

Lecture 1

SUBJECT AND METHODS OF PATHOPHYSIOLOGY. GENERAL ETIOLOGY AND PATHOGENESIS.

Pathological physiology is the science, which studies the general natural lawfulness of disease genesis, development and the end. This is the science about the vital activity of sick organism. Pathological physiology is the study of the most common options of the disease genesis and development, while clinical sciences study specific items of disease prevention, diagnostics and treatment. Pathological physiology, as a science, solves the following problems: illness essence establishment; disease causes and its beginning conditions study; illness development, display, course and the convalescence mechanisms separate explanation; diseases prophylaxy and cure general principles determination.

The pathological physiology is related to the other sciences:

- to the sciences, which study illness causing environmental factors (physics, chemistry, biology, microbiology, the social sciences), they are necessary for etiology studying;
- to the sciences, which study the organism properties and its vital functions (cytology, embryology, histology, the normal physiology, biochemistry, immunology, genetics), they create a base for pathogenesis study;
- to general theoretic sciences, which study the disease (pathological anatomy, pharmacology), in common with pathological physiology create a total picture of the illness;

- to the clinical sciences, helping to determine the basic etiological and pathogenic principles of disease prophylaxy, diagnostics and cure.

The clinic arises the problems and gives the necessary material for their solvation to pathophysiologists.

The pathophysiology, as a scientific medical base (medical philosophy), establishes illness etiology and pathogenesis and determines the main directions of their prophylaxy and cure on this base.

The medicine uses clinical, epidemiological, anatomic, experimental disease study methods.

The peculiarity of pathophysiological experiment is the reproducing of the experimental disease models upon laboratory animals with the purpose to establish the mechanisms of their genesis, development and in human organism.

The experimental disease model is the artificial reproducing of disease up the laboratory animals, which has the same lines of the proper human disease.

Though an experiment up animals does not give us the full picture of the proper human disease, it enables to observe and to study the disease course the beginning to its completion that is impossible in clinics. During the experiment one can control the environmental conditions, which influence upon the illness course and have the objective material for the scientific theories construction.

The experiment can be divided into the acute and the chronic one. The acute experiment is based on the surgical intervention in animal organism. It examines the acute disorders in organism (shock, collapse, sharp breathing insufficiency, blood circulation insufficiency, etc). The chronic experiment is a protracted one, shows the

illness development dynamics. It is used for chronic diseases modeling (diabetes, atherosclerosis, arterial hypertension, ulcerous disease etc).

Pathological physiology consists of such parts: the general pathology and the pathophysiology of the organs and systems. The general pathology unites such parts: nosology, pathogenic environmental factors action, inner factors role in pathology, typical pathological processes, and the typical metabolic disturbances.

The pathophysiology of organs and systems studies the general development of pathological processes in separate functional systems; the most widespread nosological forms etiology and pathogenesis as well.

The general nosology includes such notions: health, disease, pathological process, pathological state, pathological reactions.

According to definition of World Health Care Organization health is the condition of complete physical, psychic and social well-being, but not only diseases or the physical defects absence. In doctor's practical activity determination is used, according to which health is the condition of a norm. There is a question: what the norm is? There are two approaches to this notion determination: the statistic and the general physiologic one. According to the first one, the norm is the condition, which is the most frequently observed among people. According to the second one, the norm is the biological optimum of the organism functioning and development. The second determination reflects the scientific approach to the notion which is "a norm". However this approach remains still unrealized because of our knowledge and possibilities limitation. Therefore a doctor uses the statistic norm determination in daily activity.

The disease is a disturbance of human organism vital activity under the influence of extraordinary factors of external or inner environment which is characterized by lowering of capacity for work and adaptation with simultaneous mobilization of protective forces.

The new quality is created in the disease because of quantitative changes into qualitative transition. As a rule, there are two contrary processes, two phenomena of disease. One of them is a damage, and the other is called as a protective response of organism (which makes the first one perform the physiological measures against the disease, and the second one - pathological proper or the damage). The two beginnings of disease exist simultaneously. For example, in case of abscess we see the limited necrotic tissue area, but we can also see here the leucocytes emigration, phagocytosis which protects the organism. The treatment is always directed to damage limitation or removal that means - to protective reactions stimulation.

There is about thousand diseases nowadays. However, their amount changes in course of time. Some diseases disappear, the other appear. For example, the radiation disease did not exist before the X-rays started to be used. The cosmic medicine didn't exist either before the cosmic flights began.

