contraction) and **relaxation** period. In reply to a rhythmic irritation (namely the such one our muscles are received) the muscle is reduced lengthly (for a long time). Such contraction has received the name **tetanic** or **summarized**. If each subsequent pulse approaches to a muscle in the period, when it began to be relaxed, there is an **infused** or **incomplete** tetanus. If the interval between irritations decreases so, that each subsequent pulse comes to a muscle, at that moment, when it is in a contraction phase, there is a **smooth** tetanus.

In a certain degree the tetanus formation mechanism is explained by **superposition** phenomenon. However, it can be caused by excitability changing as well. And if to take

into account, that the excitability changes are caused by membrane potential change features during exaltation, then it is easy to explain smooth tetanus occurrence and its size. Let's try to understand this phenomenon together. If to render an irritation to muscle during its contraction (smooth tetanus) or relaxation (incomplete or infused tetanus), it is necessary on that moment the excitability increasing existance. Why it's so? At this time the slow depolarization phase develops in a muscle, when the membrane potential is lower, than in rest state, but is higher, the than threshold potential. That's why even subthreshold (subliminal) stimulus will cause the depolarization acceleration (i.e. the excitability at this time in a muscle is raised - **supernormal excitability**). Fast depolarization beginning results in the situation when the tissue loses ability to react to an irritation. This phase refers to as **absolute refracterity** (absolute inexcitability). At repolarization time the excitability is restored. This period refers to as **relative refracterity**. An excitability at this moment is below than the initial one, and only strong (epiliminal) stimuli can cause the answer-back reaction. Then when the restful (remainded) repolarization develops, the excitability grows and becomes above initial. This phase refers to as **exaltation** (hyperexcitability). During its occurrence even subliminal stimuli can cause the answer-back reaction. Precisely at this moment the threshold stimuli also cause the phenomenon of a tetanus (both infused, and smooth). That's why this reaction is more on size, than the single muscular contractrion. Further a membrane hyperpolarization comes and the excitability falls, it is a a **subnormal excitability** phase. At this moment the epiliminal stimulus is required to cause the answer-back reaction.

Under natural (physiological) activity conditions in human being organism the muscle shortness degree can be various.

One can differentiate the following ***types of muscular contraction*** according to the shortness size:

1) **isotonic** is the muscular contraction, at which its fibers are shortened at a constant external load (under real conditions such type is practically absent);
2) **isometric** is a muscular activation type, at which it develops a strain (tension) without the length change, it underlies the static work;
3) **auxotonic** is a regimen, in which the muscles develop a tension and are shortened, such reductions are the characteristic of walking, run, sailing.

The muscles have the certain force. The **myodynamia** (**muscle force)** is the greatest load size, which it can lift. There is a concept of an **absolute muscle force** - it is a maximal load, which the muscle lifts on 1 sm of transversal physiological section. For example, at a masseter it makes - 10,0 kg /sm^2. Besides there is a concept of a **relative muscle force**. It is the muscle ability to rise of a load on unit of a muscle anatomic section (is measured in kg / sm^2).

The muscular force grows during all period of a childhood, but especially intensively - in young age. At the second childhood period beginning the force of the majority of muscular groups in boys and girls does not differ. By at 12-15 years of age, the muscles force in boys becomes approximately on 30 % more, than in girls. With age especially after 8 years, the ability to performance of long muscular work – endurance - is enlarged. It is higher in boys.

The muscular work is determined by product of mass of the lifted load on muscle shortage size. All human muscles **useful action coefficient** is equal to 15-25 %, at trained

people it is higher - 35 %. There is a **law of average loadings**, at which the muscle is working for a long time at average loads in an optimum (average) contraction rhythm. At long-termed exercise the **working muscular hypertrophy** is developed. There occurs the whole musculation mass and each muscular fiber mass augmentation. At a hypodynaemia muscles atrophy comes. At long mode of operations of muscles **weariness** comes - subjective status, and then the **fatigue** develops. The objective attributes of ability to work hard decreasing join to the feeling of weariness: the force, endurance, rate of impellent (motor) reactions falls. One can distinguish the acute fatigue - the result of a hard work (for example, sport competitions) and the chronic fatigue - the result of repeated regular influence of loads without regular rest.

Fatigue reasons:

1) accumulation metabolites (lactic, pyruvic and other acids, ions suppressing an action potential) in muscular tissue;
2) power (energy) musclular stocks exhaustion (glycogen, ATP);
3) infringement as a result of a muscular circulation tension;
4) nervous centers efficiency (capacity for work) change. The efficiency is quickly restored at active rest, when there is activity kind change or change of working bodies (organs).

In musclular work there can be two statuses:

1) **dynamic** - there is a load moving and movement of bones and joints;
2) **static** - the muscular fibers develop a strain (tension), but are not shortened almost (deduction or restraining of a load). The static work is more tiring, than the dynamic one.

In a whole, the skeletal muscles play an important role not only in body moving in space, parts of a body opposite each other, pose maintenance, but also they take part in blood and lymph movement, heat producing, an inspiration and exhalation (expiration) act, they are the depot of liquids and salts, glycogen, provide mechanical protection of cavitary bodies (organs). And, at last, the movements caused by sceletal musculation work, are the powerful antistressful factor.

Smooth muscles. They are located in visceral organs and blood vessels walls. They can perform relatively slow movements and durable tonic contractions. First ones - determine hole organs content transfer (stomach, intestines, urinary vesicle); second ones – prevent gall bladder, urinary vesicle content exit (thus, these contractions are expressed in sphincters).

Smooth muscle contraction duration (comparatively to sceletal one) is more significant. It reaches several seconds or even several minutes. Relaxation occurs especially slow. Smooth muscle possesses big force at such slow contraction. Smooth muscle comes into state of strong durable contraction (like sceletal muscles tetatus) due to its slowed contraction. That's why they contract without fatigue development. Besides, energy expenditures in them are little. Smooth muscles relaxation is performed slower than in sceletal muscles, because sarcoplasmic reticulum development in them is less than in sceletal muscles and calcium ions are transported slow through cellular membrane.

Smooth muscles functional classification:

1. Muscles possesing spontaneous activity – they can contract while stimuli absence (rhythmic intestinal muscles contractions).

2. Muscles that have no any spontaneous activity.

Spontaneous muscular activity is linked with their stretching that causes muscular fiber membrane depolarization and action potentials occurence. Smooth muscles that have no any spontaneous activity are contracted under impulses from vegetative nervous system (arterias, spermatic ducts, iris myocytes).

Cardiac muscle. Main cardiac muscle ***peculiarities***:

- automatism;
- excitability;
- conductance;
- contractility.

Automatism – is ability to self-excitation under impulses occuring in myocardium itself. Its nature is not yet clear but there are some data about its connection with cells-pacemakers activity located in heart nodes. Systolic node is the first order pacemaker. Sinus node biopotentials distinguishing features: repolarization phase doesn't result in membrane potential restoration but transforms into secondary (dyastolic) depolarization which after threshold potential reaching causes new action potential occurence. Automatism possess all heart conductive system elements (atrio-ventricular node, Purkin'e fibers). It is decreased with impuls passage from heart base to its apex (from heart venous end to its arterial end). This regularity is known as *Gaskell's law (rule, gradient).*

Excitability also has its peculiarities in cardiac muscle. Myocardium is contracted with maximal force to threshold stimuli i.e. heart contraction force doesn't depend on irritation force (law "everything or nothing"). One can differentiate contractive (working, typical) myocardiocytes and conductive (atypical). Contractive myocardium possesses excitability but doesn't possess automatism. During dyastole resting potential of these cells is stable and its level is higher than in pacemakers (80-90 mV). Action potential in these cells occurs under pacemakers excitement. It reaches cardiomyocytes and causes depolarization of their membranes.

Working myocardium action potential consists of following phases:

- fast depolarization;
- initial fast repolarization;
- slow repolarization (plato phase);
- fast ending repolarization.

Important myocardium activity peculiarity is the following: cardiomyocytes action potential duration is about 300-400 msec that corresponds to myocardium contraction duration.

There is correlation between cardiac muscle excitement and contraction. Myocardial contraction trigger is action potential like in sceletal muscle. Depolarization phase coincides absolute refractiveness phase. But as absolute refractiveness is very long in cardiac muscle (up to 0,3 sec) than cardiac muscle excitability is absent in course of all contraction (shortening) period. That's why cardiac muscle doesn't give smooth tetanus. Relaxation period corresponds to fast repolarization period and relative refractiveness period. That's why it also doesn't give infused tetanus. During relative refractiveness phase superliminal stimuli can cause myocardium excitement and its contraction out of turn – extrasystole – appears as answer reaction.

Contractiveness peculiarity is also cardiac muscle subjugation *Frank-Starling's law:* the more heart is stretched in course of dyastole, the stronger its contraction is in course of systole. Besides, as it was explained above, the second law of heart muscle activity is law "everything or nothing".

***Conductance* –** is cardiac muscle ability to conduct excitement both through working myocardium fibers and conductive system.

Excitement wave conductance velocity through heart different parts:

- muscular contractive atrial fibers – up to 0,8-1,0 m/sec;
- in atrio-ventricular node – 0,02-0,05 m/sec;
- in Gis's fasciculus – 1,0-1,5 m/sec;
- in Purkin'e fibres – 3,0-4,0 m/sec.

Slow excitement conductance in atrio-ventricular node is called ***atrio-ventricular lack.*** It is equal to 0,04-0,06 sec.

Lecture 3
Nervous tissue physiology (receptors, nervous fibres, synapses).

Nervous tissue in organism is represented by different structures that are united in morphological and functional aspect and are nervous system base. All nervous system structures have row of common features and peculiarities:

- neuronal structure;
- synaptical connection between neurons and others.

Nervous system co-ordinates all organs and system activity providing its effective adaptation to changeable environmental conditions and formes purposeful behaviour.

Information about internal or external environment state is percepted by nervous system elements – **receptors.**

Receptors – are specialized structures necessary for stimuli perception and their transformation into nervous impuls.

2 main receptors types:

1. ***Sensor*** **-** providing different external or internal irritators perception:
   a) *primary – sensitive (simple)* – nervous endings of sensory neurons afferent conductors. They are located in skin, mucosae, blood vessels et al.
   b) *secondary-sensitive (complicated)* – specialized cells; as a rule they are in composition of sense organs – vision, gustation, hearing.
2. ***Cellular –*** providing perception of information transported by molecules of chemicals – mediators, hormones et al.

Other receptors classification (according to origin of percepted information):

1. ***Interoreceptors –*** receptors that percept sygnals about internal environment irritations and are located in internal organs:

- pressoreceptors (baroreceptors);
- chemoreceptors;
- thermoreceptors;
- noceoceptors;
- proprioreceptors of bones, ligaments, joints, muscles, vestibular apparatus;

- tissular receptors – localized in intersticium and cellular microenvironment.

2. ***Exteroreceptors –*** percept irritations of external stimuli:

a) *contact* – located in skin and mucosae:

- tactile;
- thermoreceptors;
- gustatory (tasty);
- noceoceptors;

b) *distant :*

- phono-;
- photo-;
- olfactory.

Common task for all sensor receptors is irritation transforming into biopotential. Irritator while its action for example on receptor cell increases its membrane permeability to sodium ions. It leads to creation of so-called ***local*** or ***receptor potential*** in it. It encourages mediator releasing, which acts to nervous ending. As a result of this analogous potential occurs but it is named as ***generatory potential.*** Later it generates nervous impuls. Further, due to charges difference in nervous fiber ending and through all its longitude action potential (nervous impuls) appears and then it is diverged through all nervous fiber.

Receptors features:

1) *Specificity* – ability to percept only definite, i.e. adequate for the given receptor, stimulus. This receptor ability has been formed in course of evolution.
2) *High sensitivity* – ability to answer to very small by intensivity parameters of adequate stimulus.
3) *Rhythmical excitement impulses generation* in answer to the stimulus action.
4) *Adaptation* – ability to adapt to stimulus action which is expressed in receptor activity and excitement impulses generation freaquency reducing.
5) *Functional mobility* – increasing or decreasing of functional receptors amount dependently of environmental conditions and organism functional state.
6) *Specialization* of receptors to adequate stimulus definite parameters. Receptors in perypheral analizator part composition are unequal as for their attitude to stimulus. One of them answer only to the origin of its action, others – on it stoppage, third – on intensivity change.

Nervous fibres and nerves physiology.

Nervous fibres possess excitability and according to morphologic principle they are divided into **myeline** and **myeline-free.** Nervous fibres form nerve or nervous stem, consisting of great amount of them. Nervous fibres transmitting excitation from receptors to central nervous system (CNS) are called **afferent;** from CNS to the effector organs – **efferent.** Nervous fibres possess: excitability, conductance, lability. Nervous tissue **excitability** is higher than muscular one. It is various in different nervous fibres. Myeline (thick) nervous fibres is significantly higher than myeline-free (thin).

Excitement **conductance** through nervous fibres obeyes definite **laws.**

Physiological integrity law

tells that excitation conductance through nervous fibre is possible only in a case of its non-interrupted anatomical structure and physiological features.

Excitement conductance two-sided law

at irritation application on nervous fibre the excitement is diverged through it in both sides from irritation place (at tooth nerve irritation pain is stretched not only on local tissues but also irradiates in other body parts).

Excitement isolated conductance law

excitation through nervous fibres being in a composition of mixed nerves (for example, vagus) is diverged separately, i.e. it doesn't transmit through one nervous fibre to another.

Excitement conductance velocity is different in nervous fibres. It depends on their diameter and structure (myeline membrane existance). All nervous fibres are divided into 3 main types according to their conductance velocity. *Type "A"fibres* – are covered by myeline membrane (sceletal muscles motor fibres), excitement wave conductance velocity is up to 120 m/sec. *Type "B"fibres* – vegetative nerves myeline fibres, excitement wave conductance velocity is up to 18 m/sec. *Type "C"fibres* – myeline-free nervous fibres (vegetative or autonomic nervous system postganglionar fibres), excitement wave conductance velocity is up to 3 m/sec.

Excitement conductance mechanism through nervous fibres. Excitement spreading through nervous fibres is based on bioelectrical potentials ion generation mechanisms. At excitement spreading through type "C" fibre local electrical currents occuring between excited locus, charged electronegatively, and unexcited, charged electropositively, cause simultaneouse membrane depolarization till its critical level with further action potential generation in every membrane point through all the stretching of nervous fibre. Such excitement conductance is called **uninterrupted.**

Myeline membrane presence, possessing high resistance, and membrane locuses, not having it, creates conditions for **"saltatory"** excitement conductance through myeline nervous fibres of types "A" and "B". Local electrical currents occur between neighboring Ranvier's nodes because excited membrane of node becomes electronegative as for the surface of neighbouring unexcited node. Local currents depolarize membrane of unexcited node till critic level and action potential occurence. Thus, excitation "jumps over" nervous fibre locuses covered by myeline, from one node to another. Such excitement conductance velocity reaches 120 m/sec. At the same time, such excitement wave conductance is more economic than the uninterrupted one.

Nervous fibres possess **lability –** the ability to reproduce definite number of excitation cycles in time unit according to the rhythm of applied irritations. Lability measure is maximal excitation freaquency which nervous fibre can reproduce in time unit according to the rhythm of received irritations. Nervous fibre lability is the highest and is approximately 1000 impulses per second.

Important characteristics of nervous fibre is its **relative indefatigueability**, which depends in many aspects on the fact that energy losses in it are insignificant in course of excitement and repair processes pass quickly. Besides, nervous fibre pass excitement wave with large underloading (it can transmit up to 100 impulses/sec but in the most cases transmits less for normal physiological reactions).

Synapses are excitement transmission place from one neuron process to other neuron body or process. There are 3 main synaptic parts:

- presynaptic membrane;
- synaptic fissure;
- postsynaptic membrane.

Such transmission may be performed by 2 ways: electrical or chemical. Main mechanism of information transmission between neurons is chemical. Information transfer in chemical synapses are realized by means of mediators (acetylcholine, noradrenaline, serotonine et al.). There are 2 types of chemical synapses: exciting and inhibiting. Exciting or inhibitng character of synapse is determined by corresponding mediator. Any mediator under impulse coming to presynaptic ending is released into synaptic fissure, where it goes into contact with special receptors on postsynaptic membrane. Result of such interaction: postsynaptic membrane permeability increasing as for sodium ions and membrane's partial depolarization named as ***exciting post-synaptic potential (EPSP).*** At multiplied mediator coming EPSE is summarized and action potential occurs.

Synapse is a morphological structure. Its physiological analogue is **nervous center.** CNS is a complicated structure consisting of large amount of interacting nervous centers. Anatomically **nervous center** is an integrity of neurons located in a definite brain part and are essential for definite reflex performing. Physiologically nervous center – is a complicated functional unity of many nervous centers located in different CNS parts and providing difficult reflectory acts and organism functions regulation due to their integrative activity. Examples – respiratory center, heart-vascular center et al.

Nervous centers features. Nervous centers possess a row of character features and peculiarities of excitation conductance, whcih significantly are determined by synaptic formations presence and structure of neuronal chains forming these centers. These synapses transmitting excitation received the name **exciting.** Some functional features are characteristics for them. They are also nervous centers features.

One-sided excitement conductance in nervous center is determined by its one-sided conductance through synapses.

Excitement conductance lack – is connected with the fact that excitation wave is transmittered slower in synapse than through nervous fibre (it's necessary time for mediator accumulation and exciting post-synaptic potential EPSP forming). EPSP – size on which membrane potential of post-synaptic membrane in decreased while mediator portion acting on it.

Excitement summation – can be temporary or simultanenous (it is connected with EPSP accumulation in one synapse) and space (linked with EPSP accumulation in different synapses of one and the same neuron).

Excitement rhythm transformation – impulses number increasing or decreasing on neuron "exit" in comparison with impulses number which it receives on "entrance".

Afteraction. Reflectory acts are ended not at the same time with stimulus action stoppage but they are lasted for long after action stoppage.

High sensitivity to hypoxy and different chemical substances. It gives opportunity to well-directed brain functions pharmacological regulation.

High fatigue is a result of nervous centers low lability and mediator consumption for EPSP forming.

There are also special **inhibitory synapses** in CNS the role of which are to inhibit excitation wave conductance. The same processes in comparison to exciting synapses take place in inhibitory ones. Main inhibitory mediator is gamma-aminooleic acid. It increases postsynaptic membrane permeability for potassium and chlorum ions causing postsynaptic membrane hyperpolarization. The difference is that inhibitory mediators cause in such synapses membrane **inhibitory post-synaptic potential (IPSP)** occurence. IPSP – is that

size on which post-synaptic membrane membrane potential is increased while action inhibitory mediator on it. Such inhibition is called postsynaptic.

Presynaptic inhibition is realized due to axo-axonal synapses. It is expressed as presynaptic membrane depolarization and exciting mediators releasing inhibiting. Presynaptic inhibiting mediator is glycine.

One of variant of neuronal integration is the possibility to regulate the size of coming information due to feed-back connection. Axonal collaterals can establish synaptic contacts with special associative neurons. For example, impulse occurence in motoneuron not only activates muscular fiber but also excites special neurons (inhibitory Renshow cells) through collaterals. Such Renshow cells establish synaptic contacts with motoneurons and inhibit them (this is so-called recurrent inhibition).

Main principles of reflectory activity co-ordination.

All reflectory activity is rather co-ordinative. Reflexes are tightly connected one to another in nervous system integrated reaction to the irritation. Inhibition in CNS is of great importance. First, it performs co-ordinative role, i.e. directs excitation on a definite way to the definite nervous centers. As a result of such action well-directed *elective excitation irradiation* occurs (irritation of hand definite locuses causes definite fingers flexing and leaving). Sometimes irradiation becomes *diffuse,* non-directed, realized on different ways simultaneously (at epilepsy). *Irradiation* is the simplest mechanism of such co-ordination. Irradiation means spreading. The stronger stimulus is the more receptors participate in answer reaction and finally more central neurons.

Excitation in nervous centers due to irradiation can *converge* from different origins to one and the same neurons. *Convergency* is the next principle of co-ordination.

Opposite to convergency – there is *divergency* - one neuron contact with great number of neurons of higher order. Role: given sygnal influence sphere becomes wider. Example: in course of physical exercises information flow is strongly enforced from proprioreceptors to next nervous system parts that leads to ending result increasing.

Occlusion is more complicated co-ordinative mechanism. It is the interference of one reflectory act influence spheres with the same of other. That's why at simultaneouse coming of several afferent sygnals to one and the same neurons they become ending result reducing.

Due to interrelations between excitation and inhibition processes in CNS *dominanta principle* is expressed in its work. It is main working principle for nervous centers activity which is expressed in temporary dominant excitation locuses occurence. Such dominant locuses have increased excitation, they are stable. There are 2 main reasons of dominanta: increased impulse coming from efferent organs (alimentary or urinary dominanta) and hormones or other biologically-active substance activity increasing (sexual dominanta).

Feed-back afferentation principle is in information conductance (return) from effector (working organ) ahead to nervous center structures where it is processed and thus nervous center performs control under effectiveness, properity and optimal level of reflectory activity.

All co-ordinative mechanisms are directed on doing answer reaction faster, more purposeful and more adequate and its performance - without excessive energy expenditures.

Besides very important role in reflectory activity co-ordination, inhibition performs important protective role or defencive function. Multiple organism reactions are formed with obligatory participation of different CNS parts on the basis of excitement and inhibition processes interaction.

Lecture 4
Different CNS levels role in motor acts regulation

Spine role in motor acts regulation.

Spinal neurons functional classification:

- motoneurons (alpha- and gamma-);
- interneurons;
- parasympathetic system neurons;
- sympathetic system neurons.

Alpha-motoneurons have direct connections from afferent ways coming from extrafusal muscular fibres.

Gamma-motoneurons innervate intrafusal muscular fibers of muscular spindle.

Interneurons – intermediate neurons; they organize connections between spine structures in realizing the influence of ascendant and descendant ways on separate spine segments cells.

2 spine functions:

- reflectory;
- conductive.

Reflectory spine function: spine performs regulation of many reflectory acts – clinically important among them are tendinous reflexes. These are multiple reflexes which are investigated by short doctor's shock on tendon. It is essential in neurology because every reflex of this group has definite spinal closage level. These reflexes are the most expressed in extensors and flexors of upper and lower extremities (knee jerk reflex, Achilles' tendon reflex et al.). For example, light shock on patella tendon causes femur muscles contraction and tibia extension. Reflectory arc of this reflex is following: quadriceps femori muscle tendineal receptors→spinal ganglion→posterior fasciculi→ posterior corns of the III-rd lumbal spinal segment→ motoneurons of anterior corns of the same segment→ quadriceps femori muscle extrafusal fibres.

Flexory reflexes – are directed into different injuring actions prevention. They occur at skin, muscles and visceral organs receptors irritation. Example: noceoceptors irritation (pinch, nipping)→flexors contraction→hand taking away. These reflexes provide protective function.

Rhythmical reflexes- walking, scratching (rhythmic contractions and relaxations, flexings and extensions).

Pose reflections - are large group of acts directed to definite pose support (standing, lying et al.).

Spinal shock - is a state observed in a case of spinal trauma and its complete intersection. Reason: stoppage of influencies coming from upper nervous system parts to

spine. It is accompanied by deep body musculature paralysis. Such muscles are innervated by spine segments located below injury place, later they are partially restored. Arbitrary movements restoration depends on pyramid ways injury degree.

Stem role in motor functions regulation.

Brain stem includes following structures:

- medulla oblongata;
- Varoli pons;
- midbrain;
- dieencephalon;
- reticular formation.

Medulla oblongata is delt with realization of vegetative and somatic, gustatory, auditory and vestibular reflexes.

Distinguishing feature of medulla oblongata reflexes is their more duration comparatively to spinal reflexes; afteraction and intersegmentarity are more expressed in them. Medulla oblongata is necessary for pose supporting (of all motor acts). These reflexes are originated from vestibular apparatus receptors (cochlea vestibule and semicircular channels), then they are switched to superior vestibular nucleus and finally processed information is transmitted to medulla oblongata lateral and medial vestibular nuclei. Role of these nuclei is the following: to determine, what muscular systems, what spinal segments must participate in pose changing. That's why the sygnal comes to corresponding spinal segments anterior corns (such segments innervate muscles) from medial and lateral nuclei through vestibulo-spinal tract.

One can tell about 2 groups of these pose reflexes:

- stathic – they provide equillibrium support and body status in space while standing, lying, sitting in different poses;
- statho-kinetic – they provide muscular tone redistribution for corresponding pose organization in course of movement, direct or rotatory (they are originated from semicircular channels receptors).

Varolii pons and midbrain. Cerebral pons – is one of brain stem structures which is tightly linked with midbrain. All ascendant and descendant ways connecting anterior brain (brain hemispheres) with cerebellum and other brain structures.

Midbrain is represented by corpora quadrigemina, nuclei - red, black substantia, of oculo-motor and trochanter nerve.

Red nucleus – regulates musculature tone, when sending corrigating impulses to spine motoneurons through rubro-spinal tract. At its function injury as well as its connection with midbrain one can see reaction described as decerebrative rigidity. It is characterized by extremities, neck and back extensors tension.

Black substantia – is located in cerebral peduncles. It regulates mastication, swallowing, provides exact movements co-ordination (at writing, playing musical instruments, performance surgical operations).

Oculo-motor and trochanter nerve nuclei – provide eyeball turning in all directions.

Corpora quadrigemina tubercles (coluses or bodies) – superior are primary subcortical visual; inferior – primary subcortical auditory centers. Main functions: reaction

"becoming more alert" ("what's this" according to I.P.Pavlov) on sudden unknown visual and auditory reactions.

Diencephalon

It consists of:

- thalamus;
- hypothalamus;
- epithalamus.

Only thalamus deals with motor reactions. Other parts activity are linked with vegetative and behavioural reactions.

Thalamus **–** is a structure in which processing and integration of practically all signals coming into brain cortex are occurred. Such signals are originated from spine, midbrain, cerebellum, basal gangliums. There are more than 120 nuclei in it, forming complexes that are divided into: anterior, posterior, medial and lateral. Thalamus complicated structure, existance of interconnected specific, non-specific and associative nuclei allow to organize such motor acts as sucking, mastication, swallowing, loughing. Motor acts are integrated in thalamus with vegetative reflexes providing these movements.

Brain reticular formation

It is represented by neurons net with multiple connections practically with all brain parts. Its participation in movement: from it to spinal and cranio-cerebral nuclei motoneurons sygnals come which organize head, trunk status and pose. Reticular ways releasing spine motor systems activity are originated from all reticular formation parts. Ways coming from pons inhibit spine motoneurons activity (the latest innervate flexors and activate extensors motoneurons). Ways coming from medulla oblongata cause opposite effect. Reticular formation irritation leads to tremor, muscular hypertony or spinal reflexes inhibiting. It occurs when pose is necessary to be regulated and one movement must be changed by other one.

Cerebellum

Cerebellum sends efferent sygnals to spine and regulates muscular contractions force, permits durable tetanic muscular contraction, saving optimal muscular tone under rest and movement states, to measure arbitrary movements to perform fast transition from flexion to extension and on the contrary. It provides different muscles contractions synergy at complicated movements for example, in course of walking.

When cerebellum doesn't regulate movements human being has different motor disorders.

- *Astheny* – muscular force contraction decreasing; fast muscles fatigue.
- *Asthasy* – loosing the ability to durable muscular contraction that makes standing, sitting difficult and even impossible.
- *Athaxy* – movements co-ordination disorders.
- *Asynergy* – co-operative movements disturbances (human being can't sit from laying state without hands help).
- *Dystony* – muscular tone unarbitrary increasing or decreasing.

- *Thremor* – fingers, hand, head trembling under rest; this thremor is enforced during movement.
- *Dysmetry* – movements equality disorders expressed either in excessive or in insufficient movement.
- *Dysarthry* – speech disorder.
- *Drunk walking* – person is walking having arranged his leg widely, having shaked from one side to another.
- *Adiadochokinesis* – person can't rotate fast his hands up and down.
- *Writing disorders* – megalography – very big letters.

At cerebellum injury medulla oblongata vestibular nuclei and reticular formation neurons are activated which stimulate spine motoneurons. Simultaneously pyramidal neurons activity is decreased and thus their inhibitory influence to those spinal motoneurons is reduced. Finally, motoneurons cause muscular hypertonus having received stimulating sygnals from medulla oblongata while absence inhibitory sygnals from cortex.

Basal ganglions.

They include 3 pair structures:

1. Neostriatum:
   - caudate nucleus;
   - putamen (shell).
2. Paleostriatum:
   - globus pallidus.
3. Claustrum.

Neostriatum – participates in musculature tone regulation. Injury symptoms - hyperkineses:

- unarbitrary mimic reactions;
- atethosis (worms-like fingers movements);
- thremor;
- torsion spasm;
- chorea (extremities and trunk trembling like at non-coordinated dance);
- motor hyperactivity as non-purposeful transfer from place to place.

<u>Caudate nucleus injury symptoms:</u>

- at two-sided injury – striving for unrestrained movement forward;
- at one-sided injury – rotatory (so-called manege) movements.

Paleostriatum (globus pallidus) triggers oriented reaction and extremities movement.

<u>Symptoms of its destruction:</u>

- hypodynamy;
- face as a mask;
- head and extremities thremor which is enforced under rest state and is disappeared at movements;
- myoklonuses (myoklony) – separate muscular groups or separate arms, back, face fast fascillations;
- movement beginning becomes difficult;

- additional and reactive movements disappearence at standing up;
- convergent arms movements injuries at walking.

Claustrum - is linked with cortex and the biggest amount of subcortical structures. Patients can't talk at its injury. At its stimulation orienting reactions appear:

- head turn;
- masticatory movements;
- swallowing movements;
- sometimes – vomiting.

Locomotion neuronal organization.

Thus, structures taking part into locomotions organization are located in all brain parts. They are interrelated one to another morphologically and functionally.

Motor functions regulatory levels:

1. *Spinal* - muscles state automatic regulation the simplest form is realized on this level.
2. *Stem* - regulates movements on descendant ways coming to spine.
3. *Programmed (the highest, cortical).*

All levels mentioned above may realize these functions both independently and with the help of other levels. Besides, every level may regulate muscular activity through spinal motoneurons both simultaneosely and paralelly. Thus, any muscular contraction may be caused by spine, stem structures and cortex. Different levels integrated participation allows to increase movements regulation reliability, their exact performance, locality, difficulty.

Every regulational level has feed-back connections about movement making from muscular system; every level sends command to spine motoneurons; at the same time it sends thy sygnal about command into other above-lying and below-lying centers. All this allows programming center to evaluate other levels commands in time and to perform movements management correction in time too.

Arbitrary movements of human being are regulated by brain cortex. Spine motoneurons management at arbitrary movements is realized by cortex precentral sulcus, partially it is performed through Betz' cells and through pyramidal tract. Besides, this realization is made through extrapyramidal tracts.

Pyramidal tract motor cortex injury in course of trauma, haemorrhagia leads to muscular tone loss (sluggish paralysis), loosing the ability to perform some movements types. Motor cortex injury due to inhibitory influence loss to extrapyramidal system, spinal reflexes causes hyperreflexy, muscular hypertony (spastic paralysis despite slugging is developed) at functions of below-lying structures restoration.

Thus, any motor reaction realizing is performed by distributory system consisting of cortical and subcortical centers, connected one with another by multiple nervous tights.

Lecture 5
Autonomic nervous system physiology and its role in functions regulation.

Autonomic (vegetative) nervous system – is a complex of central and perypheral structures which regulate internal environment functional level necessary for organism adequate reaction. Anatomically autonomic nervous system is represented by nuclear structures lying in brain and spine, nervous ganglions and nervous fibres. It is divided morphologically and functionally into 3 parts:

- parasympathetic;
- sympathetic;
- metasympathetic.

Autonomic nervous system reflexes morpho-functional peculiarities. *Parasympathetic part.* Parasympathetic unit central part is represented by nuclei, located: in midbrain- oculomotor nerve nucleus (III-rd pair of craniocerebral nerves); in medulla oblongata – facial (VII-th pair), glosso-pharyngeal (IX-th) and vagus (X-th pair) nerves nuclei; in spine – lateral corns of sacral part 3 segments. Perypheral part includes: preganglionar fibres – nervous fibres coming from nervous centers, ganglions and postganglionar nervous fibres – innervating effector organs.

Parasympathetic vegetative functions regulation is realized by both highest nervous centers (cerebral and spinal) and by perypheral ones – ganglions. Ganglion is a morphologic and functional unity of neurons. Excitement transduction from preganglionar nervous fibre to postganglionar is realized in parasympathetic ganglions by means of mediator – acetylcholine. When excitation reaches preganglionar fibre therminal, permeability increasing for extraneuronal calcium occurs. Calcium comes in presynaptic membrane zone and activates vesicules transport with acethylcholine to presynaptic membrane. Vesicular membrane is fused with presynaptic membrane. In creates the conditions for mediator releasing into synaptic fissure. Acethylcholine interacts with N-cholinoreceptor on post-synaptic membrane and sodium channels are opened as the result of which EPSP occurs. Acethylcholine is destroyed by enzyme acethylcholineestherase after this interaction. Substances acting like acethylcholine are called agonistes, inhibiting excitement conductance in ganglions – ganglioblockers.

In postganglionar parasympathetic nervous fibres on their endings realization is performed through synapses by means of acethylcholine which in visceral organs (heart, alimentary organs, bronchi et al.) acts through M-cholinoreceptors (muscarine-dependent). Such receptors are not equal. One can differentiate $M_1 \ldots M_5$ receptors. Besides, one can differentiate also N-cholinoreceptors (nicotine-sensitive), located on post-synaptic mebranes of sceletal muscles, in central nervous system. Physiologic effects depend on which receptors acts acethylcholine.

Parasympathetic influences peculiarity on different organs is the following: effect comes quickly because they mainly consist of preganglionar nervous fibres of group "B" where excitement wave spreading velocity is relatively high. But effect also disappears quickly because mediator acethylcholine is destroyed fast. That's why action of this part of autonomic nervous system is quick and in more extent local (in the place of mediator releasing).

Sympathetic part. Central part is origined from spine nuclei in grey substance beginning from I-II thoracic till II-IV lumbal segments. Perypheral part is represented by postganglionar neurons beginning from paravertebral and prevertebral ganglions. Excitement conductance in ganglions in this part of autonomic nervous system is realized by mechanisms similar to those in parasympathetic nervous system. Excitation wave is

transmitted from postganglionar fiber to effector by means of mediator – noradrenaline (or adrenaline). Noradrenaline produces in body, axonal therminal part and its varicosus dilations. Noradrenaline is located in neuronal vesicles, its part is dissolved in cytoplasm. It is released from vesicules in course of depolarization of presynaptic ending membranes that is accompanied by their permeability changes to calcium ions. Calcium releasing into synaptic fissure occurs by means of exocytosis – vesicular membrane fusing with axonal ending membrane. Noradrenaline or adrenaline reaching postsynaptic membrane interacts with specific receptors which name is adrenereceptors. They are divided into 2 groups – alpha- and beta-adrenoreceptors. In turn, every group is subdivided into subgroups. Alpha-adrenoreceptors leads to skin, mucosas, kidney, abdominal cavity organs, lung, brain, sceletal muscles vessels constriction. At the same time it results in contraction of sphincters smooth muscles and pupil ciliary muscle, causing midriasis (pupil's dilation).

Beta-adrenoreceptors activation causes vasodilatation in sceletal muscles, coronars, lung, brain, abdominal cavity organs. It also leads to heart beat, freaquency and excitement conductance velocity increasing in typical (working) and atypical myocardiocytes. Other results of such activation – pupillar muscles, biliary tracts smooth muscles relaxation; urinary vesicle tone decreasing.

Autonomic nervous system sympathetic part makes trophyc influence onto different tissues and organs. It means that metabolic processes complex occurs in tissues supporting tissue structure and providing its function and metabolic reactions in it. For example, it enforces energy substances resynthesis processes, changes receptors excitability et al. Biologically active substances – noradrenaline and adrenaline – participate in trophyc processes. They while absorbing into blood are spread to organs and tissues which have no sympathetic innervation and act to them (for example, sceletal muscles).

Comparatively to parasympathetic part, sympathetic one influences more diffusily. It is connected with adrenaline and noradrenaline action because they reach practically all tissues and organs and possess stronger effect in comparison with acethylcholine. Besides, sympathetic nervous system action and influence is more durable.

Metasympathetic part is a complex of structures providing their own nervous regulation of main visceral organs possessing functional automatism (cardiometasympathetic, enterometasympathetic, urethrometasympathetic). Its main functions are as follows as: providing excitement conductance from nervous system structures to effectors, regulatory influences co-ordination performing (of smooth muscles motor activity, alimentary tract organs secretory, excretory and absorbtive activity, local circulation regulation and others).

The base of metasympathetic part are neurons different in their shape, synapses existance, processes amount and length. This system ganglions are located intramurally – in organs walls. Parasympathetic and sympathetic fibres penetrate these ganglions. Central influencings are realized through these fibres. Ganglionar neurons receive and process the information from efectors and are under modulating and correcting influence of impulses coming from brain and spine centers. Information processing is performed in ganglions, excitement transmitting in them is realized with acethylcholine participation (through M- and N-cholinoreceptors) and noradrenaline (through alfa-adrenoreceptors). Impulses are transmitted from postganglionar neurons to effectors by means of such mediators as ATP, serotonine, noradrenaline, acethylcholine, substance "P" and others.

Significant role in realizing effects to effector tissues and organs have modulators – kinines, prostaglandines, opioid peptides, renine, angiotensine and others. They change effectors functional answer enforcing or decreasing their activity.

Thus, autonomic nervous system action onto organs and tissues is not equal. Sympathetic part causes their diffuse excitement. This is the system of anxiety, protection, mobilization of reserves necessary for organism interaction with environment. Such mobilization is reached by means of many systems and organs generalized involvement in reaction. Probably, that's why sympathetic ganglions are situated far from innervated organs and possess the ability to impulses multiplication that provides fast influencing generalization.

Slower but also generalized process appears at adrenaline releasing into blood. Such releasing is considered to be fluid sypmathetic nervous system. Sympathetic impulses activate brain activity, mobilize defence reactions, thermoregulative processes, blood coagulation mechanisms, immune reactions. Sympathetic nervous system excitement is an obligatory condition of emotional state and tension, it is hormonal reactions initial stage (link) at stress. Its influencings have adaptative and trophyc character.

Parasympathetic part and, especially, metasympathetic are the systems of current organism physiologic functions regulation. Such functions provide homeostasis. Metasympathetic neurones possess the features like brain nuclear structures. This system has its own integrative chain for information processing. If parasympathetic system influencings are mainly indirected (although there are also direct influencings to some organs) and more local than in sympathetic, metasympathetic one has only visceral functions (peristalsis saving, absorption, smooth muscles contraction) and it is base, local for these organs.

Vegetative functions regulative centers are practically all parts of central nervous system. Spinal part has segmentary and metameric organization. Its a very important for clinics (hyperaesthesia, hyperalgesia – tactile and nociceptive sensitivity increasing in limited body parts at inner organs diseases). Pains occuring at inner organs diseases are called reflected (Ged's zones).

In brain stem there are multiple vegetative structures – nuclei and centers of heart activity, vessel tone, respiration, swallowing regulation and others. They must belong such reflexes as olfactory, lacrimal, pupillar, sneeze and others to these reflectory acts.

In dieencephalon particularly in hypothalamus humans have central mechanism of homeostasis, alimentary, respiratory functions, heart-vascular activity, endocrine system, metabolism regulation, thermoregulation.

Somatosensor and other cortical zones are center of localization not only of somatic but also visceral systems.

Autonomic nervous system reflectory reactions. One can differentiate 3 reflexes groups:

- viscero-visceral;
- viscero-somatic;
- viscero-sensor.

Viscero-visceral reflexes are origined and are ended in inner organs. For example, peritoneum receptors in course of their excitement give impulses changing heart activity (Golz reflex, epigastral reflex). Such reflexes may be closed by type of axon-reflex (in limits of one axon branches). It's necessary to take into account such mechanism of their

occuring in clinic practice in course of therapeutical procedures performing (mustard plusters, cupping-glasses, compresses).

Viscero-somatic – include ways on which excitement in addition to visceral reflexes cause also somatic answers (contraction or inhibition of sceletal muscles current activity). Segmentary innervation of some organs (heart, intestines) are on the base of these reflexes. It's accompanied by integrative reactions of both visceral and somatic organs. For example, abdominal cavity receptors irritation can cause anterior abdominal wall muscles contraction or extremities movement that it is connected with afferent impulses convergence to interneurons of different spine segments. Such segments create common scheme for autonomic and somatic influencings transmission.

Viscero-sensor – include ways in which in answer to autonomic sensor fibres irritation reactions occur not only in inner organs, muscular system but also somatic sensitivity is changed. Due to segmentary organization, autonomic and somatic innervation at inner organs diseases in limited skin locuses tactile and nociceptive sensitivity increasing (reflected pains) is appeared. In course of some diseases (stenocardia, ulcer disease, cholecystitis, pancreatitis et al.) the patients's complaint is painful sensation in corresponding projectional zones.

Lecture 6.
Physiological functions humoral regulation. Interrelations between nervous and humoral mechanisms of physiological functions regulation in organism.

Humoral regulation is performed by means of special internal environment chemical regulators – **hormones.** These are chemical substances producing and releasing by specialized endocrine cells, tissues and organs. Hormones differ from other biologically active substances (metabolites, mediators) by their producing in specialized endocrine cells and because they act to organs located far from them.

One consider that hormonal regulation is realized by endocrine system. This functional unity consists of endocrine organs or glands (for example, thyroid, suprarenal glands et al.); endocrine tissue in organ (endocrinocytes accumulation for example Lanhergans's insulas in pancreas); organ cells possessing (besides their main function) endocrine function too (atriums myocytes alongside with their contractile function produce and secrete hormones influencing on diuresis).

Hormonal regulation management apparatus. Hormonal regulation has its own management apparatus. One of such management ways is realized by separate structures of CNS directly transmitting nervous impulses to endocrine elements. This is nervous or *cerebro-glandular way* (brain-gland). Other way is *hypophyseal.* Third way of some endocrinocytes activity control is *local self-regulation* (secretion of sugar-regulating hormones by Langerhans's insulas is regulated by glucose level in blood; of calcitonine – by calcium level).

