**INTRODUCTION.**

**THE SUBJECT AND METHODS OF PATHOPHYSIOLOGY. GENERAL NOSOLOGY. ETIOLOGY AND PATHOGENESIS.**

**Pathological physiology or pathophysiology (Gr. pathos- disease, logos – study) is the science about functions of diseased organism. It studies general regularities in the origin, onset, course and results of pathological processes, as well as the changes in the functions of cells, tissues, organs and systems of the organism during disease. Mechanisms of not falling ill (organism’s resistance) are also studied by pathophysiology.**

Since the pathophysiology studies the vital activity of the diseased organism, it may be referred to as physiology of the diseased organism.

As distinct from the clinical sciences, the pathophysiology studies the general regularities of departure from the norm of the functions of the cells, organs, systems and of the whole organism during diseases. It gives the physician an insight into the essence of the disease or pathological process.

The pathophysiology is the subject where the medical student for the first time comes into contact if not with patient, but with his problems. The main task of the pathophysiology is to teach the students to apply the knowledge accumulated in the bed of the patient, that is, to understand the mechanisms of the development of the diseases and recovery, to reveal the principle and general laws of the activity of the organs and systems in the organism of the diseased person.

So, the pathophysiology serves as a bridge between pre-clinical sciences (anatomy, physiology, biochemistry) in one hand and the clinical branches of the medical and surgical disciplines on the other.

To explain our thought figuratively, let us fancy a television set on a table. Can we say that the television set is standing on the legs of the table ? Maybe we can. But actually the legs hold the flat top of the table and the television set is standing immediately on that flat top. Just the same way, the pathophysiology is based on the anatomy, physiology, biochemistry and other medicobiological disciplines, while it forms the immediate basis for the clinic.

**Pathophysiology consists of three basis parts:**

1. **general nosology;**
2. **typical pathological processes;**
3. **pathophysiology of organs and systems.**

In many textbooks the first two parts are united under the title “General pathophysiology”(or General pathology”), whereas the third part is called “Special pathophysiology”(or “Systemic pathology).

General nosology deals with the concept of disease and pathological processes, the theory of the causes and conditiones of their origin (etiology) and the mechanisms of their onset (pathogenesis), the role of external and internal (heredity, constitution, etc.) factors in the development of the pathological processes, significance of the organism’s reactivity in pathology.

The second part of the pathophysiology studies the typical pathological processes, that is, the general, standard reactions of the organism, such as, various metabolic disorders, inflammation, fever, neoplasia, extreme states of the organism, etc.

The third part of the pathophysiology is concerned with the regularities of the origin, onset and course of the dysfunction of various (blood, respiratory, urinary, nervous etc.) systems of the organism – whatever the form of its manifestation. Unlike the corresponding clinics , where the concrete diseases of the same systems and their treatment are studied, the special patophysiology studies only the general regularities of the diseases of these systems and elaborates the main principles of their prophylaxis and treatment. The knowledge of the special patophysiology prepares the ground for better learning of the clinical disciplines by students.

Pathophysiology is engaged with the elaboration of the pathogenical prophylaxis, whereas the etiologic prophylaxis is the subject of the hygiene, microbiology and immunology.

Pathophysiology, as well as the normal physiology, is the science based on the experiments.

The vast number of the methods of acute and chronic experiments are applied in pathophysiological researches.

Most of them are methods of normal physiology (enervation, transplantation, stimulation, damaging, recording of the mechanical or bioelectrical activity of organs, radiotelemetry, etc.) or those of other sciences (biology, biochemistry, biophysics, immunology, radiology, cybernetics, etc.) The clinical methods are applied in the pathophysiology.

But there is one purely pathophysiological method, that is, the specific method of pathophysiology-modelling of diseases.

Thus, although the methods that are applied in pathophysiological experiments are numerous and different, but its chief methodological principle is one –to study the disturbances of the organism’s activity by the way of experiments.

Brown-Sequard attempted to obtain the model of the Addison’s disease by the way of removal of adrenal glands in animals. Pavlov produced the model of the disturbances of the gastric juice secretion by the way of damaging the mucous membrane of the stomach with silver nitrate, corrosive sublimate etc.

The acute and chronic experiments resemble the acute and chronic diseases.

The pathological processes such as shock , loss of blood , asphyxia, poisoning are studied usually in acute experiments.