The diseases classifications are based on the following criterias:

- The etiological classification is founded on the cause community for the diseases group. For example, there are the infectious and uninfected diseases. According to the same principle one can group the diseases caused by an intoxication (food, professional), genes violations and chromosomal mutations (hereditary diseases) etc.

- The topography-anatomic classification is based on the organ principle the cardiovascular diseases, diseases kidneys, diseases of nervous system etc. It is comfortable for practice. Besides, it corresponds to the modern specialization of the medical help. It combines with the classification of the functional systems: blood system, digestive system, musculoskeletal apparatus diseases etc.

- The age and sex disease classification. There are the children's diseases, the senile age diseases. The female genitals diseases are studied by the gynecology.

- The ecological diseases classification proceeds from the human dwelling conditions: the air temperature, the atmospheric pressure, the sun illumination.

- The classification according to the pathogeny commonness: allergic and inflammatory diseases, neoplasms, shock, hypoxia.

Every disease is the suffering of the whole organism irrespectively the diffuse organs and tissues damage. At the same time there are the definite localization and the scantiness of pathological changes, they are peculiar to the diseases majority.

The pathological process is combination of local and general reactions, which arise in organism retaliating to the morbidic agent damaging action. The development of pathological process depends both on etiological factor and the organism reactive properties. There are the destruction (damages) processes combinations and the protective compensational reactions, which arise at different organism levels because of pathogenic factor influence. The pathological process can develop at the molecular, cellular, tissue, organ, and system levels. If pathological process envelops the whole organism, that means disturbs its vital functions, then it turns into disease. Therefore the pathological process is not the disease obligatorily; however there isn't the disease without the pathological process.

The pathological processes may be typical; they course identically with the diverse pathogenic influences, in different organs and in different organisms. The examples of such processes are: inflammation, neoplastic process, local blood circulation disorders, hypoxia, and fever.

The pathological state is the pathological process, which develops more slowly. Herewith the sickly violations remain invariable during a long time (years, tenth anniversaries). Frequently the pathological state is the result of the pathological process. So, the inflammation of the cornea may turn into the formation of the leukoma, which preserves for all life. It's possible to reverse pathological state transition into pathological process. For example, the cancer swelling can be formed under the influence of carcinogenic factors in the place of the afterburning scar.

The pathological reaction is inadequate and biologically inexpedient answer of organism or its systems to usual or excessive irritants influence. The pathological reaction is destructive element of pathological process. There are four periods (stages) of the disease development: the latent (incubation); the prodromal; the expressed clinical signs period; the disease ending. Such division arose up to the clinical analysis of the acute infectious diseases (a scarlet fever, ah abdominal typhus). The other diseases (cardiovascular and endocrine diseases, tumours) course another lawfulness. A.D.Ado distinguishes three disease development stages: the beginning, the stage of the disease proper, and the end.

The diseases endings are following: convalescence (complete and incomplete), recurrence, into chronic form transition, the death.

The convalescence is the process, which conduces to the violations liquidation, caused by a disease, and normal relations with the environment restoration, for human beings - foremost the ability to work restoration. The full convalescence is the state

when all the disease signs disappear and organism restores its adaptation possibilities completely. When the convalescence is incomplete the disease consequences are expressed. They remain for a long time or forever. The convalescence is provided by the urgent (emergency) and lasting protectively-compensational reactions of the organism.

The remission is the temporal state improvement of the human being, which is displayed by the disease progressing slowing down or cessation, the partial reverse development or the disappearance of the pathological process clinical signs.

The recurrence is the new disease display after its seeming or incomplete cessation.

The complication is secondary as for reference to the disease pathological process.

The transition in the chronic form signifies that disease courses slowly with the protracted remission periods (months and even years). So, many diseases acquire chronic nature in old age (chronic pneumonia, chronic colitis).

The terminal states are the boundary ones between life and death. This is also the dying, which include a few stages: pre-agony, agony, clinical death, biological death.

The pre-agony is characterized by the diverse duration (during hours, days) of deep violation of the vitally important organism functions. In this period are observed the dyspnea, the decreasing of the arterial pressure, the darkening down of the consciousness. Gradually the preagony gets across in the agony.

The agony is characterized by the gradual turning down of all organism functions. The agony lasts 2-4 minutes, sometimes more.