Hypothalamus is a central structure of nervous system that regulates endocrine apparatus functions. Such hypothalamus function is connected with neuronal groups existance having the ability to synthesize and to secrete special regulative peptides – neurohormones. Simultaneously hypothalamus is both nervous and endocrine structure. Hypothalamic neurones feature to synthesize and to secrete regulatory peptides receives the name neurosecretion. I would like to mention that in fact all neurons possess this

quality – they transport proteins, enzymes synthesized in them. Neurosecret is transmitted into brain structures, liquor and hypophysis. One can differentiate 3 groups of hypothalamic neuropeptides:

- visceroreceptive – primarily act to visceral organs (oxytocine, vasopressine);
- neuroreceptive – neuromodulators and mediators possessing expressed effects to nervous system functions (endorphines, encephalines, neurotensine, angiotensine);
- adenohypophyso-receptive – realize adenohypophysal glandulocytes activity.

Lymbic system belongs to endocrine elements activity management common link with hypothalamus.

Hormones synthesis, secretion and releasing.

Hormones classification (according to their chemical structure):

1) aminoacids derivates:
- thyroid hormones;
- adrenaline;
- hypophysal hormones;

2) peptide hormones:
   - hypothalamic neuropeptides;
   - hypophysal hormones;
   - pancreatic insular apparatus hormones;
   - parathyroid hormones;

3) steroid hormones (are formed from cholesterine):
   - suprarenal glands hormones;
   - sexual hormones;
   - renal hormone – calcitryol.

Hormones are usually deponated (accumulated) in those tissues where thay are formed (thyroid follicules, suprarenal glands medulla - as granules). But some of them are deponated by non-secretory cells (cathecholamines are catched by blood cells).

Hormones transport is performed by internal environment fluids (blood, lymph, cells microenvironment) in 2 forms – connected and free. Connected (with erythrocytic, thrombocytic membranes and proteins) hormones have low activity. Free hormones are the most active, they pass through barriers and interact with cellular receptors. Hormones metabolic transformations lead to new informational molecules forming with qualities different from main hormone. Hormonal metabolism is performed by means of enzymes in endocrine tissues themselves and also in liver, kidney and tissues-effectors. Hormonal information molecules and their metabolites releasing from blood is realized through kidney, sweat glands, salivary glands, bile and alimentary juices.

Hormones action mechanism. They differentiate several kinds, types and mechanisms of hormones action to tissues-targets:

1) *metabolic action* – causes metabolism change in tissues (cellular membranes permeability, cellular enzymatic activity, enzymatic synthesis change);
2) *morpho-genetic action* – hormones influence on processes of structural elements shape-forming, differentiating and growth (genetic apparatus and metabolism change);
3) *kynetic action* – ability to switch on effector activity (oxytocine – uterus musculature contraction, adrenaline – glycogenolysis in hepar);

4) *corrigating action* – organ activity change (adrenaline – heart contractions frequency increasing);
5) *reactogenic action* – hormone ability to change tissue reactivity to the action of the same hormone, other hormones or mediators (glucocorticoids release adrenaline action, insuline increases somatotropine action realizing).

Hormones action ways to cells – targets – can be realized as 2 possibilities. Hormone action from cellular membrane surface after binding with specific membrane receptor and after that switching on biochemical reactions chain in membrane and cytoplasm. Peptide hormones realize their activity by this way. Another way – penetrating the membrane and connection with cytoplasmic receptors after which hormone-receptor complex penetrates nucleus and cellular organoids. Such way is a characteristics of steroid and thyroid hormones.

In peptide, protein hormones and catecholamines hormone-receptor complex leads to membrane enzymes activation and hormonal regulative effect secondary messengers formation. They know next secondary messengers systems:

- adenylatecyclase-cyclic adenosinemonophosphate (cAMP);
- guanylatecyclase-cyclic guanosinemonophosphate (cGMP);
- phospholipase C – inositoletryphosphate (IP3);
- ionized calcium.

In the most organism cells practically all messengers mentioned above with the exception of cGMP are present or may be formed. There are different interrelations between them (equal participation, one - main, others – agonistes, act simultaneously, double one another, are antagonistes). In steroid hormones membrane receptors provides specific hormone recognition and its transport to cell; special cytoplasmic protein – receptor with which hormone is connected – is located in cytoplasm. Then interaction of this complex with nuclear receptor occurs and reaction cycle with DNA participation and ending protein and enzymes biosynthesis on rhybosomes is switched on. Additionally, steroids change intracellular cAMP and ionized calcium content. In this aspect different hormones action mechanisms have similar features.

In last tens years tissular hormones large group has been discovered. For example, alimentary tract, kidney and practically all the tissues hormones. Prostaglandines, kinines, hystamine, serotonine, cytomedines and others belong to them. Second half of last century in biology and medicine is characterized by fast development of peptide role study in organism activity. Every year great amount of publications dedicated to different physiologic functions course appear. Nowadays from different (practically all) organism tissues more than 100 peptides are extracted. One group of neuropeptides is among them. To present time peptide regulators are found out in alimentary tract, heart-vascular system, respiratory and excretory organs. Thus, there exists diffused neuroendocrine system called sometimes third nervous system. Endogenous peptide regulators containing in blood, lymph, intersticial liquid and different tissues, can have at least three origins of their development: endocrine cells, organ neuronal elements and peptide axonal transport depot from central nervous system. Brain synthesizes constantly and thus contains with the small exception all peptide bioregulators. That's why brain is called to be endocrine organ. At the end of last century information molecules existance in organism cells was proved. These molecules provide interactions in nervous and immune system activity. They received the name cytomedines. These are substanses realizing connection between small

cellular groups that influence greatly on their specific activity. Cytomedines carry definite information from cell to cell. Such information is written by means of aminoacids sequences and conformational modifications. Maximal effect cytomedines cause in tissues of organ from which they are excreted. These substances support definite cell correlation in populations situated on different developmental stages. They perform informational exchange between genes and intercellular environment. They participate in cells differentiation and proliferation processes while changing genome functional activity and protein biosynthesis. Nowadays thesis about united neuro-endocrine-cytomedine regulatory system in organism is putted forward. I would like to mentione specially that our Normal Physiology Chair deals with cytomedines action mechanism study. Cytomedines are multiple substances group. They are of protein nature and are released nowadays practically from all organs and tissues being one of the most important links in organism physiologic functions regulation. Some of these substances were checked up experimentally particularly at our chair. Today these substances are described as medicines (thymogen, thymaline – from thymus, cortexine – from brain tissues, cardialine – from heart tissues – the preparations were received in Russia). Our collaborators studied action mechanisms of such cytomedines – from salivary glands tissues – V.N.Sokolenko; from hepatic tissues and erythrocytes – L.E.Vesnina, T.N.Zaporozhets, V.K.Parchomenko, A.V.Katrushov, O.I.Tsebrzynsky, S.V.Mistchenko; from cardiac tissues – A.P.Pavlenko; from kidney tissues – I.P.Kaydashev, from brain tissues – N.N.Grytsay, N.V.Litvinenko; cytomedine "Vermilate" from California Nematoda tissues – I.P.Kaydashev, O.A.Bashtovenko. These peptides play important role in antioxidative protection regulation, immunity, non-specific resistancy, blood coagulation, fibrinolysis and other reactions.

Interrelations between nervous and humoral mechanisms in physiological functions regulation.

Regulation nervous and humoral principles described above are united morphologically and functionally in one *neuro-humoral regulation.* Such regulatory mechanism initial link, as a rule, is afferent sygnal on entrance and informational connection effector channels are either nervous, or humoral. Organism reflractory reactions are initial in complicated integrated reaction, but only only in complex with endocrine apparatus organism alive activity regulation system functionning is provided to its optimal adaptation to environmental conditions. One of such alive activity organization mechanisms is *general adaptational syndrom or stress*. Stress is neuro-humoral regulation, metabolism systems and physiological functions non-specific and specific reactions integrity. Neuro-humoral regulation system level is expressed in course of stress as a whole organism susceptibity increasing to environmental factors action particularly harmful for organism. You will discuss stress mechanisms in details in course of pathological physiology. But now, please, put your attention to the fact that under stress conditions interrelations between nervous and humoral regulatory mechanisms are very brightly expressed. In organism these regulatory mechanisms add one another while forming functionally united mechanism. For instance, hormones influence on processes taking place in brain (behaviour, memory, study). Brain, in turn, controls endocrine apparatus activity.

Organism interrelation with external environment which influences on its functions so much is realized by analizators – special nervous system apparatus.

Lecture 7.
Sensor systems physiology (analizators and their significance for organism interrelations with surrounding external and internal environment).

Human being constantly receives information about multiple changes taking place in external and internal environment. It is realized by means of **analizators** or sensor systems. Each analizator consists of 3 parts:

1) *perypheral or receptor part*– performes stimulus energy perception and its transformation in specific excitement process;
2) *conductive part* - is represented by afferent nerves, spinal and stem centers. It performs specific excitement primary processing and its transmission to brain cortex;
3) *central, brain or cortical part* – corresponding cortical zones, where ending excitement processing – the highest analysis and corresponding sensation forming – is performed.

Thus, **analizators** – integrity of structures providing:

- irritator energy perception;
- its transformation into specific excitement process;
- this excitement transmission through CNS structures;
- its analysis, assessment by specific cortex zones with subsequent forming of corresponding sensation.

Gustatory reception. Gustatory sensitivity is oral mucosa sensor function specific peculiarity. Gustatory analizator physiology knowledge is a very important because change of its function may testifies to serious disorders both in oral cavity and in other organism parts. One can differentiate such problems with taste:

- *agevzya* –gustatory sensitivity loss;
- *hypogevzya* – gustatory or taste sensitivity reducing;
- *hypergevzya* - gustatory or taste sensitivity increasing;
- *paragevzya* - gustatory or taste sensitivity distortion;
- *dysgevzya* – gustatory substances detailed analysis disorders;
- *gustatory gallucinations.*

But gustatory analizator role and its importance is difficult to determine separately because natural adequate stimulus - food, coming into oral cavity – excites simultaneously other analizators receptors. Thus, gustatory sensation is a complicated sum of excitements coming into cortex from gustatory, olfactory, tactile, temperature and nociceptive receptors. First of all, in oral mucosa tactile receptors are excited, later – temperature and than receptors answering to chemical food content. Impulses from them go into CNS through different fibres with different velocity. Result - dyspersion on excitement spreading through nervous centers. Different shades of gustatory sensations also depend on the complex of occuring excitations. Gustatory receptor cells are united in gustatory bulbs which are primarily located in tongue papillas: fingiformed, foliatae and vallate. Taste analizator sensitivity assessment is performed by method of *gustatory sensation threshold determining* as well as by *functional mobility* method. Gustatory thresholds are defined separately for every from 4 main gustatory stimuli according to taste fields topography because separate tongue locuses possess different sensitivity to substances of

various gustatory quality in the majority of people: tongue end is the most sensitive to sweet, lateral surfaces – to salt and sour, root – to bitter. It was established by means of functional mobility method that active lingual papillas amount is constantly changed according to alimentary tract functional state. Receptor mobilization maximal level is observed on an empty stomach, it is reduced after its irritation with food. This phenomenon is known as **gastro-lingual reflex.** Gustatory receptors play the effector role in this reflex. Some dental diseases for example *glossalgia* (pain in tongue), *glossitis* (tongue inflammation) and others may appear at alimentary tract disorders. There can be taste loss and gastro-lingual reflex disorder that can be used as diagnostic criterium. Gastro-lingual reflex study in these cases help diseases aethiology assessment.

Somato-sensor analizator - system providing organism connection with environment through skin and visible mucosae.

It contains 3 types of receptors:

- tactile (mechanoreceptors);
- thermal (of warmth and coldness);
- noceoceptive (of pain).

Tactile reception. Tactile reception is an important part of somato-sensor analizator. It is represented by touching and pressure receptors. These receptors are in strong functional interconnection with mechanoreceptors and proprioreceptors. They are located in skin different regions (maximal sensitivity is on fingers endings, foot). Touching sensation or pressure can be caused indefinite points (tactile points). They are free nervous endings (Ruffini bodies, Pachini bodies et al.). Free nervous endings afferent fibres carry the information according to sensitivity type through spinal nerves, then through posterior columns fibres (Goll's and Burdach's fasciculi) to brain stem, thalamus and cortex (postcentral sulcus).

Tactile sensitivity gives the imagination about subjects shape and their surface. Multiple, freaquent irritation of them causes vibration sensation. Simultaneous several Pachini bodies involvement into reaction is the essential condition of vibration occurence in skin. Skin superficial layers local anaesthesia doesn't liquidate vibrational sensitivity and high-freaquened receptors answer reactions.

Temperature reception. Temperature analizator belongs to somato-sensor analizator too. Some sensor regions possess high sensitivity to temperature fluctuations. Temperature receptors are divided into receptors of warmth and of coldness. Coldness points amount is significantly predominant comparatively to warmth points. Their maximal accumulation is on face skin. Coldness receptors in human being are located in epidermis and directly under it and warmth receptors – primarily in derma (proper skin) superior and middle layer. Coldness receptors are connected with thin myelinized and warmth receptors – with non-myelinized fibres.

Nociceptive sensation can occur either at injured stimulus action to special "noceoceptive" receptor – nociceptor, or at superstrong irritations of other receptors. Nociceptors are 25-40 per cent of all receptors. Nociceptors both of skin and of mucosa are represented by free non-incapsulated nervous endings of different shape (hairiness, spirals, plates et al.).

Nervous fibres carrying impulses from these receptors reach spine posterior corns grey substance, where second neuron is originated from. Second neuron reaches brain columns white substance and further – thalamus from where it is projected widely into different cortical regions.

Pain analizator (noceoceptive analizator). Physicians are familiar with pain as a common symptom in people who seek medical help. They use the description of its location, quality, and time course to determine its cause and they use the reported intensity to judge the intensity of treatment. The person who is experiencing pain is obviously less objective about it. From his or her point of view, the pain complaint is a cry for help. The subjective experience includes an urge to escape from the cause or, if that it is not possible, to obtain relief. It is this overhelming desire to make it stop that gives pain its power. It can produce fear and, if it persists, depression. Ultimately, the pain sufferer may lose the will till live. People have understood this power for millenia, using painful punishment (or the fear of it) to control the behavior of others. Parents, for instance, will punish their children physically when they have done something wrong. Children learn to associate pain with actions that are disapproved of by others. Because much of our behaviour, especially in early life, is shaped by the desire to avoid pain, the psychological reaction to it can be as complex as the individual who experiences it. This complexity has been a major stumbling block for physicians trying to understand and treat pain patients, particularly those with chronic pain.

Because it is a common experience with diverse psychological consequences, there have been many definitions of pain. Webster's New Collegiate Dictionary (2-nd ed.) defines it as "a distressing feeling due to disease, bodily injury, or organic disorders". There exists such definitions more useful for clinical purposes: "pain is unpleasant sensation that is perceived as arising from a specific region of the body and is commonly produced by processes which damage or are capable of damaging bodily tissue".

It is necessary to emphasize that pain is perceived as arising from a specific place in the body in order to distinguish it from moods (e.g., sadness) or body feelings such as hunger or warmth, which may be felt as arising from the body but not necessarily a particular body region. Another reason for this refinement is that the word 'pain" is commonly used to denote emotional rather than bodily suffering ("a painful loss") and it is used metamophorically to describe irritation ("a pain in the neck"; "that person is a pain").

In most cases the sensation of pain is produced either by injury or by stimuli that are intense enough to be potentially injurious (noxious). Along with the subjective experience of pain, noxious stimuli elicit a variety of behaviours that all serve to protect uninjured tissues. Under different circumstances, tissues can be protected either by withdrawal reflexes, escape, immobilization of the injured part, or avoiding future encounters with similar damaging stimuli. Main function of pain sensory system is protective one. Some individuals can have lack of neural apparatus for noxious stimuli detection. They repeatedly injure themselves by failing to avoid high temperature, intense pressure, extreme twisting, or corrosive substances. They may be totally unaware of internal diseases that would be very painful in a normal person. On examinations they are usually found to have pressure sores, missing digits, and damaged weight-bearing joints. Loss of pain sensation can also lead to traumatic injuries in adults.

One can differentiate somatic and visceral pain. Somatic pain may be superficial (cutaneous) and deep (in muscles, bones, joints and connective tissue).

Nociceptors are divided into 2 types: mechanoreptors and chemoreceptors. Mechanoreceptors are getting excited as the result of mechanical movement of membrane that allows to sodium ions to penetrate inside and to cause nerve ending depolarization. Mechanoreceptor is located so that it provides the control of skin, epidermis, articulatory sacs, muscular surface. Excitement from the most mechanoreceptors are transmitted through "A" fibres. Chemoreceptors are located in the deeper tissular layers. They control oxidative processes level in tissues: at oxidation level reducing their self-excitement occurs. Ishemia (tissue blood supply decreasing or stoppage) independently from its reason leads to strong painful sensations development. Specific irritators for chemoreceptors are the substances released at cells injury: acethylcholine, histamine, serotonin, potassium ions, bradykinine, prostaglandines, leukotrienes, substance P. Some products of plasma, tissualr liquid may be activated while contact with side body, acid metabolic products, inflammation products and act to chemoreceptors. Prostaglandine E (is released at inflammation), blood coagulation contact factor – factor XII (Hageman's factor), plasmine, bradykinines.

Central processes are directed to medulla oblongata where they are finished on neurons of nuclear complex consisting of main sensor nucleus and spinal tract. Excitement comes from second neurons to posterior and ventral specific thalamic nuclei, from which nociceptive excitement is directed to sensor zone and medial parts of brain hemispheres orbital cortex. The result of excitements coming into central brain parts is pain sensation forming with more or less expressed behavioral, emotional and vegetative reactions directed to oral cavity tissues integrity preserving.

We would like to tell some word about referred pain. It is likely that several mechanisms contribute to referred pain. In many instances, muscular contraction, tenderness and cutaneous hyperalgesia are produced by pathology in visceral organs. In these cases it is possible that there are secondary peripheral sites of nociceptive input that account for the spread of pain. Consistent with this idea is the observation that local anaesthetic injected into the site of refferal provides significant relief. In other situations, local anaesthetic injected at the site of referral has no effect on referred pain. In these latter cases, the mislocalization of pain is clearly due to a process in the CNS because there is no nociceptor input from the site in which the pain is felt.

Reffered pain is an important phenomenon to be aware of in patients with puzzling pain problems. Pain of visceral and musculo-sceletal origin is commonly projected to a distant, unstimulated structure and this is a potential source of confusion in patients whose diagnosis in in doubt. Obviously, if the case of the pain is not within the area that hurts, the clinician may be misled when looking for objective evidence of disease. Although spatial patterns of refferal are somewhat variable from patient to patient, the spinal segmental relationship between the diseased structure and the site of pain referral provides a basis for a systematic clinical examination.

Some CNS structures perform antinociceptive functions. These are separate nuclei of medulla oblongata, midbrain, hypothalamus and big hemispheres. Besides brain structures mentioned above there exist others, cellular elements, disseminated in CNS participating in noceoceptive sensitivity control. One can say about a whole network within the CNS that can selectively inhibit pain. This network has important brainstem

components including the midbrain periaqueductal grey matter and adjacent reticular formation, which project to the spinal cord via the rostroventral medulla. This pathway inhibits spinal neurons that respond to noxious stimuli. There is also a pain-modulating pathway from the dorsoventral pons to the cord. The pathway from the rostral medulla to the cord is partly serotonineergic, whereas that from the dorsoventral pons is at least partly noradrenergic. In addition to these biogenic amine-containing neurons, endogenous opioid peptides are present in all the regions so far implicated in pain modulation. The opiod-mediated analgesia system can be activated by electrical stimulation or by opiate drugs such as morphine. It can also be activated by pain, stress and suggestion. Although by no means proven, it seems probable that this pain-modulating system contributes to the well-known variability of perceived pain in people with apparently similar injuries. Alongside with well-known opiate and serotoninergic mechanisms we should mentione dophamine-, choline- and adrenergic mechanisms switched on in noceoceptive sensitivity regulation at different CNS levels.

Pain threshold size depends on nociceptive analizator interconnection to antinociceptive system and can be modulated due to changes the activity of not only noceoceptive analizator afferent systems but also due to nociceptive system activity. Pain threshold is often changed at emotional states which in dependence on emotions type either activate antinoceptive system (aggression, fury), increasing pain threshold, or decrease its activity (fear), reducing pain threshold.

At the present time only 2 processes have definitely been associated with clinical pain syndromes: cortical epileptiform discharge, which is actually a rare cause of pain, and sympathetic efferent facilitation (or sensitization) of the peripheral therminals of primary afferents. It is not clear whether sympathetically maintained pains depend on increased or abnormal discharge in sympathetic efferents, increased sensitivity of primary afferents, a change in the central actions of afferents sensitive to sympathetic efferents, or some combination of these factors. Loss of myelinated afferent inhibition of spinal pain transmission cells contributes to clinical pain. Thus, in normal subjects, with selective blockade of peripheral nerve myelinated axons, cutaneous stimuli result in exagerrated, summating sensations that have a burning, dysesthetic quality similar to what is reported by many patients with painful injuries to peripheral nerve. On the other hand, since most patients with nerve injuries do not have spontaneous pain, it is likely that pain of nerve injury is due to a combinations of factors. For example, in causalgia, the pain may result from a combination of loss of myelinated afferent inhibition, ectopic impulse generation at the site of nerve injury, and sympathetic activation of primary afferents. In tic doloureux, and the lancinating pain associated with demyelinating disease, the sympathetic nervous system does not contribute to the pain, and ectopic impulse generation from a demyelinated patch of axon is a more likely cause of the distinctive pain pattern. With brachial plexus avulsion, the pain may be primarily due to hyperactivity of deafferented spinal pain transmission cells.

Psychologic and psychophysiologic aspect is essential in pain assessment. People experience pain freaquently. Most people accept usual pain as a normal, if unpleasant, part of life. They ignore the pain or treat themselves with over-the-counter drugs or home remedies, and go about their lives. Although there are no systematic studies of the psychological impact of common pains on the individuals who suffer from them it is likely that mild frustration, irritability, and impatience are the normal responses. Obviously, the

psychophysiological reaction will be greater when the pain is sufficient to interfere with normal activities. The telephone surve referred to above also found that functional impairment resulting from pain is very common in the general population. It is not clear why pain produces a functional impairment in some people, whereas most are able to carry on with their lives despite it. Intensity is obviously a major factor. A second important factor is the meaning of the pain to the individual. This is closely tied to location and quality. For example, chest pain in a person who has previously suffered myocardial infarction may be partially disabling because it is interpreted as life threatening. In addition, clinical observation suggest that differences in personality traits between individuals contribute to the variation to their responses to pain. Finally, there is evidence for psychological factors in the home or at work can help perpetuate pain complaints and functional impairment.

Affective responses to painful injury or disease range from annoyance to agony desperation. If a painful injury or disease occurs in a person who has psychophysiological problems, the degree of suffering is likely to be out of proportion to the severity of the somatic pain. Some common symptoms in patients with chronic (persistent) pain are the following: depressed mood, sleep disturbance, somatic preoccupation, reduced activity, reduced libido, fatigue. Thus, a major task for the clinicians dealing with pain patients especially those with chronic pain is to assess the contribution of psychological and somatic factors. Unfortunately, there is always a degree of uncertainity about such assessments because there is no way to objectively measure how intense a person's pain actually is.

The problem of assessment is also compounded by the fact that patients are often unaware of or reluctant to discuss the most relevant psychological issues. A mild somatic pain may be emphasized by a depressed or anxious patient because it is more socially acceptable to seek medical than psychiatric help. Thus, the of help sought by the patient is often inappropriate to his or her significant problem. Individuals complainting of chronic pain freaquently deny that they have any problems unrelated to their pain and resist psychiatric evaluation. Unfortunately, for many such patients approaches that ignore the psychological factors are not likely to produce any long-term benefit. Clearly, the adequate assessment and treatment of patients with persistent pain demands attention to both somatic and psychological factors. Other aspect: one more problem confronting the clinician is how to deal with a patient who complaints a somatic pain but has no obvious somatic cause for it. It is likely that many such patients actually do have a somatic cause for their pain but physicians lack the tools to demonstrate it. On other hands, a variety of psychiatric syndroms and psychological mechanisms may also contribute to the problem. It is doubtly that there are distinctly different approaches to the study and analysis of the psychology of chronic pain patients.

All mentioned underlies essential importance of nociceptive and antinociceptive system physiology and psychophysiology knowledge to doctor of any speciality.

Auditory analizator.

Ear is the organ of hearing. Ear can be divided on 3 parts:

1. external ear:

- auricle - collects sound waves;
- external auditory meatus: conducts sound waves from auricle to tympanic membrane;

2. middle ear (tympanic cavity):

- tympanic membrane: forms lateral wall of tympanic cavity; circular and concave from outside; point of maximum concavity is called umbo, where handle of malleus is attached;
- contents: air, auditory ossicles, tensor, tympani muscle and stapedius muscle;
- windows: there are 2 windows in medial wall to tympanic cavity, round window and oval window.

3. internal ear:

- cochlea;
- vestibular apparatus.

Auditory ossicles:

- malleus;
- incus;
- stapes.

Arrangements:

- handle of malleus is attached to umbo of tympanic membrane;
- other end of malleus is bound to incus by ligaments;
- opposite end of incus articulates with stem of stapes;
- foot plate of stapes lies against membraneous labyrinth in oval window, where sound waves are conducted into cochlea.

Functions:

Auditory ossicles increase pressure exerted by sound waves on fluid of cochlea. Thus, provide impedance matching between sound waves in air and sound vibrations in fluid of cochlea.

Muscles of ossicles:

1. Tensor tympani - pulls handle of malleus inward, thus, keeps tympanic membrane tenses.
2. Stapedius – pulls stapes out from oval window.

Eustachial tube – is a tube connecting middle ear cavity with pharynx.

Function: equilizes pressure on either side of tympanic membrane.

Hearing – is the sense by which sounds are perceived.

Sound **-** is effect produced on organ of hearing by vibrations of air molecules. Sound doesn't travel through vacuum. The unit of sound intensity is decibel.

Noise – is a disturbing sound.

How sound is heard

Ear receives sound waves, discriminates their freaquencies, and finally transmits auditory information onto the central nervous system where its meaning is deciphered.

Conduction of sound from the tympanic membrane to the cochlea

Tympanic membrane and the ossicular system, which conducts sound through the middle ear. The tympanic membrane is cone-shaped, with its concavity facing downward and outward toward the auditory channel. Attached to the very center of the tympanic membrane is the handle of the malleus. And its other end the malleus is tightly bound to the incus by ligaments so that whenever the malleus moves the incus moves with it. The opposite end of the incus in turn articulates with the stem of the stapes, and the footplate of

the stapes lies against the membranous labyrinth in the opening of the oval window where sound waves are conducted into the inner ear, the cochlea.

The ossicles of the middle ear are suspended by ligaments in such a way that the combined malleus and incus act as a single lever having its fulcrum approximately at the border of the tympanic membrane. The large head of the malleus, which is on the opposite side of the fulcrum from the handle, almost exactly balances the other end of the lever. The articulation of the incus with the stapes causes the stapes to push forward on the cochlea fluid every time the handle of the malleus moves inward and to pull backward on the fluid every time the malleus moves outward, which promotes inward and outward motion of the footplate at the oval window.

The handle of the malleus is constantly pulled inward by the tensor tympani muscle, which keeps the tympanic membrane tensed. This allows sound vibrations on any portion of the tympanic membrane to be transmitted to the malleus, which would not be true if the membrane were lax.

Cochlea is a system of coiled tubes.

It consists of:

1. Three tubes:
- scala vestibuli;
- scala media;
- scala tympani.
2. Two membranes:
- Reissner's (vestibular) membrane: separates scala vestibuli and scala media.
- Basilar membrane: separates scala media and scala tympani.

Organ of Corti

It lies on surface of basilar membrane. It contains mechanically-sensitive hair cells which are receptive end-organs and generate nerve impulses in response to sound vibrations.

Fluid present in cochlea:

- Perilymph: present in scala vestibuli and scala tympani. It is almost identical to cerebro-spinal fluid (liquor).
- Endolymph- present in scala media.

The basilar membrane and resonance in the cochlea

The basilar membrane is a fibrous membrane that separates the scala media and the scala tympani. It contains 20000-30000 basilar fibres that project from the bony center of the cochlea. The modiolus, toward the outer wall. These fibers are stiff, elastic, reed-like structures that are fixed at their basal ends in the central part of the cochlea (the modiolus) but not fixed at their distal ends except that the distal ends are embedded in the loose basilar mebrane. Because the fibers are stiff and also free at one end, they can vibrate like reeds of a harmonica. The length of the basilar fibers increases progressively as one goes from the base of the cochlea to its apex. The diameters of the fibers, on the other hand, decrease from the base to the helicotrema so that their overall stiffness decreases more than 100-fold. As a result, the stiff, short fibers near the oval window of the oval window

of the cochlea will vibrate at a high freaquency, whereas the long, limber fibers near the tip of the cochlea will vibrate at a low freaquency.

Thus, high freaquency resonance of the basilar membrane occurs near the base, where the sound waves enter the cochlea through the oval window and low freaquency resonance occurs near the apex mainly because of difference in stiffness of the fibers but also because of increasing "loading" of the basilar membrane with extra amounts of fluid that must vibrate with membrane at the apex.

Transmission of sound waves in the cochlea - the "travelling waves"

If the foot of the stapes moves inward instantaneously, the round window must also bulge outward instantaneously because the cochlea is bounded on the sides by bony walls. Therefore, the initial effect is to cause the basilar membrane at the very base of the cochlea to bulge in the direction of the found window. However, the elastic tension that is built up in the basilar fibers as they bend toward the round window initiates a wave that "travels" along the basilar membrane toward the helicotrema.

Corti organ functions

This organ is the receptor organ that generates nerve impulses in response to vibration of the basilar membrane. Note that it lies on the surface of the basilar fibers and basilar membrane. The actual sensory receptors are 2 types of hair cells, a single row of internal hair cells and 3-4 rows of external hair cells. The bases and sizes of the hair cells synapse with a network of cochlear nerve endings. These lead to the spiral ganglion of Corti, which lies in the modiolus (the center) of the cochlea. The spiral ganglion in turn sends axons into the cochlear nerve and hence into the CNS at the level of the upper medulla.

The auditory pathway

Nerve fibers from the spiral ganglion of Corti enter the dorsal and ventral cochlear nucleus located in the upper part of the medulla. At this point, all the fibers synapse, and second-order neurons pass mainly to the opposite side of the brain stem through the trapezoid to the superior olivary nucleus. However, some second order neurons also pass ipsilaterally to the superior olivary nucleus on the same side. From the superior olivary nucleus the auditory pathway then passes upward through the lateral lemniscus; and some, but not all, of the fibers terminate in the nucleus of the lateral lemniscus. Many bypass this nucleus and pass on the inferior coliculus where either all or almost all of them terminate. From here, the pathway passes to the medial geniculate nucleus, where all the fibers gain synapse. And, finally, the auditory pathway proceeds by way of the auditory radiation to the auditory cortex, located mainly in the superior gyrus of the temporal lobe.

There are 3 crossing of auditory ways:

- at superior oliva level – less fibres part is remained in the limit of hemisphere on the side of which perypheral auditory is located; larger part comes in opposite hemisphere into midbrain; at trapezoid bodies level is partial crossing too; small parts of direct, uncrossing, fibres come from here (trapezoid bodies and superior oliva) to midbrain;
- at midbrain quadrigemina bodies – some fibres are crossed, another part – directly go to the nearest subcortical auditory centers – medial geniculate bodies;
- at cortical level – fibres come here from geniculate bodies.

Humans have binaural interaction or binaural hearing.

Visual analizator

Vision organ is eye.

Eyeball levels:

- fibrous layer;
- vascular pigmented layer;
- retina.

Fibrous layer:

- sclera: posterior $5/6^{th}$ opaque part – it protects eyeball;
- cornea: anterior $1/6^{th}$ transparent part - it allows light to enter eyeball.

Vascular pigmented layer:

- chroroid: made up of outer pigmented and inner vascular layers;
- ciliary body: made up of ciliary ring, ciliary processes and ciliary muscle;
- iris: it is a contractile and pigmented diaphragm with central aperture, i.e. pupil – it controls size of pupil.

Retina

It is the light sensitive area of the eye.

Eyeball content:

1. Aqueous humour – it is a clear watery fluid that fills anterior and posterior chambers (both in front of lens). Secreted by ciliary processes.
   Functions:
- maintains intra-ocular pressure;
- maintains eyeball shape;
- it acts as refractory medium;
- it supplies nutrition;
- it drains metabolic end-products.

2. Crystalline lens – it is a transparent, elastic and biconvex lens.
   Function:
- It refracts light and focuses it exactly on retina.

3. Vitreous Body- it is a transparent gel enclosed by vitreous membrane. It fills eyeball behind lens.
   Functions:
- contributes to magnifying power of lens;
- supports posterior surface of lens;
- assists in holding neutral part of retina against pigmented part of retina.

Anterior and posterior chambers of eye

1. Anterior - space between cornea and iris.
2. Posterior- space between iris and lens.

Both chambers are filled with aqueous liquor.

Lens refractive power – lens ability to bend right rays. The more a lens bends light rays, the greater is its refractive power. This refractive power is measured in terms of diopter. Refractive power of eye lens – 15 diopters.

Image formation on the retina

In exactly the same manner that a glass lens can focus an image on a sheet of paper, the lens system of an eye can focus an image on the retina. The image is inverted and reversed with respect to the object. However, the mind perceives objects in the upright position despite the upside-down orientation on the retina because the brain is trained to consider an inverted image as the normal.

Accomodation – is eye lens adjustment for various distances.

Parasympathetic control of accomodation – the ciliary muscle is controlled almost entirely by the parasympathetic nervous system. Stimulation of the PNS contracts the ciliary muscle which relaxes the lens ligaments and increases the refractive power. With an increased refractive power the eye is capable for focusing an object nearer at hand than when the eye has less refractive power. Consequently, as a distant object moves toward the eye, the number of parasympathetic impulses on the ciliary muscle must be progressively increased for the eye to keep the object constanly in focus.

Sympathetic control. Sympathetic stimulation has a weak effect in relaxing the ciliary muscle, but this plays almost the role in the normal accomodation mechanism.

Visual acuity – is ability of human eye to discriminate between point sources of light. Normal clinical value: 20/20, that is, test chart is at 20 feet and person can see those letters clearly which he should normally be able to see at 20 feet.

Retina – is the light-sensitive portion of the eye, containing the cones, which are responsible for colour vision, and the rods, which are mainly responsible for vision in the dark. When the rods and cones are excited, signals are transmitted through successive neurons in the retina itself and finally into the optic nerve fibers and cerebral cortex.

Functions:

1. Vision – due to rods and cones presence, retina is responsible for photopic and scotopic vision.
2. Reflexes –concerned with light and accomodation reflexes.
3. Tone, posture and equillibrium.

Retinal impulses help to maintain tone, posture and equillibrium.

Rods and cones are photoreceptors.

Functions:

1. Rods are responsible for dark vision.
2. Cones are responsible for colour vision or daytime vision.

Photochemicals – these are light-sensitive chemicals that decompose on exposure to light and excite nerve fibers leading from eye.

1. Rhodopsin- photochemical present in rods. Composed of scotopsin plus 11-cis-retinal.
2. Iodopsin – photochemical present in cones. Composed of photopsin plus 11-cis-retinal.

Photopic vision – colour-vision or day light vision is called photopic vision.

Scotopic vision – night vision (or black and white vision).

When a person is in dark, scotopsin combines with 11-cis-retinal (derived from vitamine A) and forms rhodopsin that causes depolarization of sensory receptors which in turn excites optic nerve so the person is able to see in dark.

As soon as person comes in the light the rhodopsin splits into scotopsin and all-transretinal causing hyperpolarization which causes decreased excitation of optic nerve.

Protanopia (red blindness) – is observed due to missing of red cones.

Deuteranopia (green blindness)- due to green cones missing.

Tritanopia (due to blue cones missing).

The visual pathways

Are the pathways from the retinae to the visual cortex. After nerve impulses leave the retinae thay pass backward through the optic nerves. At the optic chiasma all the firbers of the retinae cross to the opposite side, where they join the fibers from the opposite temporal retinae to form the optic tracts. The fibers of each optic tract synapse in the dorsal lateral geniculate nucleus, and from here the geniculo calcarine fibers pass by way of the optic radiation, or geniculo-calcarine tract, to the primary visual cortex in the calcarine area of occipital lobe.

Olfactory (smell) analizator

It is a sensory modality mediated by chemoreceptors of olfactory mucosa.

Primary sensations of smell:

1. Camphoraceous.
2. Ethereal.
3. Floral.
4. Musky.
5. Pepperminty.
6. Pungent.
7. Putrid.

Olfactory membrane or mucosa lies in superior part of each nostril. Medially it folds downwards over surface of septum and laterally it folds over superior turbinate.

Olfactory cells:

1. These are receptor cells for smell sensation.
2. Mucosal end of each olfactory cell forms a knob from which 6-12 olfactory hairs or cilia project into mucus that coats inner surface of nasal cavity.
3. Cilia react to odors in air and stimulate olfactory nerve.
4. Glands of Bowman are also present among olfactory cells. They secrete mucus.

Odorants (smell-producing substances) have 3 characteristics:

1. Substance must be volatile - so that it can be sniffed into the nostrils.
2. Substance must be water soluble - so that it can pass through mucus to olfactory cells.
3. Substance must be lipid soluble – so that it can penetrate lipid bilayer of olfactory cells to stimulate them.

Olfactory adaptation – olfactory sensation decreases very rapidly with continual exposure to an odorant. Nerve fibers from olfactory region of brain pass backward along olfactory tract of inhibitory granule cells of olfactory bulb, which causes olfactory adaptation.

2 main theories of smell:

1. *Physical theory* – according to this theory, physical shapes of odorant molecules determine which olfactory cell will be stimulated.

2. *Chemical theory* – odorant molecules bind chemically to specific protein receptors in membrane of olfactory cilia and increase permeability of olfactory ciliary membrane so, receptor potential in olfactory cells is excited and action potential (impulse) is produced in olfactory nerve fiber. So, main factor is stereochemistry of smell substances. This is space accordance of smell substances to receptor locuses shape on surface membrane of olfactory microvilli.

Olfactory cells are primary sensor cells. They send axones into brain from their basal pole. These fibers forme thick fibers (olfactory fibers) under sensor epithelium coming to olfactory bulb. There occurs primary processing of sensor information. Bulb generates rhythmic potentials. Axones of cells compose olfactory tract directly or indirectly transmitting olfactory sygnals into many braci regions particularly into olfactory bulb of opposite side in structures located into subcortical structures of anterior brain, limbic brain, hypothalamus.

Lecture 8
Organism integrative activity and behavioral physiological bases (the higher nervous activity, behavioral congenital and acquired forms, memory, thinking and speech).

Human behaviour includes 2 reactions types:

1. *genotypic* – it is based on genetic proggramme;
2. *phenotypic* – it is linked with genotype, environmental conditions interactions or it may be individually aquired, based on study.

Hereditary behaviour forms

These are unconditioned reflexes, individual and of species, stereotypic organism reactions to external and internal stimuli performed by CNS. Main distinguishing feature of such reflexes – they determine reflexes expressed without preliminary study. For example, stomach juice releasing at food coming into oral cavity, hand taking off at noceoceptive irritation, winking while air coming into one's eye. Try to check them up in new-borns and you'll see that they are performed without any study.

Unconditioned reflexes – are instincts; they are fundamental phenomenon in highest nervous activity forming. One can differentiate 3 types of them:

1. Vital – they provide individual and species organism preserving:
   - alimentary;
   - drinking;
   - dream;
   - defence et al.

They are directed to organism forces economy; their disorders lead to individual's physical death.

2. Zoo-social – they may be realized only by interconnection with other individuals of the same species:
   - sexual;
   - paternal;

- territorial;
- of groups et al.

3. Reflexes of self-development – they are oriented to new spatial-temporary environments discovery; addressed to future:

- investigations;
- reflex of freedom;
- plays;
- mimicry et al.

Instincts organization

It is rather complicated. External (key) stimuli are triggers in their realizing. Every stimule switches stereotypic reactions on as a rule consequent motor acts the result of which is any reaction performance. One can differentiate 2 categories of brain reflectory processes:

- Of preparation – triggering, motivational. Their activity are connected with less specific reactions and is controlled by organism internal needs in more extent. Motivational reflexes are also called drive-reflexes (from "drive"-"motive"). They are hunger, thirst, fear, fury. Their main peculiarity is motor activity general mobilization.
- Efferent – are linked with multiple specific reactions onto stimuli.

Each unconditioned reflex is characterized by definite behaviour. For example, hunger reaction initiates food-getting reactions expressing in motor anxiety and sensor systems activation. Ending phase of food-getting behaviour is efferent reflex – mastication and swallowing. Efferent reflex triggering (alimentary one in this case) is realized with participation of sensor (olfactory, gustatory) reception, emotional-motivational aspect is important for this. Food itself as unconditioned stimulus causes congenital emotinal reaction – gustatory and olfactory receptors excitement.

Unconditioned reflexes are congenital, species, relatively constant, reactions occuring as an answer to definite receptive field irritation. Brain stem and subcortical structures are essential for their realizing. They are remained after cortex removal although naturally they are realized at its participation under norma too.

Acquired behavioural forms

This is individual experience aquirement due to environment variation. Associative or conditioned experience aquirement takes special place among these behavioural forms. *Conditioned reflexes* are formed at definite conditions of organism onthogenesis and are disappeared at their absence comparatively to unconditioned reflexes.

The earliest form of new-borns adaptation are natural conditioned reflexes onto feeding time and onto food as sucking movements. Artificial conditioned reflexes begin their formation later than natural.

Acquired reactions constant chage occurs in course of life. One conditioned reflexes are fixated, others disappear quickly and then after several time are restored. It is connected with conditioned reflexes inhibiting appearence or working out.

One can differentiate ***conditioned reflexes inhibiting 2 main types:***

- *External* – unconditioned.
- *Internal* – conditioned.

External inhibiting – appears and that's why it is congenital. It appears when in course of conditioned stimulus action onto organism other stimulus acts onto organism

(external). It may be very strong (car signal while crossing the street) or weak (rain drops or train wheels thud). These stimuli come at definite stage out off limits of their possible perception with corresponding nervous structures and inhibiting occurs due to this. Such inhibition is often called out-limited. External inhibition is also indicated as such inhibition when unusual stimulus action. For instance, someone comes in lecture hall (rector, dean), orientive reaction appears first, then – conditioned reaction inhibiting (in this case such conditioned reaction is the lecture writing) and this reaction stoppes during the stimulus action.

Uncondioned external inhibiting is expressed in children from the early beginning of conditioned reflectory activity.

Internal inhibiting – is aquired one and it has different forms of expression.