The chronic modelling makes it possible to study the diseases in detail. The experimental models of the diabetes mellitus, myocardial infarction, atherosclerosis, arterial hypertension are frequently produced.

The experimental methods made it possible to study profoundly the causes and mechanisms of nutritional and metabolic disorders, hypertensive vascular disease and atherosclerosis, fever and many infectious diseases , different endocrine disturbances.

But there are some shortcomings of the experimental method. First of all, it must be taken into consideration that man develops in a social environment and possesses a higly-organised nervous system with the development of the second signaling system.

In some human diseases great is the significance of the conditions of the work and way of life.

Some diseases (rheumatism, grippe, syringomyelia)are observed only in human beings. Up to now it was not a success to create models of bronchial asthma , Quincke’s edema , podagra.

It is important that in human beings the diseases often occur on the background of other ones (for instance , diabetes mellitus in the man with the hypertensive disease). Also, the animal tissues have greater regenerative ability than those of man.

So, the information gained in experiments on animals cannot be mechanically applied to man . It is supplemented by clinical studies of patients under different conditiones of life and under certain physical and chemical influences. Of course, these methods of investigation must under no circumstances do the organism any harm.

The clinical pathophysiology investigates the disturbances of the physiological processes in the diseased person.

The mathematical modelling of the diseases is also applied in pathophysiology.

Pathophysiology is connected with many other sciences – medical and non- medical.

To elucidate the essence of pathological processes one must know at first the regularities of the animate nature. So, the pathophysiology is closely linked with biology. Biology plays an important role, for instance, in study of pathological heredity and constitution.

To evaluate rightly the results of some experiments the pathophysiologists must know also the principles of biochemistry. For example , to study the antitoxic activity of liver Quick’s test is applied : the sodium salt of benzoic acid is introduced into organism , and appearance of hippuric acid (a product of detoxication of the benzoic acid in liver ) in urine shows the satisfactory antitoxic activity of the liver. But pathophysiologists must know that in the liver of birds the benzoic acid is converted into ornithuric acid.

In the liver of man and mammnals ammonia is converted into urea ,in the organism of reptiles and birds – into uric acid, whereas fishes excrete the ammonia without any changes.

Ascorbic acid is synthesized in the organisms of all living beings, except those of man, primates and guinea pigs. So, ascorbic acid deficiency (scurvy) must be studied on primates or guinea pigs.

Pathophysiology is most closely linked with normal physiology: knowledge of physiological regularities is necessary for understanding of pathological processes.

To evaluate the activity of organism’s systems and organs in pathological conditions one must know the physiological (normal)indices of their functions. Besides, pathophysiology applies the same methods of research that the normal physiology does.

The pathophysiology is closely connected with the pathological anatomy. If the pathological physiology studies the disturbances of functions in diseased organism , pathological anatomy studies the morphological changes occurring in the diseased organism. Both sciences supplement each other and together they form the extensive branch of medical science known as pathology.

Pathophysiology is connected not only with biological and medical disciplines , but also with mathematics , cybernetics and especially with philosophy.

To elaborate the philosophical problems of medicine- is one of tasks of the pathophysiology. It applies all the laws and categories of dialectics. For instance, the spasmodic character of beginning of the diseases and their sharply differing stages are explained by the law of the transition of quantitive changes into qualitative changes.

The constant struggle between the damaging reactions caused by the pathogenous factors and adaptative – defense reactions of the organism demonstrates the law of the unity and fight of opposites.

The disease denies the healthy state of the organism and the state of illness itself is denied by the state of convalescence(recovery). This may be the demonstration of the law of negation of negation.

The scientific definition of disease is one of the most important and difficult problems of nosology. It is important because the correct approach to the treatment (as well as prevention) of disease is not possible without the exact comprehension of its essence, that is, the correct formulation of the idea of disease. And it is difficult because disease is the versatile idea to embrace all the features of which is not simple.

Before speaking of disease, we must find out what are norm and health. These two ideas are frequently used as if one and the same, and they are really very close, but not the same. Because departure from the norm is not yet the disease. For instance, in some states of organism that have nothing to do with pathological processes (the physical fatigue, pregnancy etc.), the physiological indices of the organism are considerably departed from the normal limits. Also, among the people that differ from the normal ones by some indices there are many healthy persons. On the other hand, the sick person may have some normal indices.