The clinical death is such condition when all of the visible sparks of life have already disappeared (the breathing and the heart work are ceased, however the metabolism still continues). The life can be restored on this stage.

The biological death is characterized by the irreversible changes in the organism.

The reanimation of the organism includes number of measures which are directed foremost to blood circulation and breathing renewal: heart massage, artificial lungs ventilation, heart defibrillation. The indirect heart massage is widely used for the renewal of blood circulation; it can be used at once after the clinical death setting in any conditions and even not by specialist. The artificial ventilation of the lungs also must be started as soon as possible. The heart fibrillation is observed in the terminal period ordinary. In such cases the electric defibrillation is used. A single digit to 6000 V removes the fibrillation and promotes the renewal of the blood circulation.

All of these measures are directed to renewal of cerebral cortex function. Herewith the respiratory centre is paramount significant. It is the main pacemaker of cerebral rhythms and the impulses, which promote the appearance of the electric cortex and the subcortical centres activity, vasomotoral one also. The renewal of the independent breathing promotes renewal of the blood circulation.

The etiology is the learning of disease beginning causes and conditions. The notions of causality and determinism are base of etiology. Causality reflects an objectively existent phenomenas connection, when one phenomenon (cause) inevitably causes beginning of the other phenomenon (resuh) by the definite

conditions. Any disease just like a phenomenon has its own cause. The beginning and the development of the disease are not by chance but subordinated to the definite lawfulness.

That factor without the disease can not arise in any conditions must be a cause of it.

A factor can be a cause if it exists objectively, irrespective of consciousness, co-operates with the organism, imparts the specificity of the disease.

If there is the typical pathological process or the nosological unit, then one can arrive to the conclusion about existence of many diseases causes. This is so-called principle of the polyetiology. For example, the lungs fever causes, as the nosological unit can be viruses, staphylococcus, pneumococcus, fungus, radiation, poisons.

However when concrete man's disease arises, then the principle of the polyetiology is incorrect. The assertion "one disease - one cause" is right solely in these conditions.

The conditions of the disease beginning are the different factors combination, where no one is absolutely necessary for its development. All the conditions are divided into two groups, according to the disease beginning influence:

- The conditions which increase cause action and promote disease development. For example, viruses are the cause of acute respiratory diseases, and cooling, tiredness, immunodeficiency are cooperant conditions. Sometimes these conditions can matter decisive. Without the definite conditions, in spite of cause presence, the disease does not arise (for example, the food products allergy).

- The conditions which weaken the cause action and prevent the disease development. They are the nutrition, correcting day routine organization, physical culture, correct care of sick. Sometimes the conditions may neutralize completely the cause action (for example, the presence of natural or acquired immunity to the infectious diseases). The combination of causes and conditions, relating to the disease beginning, were named the etiological factors. They are exogenous (external) and endogenous (internal). The exogenous factors are physical- mechanical influence, radiation, high and low temperature, electric current, overloading, zero-gravity and others; chemical – the inorganic and organic compound; biological – viruses, rickettsias, bacterias, Protozoas, helminths, Arthropodes; psychic - a word; social - society development level, traditions and others. The endogenous factors are; heredity, constitution, age, sex, organism reactivity.

There are risk factors as a notion, besides the etiological factors. The risk factors are the factors combinations, the presence of which in people population statistically increases morbidity by definite diseases. The belonging of these or those conditions to the risk factors is determined by epidemiological methods, which envelop the large people contingent. So it was established, that the violation of blood plasma lipid composition, arterial hypertension, the age, belonging to male, obesity, hypodynamia, hereditary factors, stress are the atherosclerosis risk factors.

The general pathogeny. The pathogeny is the study about the mechanisms of the development, the course and the end of disease. The pathogeny studies everything taking place after the cause action.

It is necessary to mention the following questions in disease pathogeny consideration: the role of etiological factor in disease development; the organism reactivity significance for the disease beginning and the course; the significance of

the general and local changes and their correlation; the basic link of pathogeny and causally-investigation intercourses; the significance of functional and morphological changes and their correlation in disease; the significance of nervous system functional changes for disease development.

There are some variants of connections between a cause and a pathogeny:

- The etiological factors play pushing role and turn the pathogeny on. The further cause existence is not obligatory for course of the pathogeny (burns, radial sickness).
- The existence of cause and pathogeny. The pathogeny continues while the etiological factor is active (the majority of infectious diseases).
- The persistence of etiological factor. The agents caused the disease stay in organism longer than pathogeny continues. Herewith the properties of etiological factor can interchange under dominance of organism (bacteria carrying after the infectious disease).