1. Extinctive – is produced after conditioned stimulus support cancellation (baby has salivation to mother breast, but after cancellation out off mother's breast this reflex disappears because it becomes useless).
2. Differentiated - it encourages the differentiation of signals similar by nature. For example, sounds differentiation in course of lection delivering. There are different sounds during this time – lecturer voice, knocking on doors in corridor, peoples' steps, transport sounds et al. But, we hope, you have answer reaction to essential sounds in this moment - lecture's voice. Thus, differentiated inhibiting produces to other sounds. Significance of this inhibition forme: we perform analysis of surrounding world due to it.
3. Delaying – is formed under the situation when conditioned stimulus goes before support and the latest one is late. Example. You set your alarm clock to the definite time for getting up. It is ringing in the morning. You hear it but don't react to it, i.e. don't get up and do it only at unconditioned stimulus action (parents or friends voice, your blanket is taken out off you).

Conditioned inhibiting (delaying and differentiating) appears in 2,5-3,0 months in children.

Thus, all inhibiting types, mentioned above, stop conditioned reflexes. Conditioned reflexes are formed not only by cortex but also by subcortical structures. Inhibiting is also formed by cortex but it appears in subcortex. Mosaic of exciting and inhibiting in CNS, codtioned and unconditioned reflexes, having been fixated in definite consequence – this is the base of one or other behavioural act.

Memory - is one of basic CNS features. Memory is responsible not only for information fixating, its keeping but also it includes mechanisms of its retention and reproduction. Memory is tightly connected with study. Study provides constant knowledge addition, new experience aquiering. Memory and study – are 2 sides of one and the same process. They have one common feature: necessity in information repeating (it is not occasionally to hear that repeating is study mother). Memory may be *genotypical* (congenital) - it is responsible for unconditioned reflexes, instincts formation. *Phenotypical* memory – is processing and preserving of information aquired in course of individual onthogenesis.

Human being has at least 3 types of sensory memory:

- *iconic (instant)*- supports exact and complete picture, percepted by eyes in course of 0,1-0,5 sec. Similar memory percepted by ears is often called as *eichoric* memory. It may transform into
- *Short-termed* or *working* memory that realizes current behavioural and thinking performance in course of seconds, minutes after phenomenon and subject action. It is significant for information selection ("morning is wiser than evening"). It is disturbed in course of ageing.
- *Long-termed* – keeps big informational volume. All that is kept in our memory more than 1 minute is transformed in long-termed memory system in course of so-called consolidation (nore often - during dream) where it is kept in course of hours, days, years, sometimes- in course of all individual's life.

Memory physiological mechanisms

Retention and reproduction memory mechanisms are not yet clear. But fixating mechanisms are explained by some theories. One group of theories consider that memory has cellular-molecular base. There also exist data that imaging fixation is based on stable changes of synaptic transmission. Initial information is kept due to structural synaptic changes. Further, after these synapses activation memory content may be reproduced. That's why memory depends on such main factors of synaptic transmission as mediators – acetylcholine, noradrenaline, serotonine; neuromediators - cAMP, cGMP and row of metabolites.

There also exists other theories group based on informational molecules participation (macromolecules – proteins, nucleic acids). We have great number of factors proving that study and memory are linked with aquired behavioural forms encoding in informational macromolecules (RNA, neuropeptides).

Scientists also propose immunochemical memory way based on possibility of formation substances playing the role of antigene for antibody in course of memory developmemt.

Other memory classification according to reasons underlying its development:

- *imagionational* – keeping in memory and reproduction of one percepted vital subject;
- *sensory-imagionational* - it operates representatives connected mainly with activity of one or other analizator- visual, auditory, gustatory, olfactory (the strongest among them), motor memory;
- *emotional* - the strongest among all memory types - reproduction of emotional state experienced before at stimulus new (repeated) action;
- *verbal-logic* - memory on verbal sygnals indicating objects or one or other events;
- *logic-verbal* – operates terms, concepts (is the highest memory type).

In course of receiving knowledge you must use all memory types. Besides, you know that people are divided into several groups according to their predominant memory: audials (ones with predominant auditory memory), visuals (visual one), kynaesthetics (cynaesthetics) which need in touching, delicious food, increased amount of sex, i.e. have enforced skin sensitivity (so have sominant emotional memory) and so on. As psychologists and physiologists tell it's better that both husband and wife belong to 1 group.

Naturally, that it's impossible to remember everything. Is it good or bad? ***Forgetting*** process – is a natural physiologic reaction. We can't keep in our memory all

information we ever delt in our everyday life. There are 2 reasons of this. First, forgetting is a passive inhibiting or steps weakening with time. It is developed by extinctive inhibition way: repeating is absent, necessity in information is absent and it is naturally extincts. Second, it is also active process: new information comes despite old one. Such phenomemon is called interpherence. The more we recognize new, the less old information is in our brain. It doesn't mean that old information is not necessary. No, it is simply used to the construction of new one and it is changed by it at a new level. It also occurs under biologically active substances influence in human organism. Endorphines and encephalines, vasopressine improve memory, decrease conditioned reflexes extinction, but oxytocine disturbs long-termed memory particularly aquired skills.

Thus, memory and study need in repeating. Recognizing way - through repeating. Speech and thinking are essential for memory and study development.

Thinking and speech **-** are the complicated types of nervous activity. *Thinking*- is any phenomena and subjects common features reflection in human consciousness as well as connections between them. One can differentiate several stages in course of human thinking (they have different expression in different people):

- analysis- differentiation of similar stimuli; it is originated from receptors; differentiated inhibition is under its base; simple analysis (single stimuli differentiation) is a characteristics of animals; simple analysis has more significant development in animals in comparison to human beings (sounds, smells differentiation and so on); both simple and complicated analysis are features of human being; complicated analysis is information differentiating in course of irritators combines action;
- synthesis – stimuli uniting, the example of which is conditioned reflexes of the highest orders; animals have simple synthesis - they can develop conditioned reflexes of only 2^{nd} -4^{th} orders; human beings- complicated synthesis- they can develop conditioned reflexes till 10^{th} or even more orders;
- comparison- search of similarity and differentiation features in subjects and phenomena; everything is recognized in course of comparison;
- summarizing – subjects and phenomena common features uniting as a result of which we can have new regularity occurence;
- classification- facts distribution on groups, subgroups, phases, classes (for instance, disease course - on stages).

Speech is essential for thinking formation. Word is a powerful social stimulus. It names different subjects and phenomena of surrounding world. Thus, human being has not only *first sygnal system* (stimuli action to sensor entrances through sense organs - food smell and its search) like animals but also *second sygnal system* (word, signifying influence). Though word is a real physical stimulus (auditory) it significantly differs because concepts about subjects and phenomena are reflected in it.

Human nervous system integrative activity is realized not only on the basis of direct sensations and impressions (*concrete thinking)* but also by operating with words, where word represents thinking and human intellectual abilities and functions. World picture becomes more perfect, more summarized, more differentiated due to word (*abstract thinking).* It is expressed in human being when he can abstract terms out off concrete reality.

Thus, thinking is a speech in its essence but speech without sounds, it is the expression of speech mechanism, writing activity, in deaf-and-dumb – of gestures mechanism.

Verbal stimuli understanding is linked with the functions of dominant speech hemisphere – left - it mainly participates in analytic processes, it is the base for logic thinking, it determines speech activity, its understanding, work consctruction with verbal stimuli. Right hemisphere also has speech functions. It allows concrete-imagional thinking, it deals with non-verbal material, musical abilities are linked with it. Left hemisphere dominates right one in its ability to understand speech. Speech fucntions in right-handed people are mainly located in left hemisphere and only in 5% of them – in right one. In 70% of left-handed speech center is located in left hemisphere like in right-handed and in 15% of left-handed speech center is situated in right hemisphere.

Thinking and speech are important constituents characterizing human mind. Mind variation is its criterium.

What makes one person more intelligent than another? What makes one person a genius, like the brilliant Albert Einstein, and another person a fool? Are people born intelligent or stupid, or is intelligence the result of where and how you live? These are very old questions and the answers to them are still not clear.

We know, however, that jusy being born with a good mind is not enough. In some ways, the mind is like a leg or an arm muscle. It needs exercise. Mental exercise is particularly important for young children. Many child psychologists think that parents should play with their children more often and give them problems to think about. The children are then more likely to grow up bright and intelligent. If, on the other hand, children are left alone a great deal with nothing to do, they are more likely to become dull and unintelligent.

Parents should also be careful what they say to young children. According to some psychologists, if parents are always telling a child that he or she is fool or an idiot, then the child is more likely to keep doing silly and foolish things. So, it is probably better for parents to say very positive things to their children, such as “That was a very clever thing you did” or “you are such a smart child”.

Thought is material. It’s a very big power! It may be positive or negative. Human being must be kind and generous in his imaginations. Bad, negative, depressed thoughs, thoughts directed onto unhappiness encourage this unhappiness. Destructive thoughts are worse. Unfortunately, the media, especially television is very often the source of negative information that doesn’t do people happy but causes opposite reaction. Negative thoughts themselves - are main sources of our diseases in more extent than action of all microbes and viruses taken together. Think with positive categories! This is one of the most important ways of health support!!!

Lecture 9.
Human higher nervous activity peculiarities (emotions, motivations, the highest nervous activity types)

External and internal stimuli may cause such reactions that initiate one or other behaviour and reflect organism needs expression. Such behaviour is called motivational.

Motivation is a purposeful behaviour. ***Aim*** is main motivation link. There are many aims in our everyday life. They may be constant, repeated or changeable. One can tells about 2 main aims types:

- The nearest- isntant satisfaction (tasty food). They don't need in durable preparing, activity and award are simultaneous at them. But they are not durable.
- Farther – they are directed (consciously or unconsciously) to love achievement of people close to us. They are achieved by hard work and are accumulated in course of a whole life.

Conscious aims:

- admiration for the strong (God, Allach, king,country, town, parents, spouse, children);
- to be strong (glory, power, applause of mass, award et al.);
- to present joy (desire to help to others unselfishely);
- to receive joy (it is reached at satisfaction of your deed).

Neither the nearest nor farther aims are not the real ending goal. Ending goal – to open yourself in all aspects of your life; to express yourself and to reach the feeling of confidence and security. One should strive for the highest skill because it receives respect, disposition and love (not only of your relatives but other people).

Hypothalamus, amygdala and cortex are responsible for motivational behavour. Biochemical base of motivation forming are biologically and physiologically active substances: neuromediators (acetylcholine, noradrenaline, serotonin, dophamine and others), hormones (catecholamines, vasopressine et al.) and neuropeptides (angiotensine, morphine and others). Emotions have a significant place in motivational structure.

Emotions **-** is a language of feelings inherent both in animals and human beings. Emotional may be expressed by their internal (subjective) signs:

- joy;
- grief;
- admiration;
- disgust;
- hatred;
- love et al.

And external (objective) signs:

- mimic;
- gestures;
- voice reactions;
- vegetative reactions.

Some interesting information about gesture.

Although we are not normally aware of it, most of us use our hands when we are talking. You can see this by turning down the sound of your TV set. Notice how much the speakers use hands as they talk. Our hands can show the shape and size of things (try describing a spiral staircase without your hands usage!) and emphasize what we are saying. Some gestures, though have special meanings; what do these people seem to be saying?

These gestures are not made naturally: we have to learn them and they vary from one country to another. For example, how do you call someone to you? In Spain and many

other countries you beckon someone with your palm down, which can look like the English sign for sending someone away. In Italy wave goodbye with the back of your hand which can look like the English sign for beckoning someone!

What do you mean when you nod or shake your head? Nodding seems to be one of the few gestures found in nearly every country; it seems to mean "yes" almost everywhere but in some parts of India shaking the head also means "yes". In Greece and Southern Italy and many other parts of the world, throwing the head back which can look like a nod, means "no".

When you see your friends, how do you greet them? People in many countries find the English cold and unfriendly because they often do no more than say "hello". Even adults shake hands usually only the first time they meet. French people, including schoolchildren, shake hands with their friends or kiss them on bolth cheeks if they are close friends, each time they meet and when they leave one another. At home they do not go to bad without kissing everyone in the family good night on both cheeks, and shaking hands with any visitors. The same thing happens in the morning. How do you think a French child might feel staying in your family?

Other countries have different ways of greeting. The Eskimos rub noses. In Samoa people sniff one another and in Polynesia you take hold of your friend's hands and use them to stroke your face. In Tibet it is very polite to stick your tongue out at someone; you are saying "there is no evil thought on my tongue"!

In some parts of East Africa it is considered very unlucky to point with your fingers and so people turn their heads and pout their lips in the directions they mean. In Britain some people "cross their fingers" for good luck but in Austria and Germany they hold their thumbs. In Britain if the people in an audience do not like a performer and if they are not very polite thay may clap their hands slowly to "go away"! In other parts of Europe the slow hand clap is a great compliment! In Britain people may stand up as a sign of respect. In some other countries they sit down to show that they look up to the person.

There are many other signs used in different countries, and what is an insult in one country may not be understood or may have quite a different meaning in another. The English do not use gesture as much as many other people and it is very easy for misunderstandings to arise.

The head toss

One of the common body gestures is the head toss. This is when the head is tossed quickly upwards and backwards and then it is lowered again more slowly. The eyebrows, the line of hairs above the eyes, are usually raised and often the eyes are rolled back. Sometimes the eyes are closed. The person may make a soft noise with their tongue which we call a "click". However, the head toss does not mean the same in every country. Most people use it to mean No. Researchers asked 1200 people in 40 places whether they used the "head toss". 584 said they did not use this gesture, 302 people said they used it and it mean No. 314 people used it for seven other different meanings. This means that the "head toss" is often misunderstood. So when we are talking with people from other cultures we must learn to interpret their body gestures correctly.

There are polarities between emotions (positive and negative). One can say that alive organisms have positive and negative emotions.

Positive emotions (main):

- pleasure;

- joy;
- interest;
- agiotage et al.

Main negative emotions:

- distress-grief;
- misfortune;
- disgust;
- wrath-fury;
- disregard-contempt;
- surprising-fright;
- shame-shyness-humiliation;
- fear-horror.

But you should remember that positive emotions have negative aspects (joy, enjoyment without any measure - is an unhappiness). At the same time some negative emotions have positive aspects. For example, grief unites people, fear or wrath mobilize our spirit and our forces. Positive part of all negative emotions is named as sthenic, and really negative – asthenic.

Now some words about ***fear***. "Are you a man or a mouse?" When people ask this question they want to know if you think you are a brave person or a coward. But will never really know the answer to that question untill you are tested in real life. Some people think they are brave, but when they come face to face with real danger, they act like cowards. Other people think of themselves as cowardly, but when they meet danger, act like heroes.

When you are in a very dangerous situation and feel afraid, the body automatically produces a chemical in the blood. This chemical is called adrenaline. With adrenaline in the blood system, you actually feel stronger and are ready to fight or run away. However, when you are absolutely terrified, the body can produce too much adrenaline. When this happens, the muscles become very hard and you find that you cannot move at all. You are then paralysed with fear. That is why, when we are very frightened, we sometimes say that we are "petrified". This word comes from the Greek word "petros" which means "stone". We are so frightened we have become like stone.

Stress and anger

Every day you read in newspapers, books and magazines that it is important to avoid stress. Stress can kill, they say. Stay calm. Be relaxed. Slow down. Don't worry so much and don't work so hard. Unfortunately, this is difficult. There are always many problems in our everyday life. Our cities are full of traffic and noise. Stressful situations seem to be everywhere.

When people are under stress they react in different ways. Signs of stress you can quickly recognize include poor sleep, over-eating or drinking, repetitive mannerism like nail-biting or pencil-tapping. Some people find it difficult to stay calm and often become tense. Little things, like a baby crying, can make them irritated. They get very annoyed if they have to wait just a few minutes too long – in a shop, stop or restaurant. These people are usually very moody. One minute they are fine and the next they can be really angry-absolutely furious. Other people seem to stay calm almost all the time, and rarely get angry. For example, if they are caught in bad traffic, they don't get frustrated. They sit

calmly in their cars, telling themselves that there is nothing they can do about the situation. These people are not moody at all. They don't change from moment to moment, but always seem to be in control of their emotions.

Some doctors give names to these 2 personality types. Type A people and type B people. Type A people work very hard, worry a lot and are often bad-tempered. Type B people are the opposite. They don't worry. Work is not so important to them and they don't get angry easily. They like to relax a lot and have fun. These doctors say it is better for your health and your heart if you are a type B person.

Stress can be alleviated by mental discipline, conscious relaxation and the right kind of food. First of all, it's necessary to try to get rid of the feeling of worry that often make us tense. Before going to bed, aid to empty your mind of worries. Take paper and pencil and dreg them out into the open, writing down every nag in your mind. Having written them down, study them carefully. Can you do anything about this one, for example? No? Then take your pencil and strike it out. The very act of putting your pencil through it will get it off your mind. This worries now? You can do something about that!

Well, write down just what you can do and resolve to do it on such and such a date. Do this every night, clearing your mind of worried feelings and watch your stress symptoms disappear.

Stress stages:

- adaptive – it increases organism internal reserves and we can perform one kind of work;
- sthenic negative- with tension growth in course of activity all organism reserves are used and "vegetative storm" occurs – blood pressure and heart beats increasing, fury et al.
- asthenic negative- energetic and intellectual abilities are inhibited leading to fear, horror, boredom, anguish;
- neurosis- highest nervous activity disruption and diseases possible development.

How to be at emotional tension development and not to lead youself to the 3rd and moreover to its 4th stage? The best discharging – physical loading, communication with interesting people, sometimes – falling in love.

"Emotional" brain:

- reticular formation;
- hypothalamus;
- limbic system;
- cortex.

One can tell about emotional hemispheres asymmetry. Temporary left hemisphere switching off (in everyday life and in clinics) is accompanied by movement towards negative emotions (bad mood, pessimism); right one – good mood, irresponsibility, complacency, carelessness. Thus, right hemisphere is responsible for negative emotions, left one – for positive. Interhemispherical interrelations are usually disturbed at shizophrenia, maniac-depressive psychosis, brain traumas. There exists so-called lateral therapy which allows to release suffering of such patients by selective switching injured hemisphere off and thus by changing the profile of their interhemispherical asymmetry.

Sense organs are significant for emotions formation. First place has vision organ (up to 90 per cent of all emotional states are connected with it), then auditory organ and others.

Vision gives us the presentation about colour, environment changings and subjects dysposition. It provides corresponding emotional state to us (red colour- excitement; blue – grief). Remember your state when sun is shining or it is raining. Hearing – high sounds excite, low- cause fear, monotonous – inhibit all the emotions; rock-music intensive hearing leads to mental abilities decreasing; classical one – one the contrary; it also may be used at different diseases (music-therapy, art-therapy). Smell also forms different emotional states (for example, smell of chocolate increases immunity, stinking or smelly – decrease it). It is well-known that 40 minutes of everyday listenting to the lovely music is a brilliant anti-stressful therapy.

Emotions are essential for work reproductiveness. Positive emotions and sthenic part of negative emotions increase it; negative emotions in their asthenic stage – decrease it.

There are interrelations between emotional state and morbidity. Fear emotions cause heart diseases, wrath – liver, anguish – stomach.

Keeping healthy life style, we create all conditions for emotional tension relaxing.

Emotions depend on individual ***(typologic)*** subject features. People under one and same situations have different behaviour. But one can differentiate common ***behaviour schemas or types*** despite all multiple reactions.

This phenomenon was seen long long ago. It was the base of Greek medicine according to which there were 4 elements (air, water, fire and earth) or matters (blood, lymph, bile and black bile). Combination of them determines temperamentum of behaviour. Theses data were the base of Hippocrate's temperaments classification. He considers that human availability level depends on correlation of all these liquids (fluids) in organism. These fluids mixture (taking into account translating from Greek into Latin the word "mixture" sounds as "temperamentum") and defines individual peculiariry of any person. According to this learning, one can differentiate:

- sanguine person – with blood (sanguis predominance in this mixture);
- choleric – with bile (chole) predominance in this mixture;
- melancholic – with black bile (chole) predominance in this mixture;
- phlegmatic- with mucus (phlegma) predominance in this mixture.

These names are actual till nowadays.

I.P.Pavlov (1910-1935) connects temperamentum's types with such nervous system features as force, stediness and motility. People are divided into strong and weak types according to force. Strong type – acts to the irritation according to the law of force interrelations; weak – doesn't act according to it. According to steadiness – steady and unsteady. Steady – person in which excitement and inhibition processes are equal (in equillibrium). Unsteady – if excitement process predominates over inhibition. According to motility – agile and inert (sluggish). Agile type – excitement and inhibition processes changing occurs quickly. Inert type – if inhibition is predominant comparatively to excitement.

According to these data next combinations were done:

- Sanguine person – strong, steady, agile.
- Choleric – strong, unsteady, agile.
- Phlegmatic – strong, steady, inert.
- Melancholic – weak type.

One can also differentiate ***properly human types of the highest nervous activity***:

- *Artist* – first sygnal system (and right brain hemisphere) is dominant.
- *Mental* – second sygnal system (and left brain hemisphere) is dominant.
- *Mixed* – without any dominance.

There are many new classifications during last years:

- *Extraverts:* people with orientation to environment – sanguine person (stable) and choleric (unstable).
- *Intraverts:* people with orientation to their internal world – phlegmatic (stable) and melancholic (unstable).

Of course, to determine human type finally is rather difficult. Moreover, every human being, depending on the situation, can express the features of all mentioned 4 types. In addition, every person in course of his or her life comes through age and temperamentum periods: childdhood – sanguine person, adolescence – melancholic, adulthood – choleric, elderness – phlegmatic. Children can express individual typologic peculiarities from 6 months of their life but especially brightly in 5-6 years. Children are different according to excitement and inhibiting processes force, steadiness and motility signs. But they are changed in course of human ageing. One can see similar regularity due to seasons changing: spring - choleric, summer – melancholic, autumn – sanguine person, winter – phlegmatic. ***Human biorhythms*** are also essential for this. Our behaviour depends on biorhythms in big extent. Biorhythms – are harmony, phenomena periodically repeated. *Biorhythms types:*

a) High-freaquened – from msec till 30 min:

- breathing,
- heart activity et al.

b) Middle-freaquened:

- ultradian – up to 20 hours;
- circadian – 20-28 hours;
- infradian – more than 28 hours;
- circaseptan – up to 7 days.

Examples:

- sleep and waking state;
- metabolism changes near 24 hours;
- hormonal changes near 24 hours et al.

c) Low-freaquened- up to months, years:

- seasonal;
- year;
- sunny et al.

There are several important terms in medicine delt with biorhythms – ***chronogram*** and ***chronotherapy.*** Organism, its separate organs and systems activity chronogram is essential at patients diagnosis. Chronotherapy should be taken into account at medicines application.

Learning about highest nervous activity types is very important for doctor from different aspects. At diagnosis statement, patients location in a ward, therapy. But it is also

of great significance in other spheres of our life: marriage, people groups creation, interrelation head-subordinate and so on.

Lecture 10
Waking state, sleep, dream and hypnosis.

Waking state. Most time in course of 24 hours human being is under waking state, but attention to surrounding events is cyclically changed at this. Attention fluctuations cycle is 90-100 minutes (it is not occasionally due to this one make breaks in activity for example between practical classes or lectures). Brain structures responsible for waking state support:

- Varolii pons internal region.
- Stem internal region.
- Midbrain internal region - reticular formation.

For example, there are noradrenaline-containing neurons in pons blue spot, serotonin-containing neurons in suture dorsal nucleus. Both cells are maximally active in course of waking state. The same neurons are active in periods of increased answer (reacting) to surrounding situation. Thus, in course of increased attention (pricking up one's ears, head turn towards attention object). Serotonin insufficiency in blood leads to continuous waking state, serotonin increasing – to falling asleep; noradrenaline content increasing – to waking up. At blue spot injury neurons of which produce noradrenaline animals sleep rather longer in comparison with norma.

Sleep – is organism specific state which is characterized by almost complete absence of reactions to new stimuli and immobility. Why do we sleep? The answer to this question is not so simple. People always try to answer this question but it was not any clear answer till the 20-th century. There were large amount of different theories (mainly delt with dreams problem). The beginning of last century was characterized by occurence of 3 simultaneous approaches to this problem.

1. Sleep is the result of hypnotoxines accumulation in blood (Legandr and P'eron – hypnotoxines theory).
2. Theory of sleep center (Gess, Economo) – some thalamic and hypothalamic neurons excitement causes sleep.
3. Theory of I.P.Pavlov about dispersed cortical inhibition.

The latest point of view is not proved for now. Additionally to mentioned biologically active substances multiple peptides were extracted influencing on sleep. Peptide of sleep – factor "C", Uchizano factor, Nagasaki factor and others are among them. They are secreted in thalamus and hypothalamus.

There are 2 kinds of sleep. One can differentiate ***fast (paradoxal) sleep period*** in course of sleep. This name is originated from the following: brain is under active state, vegetative indexes are changed. They aquire the state similar to waking state. Blood pressure is increased, heart rhythm and breathing is freaquened. This is the phase of deeper sleep when all body muscles with exception of ocular are relaxed. Human being as a rule see dreams under this phase. According to other point of view, you dream in both deep sleep and REM sleep, but in REM sleep you dream in pictures. If you wake up in REM

sleep you can usually remember your dream. That's why fast sleep with rapid eye movements are considered to be dreams period. This is also called rapid eye movement sleep (or REM sleep). Decision of informational problems – tasks, ideas come, comparison and summarizing, short-termed memory can transforms into long-termed (consolidation) are performed in REM sleep. It is known for sure that learning of necessary material before sleep helps to remember it better.

REM sleep is expressed distinctly in new-borns. Its duration in them is bigger, it lasts about 50 per cents of all time (10 hours). In adults there are 4-6 phases of paradoxal sleep in course of 1 night with duration about 20 min; it is about 1,5 hours from all sleep duration. This sleep predominance in new-borns encourages nervous elements maturation and nervous connections formation.

The rest of time - is ***orthodoxal or slow sleep***. When you go to sleep you go into this slow sleep. More energetic tasks are solved during this period (fatigue liquidation). That's why when we wake up in this phase we feel ourselves in a good relaxation. Our temperature falls, our body relaxes and we breathe slowly.

Our natural sleep is characterized by cyclic changing of slow and REM-sleep. Full cycle consisting of slow sleep change into rapid with the further recurrence to slow sleep is 60-90 minutes in human being.

Why we sleep in the night?

- According daily biorhythm.
- According conditioned reflex – definite procedure of going to bed: all sounds and light switching off, relaxation in our bed.

Norma for sleeping is rather complicated to be determine. The most common point of view to this – human being must sleep from 2 to 9 hours. Moreover, one should take into account that people who sleep less are more adaptive to life, can ignore different psychologic problems better. People who have long-termed sleep are always under social and psychological problems. It's important to strive to go to bed and to wake up regularly, in one time every day.

<u>Sleep duration:</u>

- new-borns – 20-21 hours per day;
- 1-3 months – 16-19 hours;
- 1 year – 14 hours (3 times a day with the most significant duration in the night);
- early children have bicyclic sleep;
- schoolchidren and adults – monocyclic;
- teenagers – 8-9 hours;
- adults – 7-8 hours.

People can sleepwalk in deep sleep and sleepwalkers do amazing things. They open doors and windows, they ride bicycles and drive cars. They cook, they take a bath or a shower (often in their pijamas), they shave, they clean their teeth, they get dressed, they dig the garden and they get into the beds of other people. Example. A man from Scotland woke up in his car 2 miles from his house. He had no clothes on. A girl from Wales woke up at 5 o'clock in the morning in a launderette. She had a shopping bag and the dog with her. Sleepwalkers are asleep, but they have their eyes opened and they can see. They can't wake up easily. If they do, they can't remember anything.

Dreams, levitation or sleepwalking, meditation, narcosis, clinical death and some other states are considered so-called unusual mind states. All processes occuring in course of our sleep are unconscious, in course of waking state – counscious. All people see their dreams. They can occur 4-6 times per night. If we are waking up in course of slow sleep, we'll tell about our dreams in 70-90% of cases; in REM-sleep – only in 7-10% of cases. Why can we see dreams?

Dreams main theories:

- dreams – the signs of diseases; healthy sleep must be without any dreams;
- dreams – is a special soul state;
- brain psychical activity is continuous during sleep;
- sleep – is a psychical activity decreasing or even stoppage;
- under sleep state human being can see something he has never done, known, felt;
- Z.Phreud: dreams are realizing of our clerished desires;
- I.M.Sechenov: dreams – are unusual combination of usual impressions.

Modern data- 3 factors in dreams occurence:

1. External sygnals.
2. Internal sygnals.
3. Steps of daily impressions.

Dreams peculiarities:

- they are short-termed (events are pressed in them like in movie);
- weak sygnals are enforced in course of sleep;
- many people don't remember their dreams or forget them rapidly;
- dreams can be prognostic, prophetic, creative (of art).

Hypnosis is well-known for long. Its mechanism is still out of clearance. It is dream variation but it is not a dream. It differs from usual dream by tight connection with hypnotizer. Besides, there is special muscular state in course of hypnosis and ability to suggestion. One must use following techniques in course of hypnotic dream reproduction:

- monotonous stimuli influencing (eyesight fixation, monotonous speech, rhythmic passes or movements);
- muscular relaxation (it prepares CNS to the rest, to transition from waking state to sleep, passive rest);
- ability to suggestion (it appears better under CNS weakening states – diseases, grief, fear, fatigue et al.).

Hypnotic dream stages:

- letargic – sleepiness, relaxation for example in course of listening to the music, service into the church;
- cataleptic – muscular relaxation, one can't raise his arm, body wax flexibility;
- somnambulic – renouncing from external stimuli, complete amnesia about listened and experienced events.

Hypnotic states are sleep-like with speech connection preservation. Human hypnability depends on age, sex, health, fatigue, intellect. Children up to 10 years practically don't possess any hypnability. Approximately up to 6 per cents of the adult don't have such ability too. There are such statistic data: 29 per cent of people have weak ability to suggestion; 49% - good; 15 per cent are easily suggested.

Lecture 11.
Blood circulation system. Heart physiology (cardiac activity phases, heart tones, electrocardiogram).

Blood circulation system provides continuous blood movement through vessels. As it is well-known, it consists of 2 main parts – heart and vessels. Heart work beginning is ***atriums systole***. Right atrium contracts before left atrium on 0,01 sec because main pacemaker is in right atrium. Excitement spreading through heart begins from it. This phase duration is 0,1 sec. During atrium systole pressures in atriums are increased: in right – to 5-8 mm, in left – till 8-15 mm mercury col. Blood moves to atriums and it is accompanied by atrio-ventricular foramens closage. ***Ventricles systole*** takes place simultaneously (atriums are relaxed in that time). Ventricles systole duration is about 0,3 sec. Ventricles systole begins with *asynchronic contraction phase.* It lasts about 0,05 sec and is the process of excitement spreading and contraction through myocardium. Pressure in ventricles is practically constant. While further contraction when pressure in ventricles increases to the size sufficient to atrio-ventricular valves closage but insufficient to semilunar valves opening, *isometric contraction phase* occurs. Its duration is up to 0,03 sec. Sometimes these phases are united in one and are called by *tension phase* (0,05-0,08 sec). In this phase pressure in right ventricle increases up to 30-60 mm merc.col., in left one – up to 150-200 mm merc.col. Tension is increased (valves are closed) and muscular fiber length doesn't change in course of asynchronic contraction. In the end of tension phase pressure provides semilunar valves opening and ventricle systole next phase is begun – *of fast blood expulsion.* In course of this phase which lasts from 0,05 to 0,12 sec, pressure reaches its maximal ziphras. Later pressure reduces up to 20-30 and 130-140 mm merc. col. in corresponding ventricles and this moment of their work is called *slow blood expulsion.* This ventricle systole phase duration is from 0,13 to 0,20 sec. Pressure is sharply reduced with its ending. Pressure is decreased rather slower in magistral arteries that provides later clapping of semilunar valves and prevent blood regurgitation. But it occurs in the moment when ***ventricle*** muscle begins its relaxation and their ***dyastole*** takes place. Space time from ventricles relaxation beginning to semilunar valves closage is first dyastole *phase – protodyastolic*. Next dyastole phase – *tension reducing* or *isometric relaxation* takes place. It is expressed at closed valves and lasts approximately 0,05-0,08 sec from the moment when pressure in atriums is higher than in ventricles (206 mm.merc.col.) that leads to atrio-ventricular valves opening after which blood comes in ventricle. First, it occurs quickly (for 0,05 sec) – *ventricles fast filling with blood phase* and then slowly (for 0,25 sec) - *ventricles slow filling with blood phase.* Uniterrupted blood coming from magistral veins both in atriums and in ventricles takes place at the beginning of this phase. And, finally, last phase of ventricles dyastole is their filling due to atriums systole (0,1 sec). If to sum ventricles systole and dyastole time than we will receive time corresponding to complete **cardiac cycle** which is 0,8 sec in adults. In course of heart work there is such moment when both atriums and ventricles together (simultaneously) are in dyastole state. This heart work period is called **heart pause** the duration of which is 0,4 sec.

In course of systole heart pumps in blood circulation up to 70-100 ml of blood. This blood volume is known as **systolic volume (SV).** If SV multiply on heart contraction freaquency (HFC) we will receive **minute volume (MV)** of heart work the size of which is about 4,0-5,0 l.

Heart tones. These are sound phenomena by which heart work is accompanied by. Different heart structures fluctuations (of valves, muscles, vessel wall) are on the basis of their occurence. As any fluctuations, tones are characterized by intensivity (altitude), freaquency and duration. There are 2 clinical methods of their assessment: auscultation (hearing by sthethoscope) and graphical one – phonocardiography.

I-st tone – systolic – is lower and more prolonged, it occurs in atrio-ventricular valves region simultaneously with ventricle systole beginning. Duration: 0,08-0,25 sec, freaquency – 15-150 Gz. Optimal place for auscultation: heart apex. Its reasons:

- atrio-ventricular valves closage and tension;
- heart cavity walls fluctuation in course of systole;
- ventricles musculature contraction.

II-nd tone – dyastolic – is higher and shorter. Its duration is 0,04-0,12 sec, freaquency – 500-1250 Gz. Optimal place for auscultation: second intercostal space on the right and on the left from sternum. Reason: semilunar valves fluctuation. Sometimes these fluctuations are so expressed that tone's division into two is observed.

III-rd tone – ventricular gallop – is delt with ventricles muscular wall fluctuations at their stretches right after the second tone. It is sometimes called as tone of filling. It is most often auscultated or registrated on phonocardiogram (PCG) in children and sportsmen. One can hear it as a weak, muffled sound, the most comfortable place – on heart apex (when patient is lying) and sternum region (when he is standing).

IV-th tone – atrial gallop – is connected with atriums contraction when they fill actively ventricle with blood. It is auscultated seldom, more often it is registrated on phonocardiogram.

Registration and analysis of electrical potentials occuring in course of heart activity has received the widest spreading in clinical practice.

Electrocardiogram – is a curve, periodically repeated and reflecting heart excitation process spreading in course of time. Separate ECG elements have received their special names: denses, segments, intervals and complexes. Every ECG element reflects excitation process spreading through definite heart regions and has time (in seconds) and high (in mV) characteristics. ECG analysis independently from abduction (lead) is given on the base of denses study (P,Q,R,S,T), intervals (PQ, ST, TP, RR), segments (PQ, ST) and complexes (P – atrial and QRST – ventricular).

As cardiac cycle begins with atriums excitation the first dens on ECG – is ***dens P.*** It characterizes atriums excitement. Its ascendent part – of right, descendant - of left one. Its characteristics under norma: duration - from 0,07 to 0,11 sec, altitude - from 0,12 till 0,16 mV. It may be absent in III-rd standard lead (abduction) it may be absent, two-phased or negative. In V_1-V_2 - it is positive, V_3-V_4 - it is gradually increased. In one-poled abductions form extremities: aVR – it is negative, in aVL and aVF – positive.

Segment PQ – is a right line section on isoelectric axis from dens P end to dens Q beginning. It characterizes atrio-ventricular lack time and is about 0,04-0,1 sec.

Interval PQ - ECG locus from dens P beginning till dens Q beginning, it characterizes excitement distribution from atriums to ventricles. Its duration is 0,12-0,21 sec.

Dens Q – characterizes interventricular septum and papillar musculature excitement. Under norma its duration is from 0,02 till 0,03 sec, altitude – up to 0,1 mV. It may be absent in the I.

Dens R – characterizes main ventricles musculature excitement. Its altitude is 0,8-0,16 mV, duration – 0,02-0,07 sec. In thoracic abductions V_1-V_2 it is small, V_3-V_4 - it is increased, in V_5-V_6 it is reduced again.

Dens S – describes excitement in distant ventricles locuses. Its altitude reaches up to 0,01 mV and duration – up to 0,02-0,03 sec. It may be absent in I. In V_1-V_2 it is deep, then it is decreased, in V_5-V_6 it may be absent.

Segment ST - is a right line section on isoelectric axis from dens S end till dens T beginning and describes the moment when both ventricles are simultaneously excited. Its duration is from 0,1 till 0,15 sec.

Dens T – describes myocardium repolarization process, it altitude is 0,4-0,8 mV, duration – 0,1-0,25 sec. In I it is always positive, in II - often positive and in III – may be positive, two-phased and negative. In V_1-V_2 it is negative sometimes, in aVF – negative.

Interval TP – characterizes common heart pause, its duration is 0,4 sec.

Interval R-R – characterizes complete cardiac cycle, its duration is 0,8 sec.

Complex P – atrial.

Complex QRST – ventricular.

As heart excitation begins from its base, than this region is a negative pole, apex region – positive one. Heart electromoving force (EMF) has its size and direction. EMF direction is considered to call ***heart electrical axis***. In the most common cases it is located in parallel to heart anatomical axis (*normogram*). Direction of one or another dens on ECG reflects an integral vector direction. When vector is directed to heart apex, one can registrate positive (as for electrical axis) denses, if to the heart base - negative. Due to definite heart location in thorax and human body shape, electrical force lines occuring between excited and unexcited heart locus, are distributed unequally on body surface. If heart axis becomes horizontal (lying heart) than such situation is called *left-gram*, in a case of its vertical localization (hanging heart) – *right-gram.*

Lecture 12.
Vessels physiology. Blood pressure. Pulse. Capillary and venous circulation. Lymphatic supply.

Functional vessels classification:

1. Elastic:
- aorta;
- pulmonary artery;
- other large vessels.
2. Muscular:
- middle arteries;
- shallow arteries.
3. Resistive (vessels of resistance):
- ending arteries;

- arterioles.

4. Of exchange (exchangeable):

- capillaries.

5. Cavitary:

- veins;
- venules.

Blood movements through the vessels obey to some regularities known as hydrodynamics laws. But they are named as haemodynamics laws according to blood vessels.

Factors determining haemodynamics peculiarities (3 first are the main, rest are additional ones):

- pressure;
- resistance;
- velocity;
- vessel diameter and length;
- blood content;
- blood viscosity et al.

Circulation peculiarities:

- one-sided blood traffic through vessels;
- its continuosity;
- laminarity;
- turbulent character.

One-sided movement **-** is provided by pressure gradient (difference) at the beginning and at the end of vascular system. It is 120-150 mm merc col. in initial circulation part and 5-0 mm merc col - in ending part (veins inflowing into heart).

Circulation continuosity **–** is linked with vessels elasticity, when blood is pumped in aorta by heart (it possesses elasticity) then all its volume can not come through the vessels at once. More blood part is remained temporarily in dilated (due to elasticity) aorta region and then (in course of dyastole) leaves it due to aorta walls muscular contraction. The more elastic is aorta and other large arteries, the better circulation continuosity is realized. And on the contrary, at elasticity loss (with ageing, at sclerosis and other vessels injuries) circulation continuosity is disturbed.

Laminar or streamline and turbulent character of blood circulation movement character through vessels. *Laminar circulation* - is blood movement by separate layers in parallel to vessel axis (it is realized practically in all vessels). *Turbulent circulation* – with blood turbulence – occurs in the places of dilations, constrictions, flexures and pressures on them.

Vessels activity main indexes:

- velocity,
- pressure,
- pulse.

Blood movements velocity types:

1. *Volumetric velocity* – blood amount flowing through transversal vessel section in time unit. It is expressed in ml/min and depends on pressure gradient at vessel beginning and

end as well as on resistance to blood stream. Its size depends on organ state (for instance, in course of muscular activity this velocity increases in them in tens times). This velocity is determined by rheography method.

2. *Linear velocity* – distance which blood particle passes through time unit. It is determined in m/sec and is under norma:

- in aorta – 0,5-1,0 m/sec,
- large arteries – up to 0,5 m/sec,
- in veins – 0,25 m/sec,
- in capillaries – 0,05 m/sec.

Investigation methods: direct – stains and different substances introduction; indirect – ultrasound.

3. *Circulation velocity* – blood transport time on circulation circle. Norma: 14-20 sec.

Investigative methods: radioactive.

Blood pressure – force whith which blood presses onto vessel walls.

It depends on:

a) heart activity,
b) vessels resistance,
c) their diameter,
d) their length,
e) blood viscosity.

Maximal (systolic) pressure is registrated during heart systole. Its size is equal to 100-130 mm merc col (on brachial artery). There is a tendency to this pressure increasing during last years of practically healthy children even of school age. Its level depends mainly on heart activity.

Minimal (dyastolic) pressure is characterized by size registrated during dyastole. Norma: 65-90 mm merc col. Vascular wall tone is a dominant factor determining this pressure.

Pulse pressure – matematic difference between systolic and dyatolic pressure level. Its maximal size is in arteries near heart. The farther from heart the pressure pulse difference is decreased and beginning from arterioles it disappears.

Middle-dynamic pressure – expresses energy with which blood is moved, it provides blood movement through vessels and it is the average resulting size for all pressure fluctuations (oscillations) alongside all vascular system. Its level is less than systolic but more than dyastolic. Norma: 90-100 mm merc col.

Pressure changings in course of transport through all vessels:

- aorta – 120-130 mm merc col.;
- arteries – 100-120 mm merc col.;
- arteries- 40-80 mm merc col.;
- capillaries – 20-40 mm merc col.;
- veins – 5-10 mm merc col.;
- vena cava - up to 0 mm merc col.

Arterial pulse – or push, arterial wall fluctuation caused by systolic pressure increasing in arteries. Pulse wave appears in aorta when pressure is sharply increased in it and its wall is stretched. This wave is spread with velocity 3-15 m per second from aorta to

arterioles. It may be registrated on large, superficially located arteries, by palpation or graphically *(sphygmogram).* At palpation its necessary to perform on both hands simultaneousely (hands must be at heart level) in one and the same patient location from initial investigation. If one can not determine any difference further pulse investigation should be performed on one hand (at pulse difference on both hands pulse is called different). Different pulse may be diagnostic sign of mitral valve stenosis, aortal aneurisme.

One can differentiate on sphygmogram:

- anacrote (it corresponds to ventricles systole) – curve ascent (rising);
- catacrote (it corresponds to blood slow exile from ventricules in its beginning, rest part – ventricules dyastole) – curve descent (falling down, drop);
- dycrote – there is dycrotic ascent on catacrote, it corresponds to blood return to heart during dyastole ans its shock to semicircular valves.

Pulse clinical characteristics main indexes:

1. *Freaquency* – shocks (beats) amount per minute. Norma: 60-80 per minute (sometimes it is considered to 90). It may be estimated both on sphygmogram and by palpation.

A) Freaquent pulse (tachycardy, trachysphygmy) – it takes place at hyperthermia, in course of physical loading. At body temperature increasing on 1°C in adults pulse freaquency increases on 8-10 beats, in children – on 15-20 beats per 1 min.

B) Seldom pulse (bradycardy, bradysphygmy) – in sportsmen, in well-trained people.

C) Pulse freaquency is changing in course of ageing:

- new-borns – 130-140 beats per min;
- 1 year – 120-130;
- 7 years – 90-100.

2. *Rhythm* – is determined both on sphygmogram and by palpation.

A) Rhythmical (regular) pulse – it is observed at equal spaces between pulse waves.

B) Arythmical (irregular) - it is observed at unequal spaces between pulse waves. Physiological arhythmias may be at intensive muscular loading, thermal procedures.

3. *Pulse velocity* – intensivity with which pressure in artery is increased during pulse wave arising and is reduced in course of its drop (it is determined the best on sphygmogram).

A) Rapid pulse - it may be in course of physical activity, aortal valve insufficiency.

B) Slow pulse – at faint, aortal ostium constriction.

4. *Pulse altitude* – is determined on sphygmogram.

A) High pulse -it is rapid or fast at the same time.

B) Low pulse – it is slow at the same time.

5. *Pulse tension* – vascular wall force or resistance degree to its pressure with fingers.

A) Solid pulse – pulse is accelerated and becomes stronger after vessel wall pressure. As a rule, it is observed at elderness due to vascular elasticity reducing; at hypertonic disease.

B) Soft pulse – pulse becomes slower and low-expressed after vessel wall palpation. It is under norma.

Diagnostic value: on tension degree one can tell about maximal blood pressure level. There is direct correlation between these 2 indexes.

6. *Pulse filling* – consists of pulse altitude and its tension. The higher systolic pressure plus blood volume and pulse altitude, the filling is stronger.

A) Full pulse.
B) Empty pulse – if pulse is small by its size, it is empty, as a rule.
C) Filliformis pulse – it is practically unexpressed - it is observed at strong bleeding, collaps and so on.

Capillary circulation and its peculiarities

Circulation in this part provides its main function – exchange between blood and tissues. That's why main link in this system – capillaries – they are called exchangeable vessels. Thir function is tightly linked with vessels they are originated from - arterioles and vessels they come into (inflow) – venules. There exist direct arterio-venous anastomoses, connecting them out off capillaries. Mentioned vessels plus lymphatic capillaries are ***microcirculation system.*** This is main link of blood circulation system. Main reasons of diseases biggest part are in this region. Capillaries are the base of this system. Under rest state in norma only 25-35 per cent of them are opened, i.e. in working state; if more – one can see haemorrhagias and even organism death from internal bleeding, because blood is accumulated in capillaries and doesn't reach heart.

Capillaries are located in intercellular spaces and that's why metabolism occurs between blood and intercellular fluid.

Capillary exchange factors:

1. Hydrostatic pressure difference between capillary origin and its end (30-40 mm and 10 mm merc col correspondingly).
2. Low blood movement velocity (0,05 m/sec).
3. Filtration pressure (difference between oncotic pressure in intersticium and hydrostatic pressure in arterial capillary end – 15 mm merc col.). At its increasing – liquid comes into vessels and cellular dehydratation is developed.
4. Reabsorbtion pressure (difference between hydrostatic pressure in venous capillary end and oncotic pressure in intersticium – 15 mm merc col.). At its increasing – liquid (fluid) maily comes into tissues and oedemas are developed (for example, at proteins deficiency).

Capillary pulse (or Kwinke pulse) – pseudopulse, linked with rhythmical oscillations at small arteries dilation in course of ventricules systole. It is easily observed at thermal procedures: if one attaches mirror to lips small vessels pulsation is seen. But more often such pulse is pathology sign: aortal insufficiency, thyreotoxicosis.

Venous circulation

Veins are cavitary vessels, approximately 70-80 per cent of blood are located in them; they possess large ability to stretching and comparatively low elasticity. Their internal surface has valves (with exception of shallow veins, portal veins and cava veins) which:

- encourage blood stream to the heart;
- prevent its regurgitation (movement ahead);
- protect heart from excessive energy consumption to blood oscillative movements overcoming.

Blood in veins come rapidly despite low pressure in them. Why?

- Pressure gradient in blood circulation arterial and venous ends;
- heart residual force;

- thorax suckering action (respiratory pump);
- sceletal muscles contractions (muscular pump);
- diaphragm activity.

Venous pulse – pressure and volume fluctuations in veins in course of one cardiac cycle delt with blood outflow dynamics into right atrium in systole and dyastole different phases. These fluctiations are transmitted in retrograde direction (ahead); one can find them out in large veins located near heart – usually cava or jugular. Pulse wave distribution velocity is 1-3 m/sec. This pulse wave reason differs from that for arterial pulse. Vein pulse reason is blood outflow stoppage from veins to heart in course of atrial and ventricular systole. In this moment blood stream is lacked in large veins that results in pressure rising up in them. This pulse is registrated graphically and this curve is named as *phlebogram.*

3 phlebogram waves:

- wave "a" - occurs in course of right atrium systole: blood outflow from veins to heart is stopped and pressure in rised up in them; when atrium is relaxed blood begins to pass in its cavity, pressure in vein is reduced and curve reaches its initial level;
- wave "c" – new wave after drop which corresponds to pulse of neighbouring carotid artery and reflects fluctuation of its wall. Carotid artery push is communicated to vein and causes occurence of increased pressure rapid wave in it. After such short-termed rising pressure is falling down because blood outflows in atrium constantly and atrium is in dyastole;
- wave "v" - after atriums filling pressure in vein is increased again, blood stagnation and venous wall stretching take place; all this causes third wave appearence.

Venous pulse can be investigated both graphically and by palpation.

Lymphatic circulation

It's necessary for fluid and substance (proteins) excessive amount, particles (microbes and others) removal; it serves as messengers between blood and cells. Blood comes into lymph, lymph – in tissues, from tissues in blood and on the contrary.

Lymphatic system:

- lymphatic capillaries;
- lymphatic vessels;
- lymphatic nodes.

Lymphatic capillaries - capillaries beginning blindly, which consist of endothelial tubules systems penetrating tissues. Their cavity is wider comparatively to blood capillary, endotheliocytes are larger, fissures between them are bigger, basal membrane is absent. Some organs don't have any lymphatic capillaries such as cutaneous (skin) epithelium, mucosae, placenta, brain.

Lymphatic vessels look like blood vessels, but they are thinner, muscular layer is less developed and there are many constrictions (valves) in them. Valves are pair intime plicas directed one opposite other and creating activity like in locks (sluices).

Lymphatic nodes perform very significant role in organism. One can tell about following main functions:

1) haemopoiesis (lymphopoiesis);

2) filtration – lack of:
- side bodies;
- bacterias;
- tumor (particularly malignant) cells;
- toxines;
- side proteins;

3) immunity –
- plasmocytes production;
- antibodies production;
- T- and B-lymphocytes differentiation;

4) participating in metabolism of:
- proteins;
- fats;
- vitamins.

Lymph

This is product of blood, cells, intersticial fluid. That' s why its content is similar to all these compounds. Its reaction is alkaline, it has proteins (fibrinogen and other coagulation factors), lymphocytes, salts, fats and other substances. Daily production is up to 2,0 l of lymph.

Lymph types (according to lymphocytes number):
- peripheral ($0{,}5 \times 10^9$/l);
- central (passing through lymphatic nodes where lymphocytes amount is from 2,0 to $20{,}0 \times 10^9$/l).

Lymph formation stages:
- tissular liquid formation;
- proper lymph formation;
- lymph movement through vessels.

Tissular fluid formation occurs in capillaries. Tissues and blood osmotic pressure difference is essential for this. Under physiological conditions lymph formation from tissular fluid is insignificant (because filtration and reabsorbtion pressures are equal - see above). At oncotic pressure reducing (at protein deficiency in fasting) filtration pressure is rised up and reabsorbtion pressure is decreased. Fluid in such a case will come in tissues that leads to swelling (oedema) development. But such phenomenon will be in course of physical training too: filtration pressure increases due to capillary presure increasing (the result of hydrostatic pressure increasing in magistral vessels). Fluid amount in tissues will grow too (muscles increase their weight to 20 per cent). Lymphatic vessels begin their active functionning and take fluid excessment off.

But tissular liquid is not yet a lymph. It becomes itself when fluid passes into lymphatic vessels. Lymph formation is a rather complicated process. One can differentiate both physico-chemical reactions (diffusion, permeability, osmotic pressure) and secretory process (cellular secretion) in it. There are some substances increasing lymph formation. They are known as lymphogonic: peptones, hystamine et al. Some food products also possess lymphogonic features: crabs, squids, strawberry et al. Leeches action is based on this.

Lymph movement is realized due to:

- lymphatic vessels walls contraction (8-20 times per 1 minute);
- negative pressure in thorax;
- muscular contractions (intramuscular lymphatic heart). This mechanism lymph movement through vessels is essential for massage performance. At hypodynamy when this mechanism is disturbed, lower extremities oedemas are developed.

Lymph while proteins return from intercellular fluid to blood participates in fluid balance (equillibrium) support into tissues.

Lecture 13

Blood circulation regulation. Heart-vascular regulation center. Blood circulation nervous and humoral regulation. Blood circulation regulation distinguishing features in separate organs.

Heart and vessels work in complicated functional interrelations. Besides, heart has its own (myogenic) regulative mechanisms. One of them – ***heterometric –*** is performed as answer to myocardium fibres length change (Starling's law). Such cardiac regulative mechanism can provide circulatory insufficiency compensation and its anomalies. It is characterized by very high sensitivity. It may be observed at introduction of 1-2 % of all circulating blood mass in magistral veins.

Second myogenic regulative mechanism type is ***homeometric.*** Myocardial fibres ending dyastolic stretching degree is not important for its realizing. The most important is correlation between cardiac contractions and aortal pressure (Anrep's effect): aortal pressure increasing causes initial heart systolic volume decreasing and then – heart contractions force increasing and cardiac discharge stabilizing at new contractions level.

Thus, heart activity myogenic regulational mechanisms may permit its contraction significant changes.

Besides, heart has sympathetic and parasympathetic innervation like vessels. At tone dominance of one of them heart and vessels activity will be different.

Efferent nerves tone support is provided by ***cardiac-vascular regulation center.*** Heart-vascular regulative center – is a rather complicated structure in which dominant importance has its "working" part, located in medulla oblongata. It was there where neurons are located from which excitement are transmitted on effector ways (parasympathetic and sympathetic) while reaching heart and vessels. That's why their reflectory regulation is always performed simultaneously. When **sympathetic nervous system tone is dominant** (**hypersympaticotony**) than heart activity is increased:

- its contraction freaquency is rised up – ***positive chronotropic effect;***
- contraction force is increased – ***positive inotropic effect;***
- excitability is increased – ***positive bathmotropic effect;***
- conductance is rised up - ***positive dromotropic effect;***
- tone is increased – ***positive tonotropic effect.***

At **hyperparasympatheticotony –** on the contrary, all mentioned effects will be negative.

Vascular tone will be changed too: in the first case – to increase, in the second – to decrease. It will influence on size of their filling with blood and arterial pressure.

"Working" part of heart-vascular regulation center consists of **2 parts**:

- *pressor* – its irritation causes vasoconstriction;
- *depressor* – its irritation causes vasodilatation.

These parts of "working" center receives the information from different receptor groups located in heart, vessels and out of blood circulation system.

That's why while characterizing blood circulation system **reflectory regulative mechanism** one can differentiate 2 reflexes types: proper and conjugated.

Proper reflexes – are such acts occuring in the structures of a given system and realizing in it. Such receptive zones in blood circulation system are vascular *presso*- and chemoreceptive zones. Special place in this reflectory group has sino-carotid zone. Reflectory act from carotid zone pressoreceptors is called as *sino-carotid reflex (Chermak's reflex).* This reflectory act is performed at blood pressure increasing in a given zone. Pressoreceptors irritation leads to nervous impuls occurence, further coming through sino-carotid nerve in medulla oblongata where it passes on vessel-motor depressor part. From depressor part information is switched to sympathetic nervous system through inhibiting reticular neurons and through exciting reticular neuron – to parasympathetic part of this system and through efferent fibres - to heart and vessels smooth muscles. As the result of parasympathetic nervous system tone predominance both heart and vessels work is decreased (heart contractions freaquency and force, systolic volume size, blood pressure are decreased).

Another blood circulation system proper reflex type are *chemoreflexes* from same vessels zones. They answer to blood chemical content change, for example, CO_2 excess in blood. Reflectory arch of such reflex is a very similar to sino-carotid reflex reflectory arch but information comes to pressor part of heart-vascular regulation center. Then information through exciting reticular neurons come to synaptic, through inhibiting – to parasympathetic part of autonomic nervous system. Result: hypersympatheticotony and further heart activity enforcement and vascular tone increasing (heart contractions freaquency and force, systolic volume size, blood pressure are increased). CO_2 is more effectively removed from organism due to such mechanism.

Conjugated reflexes – reflectory acts that are originated from different receptive groups located out of blood system boundaries. As it is known, there are many such zones in organism but according to receptors classification one can differentiate 3 types of such reflexes:

1) *Proprioreceptive* – are originated from supporting-moving apparatus receptors for instance in course of physical activity. From these receptors (they are localized in muscles, tendons, ligaments) the information occuring in them comes to heart-vascular regulation center pressor part that leads to heart and vessels activity enforcement (see above the mechanism). Pulse freaquency and blood pressure increasing in course of physical training is explained by this (probe with physical activity).

Reflexes of localization are too closely to these reflexes. One of them is known as orthostatic probe: one determine pulse freaquency and blood pressure in investigated person while his lying on the bed. Then the investigated person must be gradually putted into vertical state and the measurements are repeated. Under norma these indexes are increased in course of orthostatic probe. The explanation: information flow from

proprioreceptors (while someone's staying muscles, joints, ligaments are tensed) is increased in spine. Then information goes to medulla oblongata, to pressor part of heart-vascular regulation center. Clinosthatic probe is the directly opposing to the previous probe: the investigated person is gradually putted from vertical to horizontal status. The information from proprioreceptors is significantly decreased and depressor part of regulative center became dominant that leads to pulse and pressure reducing.

2) *Interoreceptive* – are connected with different inner organs activity. Everyone knows very well that heart and vessels activity is always changed in course of respiration, digestion, excretion changings. For example, if one presses on epigastrial region (epigastrial reflex) it's accompanied by vessels hypotony, blood pressure and heart freaquency reducing. Mechanism: at peritoneum receptors irritation (that occurs at pressure to epigastral region) information finally reaches depressor center and then to heart, vessels leading to their function decreasing or even stoppage. That's why fights are so dangerous because they may be accompanied by shocks to epigastrial region and in the most horrible cases even to instant (moment) death.

3)Extero-receptive conjugated reflexes are multiple nervous acts group occuring at the irritation of body surface and mucosae separate receptive fields. Example: ocular-heart reflex (Danini-Ashner's reflex): at pressure to eyeballs information comes to depressor centre. Result: heart contraction freaquency and blood pressure decreasing.

4) One knows very well vascular reactions to warmth (dilatation), coldness (constriction), pain (moderate pain leads to vasodilatation, strong – to constriction), touching (especially of lovely person). Due to separate points irritation (acupuncture points) on skin surface one can achieve definite success in heart activity and vessels tone regulation that is widely used in clinical practice particularly in facial-maxillary region (at neurites, myosites, myalgias et al.).

Humoral-chemical regulation

of heart and vessels activity is determined by hormones, mediators and different chemical substances (metabolites) action.

Substances increasing heart and vessels activity:

Hormones:

- adrenaline;
- noradrenaline;
- vasopressine;
- thyroxine;
- insuline;
- renine et al.

Mediators:

- noradrenaline;
- serotonine and others.

Metabolites:

- calcium excess;
- oxygen excess.

Substances decreasing heart and vessels activity:

- acethylcholine;
- hystamine;

- many prostaglandines (f.ex. prostacycline);
- acids (lactic et al.);
- CO_2 surplus (excess).

Acid products (lactic acid, CO_2) accumulating in course of physical activity decrease tone of working muscles blood vessels increasing blood supply to them. At this time magistral vessels are in increased tone due to adrenaline and noradrenaline concentration increasing in answer to load. Such tone redistribution in different vessels of blood circulation system provides high reliability of a given system functionning.

Thus, we see that heart-vascular activity regulation is a complicated process in what both reflectory (conditioned and unconditioned) and humoral-chemical mechanisms take part.

How and in what sequence these mechanisms are switched on under physiological conditions for instance in course of physical work? At this activity type increased oxygen consumption and enforced carbon dioxide releasing occurs. It may be achieved due to increased activity not only of respiration system but also blood circulation apparatus. Describe the consequence of switching of all these regulatory mechanisms on. At the early beginning, in the period of preparation to work the blood circulation system activity is increased by means of 2 mechanisms: conditioned-reflectory and humoral. Conditioned-reflectory – the situation itself before physical activity (sportsmen before running) is conditioned stimuli complex (in example with sportsman these are running way, stadium, spectators, referees and so on) which will cause the changes from the side of heart and vessels. Emotional load at this is a reason of enforced adrenaline releasing from suprarenal glands. The result of this is more expressed increasing of heart and vessels activity. Organism prepares given (cardiac-vascular) system to future wok in such a way.

In course of performing of physical activity itself conjugated reflexes from proprioreceptors, proper reflexes from chemoreceptors (metabolism products accumulation and first of all CO_2) are involved into regulation and hormones (adrenaline, vasopressine et al.) continue to be released. All these factors encourage further heart and vessels activity increasing. At the same time in working organs (muscles) acid products are accumulated, decreasing vessels tone in these organs and blood fills them in more extent providing feeding and removal of metabolism exchange.

After physical activity performing everything came ito its initial level due to involvement ito the work proper receptors from pressoreceptors directed to heart and vessels activity restriction (restoration).

Circulation regulation peculiarities in separate organs

There are both blood circulation and its regulation several distinguishing features in different organs. It is connected with different organs innervation and their various sensitivity to hormones, mediators and different chemicals which can influence on vascular vessels activity.

Circulation in heart

It is performed by coronary arteries, big capillaries amount. Circulative conditions in coronary arteries differ greatly from circulation in other organs. In course of ventricules systole myocardium presses vessels in it. That’s why blood circulation is weakened, oxygen supply is decreased to the tissues. Right after systole heart blood circulation is

increased. Main regulative role of sympathetic and parasympathetic influencings interrelations is in rapid and adequate coronary circulation adaptation to current organism organism needs. Vagus excitement leads to coronars dilation. Cardiac sympathetic rami (branches) excitement results in coronarodilation and blood stream activation in them. Oxygen myocardial consumption sufficiency is important for coronary circulation regulation. Cardiac muscle hypoxy results in myocardial chemoreceptors excitement which leads to reflectory arterioles dilations and blood stream activation. Carbonic dioxide accumulation in blood causes the same effect (that's why coronary circulation is increased at respiration lack).

Circulation in brain

It is more intensive in this region comparatively to all others. About 15 per cent of blood from every cardiac discharge in large circle comes into brain vessels. Brain vessels are muscular, with excessive adrenergic innervation that allows them to change their cavity in wide limits. Circulation distribution in brain is rather unequal: its maximal level is in hypothalamus and cortex.

Brain circulation independence from general (systemic) circulation is its important feature. It is explained by skull rigidity and brain disability to be pressed. That's why all liquids volume in intracranial vessels is practically constant. Even small increasing of this volume caused by significant arterioles dilation that leads to circulation increasing is compensed easily with insufficient veins constriction the volume of which is rather more.

Under norma, vasonstricting nervous fibres influence on brain blood stream insignificantly. Such weak brain innervation with vasoconstricting nerves is favourable for it. When blood pressure decreases for instance after strong bleeding (at which peripheral vessels are constricted), brain vessels are dilated. Brain circulation remains constant even under such conditions due to autoregulation (but only if blood pressure is not less as 50-60 mm merc col.) At further blood pressure decreasing blood circulation will be reduced in brain too that may leads to unconscious state.

In brain vessels tone regulation local factors are of great importance too. Merabolism intensivity activation in brain, blood content change (CO_2 level increasing) causes brain vessels dilation. H^+-ions role, oxygen tension are very important in these reactions too (at oxygen low tension – brain vessels are dilated, at high tension – are constricted, on the contrary). At oxygen content increasing in air brain vessels are constricted.

Blood circulation in lungs

Lung circulation peculiarity: circulation small circle vessels are relatively short, resistance in them is less; that's why pressure in them is in 5-6 times lower comparatively to aortal. Lung vessels capacity may be increased or decreased. Thus, due to this mechanism, lung filling with blood may varies in the limits of 10-25 per cent from common blood amount in organism. It provides blood depot creation. Lung net vessels big ability to stretching creates favourable conditions for easy blood stream and volume change. Inspiration leads to blood regional content increasing and to regional resistance decreasing to blood in course of usual breathing or even in course of hyperventillation.

At hypertony in reflexogenic zones vessels with parallel reflectory heart activity weakening and large circle vessels dilation lung circle reflectory filling takes place. Due to this blood pressure is leveled and blood distribution between circulation big and small

circles occurs. At pulmonal arteries pressure increasing, when small circle is overfilled with blood, reflexes from pulmonal artery receptors occurs on large circle vessels. As the result of this blood amount is increased in large and is decreased - in small circle. It prevents blood stagnation in lungs and provides heart activity and blood circulation as a whole.

Lecture 14
Blood physiology – blood functions. Blood physico-chemical peculiarities. Erythrocytes and erythropoiesis.

Blood system includes:

- circulating blood;
- haematopoiesis organs;
- blood destruction organs;
- regulative organs.

Circulating blood - is internal environment liquid or tissue, contained into blood circulation system. Its amount is 6-8 % from body weight; in average – 4,0-6,0 litres. In women this amount is on 1,0-1,5 l less in comparison to men.

Blood amount:

- in new-borns - 15 per cent from body weight (11,0-20,0 %);
- in 1 year - 10 %;
- in boys it is bigger than in girls.

Normovolemy - normal blood volume.

Hypovolemy - blood volume decreasing. Reasons:

- haemorrhagias (bleedings);
- hard physical activity;
- hyperthermy.

Hypervolemy – blood volume increasing. Reasons:

- liquid big amount usage;
- oligoanuria (kidneys and urinary tract pathology).

2/3 of blood is concentrated in veins, 1/3 - in arteries; 1/3 (1,5 l) – in ***blood depot***:

- spleen;
- liver;
- skin et al.

Deponated volume decreasing main reasons:

- physical activity;
- environment or body temperature increasing;
- tissular hypoxy;
- bleedings.

Deponated volume increasing main reasons:

- pregnancy;
- hyperadrenalinaemia and other cases.

There is definite correlation in blood between plasma and formed elements – ***haematocrit.*** Normal values:

- in men - 40-48 per cent;
- in women - 36-44 per cent;
- in new-borns – 55-60 per cent;
- in 1 month - 40-45 per cent;
- in 1 year – 35-40 per cent;
- in capillary blood - 32 per cent.

Main blood functions:

1. *Transport* – oxygen, nutrients delivery to peryphery, carbonic dioxide and metabolites removal.
2. *Protective*:

- immunity;
- phagocytosis;
- complement system;
- haemostasis;
- fibrinolysis;
- antioxidant system and so on.

3. *Regulatory:*

a) humoral regulation:
   - hormones;
   - mediators et al.;

b) physico-chemical regulation:
   - temperature;
   - osmotic pressure;
   - oncotic pressure;
   - acid-alkaline equillibrium and others.

Blood physical-chemical peculiarities and constants.

1. *Blood colour* - depends on haemoglobine. Arterial blood is brightly red because of oxyhaemoglobine (haemoglobine connected with oxygen) big amount. Venous blood is dark red with blue shade. Such blood colour is linked with presence not only of oxydated haemoglobine but also reducted haemoglobine.
2. *Blood viscosity or internal friction*. It is often determined comparatively to water viscosity: if the latest one is equal to 1, blood viscosity is equal to 4,0-5,0. In new-borned - 10,0-14,0; in 1 month – like in the adult. In girls this index is less than in boys. Main reasons for viscosity increasing:

- in mountains;
- hypercapnia (carbonic acid content increasing in blood);
- inflammations;
- hypertony;
- atherosclerosis;
- at feeding of mainly animal food (proteins-rich) – meat, eggs.

Main reasons for viscosity decreasing:

- at vegeteranian feeding.

Viscosity depends on formed elements (mainly erythrocytes) amount and proteins concentration.

3. *Blood density* – 1,056-1,060. It is increased at blood condensation; it is decreased – at its liquerfaction. Density level depends on formed elements (mainly erythrocytes) amount and proteins concentration.
4. *Osmotic pressure* – force that makes water transmit from less concentrated solution in more concentrated. Sodium chloridum is essential for its support (60 per cent of this pressure depends on it). It is the same in all internal environment elements (blood, lymph, tissular liquid). It remains constant even at big water and salts passing into the blood because of their removal by kidneys. Osmotic pressure is supported by means of receptors located in vascular vessels wall and in hypothalamus. Normal value: 7,3-7,6 atmospheres. Solutions with equal osmotic pressure are called isotonic (for example, 0,85% solution of sodium chloridum, 5,5 % solution of glucose). If osmotic pressure in solution is more - it is called hypertonic and, correspondingly, if less - hypotonic.
5. *Oncotic pressure* - is created by blood proteins (mainly low-weighted albumines). Its level is fluctuated from 25 till 30 mm merc col under physical conditions. It is essential for:

- transcapillary exchange;
- uropoiesis;
- absorbtion;
- lymph formation (lymphopoiesis).

6. *Acid-alkaline equillibrium* – correlation between acid and alkaline equivalent in blood. This is reaction caused by H^+-ions concentration. PH or hydrogenium index is used for its evaluation. If pH is equal to 7,0 the environment is called neutral; less than 7,0 – acid; more than 7,0 – alkaline. Norma: in venous blood – 7,34, arterial blood – 7,4; blood in a whole – 7,35-7,47. At birth acidosis is physiologic. Ph is supported by: buffer systems, excretory organs and lungs.

Buffer systems:

- bicarbonate,
- phosphate,
- protein,
- haemoglobine (75 per cent of all system).

At muscular tension increasing acid products come into blood (lactic acid, carbonic acid) and movement to acid side (acidosis) is observed. At increased carbonic acid releasing (with lungs at hyperventillation) movement to alkaline side (alkalosis) occurs.

Blood protheins are 7-8 % or 65-85 g/l. Their population is not homogenic.

Albumins – (60 % or 35-50 g/l) produced in liver; are agile, low-weighted, they are important for:

- oncotic pressure support;
- bilirubin transport;
- hard metals salts transport;
- fat acids transport;
- medicines transport (proteins increase action periods for them).

Globulins (40% or 30-35 g/l) are formed in liver, bone marrow, spleen. Role:

- form antibodies;

- antitoxines;
- agglutinines;
- blood coagulation (some of them are clotting factors);
- phospholipid transport;
- cholesterol transport;
- steroid hormones transport;
- oncotic pressure support (less than albumins);
- blood density support;
- buffers;
- blood viscosity determination;
- nutritive function.

Erythrocytes Er (red blood cells RBC)

They were discovered in 17th century. They vary in their shape:

- discocytes (76 per cent);
- stomatocytes;
- echinocytes;
- spherocytes;
- torocytes;
- dacryocytes;
- planocytes;
- spherocytes;
- ovalocytes;
- acanthocytes and others.

Poikilocytosis - if one can see erythrocytes of different shape in 1 eyesight field simultaneously. Discoid shape the most widely-spread among RBC allow them transmit capillary better.

Er also differ in their sizes:

- normocytes - cells with diameter 7,5-8,3 mcm and width about 2,1 mcm (their amount is approximately equal to 68 per cent);
- microcytes – if diameter is less (about 15 per cent);
- macrocytes - with larger diameter.

Anizocytosis - if one can see erythrocytes of different size in 1 eyesight field simultaneously.

Human erythrocytes have no any nucleus. This fact allows them to come through capillary easily. Er is covered by membrane which has antigenic features. This membrane can adsorb and desorb substances coming into blood. Human Er possess large adsorbtive-desorbtive potential. RBC membrane permeability is important for organism availability. Er membrane may be destructed in hypotonic solutions (water, acid et al.) that leads to ***haemolysis*** development.

Haemolysis kinds:

1. According to causative agent action:

- mechanic (shaking up, vibration);
- chemical (chlorophorm);

- physical (electrical current);
- osmotic (sodium natrium action);
- biologic (some snakes poisons).

2. According to localization:

- intracellular;
- intravascular (at blood transmissions, toxic animals and insects bites and so on).

Osmotic resistance (ability to resist osmotic forces) is index characterized intravascular haemolysis. Norma: 0,32-0,48% of sodium chloridum.

Er membrane is charged negatively; at this negative charge decreasing RBC can glue together and sedimentate. This reaction received the name ***velocity sedimentation rate (VSR).*** Under norma:

- in men – 2,0-10,0 mm/h - widely-spread among doctors (according to new data – 6,0-12,0);
- in women – 2,0-15,0 mm/h (according to new theoretic data - 8,0-15,0) (up to 15,0 - at pregnancy due to hyperfibrinogenemia and at menses as a result of erythrocytes number decreasing because erythrocytes are easily to sedimentate under such conditions);
- in new-borns – 1,0-2,0 mm/h;
- in babies (1 year) – 4,0-10,0 mm/h;
- in the old of both sexes – up to 15,0-20,0 mm/h.

VSR depends on fibrinogen concentration in blood: if its content is more than 3,0 g/l (norma – 2,0-4,0 g/l) VSR is increased. It's observed in pregnant women and at inflammatory processes. VSR reducing less than 2,0 mm/h – is unfavourable diagnostic sign. But at the same time this index increasing up to 40-100 mm/h (especially to upper limit) may be the sign of tumors particularly malignant.

Erythrocytes amount under norma in men 4,4-5,0 x 10^{12}/l; in women – 3,7-4,5 x 10^{12}/l. *Erythrocytosis* means Er amount increasing:

1. Physiological:

- in new-borns;
- at physical work;
- in mountains.

2. Pahological:

- real polycytaemia - Vakez' disease.

Erythropenia – RBC amount decreasing:

- in pregnant;
- at irradiations et al.

Haemoglobine is an essential structural part in Er. Normal values:

- in men – 135-180 g/l;
- in women – 120-160 g/l;
- in new-borns – up to 200 g/l;
- in pregnant women – up to 110 g/l (physiological hypochromic anaemia).

Main role: oxygen transport (oxyhaemoglobin) and CO_2 (carbohaemoglobine). Adult haemoglobine consists of fractions: "A" – 95-98%, A_2 – 2-3%; fetal haemoglobine (Hb F) – 1-2%.

One can tell about Er saturation by haemoglobine on so-called ***colour index (CI).*** It is relative index characterizing Er saturation with Hb. Under norma this index is equal to 0,75-1,0. Er at such CI are called *normochromic*; if it is more than 1,0 – *hyperchromic;* less than 0,75 – *hypochromic.*

Erythrocytes functions:

1. Respiratory – O_2 and CO_2 transport.
2. Metabolic – participation in proteins, fats and carbohydrates, water and salts exchange.
3. Transport - proteins, fats, carbohydrates, medicines.
4. Buffer (haemoglobine buffer).
5. Participation in iron metabolism.
6. Bile-formation regulation.
7. Erythropoiesis.
8. Antitoxic function.
9. Blood coagulation and fibrinolysis.

Erythropoiesis and its regulation.

RBC life duration is 60-120 days (in males – on 10-20 days longer). They are formed in bone marrow from reticulocytes. At this stage reaching capillary wall is stretched, vessel is opened and Er are washed into blood stream, where they are transformed into young Er (normocytes) after 35-45 hours. Er die in liver, spleen. Destructed Er amount corresponds to formed Er amount. This closed system with all mass of Er circulating into organism received the name ***erythron***.

Erythropoiesis regulation is performed by humoral and nervous-reflectory way. ***Humoral way*** is main and it's more complicated. It includes 2 ways:

1. *Specific* - is linked with special substances - cytokines. Erythropoietin is the most essential among them from this point of view. This is polypeptide, produced in kidneys, uterus, salivary glands. Its amount is increased at:

- bleedings;
- low oxygen partial pressure;
- ascent to haltitude (in the mountains);
- muscular activity.

Action mechanism:

- stem cells transition into erythroblasts acceleration and enforcement;
- cellular mitosis increasing;
- interphase decreasing;
- normoblasts and reticulocytes maturation increasing;
- DNA, RNA and ferritin amount increasing in erythrocytic predecessors;
- circulation activation in erythroblastic bone-marrow insulas.

Other cytokines delt with erythropoiesis - haemopoeitines (they produce by leucocytes, macrophages and endotheliocytes):

- interleukines acting to bone-marrow;
- growth-stimulating factor;
- colony-stimulating factor;
- colony-forming factor.

2. *Non-specific* way – microelements, vitamines and hormones action.

a) Microelements:

- Iron is the most essential among them. It comes into bone-marrow from destructed erythrocytes (about 21 mg per day). But this amount is insufficient for normal erythropoiesis performance. Additional amount must be approximately 4 mg/day. 12-15 mg must come with water and food while normal urtilization in alimentary tract. If no – iron-deficient anaemia is observed (in pregnant, at stomach and intestine diseases). Ascorbic acid enforces iron absorbtion. Transferrin – special iron transporter – is located in intestinal mucosa; iron forms complex with protein ferritin in cells and is preserved in cells in such a form. Liver is main iron depot in organism.
- Copper provides iron mobilization from tissues and its utilization. Copper is utilized by bone-marrow and participate in haemoglobine synthesis. When copper absence RBC maturate only till reticulocytic stage.
- Cobalt is a haemoglobine constituent.
- Fluorum is erythropoiesis inhibitor, that's why at its excess in environment (water, air, foods) anaemia may be developed.

b) Vitamines: of B-group are the most essential:

- B_{12} (cyancobalamine) - haemopoiesis factor. It is synthesized by microorganisms, ray fungi and some weads. Cobalt is essential for cyancobalamine formation. This vitamine comes into human organism with liver, meat, eggs. This vitamine takes part in haemoglobine synthesis. It is accumulated into liver; its depot is very large (for 5-10 years).
- B_9 (folic acid) – is contained in plant food, liver, eggs. It participates in globine synthesis influencing on erythroblasts.
- B_6 (pyridoxine) catalyzes folic acid formation and cyancobalamine action.
- B_2 (rhibophlavine) participates in iron consumption, it also is necessary for haemoglobine synthesis.
- C (ascorbic acid) – encourages iron releasing from intestine and regulates haemoglobine synthesis.
- A (retinol) and E (tocopherol) – influence on haemopoietic tissue functions, protect Er membrane from free radicals action.

c) Hormones:

- Hypophyseal erythropoietical hormone, ACTH, STH - enforce erythropoiesis.
- Suprarenal glands – glucocorticoids, adrenaline - enforce erythropoiesis.
- Parathyroid - parathormone - enforces erythropoiesis.
- Female sexual organs – erythropoiesis weakening.
- Male sexual organs - enforce erythropoiesis.

Besides erythropoiesis activators there are also erythropoiesis inhibitors in blood.

Neural-humoral erythropoiesis regulation

It is of less importance than humoral one. But it is well-known than some hypothalamic nuclei can stimulate or inhibit erythropoiesis. All these influencings performance is realized through vegetative nerves. Sympathetic nervous system excitement is accompanied by erythropoiesis activation. That's why active life position and positive emotions - are important erythropoiesis activators.

Lecture 15.
Protective blood functions connected with leucocytes. Blood groups.

Leucocytes or white blood cells (WBC) were described in the middle of 18th century. It is known that they are divided into 2 groups:

1. Granulocytes:
- neutrophils;
- eosinophils;
- basophils.
2. Agranulocytes:
- lymphocytes;
- monocytes.

Leucocytes norma: 4,5-9,0 $x10^9$/l. Their amount is bigger right after birth and can reach up to 20,0 $x10^9$/l and even more. This number can increase in course of the first 24 hours of life. In 1 year – their amount is fluctuated from 6,0 till 12,0 $x10^9$/l. Adult ziphras are achieved to 9-10 years. WBC content depends on season (it is bigger in autumn and winter; less – in summer and spring) as well as on day time (less in the night than in the afternoon).

Leucocytosis means leucocyte amount increasing.

1. *Physiological (distributive):*
- muscular - at football, chockey et al. when bone-marrow function is activated in muscles;
- emotional;
- noceoceptive (in course of pain especially moderate; while at strong pain – leucocytes amount is decreased);
- in ovulation (mainly due to neutrophils amount increasing);
- in pregnant women (in uterus submucosa);
- in new-borns (child's organism is under strong stress due to transition into new environment);
- alimentary (linked with protein food taking due to increased antibodies production to proteins).
2. *Pathological (reactive):*
- inflammational;
- infectional.

Leucopenia - leucocytes amount decreasing:
- infectional;
- radiational;
- as answer reactions to some medicines action.

Leucocytic formula:

- basophils – 0-1,0 %;
- eosinophils – 1,0-4,0 %;
- neutrophils - 50,0-70,0 % - among them:
- juveniles – up to 1,0%,

- rod or stab neutrophils – 1,0-4,0 %,
- segment-nuclear neutrophils – 50,0-65,0 %;
- lymphocytes – 25,0-40,0 %;
- monocytes – 2,0-10,0%.

Movement (shift) to the left - is called regenerative movement (blood renewal, sign of so-called young blood); is characterized by juveniles and rod (stab) neutrophils increasing in blood. Reasons:

- infectional diseases;
- leucoses;
- inflammational processes.

Movement (shift) to the right - is called degenerative movement (sign of old blood): is characterized by juveniles and rod (stab) neutrophils amount decreasing and segment-nuclear leucocytes number increasing. It may be observed at:

- aplastic anaemias;
- leucoses.

Crossings.

In children beginning from the 2nd day of their life lymphocytes is increased and neutrophils amount is decreased. 5-6th days of their life are characterized by equality of neutrophils and lymphocytes amount (42,0-45,0%). Such equality is named as first crossing of neutrophils and lymphocytes amount. Then with ageing neutrophils number is decreased, lymphocytes – increased. To 5th month of life neutrophils are 25,0-30,0%, lymphocytes – 65%. Such situation is up to 9-10th months of life. Then gradually neutrophils amount is increased, lymphocytes – is decreased. In 5-6 years – second crossing. To puberty – all indexes become like in adulthood.

Separate leucocytes physiology.

Neutrophils – are produced in bhone-marrow, live 8-10 hours, part of them are in circulation, another one – into marginal state and significant part leaves blood and dies in tissues. Functions:

- participating in phagocytosis;
- apoptosis triggering;
- interleukines-1,6,8 and 12 formation;
- interpherone formation;
- immune reactions;
- participation in mitosis;
- reparational and regenerational processes;
- haematopoietic reactions;
- blood coagulation;
- fibrinolysis (they contain plasminogen activator).

Neutrophilesis – amount increasing – sign of inflammational process.

Neutropenia – amount decreasing:

- viruse diseases;
- roentgen and radiorays action.

Basophils – are formed in bone-marrow, live up to 12 hours. Their relatives - fat cells (mast cells, mastocytes) live for years. Role:

- anticoagulation - heparin production;

- hystamine – allergy reactions, migraine;
- hyaluronic acid – participates in membrane permeability increasing;
- platelets activation factor synthesis;
- thromboxanes production – see next lection;
- leucotryens – participate in multiple organism reations;
- prostaglandines – the same + next lecture.

Basophily - basophils amount increasing:

- menstruations;
- allergy;
- stress;
- leucosis;
- inflammation.

Eosinophils – are produced in bone-marrow, live from 4 to 12 days. They are only several hours in blood stream, then penetrate into the tissue for destruction. Functions:

- phagocytosis;
- antitoxic function;
- kallikrein-kinin system components activation.

Eosinophily- their amount increasing:

- allergic diseases;
- haelmintoses;
- rose sundown of speedy recovery after infectious pathology – very favourable and long-awaited diagnostic criterium.

Eosinopeny – their amount decreasing:

- hard infectional diseases – unfavourable diagnostic sign.

Monocytes – are formed in different haemopoietic organs:

- bone marrow,
- lymphatic nodes;
- connective tissue.

Life duration – 36-104 hours. They leave tissues and form macrophagal family there. Role:

- strong phagocytosis;
- contain monokines influencing on lymphocytes;
- antiinfectional action;
- antitumorogenic activity;
- blood coagulation;
- fibrinolysis;
- complement system components synthesis.

Monocytosis – monocytes amount increasing:

- infectious diseases;
- fester (pus) processes;
- tuberculosis;
- haelminthes.

Lymphocytes – are originated from bone marrow and come into circulation. There one of their population comes to thymus where their differentiation in T-lymphocytes

takes place. Other part – to bursa of Fabricius analogue (in birds) in small intestine cellular formations, tonsills, appendix, bone marrow and are differentiated in lymphocytes (bursa-dependent). This lymphocytic part is not differentiated in immune organs and such lymphocytes are calles zero-lymphocytes (neither T-, nor B-).

T-lymphocytes have several types. In a whole, they are responsible for cellular immunity. Their amount is 40-70 per cent of all lymphocytes amount.

B-lymphocytes also have several types. They provide immunoglobulins formation and thus delt with cellular and especially with humoral immunity. Their amount is 20-30 per cent of all lymphocytes.

Zero-lymphocytes secrete proteins (perphorines) possessing the ability to make the foramen in side cells membrane and while protheolytic enzymes (cytolysines) pouring in them destroy them. That's why they are often named as natural killers. Their amount is 10-20 per cent of all lymphocytes.

Main white blood cell function is to participate in defense organism reactions against foreign agents. There exist the natural (non-specific) and specific defence forms.