The pathogeny of disease always includes two types of processes and phenomenas. On the one hand it is damage, destruction that is properly pathological changes and processes. They conduce to the violation of homeostasis. On the other hand this is protective, adaptation reactions and processes. They direct to the remove of homeostasis violations, creating under the dominance of pathogenic factors and destructive processes in organism.

The adaptation is suitability of the organism and its structures to environmental conditions changing; it provides the preservation of homeostasis and prevents the damage of environmental factors influence conditions.

The compensation is the state, which develops as the realization result of the compensatory reactions and processes, directed to renewal of changed homeostasis along with pathogenic factors influence. The compensation liquidates the damage consequences.

The base of adaptation and compensation are the same mechanisms which are named protectively-adaptation or protectively-compensatory. The distinction between these notions: is adaptation develops in augmentation of the action intensity of usual factors environmental. The damage hasn't happened yet, and the homeostasis indexes are coming to the extreme norm borders. The compensation develops in the action of the pathogenic factors when damage takes place and the homeostasis indexes are beyond the extreme borders norms.

There are two adaptation and compensation development stages:

- The stage of immediate adaptation and compensation. The mobilization of existing mechanisms and reserves begins and as a result of loading on functioning system unit increases, its hyperfunction develops. On this stage the events develop according to such scheme: the action of pathogenic factors → the violation of homeostasis → the perception of homeostasis violation → regulatory centres → immediate protective reactions (specific and unspecific) → the hyperfunction of proper structures, supporting homeostasis.

- The stage of the long duration adaptation and compensation. The augmentation of systems power, responsible for adaptation and compensation is its base. It is reached by the augmentation of the structures amount, providing a hyperfunction, so hypertrophy develops. The following changes sequence develops on the cellular level. The hyperfunction → violation of intracellular homeostasis →

activation of genomes → the augmentation of the proper albumens synthesis → cell hypertrophy.

The changes in organism which arise during disease development are in definite causally-investigation relations, it means that the same phenomenon of pathogeny is the result of violations and cause of other. Such type of causally-investigation relations when the definite links the pathogeny over violation sequence bring to their heightening over so called "the vicious round". It supports itself the pathogeny of the disease and redoubles its course. So, in pathogeny of any shock lowering of arterial pressure has big significance that becomes cause of anoxaemia. The cerebral hypoxia brings to the oppression of vasomotor centre and greater lowering of arterial pressure (a circle locked).

The main link of pathogeny is the process which is necessary for a development of all the rest. The liquidation of the main link in time brings to removal of pathological process as a whole. The main principle of pathogenetic diseases cure is founded on it. So, in diabetes mellitus the insulin lack is the main link of pathogeny. Its liquidation (the introduction of hormone) brings to disappearance of other displays (hyperglycemia, glucosuria, polydipsia, ketonemia, comas).

In pathogeny specific and unspecific processes and mechanisms are always combined. The specific ones depend on the cause properties and determine the basic disease descriptions. A search of the specific signs lies in base of diseases recognition (diagnostics).

The unspecific ones are determined by the genetic organism properties. They are the mechanisms of standard answer of any pathogenic factor. They are directed to reinforcement of the organism resistance to damage and get performed in participation

of the nervous and endocrine regulation systems. So nervous and endocrine unspecific mechanisms of pathogeny are picked out.

There are two types of connections between local and general in pathogeny:

- The local violations develop originally. They can bring to general changes of the organism proper conditions. So, inflammation, neoplasms, burns - are the local violations. However if their expression arrives to definite level they can cause the development of general violations: fever, cachexia, burn disease.

- The general violations develop originally. They can be displayed by general changes. So, in diabetes mellitus (general disease) the local processes - furuncles, defeats of the joints, nerves, kidneys, eyes retina develop secondary. The general changes of the lipid metabolism in the organism conduce frequently to the development of atherosclerosis that can be displayed by such local defeats as myocardium heart attack, strokes, and the gangrene of lower extremity. The structural changes on different levels (molecular, subcell, cultural and etc.) are in base of any functional violations. It means that there are not clear functional diseases. On the other hand the functional violations may be the cause of structural development changes. So, cells and organs hyperfunction appropriately brings to their hypertrophy (the structural changes).

So, each disease includes the complex of complicated specific and unspecific, general and local, morphological and functional changes of the organism.