The non-specific defence is directed to any foreign agent eliminating. The phagocytosis, the complement system and others humoral defense factors are the main types of such reactions. **Phagocytosis** consists of engulfing the microbes and cells via the formation of the pseudopods followed by endocytosis of the phagocytic vesicle. Next, the endocytotic vesicle is incorporated into the lysosomes of the phagocytes where the microbes and cells are digested by lysosomal enzymes. This phenomenon is adequate to the neutrophiles, monocytes, eosinophiles, macrophages and thrombocytes. In the course of the phagocytosis process we differentiate such stages as the phagocyte approaching to the phagocytized object (or ligand), the ligand contact with the phagocyte membrane, the ligand engulfing, digestion and destruction of the phagocytized object. The phagocytes find their way to the site of injury by chemotaxis or similar guiding mechanisms.

Complement system - is a special enzyme system consisting of the proteins (more than 20 types). In includes 9 components (C1…C9). During the activation process some of its components are cleaved in the fragments influencing directly the course of specific and nonspecific defense reactions. There exist the classical and alternative ways of complement system activation. The destruction of foreign and old cells, the phagocytosis and the immune reactions course activates, the vessel wall permeability increases, the blood coagulation hastens at the complement system activation that influence the pathological process.

The other humoral defense factors – defense reactions connected with the action of such substances as lysozyme and interferon. **Lysozyme** as a protein possesses the enzyme activity suppressing the growth and the development of causative agents and destroying some of the microorganisms. It can be found in nasal mucosa, intestines, salivary secret, lacrimal fluid etc. In small amounts one can find it in the granules of polymorphonuclear leukocytes, in macrophages and when destroyed they fall into the extracellular fluid. **Interferon** as the globulin of blood plasma can be located in the lymphocytes providing antiviral defense and delaying the cancer cell growth.

Specific defense – immunity – is a reaction complex directed to maintaining the homeostasis on meeting the host's body with the antigens which are considered as foreign (despite their forming in the organism itself or if they come into it from outside). Under the action of antigen the host body forms the antibodies, activates lymphocytes and thus

they get the ability to participate in the immune response. This antigen ability to cause the specific immune response is due to the presence of multiple determinants on its molecule. The active centers of forming antibodies specifically correspond to the determinants like the key to the lock. The antigen interacting with its corresponding antigen forms the immune complex.

The immune organs are divided into central (thymus, bursa of Fabricius, bone marrow) and the peripheral (lymphatic nodes, spleen etc.). There are two categories of acquired immune responces – humoral or antibody-mediated and cell-mediated.

In addition to the above mentioned information we can say that not only the nervous and humoral regulation of various organism functions but the immunological one exist in the human body. Thus, the lymphokines and monokines secreted by the lymphocytes, the monocytes and the macrophages are capable of changing the central nervous system, the heart, the vessels, the respiratory and digestive organs action. As for the interleukines they are involved in all the physiological body reactions. The immune system itself is not only the defense system (especially the antiinfectious) but the important regulative system too. Functionally it is tied with both nervous and the endocrine organism system. Such an approach to functionning of this system not only extends our data about its activity but permits to outline the new therapy ways of acquired and hereditary disorders.

Leucopoiesis regulation.

Like erythropoiesis regulation it can be performed both specific and non-specific ways. ***Specific way –*** is *leucopoietines* action (they are produced into liver, spleen, thymus, kidneys). Their action mechanism is in involving into bone marrow cells differentiation process. ***Non-specific way*** – is:

a) vitamines action (especially of groups "B_{12}" and "C");
b) hormones:
- ACTH;
- thyroid;
- sexual;

c) microelements;
d) leucocytes, tissues, toxins, microbes metabolic products have special importance for leucopoiesis regulation. The more leucocytes are destroyed, the more new forms are formed.

Blood groups.

Membranes antigenic features (particularly erythrocytic) underlie individual blood group characteristic. These antigenes have received the name agglutinogenes. One can differentiate antigenes "A" and "B". Their amount is large on the surface and it depends on agglutinogene type. "A_1" contains approximately 900000-1700000; "A_2"- 250000-260000. Their distribution on blood groups in ABO-system is the following: I-0, II-A, III-B and IV-AB. Besides agglutinogenes, in plasma or serum there are also agglutinines (antibodies). They are designated by letters α- and β-. Blood of one individual can not have similar agglutinogenes and agglutinines. There are also haemolysines in plasma and serum (they are designated like agglutinines). One can see conflict at blood haemotransfusions at meeting of one-named agglutinogenes and haemolysines (they act at 37-40°C). At room temperature, if one-named agglutinogenes and agglutinines meet each other agglutination reaction occurs –the criterium of group characteristic. There are also

antiagglutinines in blood of II, III and IVth groups. These are agglutinogenes which left erythrocytes. They are designated as “A” and “B”.

High resistance to temperature, blood preservation terms are the characteristic of all agglutinogenes. That’s why they contain practrically in all tissues of given organism and its fluids. That’s why agglutinogenes content is essential to be known, when blood is received from donor with its further usage for transmission. On the contrary, agglutinines are unstable comparatively to agglutinogenes and they are easily destroyed while contact with side surface, while temperature changing. That’s why they are not important in donor blood, but their determining is quite essential in recipient blood.

Rhesus-system was discovered in the middle of last century. 85 per cent of people has agglutinogene of this system (Rh-rhesus) and these people are called rhesus-positive. 15 per cent of people have no this antigene ans correspondingly they are known as rhesus-negative. Rh-system is rather complicated, it includes more than 40 antigenes. They don’t have one-named agglutinines, but the latest can appear in recipient blood in course of multiple transmission of Rh^+ - blood to them. This factor is inherited. That’s why it is important in obstetrics. If woman is Rh^- ad man Rh^+, then embryo approximately in 100 per cent of cases will inherit Rh-factor from father. It may result in Rh-conflict.

Other antigene systems are more seldom (Luteran, Daffi, Kell-Kellano, MNS et al.). Scientists tell nowadays about 500 antigenes only on erythrocytic membrane. If to add others to them, then their amount will predominate number of all residents on the Earth. With other worlds, every person has his or her own blood group, that is quite essential to know and to use in clinical practice.

Blood groups systems knowledge importance for doctors.

1. Problem delt with blood transmission. We should perform it very seldom if we really wonder to help our patient. Blood transmission can hurt more! If it is necessary we should follow such rules as:
- donor environment must corresponds to recipient environment (agglutinogenes should be taken into account in donors, agglutinines – in recipients);
- to determine Rh-characteristic always;
- if it is possible – other blood group sytems;
- to determine always blood compatibility and to transmit only one-grouped blood!
- Remember! Universal donors and recipients are absent!!!

2. Problems delt with tissues compatibility at organs and tissues transplantation.
3. Problems linked with paternity (MNS-system).
4. There are some data about correlation between blood groups and disease.
5. About correlation with temperamentum.
6. About such interrelations with feeding.
7. With physical loadings.

All the mentioned above can be taken into account in course of individual approach not only to his patient but also to himself. As blood determines our soul than the best soul affinity – is the same blood group! It was not occasionally observed that the most happiest marriages are among people with 1 blood group!!!

Lecture 16.

Platelets (thrombocytes) physiology. Haemostasis (vascular-platelet and coagulational).

Thrombocytes or blood platelets are formed from red bone marrow giant cells – megacaryocytes. Their diameter is fluctuated in the limits between 2 and 4 mcm, volume is 6-9 mcm^3. They are two-membraned, nucleus-free but there are lot's of different granules in them. They are activated in course of side surface, many (up to 10) processes are appeared in them as a result of which their diameter is increased in 5-10 times. There are integrines on platelet membrane serving as receptors. They participate in thrombocytes interaction one to another and to injured vessel. They have glycoprotein nature expressing fibrinogen, collagen, Willebrandt factor (FW) and other substances.

Platelets contain many granules with great number of biologically active substances. One can differentiate:

1) *Alpha-granules* – contain more than 30 proteins delt with haemostasis and other reactions:
- platelet factor 4;
- fibrinogene;
- thrombostenin and so on.

2) *Dense granules* – they contain biologically active substances delt with vascular tone and haemostasis:
- ADP;
- adrenaline;
- serotonin;
- thromboxanes et al.

3) *Lysosomal granules:*
- kinases;
- enzymes.

Platelet number under norma is:
- in adults - 150-350 x 10^9/l;
- in new-borns - 200 x 10^9/l (in average – fluctuations 100-400 x 10^9/l);
- 7-10^{th} days – 150-200 x 10^9/l;
- 14^{th} day – like in adulthood.

Thrombocytosis - their amount increasing:

1) *Physiological:*
- pain (noceoceptive);
- stressogenic;
- muscular (in course of physical loading).

2) *Pathological:*
- spleen pathology;
- spleen removal.

Thrombocytopenia – as a rule, is pathology sign and is observed at:
- radiation disease;
- congenital blood diseases;
- acquired blood diseases.

But in women on course of menstruation period platelets amount may be reduced though they are seldom out of normal limits. But it should be mentioned that even at strong thrombocytopenia reaching up to 50 x 10^9/l, there is no any bleedings and women mustn't be under medication at these situations. Only when reaching critical ziphras – 25-30 x 10^9/l - light bleedings may occur at which treaty measures are essential. It testifies that platelets amount in blood is excessive.

Platelets functions:

1. Participation in vascular-thrombocytic and coagulational haemostasis (properly blood coagulation).
2. Angiotrophyc function – vascular walls feeding (15 per cent of all thrombocytes daily). At this function disorders: vascular wall permeability increasing and resistance decreasing.
3. Protective function:

- phagocytosis;
- contain immunoglobulins;
- lyzozyme source;
- they are essential for reparation;
- cytokines source.

Thrombocytopoiesis regulation

1. Specific:

- thrombocytopoietins;
- interleukines-3,6,7,9,11,13.

2. Non-specific:

a) hormones:

- adrenocorticothropic;
- adrenaline;

b) food products:

- nettle;
- fungus puff-ball;

c) sympathetic nerous system excitement.

Haemostasis – is the reactions complex aimed at the blood loss stopping. In fact the significance of haemostasis system is much more complicated and far exeeds the limits of fighting with blood loss.

The main tasks of the haemostasis are the following: the fluid blood state storage, the transcapillary exchange, the vessel wall resistence regulation and the influence on the reparation processes and so on.

They distinguish the vessel-platelet haemostasis and blood coagulation (clotting). Speaking about the first case the question is about the blood loss stopping from the small vessels with low blood pressure; the second one is connected with the blood loss fighting at the arteries and veins rupture. Such division is rather conditional as both at small and large vessels rupture together with the thrombocyte plug forming the blood coagulation is occured. On the other hand such a division is very suitable for clinical practice because at the vessel-platelet haemostasis disorders the finger skin puncture (or the ear lobe) is accompanied by prolonged coagulation time whereas the bleeding time remains normal (for example at haemophilia because of normal platelet count in hemophiliac).

Haemophilia is a wide-spread hereditary pathological state. It is the excessive bleeding caused by a congenital lack of a substance (plasma coagulation factor VIII, IX, X or XI) necessary for blood clotting. Treatment consists of administration of the deficient factor.

Vessel-platelet haemostasis comes to the platelet plug (or thrombus) forming. Conditionally it is divided into three stages. The first stage is ***temporary (primary and secondary) vasoconstriction*** - immediately in a few seconds after the injury the primary vasoconstriction occurs due to it the bleeding at the first moment may not happen or bears the limited character. It is caused by the adrenaline or norepinephrine releasing in response to the pain irritation and lasts for about 10-15 sec. Futher, the secondary vasoconstriction occurs because of the platelet activation and the releasing from them in a blood the vasoactive substances - serotonine, adrenaline, thromboxanes.

The second stage is the ***platelet plug forming*** because of the ***adhesion*** (the binding to the foreign surface) and the ***aggregation*** (clumping of the platelets). The adhesion takes place immediately after the injury to the collagen and other adhesion subendothelium proteins. It occurs because of the glycoproteins action by means of which the platelets clump to the collagen fibres and by means of the Willebrand factor as well that one of its active centers usage is bound up to the platelet receptor and the other of its receptors to the collagen or subendothelium. From the adhesive platelets and the injured endothelium as well the ADP (adenosine diphosphate) is released, which is one of the major factors of platelet aggregation. Under the unfluence of ADP the platelets clump, so forming the aggregates. This reaction increasing is due to the platelet activation factor (PAF), thrombin and adrenaline. On this stage the aggregation is ***reversible*** and the ***desaggregation*** may happen. To complete the platelet plug forming a number of additional mechanisms (they are associated mainly with the platelets) are required. When the sygnal comes into the platelets the calcium content increases in them and the phospholipase A2 activation occurs. The latter one leads to the arachidonic acid releasing from the platelets membranes that further converts into the very active prostaglandines and thromboxanes. When removing from the platelets they make the aggregation ***irreversible*****.** As a result the platelet plug or thrombus is formed. But at first it is capable of passing the blood as it is loose. After releasing the actomyosine (thrombostenine) from the platelets during their aggregation the platelet plug is shortened and reinforced. This is the third stage of the vessel-platelet haemostasis – the ***platelet plug retraction***.

Under the normal condition the blood loss stoppage from small vessels lasts from 2 to 4 minutes. Such index in the clinic is known as the ***bleeding time***.

The arachidonic acid derivates – prostacyclin and thromboxane A2 - play a very important role in the vessel-platelet haemostasis regulation. Prostacyclin is produced by endotheliocytes under the enzyme prostacyclinsynthetase influence. Under the physioilogical conditions prostacyclin predominates over thromboxane – powerful platelet proaggregant. At any endothelium injury in the trauma place the prostacyclin producing disturbs and the thromboxane action begins to be predominate. Thus, the favourable conditions for the platelet aggregation emerge. Some vitamins (A,C,E) and foods (onion, garlic) are the platelet aggregation inhibitors.

Blood coagulation is an enzyme process where both the plasmic and the cell factors participate. Most of the haemocoagulation plasma factors are the proenzymes and their activation occurs due to the limited protheolysis and is accompanied by the peptide

inhibitors cleavage. They are designated the Roman figures. There are 13 such factors in plasma.

The platelets play an important role in a blood coagulation process. They contain a lot of (more than 30) different substances which deal with the haemostasis process. Some of them (according to the various literature scientific sources from 5 to 15) are called the **platelet (thrombocyte) coagulation factors** that are designated the Ciphers.

In the erythrocytes one can find a number of substances like the platelet ones. They are known as the **erythrocyte blood coagulation factors**. They have no figure designation. The leukocytes have the coagulation factors called **leukocyte factors.** For example, monocytes and macrophages upon antigen stimulating synthesize the protein thromboplastine part namely apoprotein III (tissue factor).

Tissue factors the main component of which is thromboplastine play a significant role in a blood coagulation. Thromboplastine or tissue factor consists of the protein part apoprotein III and the phospholipid complex and it is often considered to be a cell membrane fragment. Upon the tissue destruction or endothelium stimulation by means of proinflammatory cytokines or endotoxin the tissue factor can be released in a blood circulation. In various blood circulation regions in the vessels its content differs (e.g. in veins and arteries, lower or upper extremities, on the right or on the left in ones of the same name).

Plasmatic blood coagulation factors.

I, *fibrinogene* – protein, synthesized in liver, transforms into fibrin in course of blood coagulation. Fibrinogen is also essential for platelet aggregation, tissular reparation. Normal values into blood – 2-4 g/l (minimal level – 0,8 g/l). One can meet hypo- and hyperfibrinogenaemia.

II, *prothrombin* – glycoprotein, synthesized in liver at vitamine K presence. Prothrombin transforms in fibrin under prothrombinase. Norma: 0,1-0,15 g/l. Minimal level – 40%. One can tell about hypo- and hyperprothrombinaemia.

III, *thromboplastine* – consists of protein apoprothein III and phospholipid complex. It is in membrane structure of many tissues. It represents matrix for prothrombinase formation on external way.

IV, *calcium* – is essential for prothrombinase production, platelet aggregation, releasing and retraction reactions. Under norma: 0,03-0,04 g/l. Blood coagulation process remains normal until calcium level reducing to fits development.

V, *accelerator-globulin* – protein, synthesized in liver, is activated by thrombine, is in prothrombinase complex composition. Norma – up to 0,01 g/l. Minimal level -10-15%. Owren's disease or parahaemophilia occurs at its absence.

VII, *proconvertine* – glycoprotein, vit K is essential for its synthesis, is synthesized in liver. Participates in prothrombinase formation on external way. Norma: about 0,005 g/l, minimal level – 5-10%. Alexander's disease or parahaemophilia occurs at its absence.

VIII, *antihaemophilic globulin (AHG)* – glycoprotein, it is formed in liver, spleen, vascular wall. It is essential for prothrombinase formation on internal way. It forms complex with FW in plasma. Norma: 0,01-0,02 g/l. Minimal level – 30-35%. Haemophilia A appears at its absence or strong reducing of its concentration.

IX, *Cristmas' factor, antihaemophilic factor B* – glycoprotein, is formed in liver at vit K presence, takes part in prothrombinase formation on internal way. Norma: 0,003 g/l.

Minimal level- 20-30%. Haemophilia B (Christmas' disease) is developed at its absence or strong reducing of its concentration.

X, *Stuart-Prauer's factor* - glycoprotein, is formed in liver at vit K presence. It is prothrombinase complex main part. Norma: 0,01 g/l. Minimal level - 10-20%. Haemophilia D (Stuart-Prauer's disease) is developed at its absence or strong reducing of its concentration.

XI, *Rozental's factor, plasma thromboplastine predecessor* - glycoprotein, is formed in liver, takes part in prothrombinase formation on internal way. Norma: 0,005 g/l. Haemophilia C (Rozental's disease) is occured at its absence or strong reducing of its concentration.

XII, *Hageman's or contact factor* - protein, is activated by negatively charged surface, adrenaline, kallikrein. It triggers prothrombinase and fibrinolysis external and internal ways. Norma: 0,03 g/l. Bleeding doesn't occur even at its concentration decreasing up to 1 per cent.

XIII, *fibrinase, fibrin-stabilizing factor (FSF)* – globulin, is synthesized by fibroblasts, megalocaryocytes; it stabilizes fibrin. It is necessary for reparational processes normal course. Norma: 0,01-0,2 g/l. Minimal level: 2-5 per cent.

Fletcher's factor, prekallikrein- protein, participates in XIIth factor, plasminogene, high-molecular kininogene activation. Norma: 0,05 g/l. Minimal level - 1%.

Fitzgerald's-Flozhe factor, high-molecular fibrinogen – is activated by kallikrein, is involved in XI, XIIth and fibrinolytic agents activation. Norma: 0,06 g/l. Minimal level: 1 per cent.

The **blood coagulation process** may be divided into 3 phases. The first one includes the complex of consequent reactions leading to the ***prothrombinase forming***. The prothrombinase forming can be realized via two routes: extrinsic (from injured tissue) or intrinsic (from blood). The ***extrinsic route*** of the prothrombinase forming provides the obligatory presence of the thromboplastine (or Factor III, tissue factor). The prothrombinase forming via the extrinsic route begins with the factor VII activation by the interaction with the thromboplastine. In its turn, the factor VII transforms the factor X into the active state. Futher the factor Xa activates the factor V. The factors III+IV+ Xa +Va form the complex compound named the prothrombinase. Via the extrinsic route the prothrombinase is synthesized very quickly (it takes the seconds!).

The factor XII (the contact factor) is an important initiator of the ***intrinsic*** prothrombinase forming ***route*.** The kallikrein and high – molecular kininogen (HMK) are the participants of this reaction. The contact factor is activated by any injured surface, skin, the collagen, the adrenaline and transforms the factor XI in its active state. The XIa influences directly the factor IX, transforming it into the factor IXa. Its specific activity is directed to the factor X protheolysis (converting it into its active form) and occurs on the platelet phospholipid surface at the necessary factor VIII participating. The whole factor complex on the phospholipid platelet surface received its name as the ***thenase*** (the **thenase complex**). As it was mentionned above, the kallikrein and high – molecular kininogen (HMK) are the participants in a blood coagulation process by means of which the extrinsic and intrinsic routes combination takes place. The intrinsic pathway is more prolonged in time (up to 5-6 minutes) as it is accomplished with a great number of different blood coagulation factors. It is also implemented without vessel wall injuring (e.g. at the adrenaline concentration increasing that activates the factor XII).

The second phase of blood coagulation is a ***transition of prothrombine to thrombine*** which is performed by the prothrombinase. It is a proteolytic prothrombine cleavage resulting in the enzyme thrombine presence. This enzyme possesses the coagulative activity. It takes only several seconds.

The third phase of blood coagulation is a ***fibrinogene transition to fibrine***. At first under the influence of the thrombine two fibrinopeptides A and two fibrinopeptides B are released. As a result of it the fibrine-monomere is formed. Futher, the soluble fibrine is formed due to the polimerization process. But because of the XIII factor (fibrinase) activation its transition into the insoluble fibrine (fibrine-polymere) is taking place. Next, this fibrine plug is reinforced thanks to the platelets action (they release the protein thrombosthenin). This process is known as a ***retraction***. The plug in its turn is named a clot. The fibrine net becomes gradually tight. That's why the clot causes the vessel occlusion and the bleeding is ceased.

One observes II,VII,IX,X,XI,XII and XII factors physiological decreasing in new-borns. On the contrary, V and VIIIth coagulational factors concentration is at adult level in them. In low-weighted, immature new-borns one can see more expressed decreasing of these factors.

Umbilical cord bandaging terms and first child attaching to mother's breast time influence greatly on haemostatic indexes. One must hurry up with the first and to perform the second as soon as possible. On the 3rd day of child birth procoagulants level is decreased thet leads to hypocoagulation. Further, blood coagulation factors begin their increasing practically till adult level.

Lecture 17.
Anticoagulants and fibrinolysis.

Inspite of circulation there are all necessary factors for the clot forming. Under physiological conditions in presence of uninjured vessels a blood remains fluid. It's determined by the presence of components, preventing the blood coagulation (**anticoagulants**) in the circulation. Besides, a blood is kept fluid because of the haemostatic system **fibrinolytic components** in it.

But it's necessary to underline that blood doesn't coagulate in vessels due to others reasons too. Factors providing this feature are:

- blood stream velocity: it is well-known that where circulation velocity is the less, the more threat to intravascular blood coagulation (for example, blood is more often condensed in veins comparatively to arteries and phlebothrombosis, thrombophebitis is occured); it also observed in blood circulation regions where circulation is changed, for instance at bifurcations places;
- similar charge (negative) of vascular vessels internal layer;
- formed elements negative charge;
- most coagulational factors negative charge: charge similarity of blood vessels internal layer and blood coagulation factors creates forces for pushing away; at vascular walls injuries vascular wall charge is decreased or even is changed onto positive that creates additional conditions for intravascular coagulation initiating;

- blood coagulation factors are inactive in blood; blood coagulation are not triggered until factors are under unactive state;
- there are inhibitors to active blood coagulation factors ($VIII_a$, IX_a, X_a, XII_a): even in a case of any factors activation further process development is not obligatory.

Probably, you paid your attention that blood coagulation is origined from XIIth factor activation. It is activated by side surface or hyperadrenalinemia and it becomes XII_a only after this. Reaction cascade (chain) is begun directed to other blood coagulation factors activation. Moreover, this reaction is not spontaneous, it looks like stairs (fall) when one factor activates other one in definite order, in definite sequence.

But anticoagulants are essential factors preventing possible blood coagulation activating.

The natural anticoagulants are divided into primary and secondary ones. The ***primary anticoagulants*** are such substances that are constantly present in the circulation. They may be of three groups: antithromboplastines, antithrombines and fibrin forming inhibitors. Otherwise, all these anticoagulants are the substances that act depending on the blood coagulation process stage.

The substances preventing the prothrombinase forming are the *antithromboplastines* (they are secreted by the vessel wall endothelium, their content in veins is larger than in arteries), vitamin K-dependent protein C (inhibits the factors V, VIII), protein S, the endothelium protein – thrombomodulin, the placenta anticoagulant protein and others.

The substances inhibiting thrombine action are *antithrombines*. They are of different groups but the most important of them are: antithrombin III and heparin. *Antithrombin III* – is a prothein of a globulin origin that is formed in liver, kidneys, spleen, lungs and blood vessels as well. Its content reduces with the age, its concentration is less in women as compared with men (NB! Women have the thrombophlebitis and phlebothromboses more often than men), its content in pregnants gets smaller. Its content is smaller in human beings with the II(A) blood group and the people eating fat food (particularly of animal origin). Its activity decreases at the diseases of those organs where it is formed. Antithrombine III is a heparin co-factor. Besides, it inhibits up to 70 per cent of thrombine occuring in blood as well as the factors IXa, Xa, XIa, XIIa. There are cases of its hereditary insufficiency.

Heparin – is also an antithrombine. It is a polysaccharide transforming antithrombine III in anticoagulant of immediate action thus increasing its activity. In absence of antithrombine III heparin possesses a weak anticoagulant activity. Moreover, heparin without antithrombine III doesn't prevent the external prothrombinase forming way. So, heparin efffect may be very weak as a result of antithrombine level decreasing in patients' blood that it's necessary to take into account at its administration. Heparin also forms the complex combinations with thrombogenic protheins and hormones which finally possess anticoagulant and fibrinolytic features. Heparin influences the thrombocyte aggregation, has antiviral action and antiinflammatory properties as well. In blood heparin can be found in basophiles, in vessels – in mast cells. It it degenerated by the heparinase enzyme in liver.

Secondary anticoagulants – are the "worked-off" blood coagulation factors (that participated in blood coagulation process) and degradation fibrin and fibrinogen products or derivates (PDF) having antiaggregative and anticoagulative action. The secondary

anticoagulants role comes to limiting of intravascular blood coagulation and thrombus dissemination via vessels.

At various diseases there may appear the pathological anticoagulants dealing with different immunoglobuline classes and inactivating separate blood coagulation factors.

Fibrinolysis – is an integral part of haemostasis system. It always accompanies the process of blood coagulation and even is activated by the same factors (XIIa, kallikrein, HMK and others). Being the important defence reaction it prevents the occlusion of blood vessels by fibrin clots and leads to the vessel recanalization after the bleeding stoppage. The fibrinolysis components play key role in extracellular matrix removal. Besides, they regulate the growth and the division of cells, the reparation of wounds, the regeneration of muscles, the growth and metastasis of tumors etc.

The main enzyme destroying the fibrin is ***plasmine*** (sometimes it is called fibrinolysin), that in a circulation is in non-active state as proenzyme ***plasminogene*****.** Under the influence of the activators there occurs plasminogene peptide junctions cleavage that leads to in it's turn to plasmine forming. Plasminogene may be found not only in plasma and in serum but in other types of liquids (sperm, follicules, saliva), in tissues and leukocytes either. This is a prothein of a globulin origin the biosynthesis of which is performed in a bone-marrow.

To transform into plasmine plasminogene needs to be activated. ***Plasminogene activators*** **-** are contained first of all in tissues (vessel wall). ***Tissue plasminogene activator (TPA)*** **–** is mainly formed in vessel wall endothelium. ***Urokinase*** as plasminogene activator is produced in kidneys (juxtaglomerular apparatus), in fibroblastes, epitheliocytes, pneumocytes, placenta, endotheliocytes either. There are also plasminogene activators in erythrocytes, thrombocytes and leukocytes.

Except plasminogen activators there exist the ***fibrinolysis inhibitors*** in plasma.

Nowadays one can tell about 4 types of plasminogen and urokinase tissular activators inhibitors.

1) The most important among them is *inhibitor of the first type* (ITAP-1), which is often designated as endothelial. Besides, it is synthesized not only by hepatocytes but also by monocytes, macrophages, fibroblasts and myocytes.

Up to 90 per cent of antifibrinolytic activity is contained in platelets alpha-granules which are realeased in blood stream at their activation. While accumulation in endothelium injured locuses platelets release ITAP-1. This reaction has an essential importance for injured vascular wall restoration.

Fibrinolytic blood activity is greatly determined by the correlation between the fibrinolysis activators and inhibitors.

2) *α_2-antiplasmine* influencing not only on plasmine but also on urokinase;
3) *α_1 –protease inhibitor (α_1-antitrypsine)* – strong plasmine inhibitor;
4) *α_2-macroglobulin;*
5) *plasminogene activator inhibitors* secreted by endothelium, macrophages, monocytes and fibroblasts.

Fibrinolysis like the blood coagulation process is performed in ***three phases***. The first phase, the forming and secreting of plasminogene activators may occur in extrinsic and intrinsic ways. The ***extrinsic way*** of plasminogene activation is due to the TAP, urokinase and some others. The ***intrinsic way*** of plasminogene activation is divided into *Hageman-dependent and Hageman-independent***.** The first of them takes place under the

influence of the XIIa, kallikrein and HMK factors that transform plasminogene into plasmine. Hageman-dependent fibrinolysis is accomplished very fast and bares urgent character. Its main designation comes to the circulation clearence from fibrin clots forming in course of disseminated intravascular blood coagulation process. The second one can be realized under the influence of proteins "C" and "S".

In the second fibrinolysis stage under the action of the activators mentionned above plasminogen transforms into plasmine. Finally, in the third stage, plasmine effects on fibrin. As a result at first the early (high-molecular) and then the late (low-molecular) *fibrin degradation products or derivates (FDP)* appear. The early PDF influence on the platelet aggregation and blood coagulation thus increasing them. The late PDF are characterized by the anticoagulant features and effort the fibrinolysis reaction.

Natural ancoagulants and fibrinolytic components level is decreased in new-borns. In low-weighted, immature babies - more expressed anticoagulants decreasing. Fibrinolytic components level is reduced on the 3rd day of life that leads to fibrin clot dissolving time increasing. Further, natural anticoagulants concentration begins its gradual increasing and becomes normal up to 14th day. Blood fibrinolytic activity reaches its normal value to this time too. But at the same time, antithrombine III concentration is remainded comparatively low in a child of the 1st month of life.

Lecture 18.
Vascular-platelet haemostasis, blood coagulation and fibrinolysis regulation.

There exist 4 levels of haemostatic system regulation.

Molecular level **–** supposes haemostatic equillibrium supporting for factors influencing on vascular-platelet haemostasis, blood coagulation and fibrinolysis. Factor excessment appearing in organism due to one or other reason must be liquidated in short time as soon as possible. Such equillibrium is constantly supported between prostacycline and thromboxanes, procoagulants and anticoagulants, plasminogen activators and inhibitors. Cellular receptors existance to many blood coagulation factors underlies haemostatic equillibrium in haemostatic system at molecular level. Receptors to coagulation and fibrinolysis factors coming off cells ("swimming" receptors) acquire new features becoming natural anticoagulants, plasmine inhibitors and plasminogene activator. Regulational molecular level may be realized with immune system by means of antibodies to activated coagulation and fibrinolysis factors – II_a, X_a, tissular palsminogene activator and others- formation. There is genetic control under factors production providing blood clot forming and dissolving.

Cellular level. In circulation constant coagulational and fibrinolytic factors consumption occurs that must obviousely lead to their concentration restoration. This process must be caused by either activated factors or their metabolic products. If it is really so, cells must have receptors to indicated substances. Such receptors were found on many cells to thrombine, kallikrein, plasminogene activator, plasmine, FDP and others. Cellular level is also provided by "near-wall" fibrinolysis occuring at fibrine accumulation on vascular wall endothelium.

Organic level- determine haemostatic system optimal existential conditions in circulation different regions. Vascular-platelet and coagulational haemostasis and fibrinolysis mosaic is expressed due to this level. Our chair collaborators scientifical works for last years have proved that blood while passing through one or other organs (for example, brain, extremities muscles, kidneys) is satiated with additional haemocoagulational and fibrinolytical factors which may be synthesized in these organs. Moreover, we (V.P.Mischenko, I.V.Mischenko, E.V.Tkachenko, E.A.Tkach, O.V.Kokovskaya, J.M.Grishko and students of different departments and courses which are members of our chair student's scientific society) demonstrate that blood outflowing from these organs on the right and on the left has different coagulative and fibrinolytic features. It was the base to consider that in animal and human organism there is haemostatic and fibrinolytic process asymmetry. Such asymmetry was found by us in different laboratory animals (hens, rats, rabbits, guinea pigs, cats) and human beings.

Nervous-humoral regulation controls haemostasis state from molecular till organ level, providing reactions integrity at organism level. It is realized mainly through vegetative nervous system sympathetic and parasympathetic parts.

First of all, one should mention that there exists cortical (conditioned-reflectory) haemostatic system regulation. There some scientific data indicating on the possibility to determine conditioned reflexes both to the acceleration and especially to blood coagulation retardation up to bleedings (bleedy tears, haemorrhagias in places analogous to wounds places, caused at Christ crucifixion et al.).

CNS separate structures (cerebellum, thalamus, hypothalamus) participate in regulation both of activation and inhibition of haemostasis system functionning. As it was proved (B.I.Kuznic, V.P.Mischenko, L.L.Goncharenko. D.S.Zazykina) hypersympathicotony (acute haemorrhagia, hypoxy, stress, intensive muscular activity, adrenaline and noradrenaline introduction) causes blood coagulation acceleration and fibrinolysis enforcement. It is linked not only with Hageman's factor activation but also with thromboplastine, tissular plasminogene activator releasing from vascular wall. But the most interesting is the fact that at hyperparasympathicotony (vagus irritation, acetylcholine and pilocarpine introduction) we observe coagulation acceleration and fibrinolysis too. Under this conditions thromboplastine and tissular plasminogene activator releasing from vascular wall occurs too. Moreover, drugs vasoconstrictors and vasodilatators by their nature cause similar answer from blood coagulation and fibrinolysis - thromboplastine and tissular plasminogene activator releasing. <u>It testifies that vascular wall is blood coagulation and fibrinolysis efferent regulator!</u>

Haemostasis regulation humoral mechanism - is hormones, mediators, vitamines and other substances action.

<u>*Hormones*</u> of suprarenal glands (corticosteroids, adrenaline), hypophysis (ACTH, STH), thyroid (thyroxine), parathyroid (parathormone) and other glands mainly activate blood coagulation, although everything depends on their dosage.

<u>*Mediators*</u> – noradrenaline, acetylcholine and others mainly activate blood coagulation too.

<u>*Vitamines*</u> have different influence on haemostasis process.

<u>Vitamine "A"</u> - inhibits coagulation and activates fibrinolysis.

<u>Vitamine "E"</u> – accelerates blood coagulation and suppresses fibrinolysis.

<u>Vitamine "PP" (nicotinic acid)</u> – accelerates coagulation and increases fibrinolysis.

Vitamine "B_{12}" – accelerates coagulation and suppresses fibrinolysis.

Vitamine "C' - enforces blood coagulation.

But at the same time doctor should remember that this vitamines effect on haemocoagulation depends on their dosage. These data are quite important because vitamines and hormones usage is widely-spread.

Hypercoagulation occurs mainly due to time shortening mainly of the first haemocoagulation stage. That's why hypercoagulation reasons are quite different and depend on many coagulation factors located in plasma, formed elements and tissues. Hypercoagulation reasons:

1) Hypercoagulation occurs at blood coagulation factors (especially I, VIII and IX) excessment). It may be observed at:
- muscular activity;
- emotions;
- pain;
- hyperadrenalinaemia;
- in pregnant women.

3) Thrombocytosis.
4) Erythrocytosis.
5) Erythrocytic haemolysis:
- burns;
- haemolytic states;
- toxic animals bites;
- blood haemotransfusions.

6) Some leukosis forms.
7) Any tissular injuries.

But hypercoagulation may transforms into ***hypocoagulation,*** which is secondary under natural conditions and is caused by thrombocytes and plasma coagulation factors consumption as well as secondary anticoagulants formation. Primary hypocoagulation reasons are following:

1) blood coagulation congenital disorders:
   - haemophilia;
   - thrombocytopathies (Glanzman's disease et al.);
2) autoimmune hypocoagulation accompanied by bleedings.

In clinics often secondary hypocoagulation of coagulational character is observed, for instance in cource of ***disseminated intravascular syndrom (DIS-syndrom)*** development. This phenomenon is occured at many diseases, it's non-specific, universal and almost catastrophic. Letality at its acute formes reaches 30-60 per cent in adults and up to 90 per cent in new-borns.

Pathogenesis. Disseminated blood coagulation with multiple clots and formed elements aggregates forming in circulation which lead to blood circulation disorders. Possible result: dystrophic changes in tissues and organs where it occurs.

In course of this syndrom development everything is originated from blood coagulation activating, i.e. hypercoagulation (possible reasons of which – see above). Its determining doesn't require special conditions because one can see it at blood taking: blood is coagulated in neadle, in test-tube with stabilizator. This is the first sign of DIS –

syndrom. The reaction main reason – tissular injury and destruction. It results in thromboplastine big amounts coming into circulation and rapid thrombine formation.

Thrombocytopenia increases at the second stage, blood coagulation part is consumped to clots formation. This is the phase of different-dimensioned changes: laboratory analizes testify that one tests tell about hypercoagualtion, others – about hypocoagulation and the third ones are normal. Such contradictory picture is a distinguishing feature of DIS-syndrom.

Third stage - hypocoagulational; clots are formed badly or are not formed; thrombocytopenia is enforced. Haemorrhagical stage of DIS-syndrom is very dangerous, but is is not always accompanied by it. Sometimes bleedness may have local, for example organic character. Common bleedness is characterized by appearence of cruises great amount, haemorrhagias, haematomas and different bleedings (nasal, pulmonal, stomach-intestinal et al.).

On its freaquency DIS-syndrom is developed in target-organs in such an order (sequence): lungs, kidneys, liver, alimentary tract, brain.

Fighting with DIS-syndrom is rather complicated.

There exist blood coagulation disorders and DIS-syndrom *preventive physiologic methods:* healthy life style:

- constant (regular) physical training (in trained organism anticoagulants and fibrinolysis activators content is always bigger);
- individual restricted feeding (better - according to your blood group). Animal products especially rich in fats will enforce blood coagulation reactions.
  Live generously, with taste, according to needs individual to your blood – and all problems will be over!

Lecture 19.
Respiration physiology. External respiration. Gas transition and transfer by blood.

Respiration is vitally essential for human beings and animals life. **Respiration** is gas exchange between organism external and internal environment. This process is performed in several **stages:**

1) *External or lung respiration* – performes gas exchange between organism external and internal environment (between air and blood).
2) *Gas transition and transfer* – is performed due to alveoles permeability and blood transport function.
3) *Internal or tissular respiration* – performes directly cellular oxidation process.

External respiration – is performed with cycles change, one respiratory act consists of inspiration and expiration phases. As a rule, inspiration is shorter than expiration. ***Inspiration act:*** thorax volume increases in 3 directions – vertical, sagittal and frontal. Why? There are some reasons:

- Diaphragm contraction (if diaphragm in rest state is shifted on 1 cm it leads to thorax increasing on 200-300 ml of air). Result of diaphragm contraction: decreasing

(flattening) of its cupula; visceral organs (in abdominal cavity) pushing down, throrax increasing in vertical direction.

- Contraction of external oblique intercostal and intercartillaginous muscles: they are fixed to above-lied rib near spinal cord, to below-lied rib – near sternum. Result: throrax volume increasing in sagittal and frontal directions. Ribs are putted forward, up and towards. And it supports such lungs localization change.
- As lungs are connected with thorax through pleura visceral and parietal layers then lungs volume increasing occurs after thorax volume rising up. It leads to pressure decreasing in them. Pressure becomes lower than atmospheric one, air comes into lungs. Thus, negative pressure is third reason (factor).
- This negative pressure increases in course of inspiration because at lungs stretching their elastic draft - force with which lung strives for compression - is increased. Elastic draft is explained by 2 factors: there are many elastic fibres in alveoles walls - the first one – and the existance of surface tension of liquid tunic containing surfactants and covering alveole wall internal surface – the second one. Elastic draft (the 4-th factor of inspiration) is increased in course of inspiration, negative pressure is rised up in pleural cavity that encourages inspiration act.

Thus, inspiration is rather active process.

Expiration act – under usual conditions is performed passively by means of following factors:

- thorax gravity force;
- elastic graft of rib cartillages overwinded in course of inspiration;
- abdominal cavity organs pressure.

But expiration as inspiration may be also active (for instance, at hyperventillation, cough, someone's straining and so on), when internal intercostal muscles contraction occurs. These muscles are fixed near spinal cord to below-lied rib and near sternum to above-lied rib and their contraction cause pushing ribs down, ahead and inside.

Respiratory muscles in course of their activity passe through some *resistance*, 2/3 of which is elastic, defined by lungs and thorax tissues as well as surfactant action; 1/3 – non-elastic caused by gas stream friction with air ways.

Negative pressure appearence in pleural fissure is explained by following fact: new-born thorax grows faster than lungs that's why lung tissue is undergone to constant tension. Pleural layers possess large absorbtive ability that encourages negative pressure creation. That's why gas introducing in pleural cavity is absorbed after some time and negative pressure is restored in pleural cavity. Thus, negative pressure is constantly supported in pleural cavity. If thorax is wounded than pressure in pleural fissure becomes equal to atmospheric one and lung is falling down, **pneumothorax** occurs. If we have liquid, blood and pus – the names will be correspondingly hydrothorax, haemathorax and pyothorax.

One can differentiate **2 main respiration types:**

1) Thoracic (rib) – thorax dilation is connected mainly with ribs rising; respiration is mainly performed by means of intercostal muscles activity, diaphragm is moved passively according to interthoracic pressure change. This respiration type is a female.

2) Abdominal (phrenic or diaphragmal) – diaphragm contraction (flattening) is main respiration factor as the result of which interpleural pressure is decreased and simultaneously interabdominal pressure is increased. This respiration type is more effective because lungs are ventillated in more extent and stronger in course of it and blood venous return is released from abdominal cavity organs to heart. ***Diaphragmal respiration is more physiological!*** It is called male respiration. ***There exists one important rule for women: they must breath with thorax mainly only when their pregnancy!***

Air amount in lungs after maximal inspiration is known as **common lungs capacity (CLC).** It is 4200-6000 ml in adults. Its compounds are: **vital lung capacity (VLC)** and **residual volume (RV). VLC** – air amount which leaves lungs in course of maximally deep expiration after maximally deep inspiration. It is equal to 3300-4800 ml under norma (in males 4000-4800 ml, in females – 3300-4000 ml). VLC consists of 3 lung volumes:

1) *respirational volume* (RV) of air inspirated and expirated in course of each respiratory cycle under rest state – 400-500 ml;
2) *reserve inspiration volume* – additional air that one can inspirate in course of maximal inspiration after usual inspiration – 1900-3300 ml;
3) *reserve expiration volume* – additional air that one can expirate in course of maximal expiration after usual expiration – 700-1000 ml.

At usual respiration we have reserve expiration volume and respirational volume in our lungs.

Residual volume – everything that is in lungs after deep inspiration - it is equal to 1200-2000 ml. It is in our lungs even after death!

There exists one more volume – ***harmful space volume*** – air part that is remained in air ways (nasal ducts, oral cavity, nasopharynx, nasal additional sinuses, trachea, bronchi) and doesn't reach lungs (this air doesn't participate in gas exchange). Such anatomical space is about 140-200 ml. It very useful despite its name "harmful" because air passing through them (especially when its passage through nasal ducts) becomes warm, humid, protected from side particles, bacterias. ***Respiration through nose is more physiological!***

For 1 minute, at respiration freaquency equal to 16-20, one inspirates volume that has name of **minute volume (MV).** Its size depends on 2 compounds: respiration volume and respiration freaquency. Respiration freaquency 16-20 (norma indicated in all textbooks and manuals) per 1 minute is not ideally physiological. Less respiration freaquency which may be reached by corresponding training (the most often – physical training) - is more physiologic from the point of view delt with diseases prevention not only in respiratory appatarus but also in other organs and systems. Why less respiration freaquency is more physiological? Describe these advantages on concrete example of trained person respiration. Imagine, please, 2 people before us, of equal constitution, but one of them is regularly done some kind of physical activity (regular morning exercise, running and so on). Respirational volume is always higher in trained person in comparison with untrained. Example. Respirational volume in trained person – 800 ml; in untrained - 400 ml. After small physical loading their respiration freaquency is getting increased: in trained person – to 20 respiratory acts per minute, in untrained – rather higher (for example, 40). At such ziphras minute volume in both people will be equal to 16000 ml of air (400 ml x 40 and 800 ml x 20). In what are the advantages of one of them before other? In the first human being (trained) from 800 ml of respiratory volume 600 ml will come to

alveoles with every inspiration (if both subjects have harmful space volume equal to 200 ml). In the second (untrained) person only 200 ml of air will come to alveoles. At respiration freaquency 20 in first person 12000 ml of air reach alveoles for 1 minute (20 x 600 ml). At a freaquency 40 in second person this air amount will be only 8000 ml of air (40 x 200 ml). Thus, in untrained person air amount reaching lungs is lower on 4000 ml. That's why ***less respiration freaquency is more physiological!*** It is reached by training (the best – by physical one). As it is known nowadays, civilized person is healthy, active, energetic and it may be so tens of years if his minute volume is not more than 4-5 l. The more minute volume predominates over this level, the more symptoms are of differnt organs pathologies occur. In people who have such problems (these are the civilization problems!!!) minute volume is equal to 8-12 litres in resting state. One can't call such respiration healthy. Remember!!! External respiration normalization – reaching minute volume level 3-4 litres per minute! High freaquency of our breathing is delt with its uncorrect character. In the most people amount time for inspiration is approximately equal to time for expiration. Besides, the most people performes their expiration right after their inspiration – it is also out of physiology. It's necessary to lack someone's breathing after inspiration and then slower then inspiration expiration comes, after which – new lack. Such respiration type reminds respiration on Buteyko, Frolov et al. But, unfortunately, people become follow this respiration "culture" only when they fell ill. Really it's necessary to breath in such a way always! This is a Real Way to health and prevention of a great number of diseases!

Lung ventillation. Air-conductive ways, lung parenhyme, pleura, osteo-muscular thorax carcas an dyaphragm are united working organ by which lung ventillation is performed. ***Lung ventillation*** – alveolar air gas content renewal process. Such air provides oxygen coming into alveoles and carbon dioxide excessive amount releasing. Ventillation intensivity is determined by respiration depth and freaquency, harmful space. Ventillation occurs due to active physiologic process (respiratory movements). It depends on body stature (vertical or horizontal) and circulation in alveoles.

Gas transition and transfer mechanism. Pressure gradient is vitally essential factor providing gas exchange from one environment to another. What pressure does it mean? Oxygen and carbonic dioxide create definite pressure which is called ***partial pressure –*** common pressure part of a given gas in a given mixture. This part depends on gas per cent content in the mixture. The it is more, the partial pressure of given gas is more.

Oxygen transport.

Oxygen partial pressure:

- in atmosphere is equal to 159 mm merc col.;
- in alveoles – 102-105 mm merc col;
- in venous blood reaching alveoles – 40 mm merc col;
- pressure gradient for oxygen between alveoles and blood is about 60 mm merc col.

Thus, oxygen due to this difference of partial pressure and its tension in different environments passes from atmosphere into alveoles and then in blood and tissues. How oxygen is transmitted?

Oxygen transfer conditions

It is known that blood transfers 300-350 ml of oxygen for 1 minute under relative rest state (this ziphra significantly increases at physical work). One can differentiate 2 factors of oxygen transfer:

- large alveolar surface (60-100 square meters);
- oxygen fast diffusion ability – at this difference between alveoles and blood in 1 mm merc col 200 ml of oxygen will diffund; at a real difference that is 60 mm merc col – 12000 ml of oxygen (!even in course of intensive physical loading this ziphra is not more than 4000-5000 ml!). You see data about oxygen diffuse ability: it predominates the level necessary for intensive physical trainings in 2,5-3,0 times.

Oxygen transport forms

Particularly oxygen can be dissolved (in 100 ml of blood – up to 0,3 ml of oxygen, thus, in all blood – about 15 ml). Of course, it can't solve the problem of oxygen transport. Main chemical substance necessary for oxygen transport is **oxyhaemoglobine.** It was estimated that 1 g of haemoglobine can transmit approximately 1,31 ml of oxygen. 100 ml of blood contains about 14-16 g of haemoglobine, so, they can carry 18-21 ml of oxygen. This index is known as **oxygen blood capacity –** is is defined as oxygen amount transporting with 100 ml of blood till its full saturation. This index can change. It is rised up in course of physical training, at polycitaemia; reduced – at blood diseases for instance at anaemias.

Formed oxyhaemoglobine amount depends on oxygen partial pressure in blood. This dependence is linear that is proved by following data. At oxygen partial pressure equal to 0, oxyhaemoglobine isnt't formed; 10 mm merc col. – 10% oxyhaemoglobine; 20 mm.- 30%; 40 mm. – 70%; 70 mm.- 90%; 100 mm. – 96%. If we connect all this points we shall receive curve describing dependence between oxygen tension in blood and amount of forming oxyhaemoglobine. This curve name is **oxyhaemoglobine dissociation curve.** One can make some important conclusions from this curve:

1) At oxygen partial tension decreasing in blood up to 80-70 mm merc col (it corresponds to such partial pressure in mountains at a high 2500-3000 meters above sea level) amount of formed oxyhamoglobine decreases insignificantly, i.e. its amount is less only on several per cents than on plain. It gives the possibilities to successful work of mountaineers, highland workers and also to life in highlands without any additional devices and forces. At a high level above 4000 metres we'll not be able to breath without additional oxygen coming from gas cylinder.
2) Venous blood is rich in oxyhaemoglobine, i.e. it is saturated by oxygen. At partial tension in venous blood equal to 40 mm merc col, up to 70% of oxyhaemoglobine is formed in blood.
3) Difference between oxyhaemoglobine content in arterial and venous blood is 25-26%. Oxyhaemoglobine content in arterial blood is 95-96%, in venous – 70%. This index is named **arterio-venous difference.** It is rised up in course of physical training, at polycitaemia; reduced – at blood (at anaemias) and heart disorders.

Oxyhaemoglobine dissociation curve moving:

1) to the left (up) – is observed:

- at temperature decreasing;
- pH increasing (alkalosis);
- hypocapnia;

- in blood reaching lungs;
- in new-borns;
- in mountaineers;
- in fliers;
- in cosmonauts.

Essence: at less oxygen partial pressure in atmosphere to form more oxyhaemoglobine in blood.

2) *To the right (down)* – is observed:

- at hyperthermia;
- at fever;
- pH decreasing (acidosis);
- carbonic acid content increasing;
- in blood reaching tissues (for example, working muscles).

Essence: at the same oxygen partial tension oxygen forming is less and free oxygen comes to the tissue where it's necessary for redox reactions performing in them.

Carbon dioxide transport

Carbon dioxide transmission and transfer is realized by same mechanisms. Carbon dioxide tension:

- in tissues – maximal – 60 mm merc col.;
- in venous blood outflowing from tissues – 46 mm;
- in alveoles where venous blood inflows – 38 mm merc col;
- in atmosphere – 0,2 mm merc col.

It's quite naturally that pressure and tension gradient in different organism environments and compartments provides carbonic dioxide transition from tissues to blood, from blood into alveoles and from alveoles into surrounding space.

Carbon dioxide forms

Particularly, like oxygen, in little amounts it can dissolves (3-6%). Rest part comes into chemical connections both in plasma and in erythrocytes. Chemical substance of carbonic dioxide with water – carbonic acid (H_2CO_3) – appears in plasma. It takes place because partial tension of this gas is more than in blood, that's why it transfers into blood plasma where is connected to water. Carbonic acid part in plasma is connected to sodium chloride as the result of which soda is formed ($NaHCO_3$). Plasma transports carbonic dioxide in composition of these compounds. Its rest part reaches erythrocytes where under influence of special erythrocytic enzyme carboanhydrase the possibility of its connection with water is significantly increased with carbonic acid forming. Little amount of this acid is binded with potassium chloride with potassium bicarbonic ($KHCO_3$) formation. Finally, carbon dioxide part is binded to amine group of haemoglobine with the **carbohaemoglobine** ($KHCO_2$) forming. Thus, in erythrocytes carbonic dioxide is transported in a structure of H_2CO_3, $KHCO_3$ and $HbCO_2$.

When blood reaches alveoles, same enzyme carboanhydrase acts on the contrary: it helps H_2CO_3 dissociation and CO_2 comes into alveoles as the result of these processes. As oxygen partial pressure in alveoles is higher than in blood the gas passes in blood, in red blood cells with oxyhaemoglobine forming in them. Being more powerful acid than carbonic, ohyhaemoglobine takes the bases from bicarbonates and thus provides carbonic dioxide releasing. The result: CO_2 passes into alveoles. In tissues oxyhaemoglobine

transformes into haemoglobine giving bases connected with it, increasing blood saturation with CO_2. These examples testify to the fact that oxygen plays essential role in CO_2 forming and releasing.

But at all these reactions CO_2 tension in venous blood remains big (46 mm merc col) and it doesn't differ significantly from its tension in arterial blood. Thus, there exists **carbonic dioxide arterio-venous difference** equal to 6 mm merc col.

There is quite natural question: why organism has big amount of CO_2? The answer is the following: it is essential respiration regulator.

Lecture 20.
Respiration regulation.

Respiration regulation is performed by means of reflectory reactions occuring as a result of excitement of specific receptors located in lung tissue, vascular reflexogenic zones and other regions. Respiration regulation central apparatus are the structures of:

- spine;
- medulla oblongata;
- hypothalamus;
- brain hemispheres.

Main function of respiration management is performed by stem repiratory neurons which transmit rhythmic sygnals into spine to respiratory muscles motoneurons.

Respiratory nervous center – is central nervous system neurons integrity providing respiratory muscles co-ordinated rhythmical activity and external respiration constant adaptation to changing conditions inside organism and in environment. Main (working) part of respiratory nervous center is located in medulla oblongata. One can differentiate 2 parts in it: ***inspiratory*** (inspiration center) and ***expiratory*** (expiration center). Medulla oblongata respiratory neurons dorsal group primarily consists of inspiratory neurons. They give particularly the stream of descendant ways getting the contact with diaphragmal nerve motoneurons. Respiratory neurons ventral group sends primarily descendant fibres to intercostal muscles motoneurons. One can see region in pons anterior part called as ***pneumotaxic center***. This center deals with activity both of inspiratory and expiratory center parts providing the change of inspiration and expiration. Respiratory center important part is neurons group of spine cervical part (III-IV cervical segments), where diaphragmal nerves nuclei are situated.

Respiratory center excitement mechanisms are the following.

- One of the most important ways of its excitement is *automatism*. There is not one point of view to automatism nature but there exist data about secondary depolarization occurence in respiratory neurons (like diastolic depolarization in myocardium) which reaching its critical level gives new impuls.
- But one of main ways of respiratory center excitement is its *irritation by carbonic acid*. As it was mentionned above, there remains much carbonic acid in blood leaving lungs. It performs the function of medulla oblongata neurons main irritator. It is mediated through special structures – chemoreceptors, located directly in medulla oblongata structures ("*central chemoreceptors*"). Thus, the second way – through blood.

- They are very sensitive to carbonic dioxide tension and acid-alkaline state of intercellular liquor washing them.
- Carbonic acid can easily diffund from brain vessels in liquor and stimulates medulla oblongata chemoreceptors.
- Reflectory way - there are 2 reflexes groups (like for cardio-vascular system): proper and conjugated.

I. Proper reflexes – the reflexes originated from respiratory system organs and finished in it.

1) ***Reflex from lung mechanoreceptors.*** According to localization and type of percepted irritations, reflectory answer to irritation one can differentiate 3 types of such receptors: receptors of stretching, irritant receptors and lung juxtacapillary receptors.

- *Lung stretching receptors* **–** are primarily located in air ways (trachea, bronchi) smooth muscles. There are approximately 1000 receptors in every lung and they are connected with respiratory center by large mielinized afferent fibres of vagus with very high conductance velocity. Direct irritator – internal tension in air ways walls tissues. Such impulses freaquency is increased at lung stretching in course of inspiration. Lung swelling causes inspiration reflectory inhibition and transition to expiration. These reactions are stopped at vagus cutting and respiration becomes retarded and deep. Mentionned reactions are called ***Gering-Breyer's reflex***. This reflex is reproduced in adult person when his respiratory volume is more than 1 l (at physical training for instance). It is of essential importance in new-borns. Their adaptation is slow.
- *Irritant receptors* or slowly adaptating air ways mechanoreceptors, trachea and bronchi mucosa receptors. They answer to lung volume significant changes, chemical or mechanical irritators (mucus, tobacco, dust particles and so on) action to mucosa. Their adaptation is fast. At side bodies coming into respiratory ways there occurs cough reflex after irritant receptors activation. Reflectory arch of cough reflex – receptors – superio-laryngeal, glosso-pharyngeal, trygeminal nerves – expiratory part of respiratory center. Result - strong expiration – cough. At isolated irritation of nasal respiratory ways receptors second immediate expiration occurs – sneezing.
- *Juxtacapillary receptors* are located near alveolar and respiratory bronchi capillaries. Irritators: pressure increasing in circulation small circle and intersticial liquid volume increasing in lungs. Such situation is observed at blood stagnation in small circulation circle, lung oedema, lung tissue injury (at pneumonia et al.). Impulses from these receptors are directed to respiratory center through vagus causing freaquent surface breathing occurence. There may be not only freaquent breathing (tachypnoe) but also reflectory bronchoconstriction.

2) *Reflexes from respiratory musculature proprioreceptors:*

- *Reflex from intercostal muscles proprioreceptors* is realized in course of inspiration when these muscles while their contraction send information through intercostal nerves to respiratory center expiratory part and as a result expiration occurs.

- *Reflex from diaphragm proprioreceptors –* is performed as an answer to its contraction in course of inspiration. Result: information comes through diaphragmal nerves first in spine, than in medulla oblongata in its expiratory part and expiration occurs.

Thus, all respiratory system proper (own) reflexes are realized in course of inspiration and are resulted in expiration.

II. Conjugated reflexes – reflexes originated out of respiratory system.

1) ***Reflex onto conjugation of blood circulation and respiration systems –*** is originated from perypheral chemoreceptors of vascular reflexogenic zones. The most sensitive of them are located in sino-carotid zone region.
   - *Sino-carotid chemoreceptive conjugated reflex –* is performed at carbonic dioxide accumulation in blood. If its tension increases than the irritation of the most sensitive chemoreceptors (they are in this zone in sino-carotid body) occurs, excitement wave comes from them through IX pair of cranio-cerebral nerves and reaches respiratory center expiratory part. Expiration occurs which enforces releasing of excessive carbonic acid in surrounding space. Thus, blood circulation system (while this reflectory act perfomance it works more intensively: heart contractioin freaquency and blood stream velocity increase) influences on respiration system.

2) ***Exteroreceptive reflexes*** are originated from tactile (remember your breathing reaction on touching of lovely person), temperature (warmth – increases, coldness – decreases respiratory function), noceoceptive (weak stimuli and of a middle force - increase, strong – suppress breathing) receptors.

2) ***Proprioreceptive reflexes –*** are performed due to irritation of receptors of sceletal muscles, joints, ligaments. It is observed in course of physical training doing. Why? If under rest state it's necessary 200-300 ml oxygen per minute for human than at physical loading given volume must be significantly increased. Under these conditions both minute volume and arterio-venous difference on oxygen are increased. These indexes increasing is accompanied by oxygen consumption rising up. At work duration of only 2-3 minutes and its significant power oxygen consumption grows uninterruptedly from the very beginning of work and is decreased only after its stoppage. At work duration more, oxygen consumption, while increasung in course of first minutes, is supported all the time on its constant level. Oxygen consumption increases the more the harder physical work it is. Maximal oxygen amount that organism can use per 1 minute at the hardest work for it is called **oxygen maximal consumption (OMC).** Work at which person reaches his OMC level must have duration not less then 3 minutes. There exists many ways of OMC determining. It doesn't predominate 2,0-2,5 l/min in untrained people. It can be twice large in sportsmen and even more. OMC is an index of **organism aerobic productivity.** This human ability to perform very hard physical work, providing his energetic consumption due to oxygen used directly in course of work. It is known that even well-trained person can work at oxygen consumption 90-95% from his OMC level not more than 10-15 min. One having more aerobic productivity reaches better results in work (sport) at practically equal technic adn tactic preparation. Why oxygen consumption is increased in course of physical activity? One can differentiate several reasons:
   - additional capillaries opening and blood increasing in them;

- oxyhaemoglobine dissotiation curve movement to the right and below;
- temperature increasing in muscles.

For performing their work, muscles need in energy, the accumulations of which are restored while oxygen transport. Thus, there exists definite dependence between work power and oxygen amount necessary for work. That blood amount necessary for work is called **oxygen asking.** Oxygen asking can reach up to 15-20 liters per minute and even more in course of hard work. But maximum of oxygen consumption is less in 2-3 times. Does it possible to perform the work if minute oxygen accumulation predominates OMC? For correct answer this question one should remember for what oxygen is used in course of muscular activity. It is essential for macroergic substances restoration providing muscular contraction. Usually oxygen interacts with glucose and it releases the energy while its oxidation. But also glucose can be destructed without oxygen, i.e. by abaerobic way as a result of which energy releases too. These are also other substances possessing the ability to be destructed without oxygen. Thus, muscular activity can be provided at insufficient oxygen coming into organism too. But in this case many acid products are formed and it's necessary oxygen for their destruction because they are destructed by oxidation. Oxygen amount necessary for metabolism products oxidation that were formed in course of physical activity is called **oxygen debt.** It appears in course of work and is liquidated in restoration period after work end. Usually this disappearing takes from several minutes to 1 hour and a half. Everything depends on work duration and intensivity. Lactic acid plays the most important role in oxygen debt forming. To continue his work at lactate presence in blood in great amounts organism must have powerful buffer systems and his tissues are to be adapted to work under hypoxy conditions. Such organism adaptation serves as one of factors providing high aerobic productivity. All the mentionned above complicate respiration regulation at physical activity because oxygen taking in organism is increased and its blood hypoxy leads to chemoreceptors irritation. Sygnals from them come in respiratory center as the result of which respiration becomes more freaquent. A great number of carbonic acid is formed in course of muscular activity that comes into blood and it can acts to respiratory center directly through central chemoreceptors. If blood hypoxy leads primarily to breathing quickening than carbonic acid surplus causes its deepening. Both these factors act simultaneously in course of physical activity and that's why respiration quickening and deepening takes place. Finally, impulses coming from working muscles, reach respiratory center and enforces its activity. At respiratory center functionning all its parts are functionally interconnected by means of following mechanism: at carbonic acid accumulation respiratory center inspiratory part is excited from information comes in pneumotaxic part, then to its expiratory part. The latest, besides, is excited by means of a whole group of reflectory acts – from receptors of lungs, diaphragm, intercostal muscles, respiratory ways, vessels chemoreceptors. Inspiration center activity is inhibited due to its excitement through special inhibitory reticular neuron and inspiration is changed by expiration. As expiration center is inhibited it doesn't send impulses far into pneumotaxic center and information flow is stopped from it to expiration center. Carbonic acid is accumulated in blood by this time and inhibitory influencings on expiratory part are inhibited. Inspiration center is excited due to such information flow redisposition and expiration is changed by inspiration. And everything is repeated again.

Vagus is an essential link in respiration regulation. Main influencings to expiration center come through it. That's why at its injury (like at pneumotaxic center injury)

respiration is changed so that inspiration remains normal and expiration is sharply prolonged – ***vagus-dyspnoe.***

As it was mentionned above in course of coming to the highlands lung ventillation increasing occurs based on vascular zones chemoreceptors stimulation.

Heart contraction freaquency and minute volume are increased simultaneously with this. These reactions improve oxygen transport in organism a little but not not for long. That's why at durable staying into mountains with adaptation to chronic hypoxy initial (urgent) respiration reactions gradually leave their place to more economic adaptation of gas-transport organism system. In constant residents of highlands respiration reaction to hypoxy is too weak (hypoxic deafness) and lung ventillation is supported practically on the same level like in plane residents. At the same time at durable staying under conditions of highlands vital lung capacity, caloric oxygen equivalent, myoglobine content in muscles, mitochondrial enzymes activity (providing biological oxidation and glycolysis) are increased; organism tissues (particularly central nervous system) sensitivity to insufficient oxygen supply is decreased. At high more than 12000 m air pressure is very small and under these conditions even breathing by pure oxygen doesn't solve the problem. That's why at flyings at this high one need hermetic cockpits (planes, cosmic ship).

Sometimes human being has to work under increasing pressure conditions (divering). In the depth nitrogen becomes its dissolving in blood and in course of fast rising out off the depth it doesn't manage to release from blood, gas vesicles cause vessel emboly. Occuring condition is called **kessonic disease.** It is accompanied by pain in joints, giddiness, dyspnoe, unconsciousness. That's why nitrogen in air mixtures is changed on insoluble gases (for instance, helium).

Human being can delay free his breath not more than on 1-2 minutes. After preliminary lung hyperventillation this respiration delay is rised up to 3-4 minutes. But durable, for example, diving after hyperventillation is very dangerous. Blood oxygenation sharp decreasing can cause sudden unconsciousness. Under this state swimmer (even experienced one) under stimulus action caused by carbonic acid partial tension increasing in blood can inspirate water and choke (drown).

Thus, at the end of our lecture we must to remember you that healthy breathing – is nasal, as slow and seldom as possible, with its lack in course of inspiration and, especially, after it. While prolonging the inspiration, we stimulate vegetative nervous system sympathetic part work with all following consequences. While prolonging the expiration, we carry carbonic acid in blood more and longer that positively influences on blood vessels tone (decreases it) will all following consequences. Due to this oxygen under such situation can come in the farthest microcirculative vessels preventing disorders of their function and development of many diseases. Correct breathing – is a prevention and treatment of big group of diseases not only of respiratory system but also of other organs and tissues! Breath for enjoy!

Lecture 21.
Modern human being feeding (new approaches to the problem).

Feeding - organism assimilation process of substances necessary for its tissues building and renewal as well as for energy needs satisfaction. Food must contain organic substances predominant part of which have to belong to proteins, lipids and carbohydrates. If coming food amount is insufficient for energy needs satisfaction, they are compensated by means of internal reserves (mainly fats). If on the contrary, fat accumulative process is triggered (independently from food content)!

Feeding culture questions are of essential importance today. Human mood, health, ability to work, life duration – all this depends on feeding character! Food character influences on self-feeling, emotional sphere, intellectual abilities. Feeding questions are based on Nature Laws which are impossible to be denied. Doubtly, every person diet must correspond to his type, individual abilities, natural and climatic conditions where he or she lives. But feeding main laws must follow all people without any exceptions, who wants to preserve and improve his spiritual and physical health! But human being has to understand, master and recognize these laws!

Time by time mode to new definite products and way of their production are appeared in our modern society. Multiple media institutions, food enterprizes are predominant in such direction. Second, many people don't have even any primitive, elementary knowledge in feeding questions. They don't know, how much, what products when and even how to eat. They have occasional imagions about products chemical content, their features and almost know nothing about products influence on human organism. Only any disease makes these people to pay their attention to their feeding. Unfortunately, it may be too late: incorrect feeding destroyed body and one should adress to the treatment.

Human being feeding problem was always actual. Today its actuality increases in many times. It is linked with unknown or even harmful products appearence in our markets and in our shops. One can follow scienctific-practical feeding bases.

Scientific-practical feeding bases. They are based on knowledge of significance, products alimentary and biological availability, their ability to satisfact organism needs in chemical nutrients daily necessary to it. Cells consisting body tissues and organs, in which complicated biochemical processes take place, are getting old, die; new young cells replace them. Nutrients are essential for their construction and normal functionning. Organism needs in different chemicals according to age, sex, age, actvity character, living place. Such chemicals consist of such integral groups as proteins, fats, carbohydrates, mineral elements, vitamins. Products have different alimentary availability (one have more proteins, others – fats, carbohydrates and so on) and thus they can satisfact energy body nedds while usage different ways. Human alimentary ration practically constantly must contain more than 600 substances. At feeding non-correctly organized organism has insufficiency in some of them. Sometimes - in vitally important that leads to separate organs or even their whole systems activity disorders.

The most significant food components. ***Proteins.*** They consist of aminoacids, are plastic building material for practically all human organs. Biologically active substances – enzymes, many hormones – are built from proteins. You should also remember about excessive and non-excessive aminoacids.

Fats – is an energy source, first of all. But also they participate in cells construction. Fat consistention (taste too) depends on saturated and unsaturated fat acids different

content and correlation. At more expressed saturated fat acids usage (animal products) food is more hardly destructed by corresponding alimentary enzymes.

Carbohydrates serve as main energy supplier, their most significant content is in plants. They also are essential for central nervous system and muscles functionning.

Vitamines **–** belong to organic biologically-active substances which take part in all organism vital processes regulation. They are in catalizators structure. Such catalizators are biological processes accelerators; they are called enzymes. Significant vitamins part is destructed both in course of their keeping and at inproper thermal products processing. That's why any ration must contain many fresh products - vegetables and fruits. One should be careful as for synthetic vitamins – they are assimilated badly by organism but their overdosage is very easy.

Mineral substances **–** microelements, ultramicroelements. Human organism has more than 70 mineral elements. They are building material and are constituents of biologically-active substances (enzymes, hormones).

Water is about 60 per cent of human body weight. It serves as environment for complicated biochemical processes in cells, tissues and organs.

Thus, human feeding must be proper, scientifically-based, rational. Adequate feeding theory is taken nowadays as rational feeding.

Adequate feeding **-** feeding which satisfacts organism energetic consumption, provides its needs in plastic substances as well contains all vitamines, macro-, micro- and ultramicroelements, food fibres necessary for viability and alimentary ration as it is corresponds to alimentary tract enzymatic possibilities of a given individuum. Adequate feeding principles non-maintaining, highly-energetic products usage (especially potatoe, bread, confectionery, mealy foods) is accompanied by organism fatness and may result in obesity. It encourages the development of such diseases as:

- atherosclerosis;
- hypertony;
- diabetes mellitus;
- heart attack;
- stroke.

Insufficient physical activity helps in this. Remember! If human being follows proper physical regimen his needs in food is less than at moveless life style.

Physical feeding norms are based on national feeding main principles and feeding norms depend on sex, age, activity character, climate, organism physiological state. In the most widely-spread cases adequate feeding is based on energy consumptions connected with professional activity (see material about general metabolism).

Adequate feeding depends on feeding regime.

Feeding regime –

1) food taking amount in course of 24 hours;
2) daily ration distribution on its energetic availability;
3) food taking time in course of 24 hours;
4) intervals between food taking;
5) time for food taking.

Proper feeding regime provides:

1) alimentary system activity effectiveness;
2) food normal assimilation;

3) good self-feeling.

The majority of scientists consider that healthy person must follow 3-4-timed feeding with 4-5-houred spaces. It is not properly to take food less than in 2 hours after previous food taking. It disturbs alimentary tract activity rhythm. Food is masticated and processed by saliva badly in course of rapid feeding. It leads to excessive loading to stomach, digestion and food assimilation disorders. At fast feeding saturation feeling appears slower that encourages overeating. Last food taking must be performed not later than to 1,5 hours to sleep. Excessive food before night sleep enforces heart attack, acute pancreatitis, ulcer disease complication development possibility as well as other diseases.

But one should remember that need in food is linked with organism function daily biorythm individual features. In people greatest number these functions level increasing is observed in the first day half. That's why one should prefer "*morning feeding regime*", which corresponds to famous proverb: "Eat your breakfast by yourself, to divide your dinner with your friend and to give your supper to your enemy". Maximal breakfast, according to this system, means 40-50 per cent of daily ration. 25 per cent – to dinner and 25 per cent – to the supper. But this theory is not of no doubt. It is well-known that after excessive food one have feel relaxation, sleepness and as a result working activity is reduced. Such regime is not proper to working person especially for mental activity.

It was occured the theory of *"equal loading"* due to this. It tells about equal on calorage 3-4-timed feeding. But under real conditions delt with working activity equal loading is not always proper. Because people correspond their food taking mainly with appetite feeling. Besides, equality principle doesn't take into account twenty-four-hour rhythm of stomach and intestinal juices formation as well as alimentary hormones and enzymes activity. That's why this principle is not of no doubt too.

"Evening loading regime" or maximal supper i.e. about 50 per cent of twenty-four-hour calories must be to supper, on 25 per cent – to breakfast and dinner. It was also established that stomach juice and enzymes maximum formation is about 18-19 hours. That's because such loading regime causes minimal tension and fatigue. From these positions and according to working day duration, this regime is probably the most physiological for the majority of people.

It doesn't mean that all people must follow this evening regime. Following this regime to obese person is impossible because his weight will grow constantly. Energy loss is practically absent in the evening and eated food will become accumulated as fat. For thin people this regime is the most suitable. Feeding regime choosing must be very individual. But common tendencies and approaches must be attached in the biggest extent to mentionned regimes.

Now let's describe the problem of ***feeding quality and structure improvement.*** Nowadays all tryings for feeding structure and quality improvement both at public and on personal level are faced with some objective obstacles. According to adequate feeding position, feeding ration maximal differentiation necessity for every individual is of no doubt. At the same time, it is well-known that daily food of many people is not different. There are many reasons of this. Before – it was the deficiency of one and other products, now – the deficiency of people's ability as buyers. Many people must limit their ration with the most cheap products. Such resrtricted feeding may be the reason of organism activity disorders.

Another problem is delt with established tendency of ***refined products*** production. It is difficult to say now when and by whom rafinated sugar, oils, purificated salt production was proposed from which were restricted the substances nowadays considered to be useful striving for product clearence. When eating with rafinated products human being receives insufficient amount of food fibers, vitamins, minerals. As a result – risk of early atherosclerosis, diabetes mellitus, cholelitiasis (stones in bile ducts and gall bladder), oncologic diseases occurs. And we are the witnesses of such diseases growth especially in course of last several decades. Let's describe these products more careful.

Refined sugar - is clean chemical received as a result of multistaired (multi-staged) beetroot and sugar cane processing. It doesn't contain neither vitamins, nor salts, nor other biologically-active substances. And that's why person receives only "empty calories" from it. Not completely purificated, yellow sugar, at the same time is less harmful. Comparatively to rafinated one it doesn't allow fat-protein substances formation - low-densed lipoproteids which are one of atherosclerosis reasons. But let's think. Do we really need in so often sugar usage? Why not to change it to honey – wonderful natural product containing many useful substances?

Salt – is clean chemical too. Often and obligatory making food salty leads to increased percentage of people suffering from hypertony. Sodium excessment in food - is organism water lack reason that also causes intraorbital pressure increasing, heart-vascular system and kidneys diseases. It is of no doubt that alimentary obesity is linked with oversalted food. If obese people is prescribed low-salty diet they loss very quickly 5-7 kg of body weight with liquid. Before, when salt was received from natural resources, human being receives with it not only clean sodium chloridum but also other really necessary substances for organism. That's why the best salt for usage is stone, sea and iodated. But one should underline that human being satisfacts completely his need in salts while usage different vegetables and other natural products even without any salt usage.

White flour of the highest grade (sort) – is very often product for population. The whiter flour as it is has more in calories and it is more harmful for organism. At purification and fine-ground all useful substances leave flour for bran which excite intestinal peristalsis and allow metabolites excretion. Iron, grain germ part (possessing large energy potential) also leave flour. Yeast fermentation decreases grain potential. It is more useful to eat bread from coarse-ground flour as well as flat cakes of home preparation with flour of the worst sort with bran addition.

Last years food coming from abroad became more and more often. These products don't undergo proper sanitary control because of ***alimentary additions*** existance which are harmful to human health. This is one more very important problem of modern human being feeding. Limit alimentary additions content is determined by technologic instructions. Such additions are not harmful for human organism. But these normal ranges are not usually followed and sometimes don't correspond to the reality. Alimentary additions often may be hard intoxications reasons. It is also due to technologic epoch when almost all products are produced on factories with synthetic or artificial substances application.

Human being under complicated ecological conditions obviousely receives multiple toxins, poisons – ***pesticides, inorganic fertilizers, nitrates, radionuclides*** – with air, water and food. These substances while their accumulating in organism in different doses and often in very unfavorable combinations can lead to so-called ecological poisonings. For

example, increased nitrates (nitric acid salts) amount in soil in course of the latest years. They are in nitrogenous fertilizers structure, they use in course of smoking et al. Nitrates are not dangerous themselves but they can transform into harmful substances - nitrites and nitrosamines, which increase methaemoglobine content in blood (hypoxy reason), disturb carbohydrate and protein metabolism, possess cancerogenic action.

All mentionned feeding problems belong to global ones or, at least, of state level. Doubtly, fundamental economical and technological society life reconstruction needs for their solving. Only in this case one can hope that healthy feeding will become gold rule but not the exception for the biggest population part.

Main modern human being feeding biological bases (laws):

1. Human needs in energy and nutrients depends on age, sex and performed work character.
2. Organism energy and nutrients consumption must be compensated by their coming with blood.
3. Food organic and mineral substances must be in equillibrium between each other as for organism needs, i.e are represented in definite correlations.
4. Human organism needs in some organic substances coming in a ready state (vitamines, some aminoacids and polyinsaturated fat acids) without any possibilities to synthesize them from other food substances.
5. Food balance is reached due to its variation, products involvement in the ration from different groups.
6. Food content and, correspondingly, products set must correspond to organism individual features.
7. Food must be undangerous for human being and its coockery methods mustn't hurt him.
8. Organism activity is undergone to biorhythms. Human being must follow feeding regime according to them.

But at the same time different feeding systems followers quantity grows constantly in the world. For ages, in all world cultures thinkers and doctors payed much attention to the questions of correct food taking. The wisest humanity representatives understood that any food, according to its dosage, taking conditions, combinations with other products may be both medicine and poison. Part of recommendations recounted in such works of wise ancient and modern people is accepted and used by official medicine, other part is denied or is considered to be disputed according to one or other reasons. We believe that it's a real time to find "aurea mediocritas" (gold middle).

Non-traditional feeding systems. Fasting systems and their significance for health. Modern feeding in a childhood.

There are many non-traditional feeding systems nowadays with many rational and very significant aspects for modern human being health. We'll give characteristics of the most popular systems among population.

Vegetarian system – feeding system, excluding or limiting animal products usage. Main motto of vegetarians is: "Not to eat killed animals corpses!" Such thesis was appearing many times in course of all humanity history. Although many years ago vegetarian system followers had such points of view according to their philosophyc motives. In our pragmatic century the biggest vegetarian part would like to make their health stronger, to reach their elderness, to avoid dangerous disorders. And they really

have such chance! Cholesterine's, triglycerides' amount in their blood is lower, they have lower arterial pressure level than in meat-eaters, their immunity is higher, maligmamt tumors are diagnosted rather seldom in them! As a rule, working activity is increased and common psychological state is improved in them!

Vegetarian system followers base their system choice by next fact: human organism, to their mind, is closer to herbivorous and primates organism than the one of predators. Plant food (if ration is quite different) contains all vitally essential substances. But decomposition products which exists even in the most fresh meat are absent in them. One should remember that only the most fresh meat – is a food product and if it is preserved (in any fridge), is undergone to thermal processing and coockery finishing than it contains many decomposition products (even atherogenic ones). They stimulate lipids accumulation in liver. There are little vitamines in meat, besides vitamine B_{12}. There is also moral aspect – vegetarian diet avoiding human being from the necessity to cause sufferings to animals ("anger toxins"), to spill their blood, it allows eater thoughts and feelings to be clean. Moreover, there are some data: in human organism with meat is introduced information about animal. And it is not occasional that some people have "dull cattle habits", "sheep's or mutton brains", "swinish attitude to deed". But there are also arguments based on digestion physiology data. Indeed, more energy comes to animal proteins assimilation and utilization than these proteins can give to the organism.

Main vegetarian system opponents objections are:

1) in prothein deficiency danger because animal food contains little prothein;
2) in deficiency of possible vitamines and microelements necessary for haemocoagulation;
3) many nutrients concentration in plant products is insufficient for the quickest organism development in childhood and in youth.

But it is not so. It was established that people whose food alimentary ration contains 50-60 g in 24 hours have more expressed ability to work than those who eats 100 g of protein and even more in twenty-four –hours. Haemocoagulative vitamins concentration in vegetarian serum is not less than in meat-eaters. And, at last, there exist and existed whole nations in which vegetarian customs and traditions of which are from the bottom of centuries. They didn't degrade in course of these centuries from generation to generation (unfortunately, main part of modern people prefers meat diet and degradation level is not worthy to investigate, it is visual on the surface with unarmed sight). In any case, official dietology recognizes that at least not strong vegetarian system is quite suitable for durable usage and influences favourably to health.

Raw-eating – is more seriouse vegetarian direction. Its distinguishing feature is products usage only raw, without any thermal processing. Its followers (naturopaths) consider that human being sufficient daily amount is 20-30 g of protein. They explain it by the fact that at raw-eating human organism mobilizing internal reserves, maximally uses vitally essential prothein components – aminoacids. Raw food is alive food. It contains maximum of enzymes, vitamins, microelements and in addition they are natural. All this is destroyes in course of thermal processing. There occur many unassimilated elements in boiled food which only "pollute" organism internal environment.

Naturopathy (naturopathia) – are natural feeding followers. They don't receive theory based on food calorage (calories). "Food reach in calories led us to overeating", - naturopaths consider. And there is large part of truth in it. Taking into account our unagile

or even moveless life style, we do have to diminish all norms on 800-1000 kkal (comparatively to norma being proposed by official medicine followers). Naturopaths tell that food taking – is a saint action. These are not empty words. One must act according to such wise point of view (not only to listen to them). We are sure (persuade) in feeding culture elements correctness they tell about. Here are some of them.

- If you are irritated and can't come down and don't have enough time to eat – it is rather better not to eat.
- Well-known rule – to drink before 10-15 minutes as for eating but not to drink in course of eating.
- To masticate food very carefully. Saliva will dissolve food's consistention. Thus, you don't need other liquid dissolving digestive juices and decreasing their function.
- You have to eat only if you feel hunger. Don't eat if you are not hungry!!! It's necessary to listen to nature voice, organism voice but not to follow your habit.
- If you have some pain - wait with eating. You must do the same if you have increased temperature. To feed the sick- in more extent to feed illness itself.
- Don't eat indirectly before your eating. Why? In person who have just eaten blood inflows to alimentary organs leaving brain and muscles without blood. That's why neither physical, nor mental activity will be effective after eating (especially excessive one).

Naturopaths believe that ideal food for human being – is row vegetables and fruits, containing "sunny energy", vitamins, mineral salts and enzymes. Such food has alkaline reaction, it is digested easily, it leaves little metabolites, it cleans organism. By the way, lard belongs to such products. Rest products cause acid reaction in organism (meat, bread, starch, sweated juices and drinks) and are assimilated harder. To their mind, 2/3 must be alkaline and 1/3 - acid food. And one more requirement putt this theory followers forward - food biological compatibility will human organism cells. It is better to use plants grown in your motherland but not abroad.

Thus, this system followers have many essential feeding rules which are necessary for all people independently from their feeding regime.

Divided feeding – is food products compatibility. This system main statements are based on next data: nutrients (proteins, fats and carbohydrates) decomposition is realized under alimentary enzymes action secreted in oral cavity, intestine, liver and pancreas at products coming into gastro-intestinal tract. One or others enzymes are responsible mainly for definite components processing: either proteins, or fats, or carbohydrates. Carbohydrates are rapidly decomposed under alimentary juices action to ending products. Proteins and moreover fats require more time. While simultaneous coming into gastro-intestinal tract, such food components make gastro-intestinal tract activity more intensive, more tensed, with overloading. At divided feeding alimentary system works more synchronous, without overloadings, not interrupt one another. Next statements belong to this system followers recommendations:

- protein and starch food usage must be in different time;
- one protein type must be in one food taking;
- they don't recommend to use fats with any protein food;
- melons and watermelons (all fruits) must be eaten separately.

We would like to pay your special attention to milk. It would be better to transform it into acid-milky products, to take separately or not to drink. Milky fat prevents stomach juice releasing. Milk is assimilated not in stomach but in intestine. That's why stomach doesn't answer to milk with secretion. Moreover, enzymes responsible for milk utilizing are absent in many people out of childhood.

Genetically determined feeding – is quite new feeding form based on nutrients assimilation according to blood groups. Alimentary tract of people with the I-st blood group is oriented to meat digestion. That's why they have very high hydrochloric acid concentrations in stomach juice. People of this type are also assimilated sea fishes well. But to avoid cow milk and milky products, rolls and buns would be rather better for them. Potatoe and some beans types negatively influence on these people metabolism.

Proper feeding for people with the II-nd blood group – is vegetarian one, soya products are the most useful for them. Fish, rolls and buns are very good additions to their feeding too. They are to avoid potatoe and tomatoes.

People with the III-rd blood group are practically "omnivorous" (all-eaters) and can eat different food, they assimilate good meat and meat products. But they have to avoid from corn, buckweat, potatoes. Vegetables and fruits must consist important part of feeding.

People with the IV-th blood group must refrain from meat and bird (exception: rabbit, mouton, turkey). Buckweat and corn are not desirable. With seldom exception, all vegetables and fruits are assimilated in them without any problems.

Thus, we see that there are many non-traditional approaches to feeding problem. What is ordinary human to be done, what to do, what to eat? We think that everyone must decide all this with considered and individual approach. It's necessary to remember that health strengthening and making your figure shapely – it is not avoiding from food but conscious choice and food products combination. And, due to this, one should be of special attention to organism genetically-determined needs. We are sure that big specific weight of our health is in it!!!

Medical fasting- is "waste" of fats accumulated by organism and cholesterine "mobilization", its metabolic activity increasing with further decreasing of its level till normal values. Definite parts of organs and systems which are not vitally loaded are involved in the process when it is necessary. Either sick tissues or tissues working their vital resource are undergone decomposition in the most often cases. From dying tissues biologically-active protein substances are formed which come to organism renewal and sick organs restoration. Thus, endogenous (internal) feeding with simultaneous organism health-improvement is performed. Organism is released from slags (metabolites) and ballastic substances in course of fasting. These substances cause different diseases.

There are some fasting "types" which differ one from another qualitatively and quantitatively. <u>One can differentiate fasting</u>:

- classic (up to 20-30 days);
- fractional (intermittent);
- dry (linked with drinking regime);
- cascade (24 hours- is feeded, 24 hours – is fasted).

One can use different variants dependently from the situation but only possessing special knowledge and, better, under clinics conditions and under control of specialist.

Modern feeding in childhood.

This problem is very essential. "Complicated" character of child is often the result of uncorrect feeding. Children feeding organizational questions are well-distributed nowadays and may be highly-used by responsible parents.

It is known that in course of the first life year the most natural and essential child food must be female milk. This food is not changeable. It is especially significant in course of first days and weeks. It contains not only everything necessary for baby's life but also immune bodies protecting him from different diseases.

Beginning from 3 months he begins his feeding up with berries, fruit and vegetable raw juices as well as their mixtures. Beginning from 5-6 months – one can train to porridge with breast feeding 2-3 times in course of twenty-four-hours. Beginning from 9-th month – parents can include meat products and curd cheeze. Although it would be better not to give meat to a child up to 3-5 years. It can increase his immunity and decrease the allergic reactions development possibility.

To organize proper feeding of a child elder than 1 year is rather complicated task if the regime of previous feeding was uncorrect and it was not different.

It's necessary to follow all rules and conditions mentionned above in elder age groups.

It's necessary to remember that ideal feeding regime is individual one. Food should be taken only when we are really hungry. Our feeding must be limited in its caloric equivalent due to moveless life style of many of us. And the most important thing – don't do any cult from eating. Be closer to feeding culture!!! You have separate element of this culture in this lecture. Follow them in course of your life – and you will receive strong health and additional years of active, happy life! Make food medicine, not poison! Good luck in this deed!!!

Lecture 22
Digestion, its types and functions. Oral cavity role in digestion.

Digestion – is an integrity of food products physical and chemical processing, their transformation into components without species specificity and suitable for absorbtion and participation in substances exchange.

Digestion types have been formed in course of alive organisms development and nowadays we differentiate:

- *Intracellular* – food products hydrolysis realized inside cells (it is very limited in human being, the example of which is phagocytosis).
- *Extracellular* – is performed in special cavities (oral cavity, stomach, intestine); enzymes synthesized by secretory cells are released in extracellular environment (cavity).
- *Membrane* – has intermediate state between extra- and intracellular digestion and performed by enzymes localized on enterocytes membrane structures (in zone of enterocytes mucosa striggillate margin).

Alimentary tract main functions:

1) *Secretory* – alimentary juices (saliva, stomach, intestinal, bile) secretion and releasing by glandulocytes.

2) *Motor-evacuational* – food growing shallow, its mixturing with juices, passage through alimentary tract.

3) *Absorbtional* – transport of ending digestion products, water, salts, vitamins through alimentary tract epithelium in blood and lymph.

4) *Excretory* – excretion of non-assimilated food components, some metabolism products, hard metals salts, medicines (drugs) out off organism.

5) *Incretory* – releasing of hormones regulated digestion organs functions.

6) *Protective* – bacteriocide, bacteriostatic, detoxicative action.

7) *Receptor* – many receptive zones existance in alimentary tract for excretory, circulatory system reflexes and so on.

8) *Erythropoietic* – there exists iron depot in stomach, small intestine mucosa, liver participating in haemoglobine synthesis; there is so-called internal Kastl's factor necessary for vitamine B_{12} absorbtion responsible for erythropoiesis regulation.

Digestion process is originated from **oral cavity.** This part of alimentary tract performs 2 functional groups:

1) ***Specific functions*** – food suitability assessment performes by means of chemo-, mechano-, thermo-, nociceptors, gustatory receptors in oral cavty. Information comes in central nervous system from these receptors and then – to oral cavity organs (masticatory muscles, salivatory glands, tongue). Food gustatory features determining, food mechanic processing and swallowing are performed due to their action. Food chemical processing is also originated from oral cavity (mainly of carbohydrates). Absorbtion can also perform in oral cavity.
2) ***Non-specific -***

- participation in behavioural reactions forming (hunger, thirst);
- thermoregulatory;
- protective;
- excretory;
- incretory;
- participation in articulation and speech forming.

Digestion in oral cavity is mainly realized due to salivary galnds secretory function. *Salivary glands secretory function* is provided by functionning of 3 pairs of large (parotid, sublingual and submandibular) and great amount of small glands disseminated in oral mucosa. Saliva is a secretes mixture. Saliva is a mixture of secretes. With the addition of epytheliocytes, food particles, mucus, lymphocytes, neutrophils and microorganisms (they are in oral cavity in large amounts) it formes *oral liquid.* Daily saliva secretion is 0,5-2,0 litres. Its pH fluctuates from 5,25 to 8,0.

Saliva contains up to 99,5% of water. There are many organic and inorganic substances in solid residue. One can say that almost all Mendeleev's table is in saliva (even gold!). There are many organic substances in saliva. They are protheins – albumins, globulins, aminoacids. Nitrogen-containing substances – urea, ammonia, creatine. Bacteriocydic substances – lyzozyme; enzymes – alpha-amylase or ptyalin, maltase, proteases, peptidases, lipase, alkaline and acid phosphatase.

Saliva role in digestion: it gives the beginning to food chemical processing. It occurs due to amylase acting on polysacharides (starch) while their destruction to maltose. Under other enzyme maltase influence maltose destruction to glucose can occur. But enzymes action is very limited because food is in oral cavity very little time. ***One of the***

most important digestion rules: careful (durable) food mastication due to which saliva can influence on food (in oral cavity) more effectively.

But saliva is not only restricted by food possible chemical processing. Saliva takes part in preparation of food portion to swallowing and further digestion. Food is mixed with saliva in course of mastication and is swallowed better. Saliva equally covers teeth in neutral environment forming special tunic on them. In acid environment releasing mucin covers teeth surface an encourages teeth coating and stones forming. That's why after food taking it's necessary either to brush teeth or to wash oral cavity. Teeth and mucosa state depends on saliva content and features. Saliva volume, chemical content and features change can underline many diseases of oral cavity. For example, saliva, while contact with dental enamel is the calcium, phosphorus, zinc and other microelements sourse for it. If saliva pH is 7,0-8,0 it oversaturated by calcium that creates ideal conditions for ions passage into enamel. At environment acidification (pH 6,5 and lower) oral liquid becomes deficient on calcium ions content that encourages its releasing form enamel and caries development.

According to saliva chemical analysis and even smell, colour one can tell about inner organs diseases. For instance, at nephritis, stomach and duodenum ulcer disease residual nitrogen amount is increased in saliva. At stroke on the injury (haemorrhagia) side salivary glands excrete great number of protein.

You know about oral mucosa increased regenerative ability. Quickly mucosa restoration after its wounding (it occurs practically every day) is connected not only with tissular immunity but also with saliva antibacterial features. Besides, there are substances in saliva influencing on blood coagulation and fibrinolysis. That's why oral cavity protective function is also delt with this saliva ability to influence on local haemostasis and fibrinolysis.

Saliva formation mechanism. Saliva is formed both in acinuses and in salivary glands ducts. Secretory granules are in glandulocytes cytoplasm. Granules size, amount and localization are changed in course of secretion. They are moved to cellular apex from Golgi complex. Organic substances synthesis passed with water through cell on endoplasmic net is performed in granules. Saliva formation first stage is realized in acinuses – *primary secrete* forming containing amylase and mucin. Ions content in it insignificantly differs from their concentration in extracellular space. Secrete content changes significantly in salivary ducts: sodium ions are actively reabsorbed and potassium ions are actively secreted. As a result, sodium amount in saliva becomes less and potassium – bigger.

Salivary glands in new borns secrete little saliva – 0,4 ml per minute in course of sucking, less – out off sucking. It is in average in 8 times less than in adulthood. Salivation volume is increased from 4 months and reaches up to 150 ml per day to 1 year (it is 1/10 of adult secretion). Amylase activity in new-borned saliva is low and it is increased in second half-year, reaching adult level in course of 1-2 years after birth.

Salivation regulation is performed by complicated-reflectory and humoral ways. Special place in regulation has *complicated-reflectory* mechanism. It consistes of conditioned-reflectory and unconditioned-reflectory. Conditioned-reflectory salivation regulating way is connected with food appearence, its smell (in humans and animals), communication about it and other conditioned stimuli (pictures, writings, symbols) delt with alimentary motivation. Unconditioned-reflectory appears as an answer to oral cavity

mechano-, chemo-, thermo- and gustatory receptors irritation. Nervous impulses flow comes from these receptors through V,VII,IX and X pairs of cranio-cerebral nerves to medulla oblongata in salivation center. Efferent fibres of given reflectory acts go from this center to salivatory glands. They can carry information to salivary glands through sympathetic and parasympathetic fibres that innervate salivary glands. Sublingual and submandibular salivary glands are innervated by preganglionar parasympathetic nervous fibres coming in composition of chorda tympani (facial nerve branch) to corresponding ganglions located in glands body. Postganglionar nervous fibres innervate glands secretory cells and vessels.

Parotid glands are innervated by preganglionar parasympathetic fibres of inferior salivatory nucleus of medulla oblongata coming in the composition of IX pair in auricular node. Postganglionar nervous fibres are directed to secretory cells and vessels. Sympathetic innervation is represented by preganglionar nervous fibres from lateral corns of spine II-IV thoracic segments and is finished in superior cervical node, then postganglionar fibres to salivary glands come.

At sympathetic nerve excitement small saliva amount containing mucin doing it viscous and dense is released. At parasympathetic nerve – on the contrary, saliva becomes fluid and its amount is big.

Hypothalamic anterior and posterior nuclear groups participate in salivation regulation. Salivation reflectory regulation is not unique though it is main.

Humoral mechanism is delt with hypophyseal, pancreatic, thyroid, sexual hormones action. Excessive salivation occurs due to salivatory center irritation by carbonic acid. Saliva releasing may be stimulated by vegetothropic pharmacologic substances – pilocarpine, proserine, atropine. Saliva production can decrease too. It may be connected with noceoceptive and emotional reactions, with fever states, at systematic sleeping pills usage, diabetes mellitus, anaemia, uraemia, salivary glands diseases.

Oral cavity motor activity. Essence:

- food biting;
- getting small;
- grinding;
- mixturing with saliva;
- alimentary piece forming;
- swallowing.

Oral cavity motor function main part is realized in course of mastication.

Mastication – is a complicated act. Its essence is in consequent contractions of masticatory muscles, mandibule, tongue and soft palate movements. Masticatory muscles are fixated to moveless skull part by their one end, by other end – to unique movable skull bone – mandibule. They provide mandibule status change as for maxilla while their contraction. Mimic muscles are close to masticatory muscles on their functions. They participate in food catching, its supporing in oral cavity vestibule, oral cavity closure at mastication. They are essential at sucking in new-borns and at liquid food taking. Tongue has definite role in mastication. It takes active part in food mixture, definition of its place for getting smaller on teeth.

Mastication act by its mechanism is partially arbitrary, partially – reflectory. Human being can free inhibit or enforce masticative movements, change their character. Food biting and mastication is performed at superior jaw teeth occlusion (contact) with inferior

jaw teeth. Mandibule performes rhythmic movements in 3 main directions: vertical, sagittal, transversal. Mastication is originated from assessment of received food after which food piece irritates located in oral cavity touch, temperature, gustatory, nociceptive receptors. Besides, due to sense of smell impulses occuring in these receptors come into mentionned above nervous stems in medulla oblongata in mastication center. Then they on trygeminal nerve second and third rami, facial, glosso-pharyngeal and hypoglossal nerve come to masticatory muscles. In parallel with food getting smaller its washing with saliva occurs for better swallowing. Food getting smaller degree is under oral mucosa receptors control. Non-food elements are pushed at this by tongue (bones, stones, paper et al.). One should remember about necessity of careful food processing in oral cavity. It's an essential preventive measure for many diseases not only of alimentary tract. In babies sucking corresponds to mastication which is provided by mouth and tongue muscles reflectory contractions.

Swallowing – is a complicated reflectory act due to which food is transported from oral cavity into stomach. *Phases:*

- Oral arbitrary – from food common mass in oral cavity small piece is separated which by tongue movements is pressed to hard palate. Jaws are closed, soft palate is rised closing entrance into choanes. Simultaneously with this palato-pharyngeal muscles are contracted. Septum is formed which closes passage between oral and nasal cavity in the result of these processes. Tongue moving ahead pressses onto palate and pushes food piece into pharynx. Because of this food piece is pushed down into pharynx. Entrance into larynx is closed by epiglottis, vocal cord is closed to prevent food coming into trachea. As food piece comes into pharynx, soft palate anterior arch are contracted and together with tongue root prevent food returning into oral cavity.
- Pharyngeal-inarbitrary – is originated when food piece is pushed ahead and pharyngeal-oesophageal sphincter, closing under rest state the entrance to oesophageus, is opened. Sphincter's muscles are relaxed and pressure is decreased in it, food piece passes into oesophageus and sphincter is closed again because of pressure increasing in it. Such reaction prevents food piece passage from oesophageus into pharynx.
- Oesophageal inarbitrary: food piece transmits from oesophageus oral part to cardial.

Swallowing process as reflectory act is performed due to irritation receptor endings of trygeminal, superior and inferior laryngeal, glosso-pharyngeal nerves located in soft palate and pharynx mucosa. Swallowing center is located in medulla oblongata near respiratory center and is in reciproqual (antagonist) interrelations. At swallowing center excitement respiratory center activity is inhibited; respiration is stopped in this moment that prevents food particles passage into respiratory ways. Swallowing act afferent ways – superior and inferior pharyngeal, recurrens nerve and vagus fibres. They direct nervous impulses to muscles participating in swallowing.

Oral cavity is an initial link of reflectory reactions influencing on digestion in stomach and intestine. Oral cavity receptors irritation stimulates stomach juice forming, stomach motor function. Stomach and pancreas secretion depends on mastication act duration. The mastication is less the stomach juice is less. Oral mucosa and tongue is alimentary tract mirror. One can see problems which may occur in stomach and other alimentary tract parts in it. Pathological processes in oral cavity organs can encourage some inner organs diseases occurence, cause or support different complications. In particularly, teeth pathological agility and loss leads to incomplete food processing in oral

cavity that in first turn influences on stomach and intestine motor and secretory activity. But digestion disorders in oral cavity caused by mastication change at teeth loss don't always lead to one or another pathology in alimentary tract other parts. Alimentary tract initial link (oral tract) periodically undergo to action of removable substances (solid subjects, acids, alkalins, excessively warm or cold bodies, strong mechanical actions) that causes hypersalivation occurence as mean of oral cavity and alimentary channel tissues integrity providing. Rich microbe flora containing pathogenic microorganisms comes into oral cavity with alimentary substances. It was the reason of forming tissular and cellular barriers as well as oral cavity specific and non-specific resistance in course of evolution.

Lecture 23
Digestion in stomach

Food comes into stomach after corresponding processing in oral cavity. It is (mixed with saliva) locates in stomach in course of 2-10 hours. Food undergoes both mechanical and chemical processing in stomach. These processes are possible due to stomach functional peculiarities. Such peculiarities are the following. First of all, food are ***deponated*** in stomach. Stomach is food masses reservoir. They are mixed with stomach juice in it. Stomach possesses ***excretory function.*** Some metabolites (urea, ureic acid, creatin, creatinin) as well as substances coming into organism out of it (hard metals salts, iodine, pharmacological preparations) are released with stomach juice. Its ***incretory function*** is linked with hormones formation. These hormones participate in stomach and other alimentary glands (gastrine, hystamine, somatostatine, motiline and others) activity regulation. Water, medicines and alcohol ***absorbtion*** possibility is a stomach characteristics. ***Protective*** function is very important in stomach: stomach juice possesses both bacteriocydic and bacteriostatic action. Besides, it can provide food regurgitation or return (vomiting) at its inquality preventing its coming into intestine.

But stomach secretory and motor functions are the main for it.

Stomach secretory activity is realized by gastric glands producing stomach juice. They are reproduced by 3 cellular groups:

1) main – take part in enzymes secretion (pepsines);
2) parietal – produce hydrochloric acid;
3) additional – release mucus.

Stomach juice content and features depend on several factors. For example, juice released under rest state (on an empty stomach) has neutral or weak-acid reaction (pH – 6,0). This juice consists of saliva and proper stomach juice, sometimes with chimus addition. Juice secretion is enforced in course of food taking; it contains main alimentary enzymes set and hydrochloric acid. Such juice has sharply acid reaction (pH 0,8-1,5). Stomach juice general amount in human being at usual feeding regime is 1,5-2,5 l per twenty-four-hours. Water's content in it is up to 99,0-99,5 per cent. Solid residue is represented by organic and inorganic substances (chlorides, sulfates, phosphates and other substances). But main inorganic component of stomach juice is ***hydrochloric acid.*** Juice organic part – are enzymes, mucoids (for instance, gastromucoproteid or internal Kastl's factor).

Hydrochloric acid secretion is linked with gastric carboanhydrase activation. Hydrochloric acid is very important in digestion.

1. It encourages pepsinogene transformation into pepsine and, thus, provides optimal environment reaction for alimentary enzymes action.
2. It denaturates proteins and causes its swelling.
3. It determines stomach juice bacteriostatic features.
4. It transforms milky products into curd cheese.
5. It neutralizes saliva enzymes.
6. It helps food transition from stomach to duodenum.
7. It stimulates stomach motor activity.
8. It helps gastro-intestinal tract hormones secretion (gastrine, secretine).

Stomach juice enzymes mainly influence on proteins hydrolysis to albumoses and peptines (even with little aminoacids amount formation). They separate 7 pepsinogenes types which are transformed into pepsines under hydrochloric acid action.

Main stomach juice pepsinogenes:

- pepsine "A" – decomposes proteins to polypeptides at gastric juice pH 1,5-2,0;
- pepsine "B" – destructs gelatine, connective tissue proteins at pH up to 5,0;
- pepsine "C" – acts at stomach juice pH 3,2-3,5;
- pepsine "D" – dissolves milky caseine.

Stomach juice contains *lipase* (it decomposes emulgated fats to glycerine and fat acids at pH 5,9-7,9. It's amount is small in adults but it decomposes up to 59 per cent milky fat in adulthood.

Besides enzymes, gastric juice contains *mucin* (mucus) preventing stomach mucosa from autolysis under hydrochloric acid and pepsins action. There are neutral polysacharides in mucus. They are structural part of group blood antigenes, growth factor and antianaemic Kastl's factor. Syalomucines of mucus prevents viral haemagglutination and glycoproteins (internal Kastl's factor).

Stomach secretion regulating

is realized in ***3 phases***:

1. *Cerebral* - is determined by complex of conditioned and unconditioned reflexes. It is originated from conditioned-reflectory phase, because food appearence, smell and everything delt with its preparation (sounds, for instance) cause gastric juice releasing. Unconditioned-reflectory phase begins at the moment when food comes into oral cavity. Here excitement of receptive zones known for you from last lecture is accompanied by informational flow in alimentary center bulbar part (medulla oblongata) through nervi vagi, from where through secretory fibres of the same nerves, to secretory cells. This gastric juice prepares stomach to food taking before it. It possesses high acidity and large proteolytic activity. This juice is called "appetite" one.
2. *Gastric phase*. When food comes into stomach than gastric juice releasing continues mainly due to reflectory-humoral mechanisms linked with stomach activity. That's why this phase was named gastric. Stomach juice releasing on this stage is connected with vagus participation and local (intramural) reflexes as well as it is performed due to stomach local hormones secretion. Vagus sensory fibres excitement occurs while mechanical and chemical irritators (food, hydrochloric acid, salts, digestion products) action onto stomach mucosa. They transmit information into bulbar center and return to stomach glands through its secretory fibres. Acethylcholine released on vagi

endings excites gastric glands main and parietal cells and helps progastrine releasing (the latest transforms into gastrine under hydrochloric acid influence and acts to these cells). Also acethylcholine enforces hystamine formation in stomach mucosa. This phase of gastric secretion is main.

3. *Intenstinal phase*. When food begins its gradual transition into duodenum, gastric secretion is still continue. It is possible due to next phase performance – intestinal. Stomach juice amount released during this phase is only 10 per cent of general juice volume. This phase is humorally-chemical. Gastric glands hypersecretion at this moment is linked with fresh food portion coming. Such portion didn't manage to get saturated with hydrochloric acid. Enterogastrine formed in duodenum mucosa excites stomach secretion too. One of powerful intestinal factors stimulating gastric secretion are food digestion products (especially proteins) which increase gastrine and hystamine secretion.

But gastric secretion is inhibited at some stage. First of all, it is linked with food passage from stomach. But further stomach secretion inhibiting is delt with gastrine antagonist secretine occurence in duodenum mucosa. Secretine is formed from its predecessor prosecretine under hydrochloric acid action. Especially sharp stomach secretion inhibition appears at fats coming into duodenum as well as peptide substances secreted in gastro-intestinal tract (somatostatine, vaso-active peptide or VIP, cholecystokinine, glucagon and others). Hormone enterogastrone secreted in duodenum mucosa as well as adrenaline (noradrenaline) inhibit gastric secretion too. Emotional reactions connected with hypersympathicotony inhibit gastric secretion. But not all emotional reactions and emotional excitement influence similarly on gastric secretion. Such reactions as stress, fury may cause in separate people both gastric juice activation and inhibition. Fear and anguish – inhibit gastric secretion.

Stomach juice character and amount depend on food type. Regulational mechanisms are important for this. In course of meat eating (protein food) stomach secretion increases during the 1-st hour and reaches its maximum to the 2-nd hour. It occurs due to reflectory reactions connected with oral cavity activity (tasty, organoleptic saliva features) and proteins – stocks, received at their digestion in stomach, possess the same features. Then stomach juice secretion begins its gradual decreasing and finishes approximately in 8 hours after beginning. Reaction is expressed on carbohydrate food (bread, for example) during 1-st hour. It is connected with the same reasons like on meat: stomach juice reflectory releasing on food components which are in oral cavity and stomach. Then secretion is sharply reduced and lasts about 10 hours at low level. One can observe 2 phases at milk (fat) action: inhibitory and exciting. Secretion maximum is developed only on the 3-rd hour and may last up to 6 hours. Gastric glands secretion has not only digestive tasks, but it provides several other organism reactions delt with neutral mucopolysacharides, sialomucines and glycoproteins (that is the mucus base) as it was mentionned above.

Stomach motor activity. Stomach preserves, heats up, mixes, diminishes, transforms into semiliquid state, sorts and moves content to duodenum with different velocity and force. All this is performed due to motor function, caused by its smooth-muscular wall contractions. Stomach is in recessive state, without wide cavity between its walls out of digestion phase. After 45-90 minutes of rest state periodic stomach contractions appear

lasting 20-50 minutes (hungry periodic activity). At filling with food stomach aquires sac-like shape, one part of which comes into cone.

When stomach is filled, its motor activity consists of some movements types. *Peristaltic waves* appear in initial contractive period. They are distributed from oesophageus to pylorus with velocity of 1 cm/sec, have the duration about 1,5 sec and involve 1-2 cm of stomach wall. Waves duration in pylorus is 4-6 per minute and its velocity increases up to 3-4 cm/sec. These low-haltitude peristaltic movements encourages food mixture with stomach juice and transmission of its small portions into stomach body. Carbohydrates decomposition with salivatory amylase continues inside food piece. These movements last approximately 1 hour. Strong and freaquent contractions occur periodically which mix food more active with gastric juice enzymes and pass stomach content. Peristaltic waves in pylorus were named as *propulsive contractions.* They provide content evacuation to duodenum. These waves appear with the freaquency 6-7 per minutes.

Stomach musculature state and activity is changed with reflectory mechanism at oral cavity irritation by food and removed substances. Liquid and semiliquid substances usage and psychical excitement inhibit stomach movements by reflectory way and close pyloric sphincter. Solid food substances cause by the same reflectory way stomach movements decreasing with oral cavity receptors.

Mastication is accompanied by stomach musculature tonic contractions; swallowing – stomach smooth muscle inhibiting and weakening. Stomach contractive force and its musculature hypertony degree depend on mastication intensivity and its musculature initial state. The more swallowed piece volume is, the more stomach contraction inhibition is expressed.

Under usual digestion coditions stomach contractions occur as a result of mechanical irritation and stretching of its walls with food. This is percepted by nervous plexi neurons processes situated in intermuscular and submucosal layer. Vagus enforces and sympathic nerve weakens stomach motor activity.

Stomach motor activity humoral causative agents are gastrointestinal hormones – gastrine, motiline. Motor activity is increased under serotonin, insuline. Glucagon, secretine and cholecystokinine under stomach acid content action inhibit stomach motor activity and food evacuation from it. The same action have adrenaline, noradrenaline, enterogastrone.

Food transition from stomach in duodenum is performed portially in course of antrum strong contractions. Pyloric sphincter prevents chimus regurgitation to stomach. Pyloric sphincter is opened at empty stomach. It is periodically opened and closed in course of digestion. Sphincter opening reason is pylorus mucosa irritation with hydrochloric acid. At this time food part transits in duodenum and reaction in it becomes acid despite alkaline, that causes pylorus musculature reflectory contraction and sphincter is closed. It is observed at fat introduction in duodenum that allows its lack in stomach.

Other essential factors for food transition from stomach into duodenum are the following:

- stomach content consitention (liquid and semiliquid food leaves stomach);
- chimus osmotic pressure (hypertonic solutions retard evacuation and leave stomach only after their dissolving with stomach juice up to isotonic concentration);

- duodenum filling degree: at its stretching evacuation from the stomach is retarded and even can finish;
- badly swallowed and fat food are retarded in stomach for long;
- vagus and enterogastrine enforces chimus transition, sympathic nerve and enterogastrone – inhibit it.

Stomach content may leave it in opposite direction. It is delt with cardial sphincter working peculiarity. Food piece passing into oesophageus low end, irritates its mucosa that causes cardial sphincter reflectory opening which in the adult always closes entrance into stomach. That's why stomach content can't fall down even if you are standing your head down. Cardial sphincter contraction is supported from the stomach side with reflectory way usage. Cardial sphincter tone is absent in small children and that's why stomach content is pushed ahead into oral cavity at child's turning over his head down. There can be other variant of such reaction. In course of gastro-intestinal tract receptors irritation with toxines and metabolites nausea occurs – sensation connected with central nervous system activity at reticular formation excitability significant increasing. Vomiting comes after nausea; nausea is accompanied by vegetative disorders (salivation, perspiration increasing). Vomiting – protective reaction, occuring at vomiting center, medulla oblongata reticular formation structures excitement as well as impulsation from alimentary tract and vestibular receptors. It may be caused by olfactory, visual, gustatory irritations which excites vomiting center at intracranial pressure increasing. Efferent influencings through vagus and partially splanchnic nerve are transmitted to intestine, stomach, eosophageus as well as motor nerves to abdominal wall muscles and diaphragm. At vomiting bone and larynx are rised up, oesophageal superior sphincter is opened, pharynx is closed, soft palate is opened with choans closure. Then diaphragm and abdominal wall strong contraction begin, finally, lower eosophageal sphincter is relaxed and stomach content is pushed through eosophageus. Antiperistalsis and nausea come before vomiting. Antiperistaltic waves occur in alimentary tract dystal parts and are distributed through small intenstine with velocity of 2-3 cm/sec while intestinal content return in duodenum and stomach for 3-5 min. Vomiting occurs by reflectory principle at gastro-intenstinal tract receptors irritation and automatically – at some substances (toxines) action through blood to nervous center. Sometimes vomiting is caused consciousely, specially with the aim of stomach releasing (for example, at intoxications).

In some occasions, stomach motor activity is disturbed and is realized slowly. One should take into account that bad stomach releasing – is ulcerogenesis risk factor.

Motor periodics on an empty stomach in new-borns is absent. It is delt with nervous regulatory mechanisms immaturing. Stomach content evacuation after baby feeding with breast milk occurs for 2-3 hours. It determines feedings freaquency. Feeding mixture with cow milk of the same volume at artificial feeding is retarded in stomach more – for 3-4 hours. Proteins and fats amount increasing in food retards evacuation from the stomach up to 4,5-6,5 hours. In babies evacuation inhibiting with proteins is more expressed, in teenagers and adults – with fats.

Lecture 24.
Digestion in intestine. Absorbtion in alimentary tract.

After corresponding processing in stomach food passes in small intestine, its first part - duodenum. Food undergoes to action of 3 alimentary juices in it:

- pancreatic;
- bile;
- proper intestinal.

In small intestine, mainly, nutrients decomposition to ending products (monomeres) occurs. Digestion in this part is origined from cavity (cavital), then it continues near intestine wall (parietal).

Pancreas secretory function is linked with its exocrine function – pancreatic juice releasing. It is colourless transparent liquid, containing up to 98,7 per cent of water. Its pH is from 7,5 to 8,5, amount – 1,5-2,5 l per 24 hours. Pancreatic juice contains *proteolytic enzymes:*

1) endopeptidases – they decompose internal peptide links of proteins forming peptides and aminoacids:
   - trypsine;
   - chemotrypsine;
   - elastase;
2) exopeptidases - they decompose ending links in proteins and peptides releasing aminoacids:
   - carboxipeptidase “A” and “B”;
   - aminopeptidase;
3) enterokinase – it is secreted in duodenum mucosa and transforms non-active proteases in their active state; enterokinase activates trypsinogene activation into trypsine which, in turn, causes all rest enzymes activation.

Lipolytic enzymes are also released in their unactive state as prophospholipase “A” (it decomposes phospholipids) and active as lipase (lecitinase) (it causes neutral fats hydrolysis to fat acids and monoglycerides). Both lipases are activated under bile (biliary acids) and calcium ions presence.

Amylolytic enzymes:

- alpha-amylase (decomposes starch and glycogen to mono- and disacharides);
- maltase – maltose decomposition to glucose;
- lactase – lactose decomposition to glucose.

Nucleolytic enzymes - nucleases:

- ribonuclease;
- desoxyribonuclease.

Kallikrein - is activated by trypsine.

Pancreatic juice different amount is secreted on every food type. For example, on carbohydrate and protein food (bread, meat) secretion is increased during first 2 hours from the digestion beginning and lasts 4-5 hours (on meat) and 9-10 hours (on bread). On milk secretion maximum is on the 3-rd hour and lasts to 5 hours. Fat food enforces pancreatic juice secretion.

Pancreatic juice releasing regulation has complicated character and consists of 3 phases: conditioned-reflectory, gastric and intestinal.

1) *Conditioned-reflectory phase* – complex of conditioned (occuring on food appearence, smell, situation connected with eating) and unconditioned (originating from oral cavity,

stomach and duodenum receptors) reflexes. All of them are ended by one and the same efferent link – vagus secretory fibres, carrying the information to pancreas secretory cells.

2) *Gastric phase* – is delt with stomach receptors mechanical, chemical irritations and hormones releasing from it (for instance, gastrines). Main chemical irritators encouraging pancreatic juice releasing are the following: hydrochloric acid, vegetable juices and fats.
3) *Intestinal phase-* is linked with chimus passage in duodenum; it is developed both under nervous impulses from intestinal mechanoreceptors and intestinal hormones. Secretine and cholecystokinine belong to such hormones. Secretine is formed from prosecretine under hydrochloric acid action and stimulates pancreatic juice releasing in big amount but is is pour in enzymes. Cholecystokinine causes juice secretion rich in enzymes. It is released under fat and protein metabolism products influence.

Pancreatic secretion is inhibited by autonomic nervous system sympathetic part excitement, noradrenaline, adrenaline and their analogues. Such reactions as sleep, tensed physical and mental activity, pain – decrease pancreatic secretion.

Liver role in digestion is in following: it possesses cholepoietic (bile formation) and choleretic (bile secretion) function. *Bile formation* occurs constantly by the way of several substances (water, glucose, electrolites) filtration from blood in biliary capillaries as well as by means of hepatocytic biliary acids salts and sodium ions secretion. Bile final formation occurs as a result of water and mineral salts reabsorbtion in biliary capillaries, ducts and biliary vesicle.

Bile contains products not only of secretory but also excretory liver activity, directed on excretion some substances (urea, ureic acid and others) out off organism. Twenty-four-houred bile secretion in human being is 0,5-1,5 liters. Main bile components are the following:

- biliary acids;
- biliary pigments;
- cholesterol.

Biliary acids- specific metabolism products in liver. In hepatocytes primary biliary acids (cholic and deoxycholic) are formed from cholesterol. Connected in liver with aminoacids glycine and taurine they are released as glycocholic acid sodium salt and taurocholic acid potassium salt. They are transformed in intestine under bacterial flora action into secondary biliary acids – deoxycholic and lithocholic. Up to 90 per cent of biliary acids are actively reabsorbed from intenstine to blood. They return to liver through portal vessels.

Biliary pigments - bilirubin, biliverdin are haemoglobine metabolism products and they give its colour to bile. Bilirubin predominates in human being determining bile gold-yellow colouring. Urinary and faecal pigments - urobilin, urochrome and stercobilin – are formed from biliary pigments.

Bile can pass into common biliary duct and biliary vesicle. Vesicular bile differs by its dark colour, more significant special weight, decreased active reaction (pH) - 6,0-7,0. Hepatic bile has pH - 7,8-8,6. Bile is concentrated in gall bladder in 7-10 times.

Bile formation is changed at alimentary tract interoreceptors excitement. These receptors irritators are the following: bile, secretine, glucagon, gastrine, cholecystokinine. Bile formation is activated at hyperparasympathicotony.

Bile secretion – is a periodic process occuring as a result of non-coordinated gall-bladder wall muscular activity, Oddi sphincter's and sphincter of vesicular and common biliary duct (choledoch) fusion place. Common bile duct sphincter is closed out off digestion process and bile comes into gall bladder. In course of gall bladder contraction choledoch sphincter is relaxed and bile passes to duodenum. This reflectory mechanism is triggered by oral cavity, stomach and duodenum receptors irritation with food. Excitement sygnals through medulla oblongata and vagus fibres cause gall bladder muscular contraction and Oddi sphincter relaxation as a result of which bile comes into duodenum. Cholecystokinine is gall bladder contractile activity main stimulator. Bile secretion strong stimulators are yolks, milk, meat, fats.

Bile functions:

- fats emulgation;
- fats transformation in soluble form in water environment;
- encouraging fats digestion and absorbtion;
- pancreatic lipases activation;
- connection with pepsine (it prevents trypsine destruction with pepsine);
- pancreatic proteases action enforcement;
- pancreatic and intestinal juice secretion activation;
- iron and copper absorbtion providing;
- motor activity regulation;
- bacteriostatic action;
- it enforces formation of itself.

Liver main functions:

1. Metabolic role (participation in all substances exchange):
   a) protein exchange:
   - albumine synthesis;
   - globuline synthesis;
   - fibrinogen synthesis;
   - vit K-dependent coagulation factors synthesis;
   - urea formation and some others;

   b) carbohydrate exchange:
   - glycogenogenesis;
   - glyconeogenesis et al.;

   c) pigment exchange – due to biliary pigments;
   d) hormonal exchange;
   e) vitamines exchange.
2. Desintoxicational function:
   a) biotransformation:
   - conjugation to glucuronic acid;
   - conjugation to sulfuric acid;

   b) biologically-active substances inactivation:
   - adrenaline;
   - noradrenaline;
   - dophamine;

- serotonine;
- estrogens;
- androgens.

3. Alimentary - due to bile formation and bile secretion.

Small intestine glands secretion. Intestinal juice is Lieberkuhn's crypts and Brunner's glands activity product as well as all small intestine mucosa. Twenty-four-houred stomach juice amount is up to 2,5 l. Intestinal juice enzymes releasing is delt with glandulocytes death. Intestinal mucosa dead cells form intestinal juice solid part. Intestinal epitheliocytes are regenerated for 24-36 hours, secret pH is about 7,2-7,5 and at intensive secretion it reaches 8,6. There are about 20 enzymes of all types in juice. Their releasing is activated mainly by humoral-chemical way:

I. Activators: 1. Hormones:

- secretine;
- vasoactive-intestinal peptide (VIP).

2. Mediators (acethylcholine).

3. Chemical substances:

- hydrochloric acid;
- proteins and fats digestions products.

II. Inhibitors: 1. Hormones:

- somatostatine;
- adrenaline.

2. Mediators (noradrenaline).

3. Autonomic nervous system sympathetic part excitement.

Special place in this part of alimentary tract occupies ***membrane (parietal) digestion***, realized in strigillate margin zone formed by microvillies. Pancreatic and intestinal juice enzymes are adsorbed on microvillies glycocalix. These enzymes perform mainly intermediate stages of all nutrients hydrolysis. Proper enterocytes membrane intestinal enzymes do in biggest extent proteins, fats and carbohydrates decomposition final stages. These enzymes active centers are oriented by definite way as for small intestine membrane and cavity. Enzymes catalytic centers free orientation as for hydrolyzed objects is impossible due to it that is membrane digestion distinguishing feature. Digestion initial stages are realized extremely in intestinal cavity and mainly monomeres are formed as a result of membrane hydrolysis which are transported in circulation. It is the very beginning of adsorbtion.

Small intestine motor function is digestion essential stage. One can differentiate 2 movements types in small intestine: peristaltic and pendulum-like. *Pendulum-like movements* are expressed in following: gut on its short locus is shortened and then is prolonged again. Thus, content is passed to one and then to other direction. Food is mixed due to this. *Peristaltic movements*: above the food piece isthmus (girdle) is formed, below – gut cavity dilation. These movements encourage food passage through intestine. Sometimes these movements are performed with big velocity and such movements are called peristaltic pushings (grumbling in one's abdomen).

Intestinal motor activity is regulated by neuro-reflectory and humoral way. Emotions of wrath, fear, pain usually lead to intestinal contraction inhibiting (autonomic nervous system sympathetic part excitement). But at several strong emotions, for example,

of fear sometimes wild intestinal peristalsis is observed (nervous diarrhoea). Autonomic nervous system parasympathetic part enforces intestine peristalsis.

Humoral factors influencing on peristalsis:

1. Mediators:
- acetylcholine – increases intestinal secretion;
- noradrenaline – inhibits intestinal secretion.
2. Hormones:
- adrenaline - inhibits intestinal secretion;
- secretine - increases intestinal secretion.

In course of first year of life parietal digestion in children predominates comparatively to cavital one compensating its low development. Babies feeding up increases small intestine devlopment.

Digestion in large intestine.

Ileo-caecal sphincter begins its opening in 1-4 minutes after feeding and content in small amounts (up to 15 ml) passes in large intestine. About 1,5-2,0 l of chimus comes there for 24 hours. Digestion in large intestine has some distinguishing features.

- Digestive juice has pH 8,5-9,0.
- Juice solid part contains many epitheliocytes and mucus.
- Juice contains enzymes (lipases, peptidases, amylases) in little amounts.
- Large intestine secretion increases in 8-10 times after mechanical tension.

Intestinal microflora – is a constant attribute of this alimentary tract part. It:

- stimulates natural immunity maturation,
- inhibits pathogenic microorganisms growth,
- destroys small intestine enzymes,
- decomposes biliary acids,
- synthesizes vitamines “K”, “E”, “B_6”, “B_{12}”: vit K is especially essential in new-borns when blood coagulation vit-K-dependent factors synthesis is sharply reduced (as it was mentionned above). Until this large intestine function in new-born is not enough activated (due to flora passage) he may have bleedings (haemorrhagia of new-borns);
- unchanged aminoacids synthesis;
- fermentizes carbohydrates and
- causes rotten proteins bacterial decomposition with indole, skatole, sulfuric gas and methane formation. Some of them absorbing in blood are detoxicated in liver (indole, skatole, phenole).

Normal microflora inhibiting (in course of antibiotics treatment) causes staphylococci, yeasts, Esherichia coli and other organisms multiplication.

Excrement (faeces) coloured with biliary pigments is formed in large intestine. At faecal masses formation process intestinal juice solid substances are of great importance namely mucus pieces which glue ungested food residues particles. Faeces content:

- mucus;
- mucosal dead epithelium residues;
- cholesterine;
- salts;
- bacterias;
- proteins, fats and carbohydrates (at digestion disorders).

Large intestine motor function - is quite different. *Movements types*:

- tonic – one depending on intestine filling and releasing degree;
- pendulum-like - ones directed on content mixture;
- peristaltic – provide intestine content passage;
- antiperistaltic – improve intestinal content utilization and encourage more dense faecal masses formation.

All intestinal motor movements types are regulated by intramural (metasympathetic) nervous system. Sympathetic nervous fibres from superior and inferior mesenterial plexi send inhibitory impulses but parasympathetic – activating. Another large intestine motor activity inhibitors are following:

- adrenaline;
- noradrenaline;
- serotonine;
- glucagon.

Stimulators:

- acethylcholine;
- cortisone.

Final result of large intestine motor activity is ***defecation act.*** This process is developed according to the following scheme. Rectum mucosa sensitive nerves irritation leads to external and internal sphincters relaxation; rectum exit is opened and excrement is pushed out by large intestine and rectum peristalsis. It is triggered by making an effort (straining oneself), i.e. abdominal wall muscles, diaphragm and muscles anal sphincter elevators contraction. Defecation reflex center is in spine sacral part. Inarbitrary influencings which retard defecation come from brain cortex. Inarbitrary sphincter relaxation and defecation may occur at some emotional states for instance at fear.

In first hours after birth baby's intestine is released from primary excrement - meconium. Meconium is sterile in course of 3-5 hours, then microorganisms appear in it. It is delt with feeding. Excrements are connected to meconium at first 2-3 days. Meconium disappears on 4-5th days. Children have during 1st month defecation after every feeding. It becomes more seldom since the 2-nd month. It remains 1-2 times a day till 1 year.

Absorbtion. It is substances transfer through semipermeable membrane in blood or lymph, tissular liquid. Due to it approximately 8-9 l of liquid is reabsorbed in digestive tract every day. Absorbtion is performed in all gastro-intestinal tract parts. In oral cavity – water, medicines. In stomach – water, mineral juices, vitamines, alcohol, drugs, hydrolysis products. But main absorbtion place is small intestine. Practically all substances useful for organism are absorbed here.

Absorbtion mechanism is rather complicated, it is physiological process as a result of which filtraction (it depends on hydrostatic pressure), diffusion and osmosis take place.

Different substances take their own absorbtion place. Proteins are absorbed as aminoacids in small intestine in blood. Fats – as monoglycerides and fat acids with biliary acids participation in lymph. Carbohydrates – as glucose (in children – it is possible as fructose and galactose). Water is absorbed in large intestine.

Lecture 25.
Hunger, appetite and satiation state. Substance and energy exchange, thermoregulation.

Purposeful behaviour as for food taking is in the state which has received the name ***hunger state.*** This is special motivation directed on dyscomfort liquidation, connected with nutrients insufficiency in organism. Hunger center is located in hypothalamus, its excitement is delt both with nervous and humoral factors. Important role in sensations forming connected with hunger plays afferent impulsation coming in central nervous system from alimentary tract receptors. Its different parts have their own electrical basal rhythms of food taking. Near-houred rhythms are evacuational activity regulators. Intestine main activity rhythm – is of 90-minutes. There is 20-minute period of stomach and small intestine activity, liver, pancreas and intestinal glands secretory activity in this rhythm and 70-minute period of relative rest. Activity occurs in stomach and gradually passes through small intestine. Periodic activity initial reason is physiological hunger state. Empty stomach and small intestine proximal part hungry activity increases hunger state. It causes unconscious motor anxiety in animals and, conscious, in people. Inhibitory influencings of this feeling are connected with autonomic nervous system sympathetic part. Hypoglycaemia acting on specialized hypothalamic glucoreceptors participates in hunger forming.

Appetite – is emotional sensation delt with striving for food taking. This sensation may be hunger part but also it can occur independently from physiological consumption. In this case it is the expression of congenital or aquired individual predisposition to definite food type. One should underline that food taking in human being is not always connected with hunger feeling and it is rather uncorrect. But, unfortunately, it is so. Why? The answer is very simple – habit to take food in definite time (by the way, it is not the worst variant) or because all surrounding people are eating at this time.

Satiation **-** appears as a result of food taking. It occurs because of oral cavity, pharynx, oesophagus, stomach, duodenum mechanoreceptors as well as olfactory and gustatory receptors stimulation. Such satiation is called *sensor* or *primary.* We have also *secondary* or *metabolic* satiation connected with hydrolysis products coming into blood. It appears usually after 1,5-2,0 hours after primary satiation. Peptide hormones decreasing alimentary behaviour (cholecystokinine, somatostatine, bombesine, calcitonine) or increasing it (gastrine, insuline, oxytocine) are essential for food taking regulation, hunger and satiation sense occurence.

Remember! The slower you will take food (to masticate longer, not to hurry up while transition from one dish to other) the faster and at less food amount (it is the most important!) satiation will come. Commonly, food must be taken till you won't feel that you can eat the same amount. Than you must leave the table. You are feeling hunger but after some time you will fell the satiation. This is one of elements of feeding culture!

Substance and energy exchange – is an integrity of physical, chemical and physiological processes of substances and energy transition in human organism as well as substance and energy exchange between organism and environment. Substance and energy exchange provides organism plastic and energetic needs. One can differentiate 2 interconnected but directed oppositely processes. ***Anabolism* –** is the integrity of organic substances, cellular components and other tissular and organic structures biosynthetic processes. They are growth, development, biological structures renewal and continuous macroergs resynthesis as well as energetic substrates accumulation. ***Catabolism* –** is the integrity of complicated molecules, cellular components, tissues and organs destructive processes to simple substance. Nutrients rich in energy are assimilated and chemically transformed but ending metabolism products with lower energy content are released from cell. Organism must receive energy in suitable form for it from environment and return into environment corresponding energy amount in a form suitable for further usage. This process in organism is called ***energy exchange.*** All processes generating energy that require molecular oxygen participation are formed ***aerobic exchange system.*** Energy generation without oxygen participation is called ***anaerobic exchange.***

Definite part of energy accumulated in fats, proteins and carbohydrates chemical bonds is used in course of biological oxidation process for ATP synthesis, other part is transformed in warmth. This warmth, released right after in nutrients biological oxidation process has received the name ***primary warmth.*** Energy accumulated in ATP and used further for chemical, transport, electrical processes performance, mechanical work producing transformed in warmth was named as ***secondary warmth.*** If to measure all warmth quantity having been formed in organism for 24 hours then this warmth will be the measure of nutrients chemical bonds sum energy taking into account that these nutrients underwent biological oxidation in course of measurement. According to warmth quantity having been formed in organism one can make the conclusion about energy expenditures to viability processes performance. Main energy source in organism for viability processes performance is nutrients biological oxidation. Oxidation is essential for this oxidation. Thus, having measured consumpted oxygen quantity for 1 min (1 h, 24 hours) one can say about organism energy expenditures size. There is a connection between oxygen quantity consumpted by organism for time unit and the quantity of warmth having formed in it for the same time. This connection is expressed through ***oxygen caloric equivalent* –** warmth quantity forming in organism at consumption 1 l of oxygen by it. For instance, it is equal to 5,05 ccal at carbohydrates burning.

Organism energy expenditures assessment may be performed by 2 ways:

- *Direct biocalorymetry* – is based on warmth quantity measurement directly disseminated by organism in warmth-isolated camera. It is a very exact method but it is used very seldom because it is cumbersome and expensive. This method principle is based on thermodynamics first law which means that all work transforms into warmth which we measure in calorymeters.
- *Indirect biocalorymetry* – is based on measurement oxygen quantity consumped by organism and further energy expenditures estimation with usage of data about respiratory coefficient (RC) and oxygen caloryc equivalent.

Respiratory coefficient – is released carbonic dioxide volume correlation to used oxygen volume. Given method essence can be described on the example of glucose oxidation: $C_6H_{12}O_6 + 6O_2 = 6CO_2+6H_2O$. This reaction is well known for you from

biology, chemistry and biochemistry courses. Released carbonic dioxide volume is equal to one of used oxygen. Thus, at glucose oxidation RC= $6CO_2/O_2$=1. In case of fats oxidation it is equal to 0,7, proteins – 0,8.

As all nutrients in organism are undergone to oxidation simultaneousely than after RC size determining one can approximately tell about dominant oxidation of one or other nutrient type. Every nutrient has its own energy valuation. That's why on RC size one can estimate oxygen caloryc equivalent. If we know oxygen consumped amount we can estimate energy expenditure.

Organism energy metabolism consists of basal exchange and working addition.

Basal metabolism – is minimal level of expenditures necessary for organism viability support. It is defined under conditions of relatively complete physical and emotional rest. Under relative rest energy is expended to nervous system functions perfomance, constant substance synthesis, ion pumps work, body temperature support, respiratory musculature, smooth muscles, heart and kidney activity.

Basal metabolism determining is realized: in the morning, under rest state, on an empty stomach (the latest food taking must be 10-12 hours before investigation), at comfort temperature (22-24°C). Indicated standard conditions characterizes those factors which can influence on metabolism intensivity in human being. Metabolism intensivity is subjected to daily fluctuations. It is increased in the morning and is decreased in the night. It is changed at environment temperature changing (if it is below comfort zone than metabilism reactions intensivity is increased). In winter – is rised up, in summer – is reduced. Nutrients consumption, their further digestion (especially protheins) influence greatly on metabolism level. Metabolism intensivity and organism energetic expenditures increasing under food influence as for exchange and energy expenditures level taking place before eating is called ***specifically-dynamic food action.*** It is explained by energy expenditures to food digestion. Such food action may be up to 12-18 hours. It is mostly expressed at prothein food taking increasing metabolism intensivity up to 30 per cent and less significant at mixed food taking increasing metabolism intensivity up to 6-15 per cents. In babies specifically-dynamic food action is approximately on 30 per cents weaker than in adults. Prothein food causes basal metabolism increasing in children on 15-18% (in adults – on 30%); carbohydrate – on 10% (in adult – on 15%); fat – on 5% (in adult – on 15%).

In average basal metabolism size for person with mass 70 kg corresponds to 1600-1700 kcal /day (in women – less on 5-10%). Such factors as musculature development degree, liver, brain, heart, kidney, endocrine glands state influence on basal metabolism level. Basal metabolism is increased in small children with maximal velocity in the first year after birth (approximately from 120 to 600 kcal/day). After this basal metabolism growth is retarded again and accelerated again in puberty. But in children of any age basal metabolism level on 1 kg of mass is higher than in adults. It testifies to substance and energy metabolism more intensivity in children's tissues comparatively to those in the adult. Basal metaboilsm in children depends on constitution. In thin and agile children basal metabolism is higher than in thick and dismoved. Basal metabolism is increased at fever (in average, on 5 per cent while body temperature increasing on 1°C).

Basal metabolism changes more than on 10 per cent may serves as diagnostic criterium of such organism states as thyroid dysfunctions, recovery after hard and durable diseases, intoxication and shock.

Basal energy metabolism plus working addition (something delt with working activity type) is equal to **general (gross) metabolism.** It is the characteristics of daily energy consumption. Its level depends on energy scale for different population groups.

Population groups and norm for them in kkal/day:

1-st – servant: men - 2500-2800, women – 2200-2400 (we belong to this group as people of mental activity.

2-nd – workers of light physical activity: men – 2750-3000, women – 2350-2550.

3-rd – of middle on gravity physical activity: men – 2950-3200, women – 2500-2700.

4-th – workers of hard physical activity: men - 3450-3700, women - 2900-3150.

5-th – of very hard work: men - 3900-4300. Women mustn't be in this group.

Some scientists add one group – of non-working pensionners – their energy expenditures after their work stoppage must be significantly shortened and be not higher than in people of the 1-st group.

Mental activity doesn't require too significant expenditures like physical activity. Expenditures are rised up at mental activity in average only on 2-3 per cent. But mental activity accompanied by light muscular activity, psycho-emotional tension, leads to expenditures increasing on 11-19 per cent and even more.

Substance and energy metabolism regulation. It includes regulatory systems of multiple organism functions – respiration, blood circulation, excretion, thermoregulation and others. Hypothalamus plays role of substance and energy metabolism regulator. It is explained by the fact that there are nervous nuclei and centers there influencing directly on hunger and satiation and thermoregulation. Autonomic nervous system parasympathetic and sympathetic parts serve as metabolism regulation efferent system. Mediators releasing on their endings influence directly or indirectly through secondary messengers on tissues function and metabolism. Endocrine system is managed by hypothalamus and serves as substance and energy metabolism efferent system. Hypophysis, hypothalamus and other endocrine glands hormones influence directly on cells growth and development, supporting in blood necessary level of different substances (glucose, free fat acids, mineral ions and others). Cell is essential effector in these reactions. The most freaquent effects of regulatory influencings to cell are the following changes: of catalytic enzymes activity and their concentration, modulators, adenylates, common predecessors and common intermediate products action. Glucose concentration in blood (under norma it is equal to 0,8-1,2 g/l) is one of environmental integral indexes reflecting metabolism in organism.

Thermal exchange and body temperature regulation. Temperature influences greatly on alive processes course in organism. Physico-chemical base of this influence is chemical reactions course velocity change. That's why body temperature influences upon its cells activity. Organism tissues temperature is defined by cellular structures metabolic thermal production velocity correlation to forming warmth dissemination velocity into environment. Such processes velocity correlation disorder leads to body temperature change. Mechanisms fixed in course of evolution by means of which organism may express resistance to lower and higher environmental temperature are essential for this.

All organisms according to mechanisms of homeostasis supporting are divided into 3 main groups:

- *poikylothermal* – changeable, which have no the ability to support body temperature on constant level, cold-blooded – amphibias, reptiles, fishes, crustaceas;

- *homoiothermal* – similar, warm- blooded, which can support body temperature on relatively constant level with daily and season fluctuations in the limits of 2 degrees – mammals, human beings;
- *poikylohomoiothermal* – under favourable conditions they belong to homoiothermal organisms, under unfavourable – to poikylothermal. Some insects reproduced by partenogenesis (ants, thermites, beans), colibry, crocodiles, tortoises, rodents, Chiroptera (flying mice) belong to this group.

Body temperature constant level in humans may be served only under the condition of dynamic equllibrium between heat production and heat emission. Such equillibrium is supported by thermoregulation physiologic mechanisms. One can differentiate 2 ways of thermoregulation: chemical and physical.

I. ***Chemical thermoregulation*** is performed by means of enforcement or weakening of cellular and tissular metabolism intensivity and expressed in heat production amount change. Heat source in organism are many organs and tissues but portion of their participation in heat production is rather various. Maximal heat production in organism occurs in muscles, liver and kidneys. One can say about 2 thermogenesis types:

1) Contractive – is linked with muscular thermoregulative activity. In turn, one can differentiate 2 subtypes of it:

- Thermoregulative tone - is analogous to muscular pose tone. It is performed like low-freaquened incomplete tetanus (impulses freaquency is 16 per 1 minute). Muscles of neck, trunk and extremities flexors are involved in this reaction. That's why human being changes his pose (curls up into ball).
- Shivering – in switched on when internal body temperature becomes its reducing.

2) Non-contractive – connected with activation of heat special sources is realized due to brown fat tissue existance which in comparison with white fat has more mitochondrias (brown colour is provided by iron-containing enzymes – cytochromes which are important part of mitochondrial oxidative enzymatic system. Fat acids oxidation velocity in it predominates that in white fat in 20 times.

II. *Physical thermoregulation* is realized by means of heat emission changes. One can differentiate *several heat emission ways*:

- Heat radiation – heat releasing (emission) by organism due to infrared radiation out off body surface. Under rest state heat emission by this mechanism is about 60 per cent.
- Heat conduction and convection – direct heat emission to subjects attached to skin, air. It is the more intensive the more is temperature difference of body surface, air, surrounding subjects. Organism losses up to 15 per cent of warmth by this method.
- Evaporation – the way of heat dissemination by organism into surrounding environment due to its expenditure to sweat or moisture perspiration from skin surface and moisture from mucosae. Organism looses up to 19-20 per cent of heat by evaporation.

Thermoregulation is body temperature constant level supporting. It is performed by principle of self-regulation. Receptor structures - are receptors of coldness, warmth and burning. They are located in skin and mucosae. Excitement threshold for receptors of coldness (their amount is bigger and they are located more superficial than receptors of warmth) is in limits of 20-33°C (average - 26°C); for receptors of warmth - 40-46°C (average - 43°C) and for receptors of burning – everything that higher than 45°C.

Thermoregulative center is located in hypothalamic nuclei. Physical thermoregulation is performed by hypothalamic nuclear group located between anterior comissure and optic chiasma (heat emission center). Shortly, heat production center is located in posterior hypothalamus while heat emission - in the anterior one. Under comfort (thermoneutral) conditions thermal equillibrium providing body temperature support at normal level is not in need of correction by special thermoregulative mechanisms. Environment temperature below than comfort causes activity increasing in perypheral receptors of coldness. This "cold" information increases the posterior hypothalamus efferent structures tone and causes hypersympathycotony as the result of such increasing. It is accompanied by cutaneous and subcutaneous vessels tone increasing. Result of these reactions: organism isolation increasing and heat serving by means of heat emission reducing. This process also leads to ***pilomotor reflex*** occurence (activation of smooth muscles fibres function rising hair covering). Parallely to this due to posterior hypothalamus work activating pose muscular tone regulatory system (thermoregulative tone and trembling appearence) heat production increasing occurs in organism (contractive thermogenesis). Due to adrenaline and noradrenaline releasing in course of this reaction energetic exchange in all tissues becomes stimulated particularly in brown fat tissue (non-contractive thermogenesis). Such heat production adrenergetic stimulation is triggered by thyroid hormones action the releasing of which is increased at cooling. When organism is warmed up coldness receptors activity is reduced that leads to hypothalamic efferent structures tone decreasing. As a result sympathetic nervous system influencies on cutaneous and subcutaneous vessels are reduced and this reaction is accompanied by cutaneous blood supply increasing. Heat exchange adrenergic and thyroid activation is decreased in parallel to this. Thermoregulatory center influencings decreasing causes muscular tone and thermogenesis reducing connected with it. Under over heating conditions special sympathetic structures are activated managing perspiration through cholinergic nervous fibres. Heat emission through evaporating is increased as a result of this. Also thyroid hormones participate in heat-production. Hyperthyreosis is accompanied by hotness, hypothyreosis – on the contrary, coldness.

Human body temperature under norma is about 37°C. It is changeable in course of 24 hours: maximal - to 16-18 hours, minimal – to 4 hours. If temperature is decreased - it's hypothermia, if it is increased – hyperthermia. At temperature reducing below 35°C behaviour disorders take place, up to 31°C - human being is unconscious, at 24-26°C - he is dead. At body temperature increasing up to 39-41°C delirium can begin; at 41-43°C – heat shock and above 43°C - death. Sweat glands activity is essential for heat regulation. Their general amount on human body is up to 2,5 mln. The biggest number – on face, palms, soles, axillas (arm-pits). One can see constant (invisible) evaporation during which sweat is released from skin surface right after its emission. When forming sweat amount is big, it is accumulated near skin surface in drops (visible evaporation). Sweat releasing is observed not only in course of physical activity but also during mental activity. In course of psychical excitement and some emotions (fear, wrath, pain) cold sweat appears in people. Coldness sensation occurs because of skin cooling as vessels are constricted and skin blood supply is decreased simultaneously with sweat emission. Sympathetic nervous endings in sweat glands are considered to be cholinergic i.e. containing mediator acetylcholine releasing while excitement. Impulses causing sweat emission at temperature increasing come into sweat glands through cholinergic nervous endings while causing

emotional sweating (sweat releasing) – through adrenergic. Under norma sweat amount per day reaches up to 500-900 ml, in summer – in 2-3 times more. At high temperature and hard physical activity – in 5-10 times and even more significant.

In a child who has just born rectal temperature is 37,7-38,2°C. In 1 hour it becomes its decresing up to 35 and even lower than 32°C; but then it is increased and in 12-24 hours it reaches 36-37°C. New-borns temperature depends greatly on external (environmental) temperature. Part of children have transitory fever in 2-3 days – temperature increasing up to 39-40°C. It is linked with protein excessive coming into organism and with water insufficiency. Fever may last from several hours to several days and goes away without any consequences. Temperature in children has some peculiarities. First, skin temperature is higher in children due to better vascularization. Second distinguishing feature: children have right-left asymmetry in cutaneous temperature. Third, thermoregulation in children is less perfect than in adult. It is expressed in unconstant body temperature. Fourth, thermoproduction increasing is expressed weakly, cold trembling is absent. Thermoregulation insufficient effectiveness is also delt with relatively large body surface as well as organism low thermoisolation. Fifth, conscious body temperature control develops weakly in children of the first years. Children may not complaint on temperature dyscomfort at coldness and overheating, that's why the adult must take care of baby cloth's temperature to air temperature and humidity. It's beyond compare that this information is essential not only for future doctors but for all people as parents. Thermoregulation development and thermal exchange conditions reach adult indexes at 15-16 years.

Lecture 26.
Excretion (separate organs and systems role). Kidneys functions.

Excretion - is metabolism part realized by ending and intermediate metabolism products, side and excessive substances excretion out off organism for optimal environment content and normal viability providing. Excretion is closely connected with water exchange because main part of substances to be excreted from organism is released in a state soluble in water. Kidneys are main excretory organ secreting and releasing urine and substances necessary for excretion out off organism. Also kidneys are main organ of water-salty metabolism providing.

Excretory organs are following:

- kidneys;
- alimentary tract;
- lungs;
- skin;
- mucosae;
- salivary glands;
- lacrimal glands;
- sweat and sebaceous glands;
- milky glands (during lactation).

Excretory skin function – is mainly provided by means of sweat, sebaceous and milky glands. ***Sweat glands*** are essential for destruction products having been formed in course of metabolism, in heat regulation (sweat evaporation from skin surface enforces heat emission), in osmotic regulation (by means of water and salts excretion). Sweat contains up to 98-99 per cent of water, inorganic substances (sodium and potassium chloride), organic - urea, urinary acid, creatinine, flying fat acids. Up to 300-1000 ml of sweat is excreted in average for 24 hours. ***Sebaceous glands*** have less importance as for excretion than sweat (up to 20 gramms per day). Sebum cutaneum softens skin and lumbricates hairs. It consists of neutral fats. Sebum cutaneum is destructed under sweat acids with fat acids formation possessing special smell. ***Milky glands*** excrete milk, essential feeding product for new-borns. It contains proteins, fats, carbohydrates, vitamines, mineral substances, water. There are bacteriocydic substances, antibodies for chidren passive immunity in milk. Milky hormones are essential for growing organism. Good mother's mood helps normal milk secretion. Hard psychical emotions, fear, inhibited mood decrease milky secretion or ven may lead to its complete stoppage. Particularly, rock-music has such influence.

Liver and alimentary tract excretory function is the following: these organs excrete some metabolism products with alimentary juices under normal conditions. ***Liver*** excretes haemoglobine and other porphyrines ending metabolism products with bile as bile; ending cholesterine products - as biliary acids. Thyroxine, urea, calcium, phoshorus, medicines, poisons are excreted with bile out off organism. ***Stomach*** provides metabolism products excretion as juice components (urea and urinary acid), medicines and poisones (mercury, iod, salicylates). ***Intestine*** excretes food metabolism excessive and harmful products; alimentary juices and bile components, hard metals salts, proteins, water.

Lungs and respiratory ways excretory function is in flying metabolites and exogenic substances - carbonic dioxide, ammonium, acetone, ethanole and others – excretion from organism internal environment. Bronchi ciliate epithelium excretes lung tissue metabolism products as well as surfactant degradation products. Water is partially excreted through lungs as steam (from 400 ml under rest to 1 l at increased breathing).

Kidneys functions are various; but excretory function is dominant. Kidneys participate in organism water and ions equillibrium, osmotic constant level, acid-alkaline balance support; proteins, lipids and carbohydrates metabolism, erythropoiesis and haemostasis regulation thus performing excretory and non-excretory functions.

Uropoiesis is main kidneys function. Urine produces in kidneys from blood. Uropoiesis in kidneys is originated from blood plasma ultrafiltration in kidney glomeruli. 2 mechanisms are essential in this process: filtrating membrane and pressure gradient. ***Filter*** providing uropoiesis consists of 3 layers:

- *capillary endothelium* – it has foramens with diameter up to 100 nm, through which water with substances dissolved in them comes free;
- *basal membrane* – it has very small pores through which formed elements and large molecules don't pass;
- *layer consisting of podocytes* between which fissure-like diaphragms with diameter about 10 nm are remained. These podocytes processes are contracted and relaxed due to myofibrilles and pump filtrate in capsule cavity as micropumps.

Filtrational pressure is created due to blood hydrostatic pressure difference in glomerular capillaries (it is equal to 70 mm of mercury column) and pressures sum

impeding filtration (oncotic pressure - 30 mm merc. col. and ultraphyltrate capsular pressure –20 mm merc col). As a result, filtration pressure under norma is equal to 20 mm merc col. Filtration process is stopped when blood hydrostatic pressure in glomerule capillaries is reduced up to 40 mm merc col. Filtration level depends on afferent and efferent vessel cavity namely: efferent vessel constriction leads to filtration increasing, afferent vessel constriction – to its decreasing. Primary urins daily amount is about 180 l per day. It is identical to blood plasma only with protheins exception.

Uropoiesis second stage – is ***channel reabsorbtion*** and secretion. Water reabsorbtion and substances having filtrated in glomeruli occurs in nephron channels. One can tell about proximal and dystal reabsorbtion.

- *Proximal reabsorbtion* determines complete glucose reabsorbtion (that's why sugar glucose is absent in ending urine), protheins, aminoacids (that's why there is no prothein in secondary urine), water and sodium biggest part, potassium, chlorum, urinary acid, urea reabsorbtion. 1/3 ultrafiltrate volume is remained to proximal channel end. Glucose and aminoacids proximal reabsorbtion is performed by special transporters and is tightly connected with sodium transfer. Such transfer is called active. Water absorbtion is realized passively and depends on sodium and chloridum reabsorbtion.
- *Distal reabsorbtion* – ions absorbtion (about 10 per cents of sodium and chlorum ions) and water. Water is reabsorbed alongside all the channel. Reabsorbtion velocity is increased twice in dystal channel part. Henle loop descendant part epithelium passes water good, and ascendant – actively transports sodium ions from primary urine to tissular liquid due to kidneys outflowing-turning system. Urine concentrating and dissolving occurs in this system because substance transport processes in one knee of system are enforced (multiplied) by means of other knee activity. Ascendant knee performs dominant role in outflowing mechanism. Its wall actively reabsorbs sodium ions in surrounding intersticial spaces. Ascendant knee wall is permeable for water which comes passively from cavity in intersticial hypertonic environment. Urine becomes more and more hyperosmotic alongside descendant knee. Urine becomes less and less osmotic in descendant knee because of absorbtion and hypotonic urine comes in dystal channel cortex. Collecting tube formes outflowing system with ascendant knee. At vasopressine (antidiuretic hormone) presence collecting tube wall is permeable for water. With urine passage through collecting tubules into the depth of medulla water passes passively in intersticium hypertonic content and urine becomes more and more concentrated. There is also vascular outflowing system.

Outflowing systems action result – is ending (secondary) urine forming. Its character, finally, depends on blood osmotic pressure. Osmotic pressure increasing leads to hypothalamic osmoreceptors excitement, then information moves into neurohypophysis, releasing antidiuretic hormone. This hormone enforces dystal channel wall permeability for water and as the result of this urine becomes hypertonic. If osmotic pressure is reduced mentionned reactions will be weakened and urine will be hypotonic. Children on mother milk excrete hypotonic urine, on caw milk or artificial feeding mixture – more often are released hypertonic urine.

In ending uropoiesis definite place takes ***channel secretion.*** This is channel epithelium active transport in urine substances containing in blood or forming in channel

epithelium cells. Channel secretion determines potassium, hydrogenium ions, organic acids, ammonium and other substances passage into urine.

Secondary or ending urine is about 65-80 per cent of used water, this is daily diuresis for 24 hours which is equal to 0,7-2,0 l. Urine reaction is usually light acid, but everything depends on food character. At primarily plant food urine becomes more alkaline, and at animal or prothein – more acid. It has definite colour, transparity, sediment.

Uroreleasing is performed in the following order. First, urine comes into renal pelves. Renal pelvis and ureter smooth muscles possess automatism. With pelves filling by urine mechanoreceptors irritation occurs that causes pelvis musculature reflectory contraction and ureters opening. Urine passes into urinary vesicle due to their smooth musculature contractions like peristaltic. It stretches walls while its filling. But this stretching doesn't cause refelctory reactions directed to urine releasing till definite vesicle volume (it is approximately equal to 250-400 ml). But when urine volume predominates these ziphras urinary vesicle wall mechanoreceptors irritation begins right after this that results in urine releasing. This process is under control of spine sacral parts. Impulses from this part cause urinary vesicle wall smooth muscle contraction and sphincter relaxation through parasympathetic fibres. In the adult day diuresis predominates night one in 2-3 times.

Kidney excretory function is essential for nitrogen metabolism products releasing - urea, urinary acid, creatinine and others. These substances accumulation in blood may cause toxic phenomenon development called uraemia. Uraemia leads to nervous system excitability reducing up to unconscious state (coma), external and tissular breathing, blood circulation disorders, body temperature decreasing and even to exitus letalis. If one kidney works normally uraemia won't occur. In uraemia case haemodyalisis is performed – kidneys artificial clearence from accumulating metabolites. One differentiates extra- and intracorporal haemodyalisis. The first one is artificial kidney, the second one – abdominal cavity washing.

Kidney metabolic function is provided by substrates and metabolites excretion. Kidneys metabolize small-sized peptides, denaturated peptides filtrating with urine and return them into blood. Kidney tissue possess the ability to perform gluconeogenesis. Such ability is higher in kidney than in liver if to count on mass unit. For example, almost 50 per cent of glucose is produced by kidneys in course of durable fasting.

Kidneys role in blood arterial pressure supporting is realized by following way: several substances the function of which is connected with vascular vessels cavity regulation are formed in kidneys. One of them is produced in juxtaglomerular apparatus and is called *renin.* Renin itself doesn't influence on vessels. It is the essential component of so-called renin-angiotensine-aldosterone system that regulates vascular vessels tone, sodium equillibrium in organism, circulating blood volume. Renin passing into blood circulation transforms angiotensine into angiotensine I. Further, in lungs (under special converting enzyme action) it transforms into angiotensine II. Blood pressure level depends on this substance concentration and activity. Renin secretion is increased at blood pressure decreasing (for instance, as a result of blood loss, hypotension of medical origin and other reasons), intrachannel pressure increasing (it can be found at ureter constriction, stones in kidney and ureter), at blood pressure reducing in afferent glomerular arteriole; at

hypersympathicotony, sodium concentration increasing into dystal urine (urine of dystal channel).

Arterial pressure level in blood depends not only on renin synthesis in kidneys. Kidneys possess antihypertensive function due to depressors production - neutral medullar lipid, prostaglandines, kinines. Kidneys excrete water and electrolytes and their content in blood, extra- and intracellular environments is essential for arterial pressure support. Kidneys may also regulate arterial pressure on mechanism "pressure-diuresis". Arterial pressure increasing accelerates blood circulation through kidney medulla direct vessels. It leads to sodium and urea osmotic gradient washing (reducing) that decreases water reabsorbtion and, thus, weakenes kidney concentrational ability. Diuresis increasing decreases blood circulating volume and makes blood pressure normal. At moderate (physiological) water consumption saliva and chimus osmotic pressure is reduced, that is percepted by oral cavity, alimentary tract osmoreceptors and liver osmo- and sodium-dependent receptors. Sygnals from these receptors with reflectory way usage before sodium and osmotic pressure level change in systemic blood circulation decrease vasopressine (antidiuretic hormone) neurosecretion and enforces uropoiesis right after drinking. Blood volume is restricted because of drunk water absorbtion as a result of sodium and water excretion by kidneys. It also can influence on blood pressure level and reflects ***kidneys homeostatic function.*** Excessive water consumption leads to hyperhydratation, osmotic pressure and plasmic sodium content reducing that also inhibits vasopressine neurosecretion. Water surplus is excreted out off blood as water reabsorbtion decreasing in dystal channels and collecting tubules. This process is triggered by urea absorbtion absence in collecting tubules that decreases kidney medulla intersticium osmolarity and restrictes water reabsorbtion in more extent. At described mechanisms insufficiency water is remained in organism. From one side, it may influence on blood pressure level, from another - it causes water exit in tissues and oedemas (swelling). Excessive hydratation leads to water poisoning and, finally, to brain haemorrhagias. On the contrary, water fasting or water excessive loss leading to circulating blood volume decreasing, causes renin secretion enforcement. Angiotensine-II appearing as a result of this, causes thirst development while drinking center stimulation. Angiotensine-II may be produced in brain tissue itself leading to thirst forming. Water fasting or excessive water loss cause cellular dehydratation and potassium ions exit with water that leads to strong disorders especially of central nervous system.

Kidneys participate in ***erythropoiesis regulation.*** Hormone-like substance *erythropoietin* is secreted in juxtaglomerular apparatus. It is as it is well-known is the only specific erythropoiesis regulator. Its concentration increases in blood at blood losses, oxygen low partial pressure (it is essential both for mountain regions residents and for those rising into highlands), at heart and lungs diseases. Erythropoietin action way: it accelerates and enforces stem cells transformation in erythroblasts, increases cellular mitosis amount, accelerates normoblasts and reticulocytes maturation.

Kidneys are delt with ***blood coagulation and fibrinolysis.*** They synthesize substances influencing on all haemostasis links: vessel-thrombocytic, blood coagulation and fibrinolysis. First of all, kidneys are vessel-thrombocytic haemostasis regulators. Probably, it is necessary for activity of kidneys themselves. They contain (and can release into circulation) different prostaglandines (particularly prostacycline), influencing directly on platelets aggregation activating and inhibiting. They either produce coagulational

factors (for instance, thromboplastine) or release coagulation factors surplus accumulating in them (for example, fibrin degradation products and others).

Kidneys are essential for fibrinolysis regulation. *Urokinase* – natural plasminogen activator – is excreted from kidneys. This plasminogen activator receives from urine for thrombosis, thromboembolic diseases, thrombotic disease treatment. In organism there exists very interesting dependence of urokinase producing on sodium chloridum concentration. The more sodium chloridum in organism the worse urokinase is produced. It should be taken into account by all lovers of salty products. In many aspects urine antiinflammational effect is connected with urokinase. People have been using urine for ages at inflammations on skin for example, burns, combustions, traumas. It is not occasional. Active fibrinolytic system is necessary for reparation, regeneration, restoration. Urine is natural product containing plasminogen activators. That's why urinotherapy is considered to be very widely spread nowadays in "folk medicine". Having detemined urine coagulational and fibrinolytic activity one can tell about kidneys functions and their disorders.

Lecture 27
(Final).
Healthy life style physiological bases.

According WHO (World Health Organization), ***health*** is complete body (physical), spiritual and social welfare. Having studied Physiology at lectures and practical classes, everyone of you may have your own definition of health. But, nevetherless, let's describe separate statements of WHO health definition.

"Complete body (physical) welfare" – is it really in life? Many of you can tell: "I am physically in a good health". But is it so? Of course, when you are 18-20 years old, it's very easy to make such a conclusion. But look to people who are around you. One carries glasses, others – have problems with his or her leg and so on. And amount of such people is rather big. But, unfortunately, after careful control, - this number is even bigger, frankly speaking, the most of people have problems with their health. On the base of which indexes we tall about health? As a rule, having investigated pulse, pressure, temperature, having determined weight, growth and so on. If you go to the psychiatric clinics and try to measure all these indexes, you will have normal levels in the most people who are there. But whether they are considered healthy? Thus, these indexes determining is not health evaluation criterium. It's necessary to have psychical health too.

"Complete psychical welfare" - it is the unity of consciousness and underconsciousness. We are often so far from this unity. That's why it's very difficult to decide who is psychically healthy, who is sick. According to the statistic processing, every 4^{th} person is psychically unhealthy in Europe. But it was so 10 years ago. And, besides many people are gone by such official statistics!

"Complete social welfare" - probably, this phenomenon is very difficult to be achieved for the most people. Human being is always surrounded by one or other social problems!

"Complete spiritual welfare" – this index evaluation is more difficult. Spiritual health – is a principle of natural kidness to everything and to everybody. Whether many of us can say about their kind attitude to environment, surrounding people, even to our relatives. We can see at every step indifferentness to other people misfortune, troubles; ruthlessness, cruelty, violence, sadism and other expressions testifying to low (the lowest!!!) spiritual level of many people.

What is the conclusion of performed analysis? Thus, we have very grief picture because one can't find human being corresponding to all these requirements "in the afternoon with a fire". What to do to be closer to the term "healthy person"? To gain this goal, it's necessary to drive your life maximally to so-called "healthy life style". What factors does it depend on?

If we take all health for 100 per cent, than different factors contribution in it will be following:

- environment – 20 per cent;
- social factors - 20 per cent;
- rest 60 per cent (according to several data – all 80 per cent) – life style.

We have practically told about social factor. That's why we shall only add a few words about medicine role in health preservation and supporting. The most investigators consider that medicine role in health preservation is rather humble and its share is about 6-8 per cent. More probably, it performs its functions of organism support at definite level relatively close to healthy state. And we are sure that any supermodern diagnostical devices, any superlaboratory service, any supereffective medicines, supermodern clinics and supermediocre doctors health problem won't decide and don't decide. Sick people amount despite all these "super" is growing up and growing up. And, the most important, will increase and increase. Remember! The more medicines and more pharmacies we have (one can see this now with unarmed eye), the more patients we have.

One can tell many things about ecological factor. But the most important in this problem – complete ecological people's incompetence. Remind, you go alongside the road and see fastened animals. This is the solving of feeding problem. This is the example of people's "ecological incompetence". And vegetables and fruits chemical processing out off any control while their cultivation! Chernobyl is out off comments!!! Certainly, all this influences on our health. But at the same time it is the result of human activity. Thus, we do something wrong.

And, at last, main factor our health depens on – modern human being lyfe style. It is not occasionally that it is about 60-80 per cent of our health. What do we mean telling about healthy life style? It includes many constiutuents. All of them are tightly connected one with another. The most essential among them are the following:

- thoughts;
- movement;
- air;
- water;
- feeding;
- harmful habits;
- active psychical activity.

We consider, that human ***thoughts*** – are one of the most important and of the main healthy life style elements. May be you know the proverb: “Healthy spirit - in a healthy body”. It is not correct. Because it is on the contrary: “Healthy spirit – healthy body”. We have discussed this while the highest nervous activity physiology study. Thoughts may make human being sick and they may treat him.

The second essential health factor is ***movement.*** Aristotel wrote many years ago: “Nothing malnourishes and destroys human organism so like durable physical inactivity”. And we must completely agree with this statement, especially at present”. Why especially at present time? Because, human motor activity is very-very low; the most of them doesn’t perform the most elementary norms of physical activity our organs are intended for. But we forget that all the world (we are particle of this world), everything in it is in movement and moreover in harmonic one. If such harmony is destroyed “chaos” occurs. It is disease itself if it is described at human organism level. Remember! Because of physaical inactivity strong organ is degenerated, weak one – dies at overloading. We discuss advantages of systems and organs functionning in trained people in course of Physiology study. Here – next example. Collaborators of our chair investigated more than 100 indexes characterizing different organism systems activity in big people group (more than 700), part of which was control, another one was performing healthy running. As our results have demonstarated, running people (in the age from 20 till 75 years, of different sex, various professional groups) have in their blood more formed elements amount, low blood coagulation indexes, higher prostacycline level in vascular wall, lower blood pressure level. We can continue this list. According to literary data, people dying in accidents performing healthy running before this regularly, practically don’t have any vessels sclerotic injuries.

One can deliver separate lecture on the basis of this material. But during last years there occur very interesting data about movement as healthy life style factor. Indeed, as it was mentionned above, healthy running influences differenly on effectiveness velocity and depends on load intensivity (distance having been runned in course of training, running velocity, running freaquency in a week) in different people (taking into accout their emotional characteristics, typological distinguishing features). Nowadays it was demonstrated that human physical activity should be in correspondence to their genetical features which one can evaluate on blood groups. Authors of this textbook share this opinion and consider that this statement must be taken into account all the people who do physical exercises.

I-st blood group – intensive loadings types are necessary – running, swimming, rapid walking (4 times a week).

II-nd blood group – walking and running of middle intensivity combination with calming loadings (meditative exercises). Such combinations must be 3-4 times a week in them.

III-rd group - intensive loadings are recommended (walking, running – 3-4 times a week) and relaxating (gymnastics - 1-2 times a week).

IV-th blood group - loadings close to those like in people with II-nd blood group are essential. They must avoid games with competitive elements.

Such exactments delt with blood groups make human loadings more adequate and their preventive effect must grow due to this.

Essential factor of healthy life style is correct ***breathing training*** and also ***air*** we breath in. We've told about correct respiration above. Let us remind you shortly. We breath only with our nose; with lack in inspiration and especially in expiration; we are trained to have healthy respiration freaquency – 6-8 per minute. Physical trainings will lead you automatically to this.

We must inspirate air with maximal amount of negative ions. Such air is in mountains, near reservoirs, finally, in the street (especially – in the forests, in the parks). There are much positive ions (or aeroions as they are called by the scientists) in any room the most suitable and ideal for staying there. These positive ions make us sick.

Water – is the most important healthy life style factor. Our organism needs constantly in it. But what water do we drink? Naturally, everyone has to strive for clean, purified, spring water usage.

Next factor – it is ***feeding.*** This factor is tightly connected with movement. That individual who is trained regularly doesn't have any problems with feeding. He isn't never overeating or overdrinking. The most important approach to feeding problem – is food limited usage. We'll be more healthy in 100 times while restricted food usage comparatively to the people which can't restrict themselves in food and drinking. The most of us consume more than use. It is not occasional that every second person has the excessive weight. Excessive weight – it is disease.

Next group factors – ***harmful habits.*** It is well-known to everyone how easy to aquire them and how difficult to fight against them. Be the example to your relatives. Leave smoking, drinking alcohol, drugs, medicines. ***Only health person can make other (sick) person healthy!!!***

Active psychical activity- is other health factor. What does it mean? One scientists differentiate 2 aspects in this: labour joy and sexual health.

Labour joy – it is interest to your work. There exists psychological optimum which means that being busy with any kind of work corresponds to physiological, intellectual, social and other factors. Are you satisfied with your work? Do many people today are in joy while performing their daily work? Unfortunately, the percentage of such people is very insufficient. But we spend our main lifetime at work. If it doesn't carry joy to us, it doesn't add any health to us. On the contrary.

Sexual health – is complex of somatic, emotional, intellectual and social factors. We are talking about sexual explosion today. What is it? Church preaches asketism (refraining particularly sexual one) in Middle Ages. Intimal life was considered as fornication, lechery. There were many ignorance in intim and, it's quite naturally, that ignorance may born only ignorance. Tht's why it is remained till nowadays.

Finally, it was occured something that did very big gap between civil and sexual maturity. If civil maturity becomes in 18-20 years (in girls) and 22-23 years (in guys), than sexual one becomes significantly before (in 12-14 years in girls and 15-16 years in boys). The gap of the first from the second is approximately 5-7 years and even more. At this period (early sexual) there are only 2 constituents of sexual health – somatic and emotional. That's why sexual life early beginning causes degradation both mental and physical (fading, impotence).

One can add many small, secondary, insignificant factors to factors mentionned above but it is not important and it doesn't change the essence of deeds. It is clear only one thing: ***human health is mainly in his or her own hands!!!*** If you would like to see one

responsible for (guilty in) all your diseases and tragedies, look in the mirror and you will see him in all his (her) beauty!!!

In conclusion, telling "Good-bye" to you we would like to wish you following:

1. Stop to moan, to complaint on smth, to search for guilty every time – because these are main reasons of all your problems.
2. Don't ignore physical loadings, don't do physical trainings the company. Having started to do any physical exercises – continue all your life according to your genetical possibilities.
3. Don't forget that it's necessary to eat for live, not on the contrary. Remember: each 2,5 cm of waist circle as for breast are equal to 2 years of life.
4. Stop smoking, taking drugs and medicines and achieve this from other people.
5. Don't afraid any risk, life difficulties, go forward to them and learn to overcome them. Life is too short to loose it for triviality. Truth and politeness are the most valuable in this life. Smile, clever joke, truly word will help you and your relatives more than all medicines in the world.

Take in your Way your knowledge, love to work, because the of sweet "doing nothing" is over and world – is not a hall for loafers but great workshop! Create in it! Have a good journey through the country the name of which is Your Life!

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