Many forms of norm are distinguished. The idea of norm that is frequently applied in practical medicine (“normal body mass”, “normal body temperature”, “normal blood count”) expresses the average statistical values of corresponding indices in the healthy persons. This is called the average statistical norm.

The adaptive norm shows the fluctuations of physiological and biochemical indices of the organism within the normal limits under the influence of factors of the external environment. For example, increase of the number of erythrocytes in high altitude regions serves the adaptation of the organism to the atmospheric air with the low oxygen content. Though the adaptability is characteristic of also the sick organism, but in that case departure from the norm of the above-mentioned indices of organism is observed.

The dynamic norm expresses the individual changes of the normal indices caused by the functional mobility and compensatory reactions of the living organism.

There are also the homeostatic norm, ecological norm, correlative norm, etc. The latter is more complex idea, because it takes into account most of the above-mentioned factors.

Health is such a form of the vital activity of the organism which ensures its most perfect and optimal functioning and adequate conditions of existence in the environment. To define the health a number of important indices of the organism are taken as a basis: body temperature, blood count, blood pressure, blood sugar, blood content of proteins, gastric juice acidity, absence of any unpleasant sensations in the body, general condition and so forth. For man as a social being, the health is the existence that permits also the participation in the social and labour activity.

***The following is the definition of the health in the preamble of the charter of the WHO (World Health Organization): “Health is the state of the complete physical, psychical and social well-being, but not only the absence of the diseases or the physical defects”.***

Disease is qualitatively a new process for organism. But it is, first of all, the vital process in which all the signs of the life exist, though changed one way or another. They disappear only after the death.

A number of scientists paid attention to different changes in the organism during disease and regarded them as principal ones: departure of vital functions from normal, disturbance in the relations between the organism and its external environment, disturbance of the adaptability of the organism, sensation of pain or discomfort, decrease of capacity for work and so forth. But definitions of disease based only on one or even several of these changes are one-sided.

The shortest definition of disease belongs to Virchow: “Disease is the life in abnormal conditions”. But what is normal under some conditions, may be completely abnormal under other ones.

The same way do not justity themselves the definitions based on other signs of disease.

For instance, many diseases (blood, endocrine psychical diseases) go on without pain, and, on the contrary, some physiological processes (delivery, dental eruption, etc.) cause a pain. Or a number of mental diseases do not cause the rough morphological changes in tissues. Disturbance of the adaptability of the organism is observed not only during the disease but also in pregnant women and old persons. Even the definitions that to a certain extent correctly express the essence of disease, are one - sided, because they do not point out the defense – adaptative processes in the diseased organism.

Pavlov’s conception about the essence of disease answers the dialectical law of the unity and fight of opposites: two closely associated phenomena must be distinguished in the picture of any disease - the injury and the organism's counteraction to the injury, or the "physiological measures” against it. From this point of view the following definition of disease is acceptable: ***Disease is the life of the injured organism with the participation of the processes of compensation of the disturbed functions. Disease reduces man’s working capacity.***

The beginning of disease occurs by the way of qualitative leap according to the dialectical law of transition of quantitative changes into qualitative changes. But before these macroleaps a number of microleaps also occur.

There are some transitional forms between health and disease: the incubative period of infectious diseases, the period of sensibilization of allergic diseases, the temporary disturbances of vascular tension at the initial stage of the hypertensive disease. These are called premorbid states. This expression first appeared with the connection of precancer (or precancerosis). At present the list of the precancer diseases is widened and it includes also such diseases as ulcerative colitis, Addison – Biermer’s anemia, etc., which relatively rarely lead to the development of the cancer.Such terms as prediabetes are widely used in modern medicine. Premorbid state creates the initial condition for the disturbance of the health. One of the principal signs of the premorbid state is development of the compensatory processes in the damaged tissues and cells. The gradual exhaustion of the regulatory and compensatory mechanisms cause the transition of the premobid state into disease.

The concept of disease includes also the ideas of pathological process, pathological reaction and pathological state.

***Pathological process is the combination of pathological and defense – adaptative reactions in damaged tissues, organs or organism.*** Although the pathological process, as the organism’s reaction to unusual stimulation, is based on a disturbed function and structure, it is not a definite picture of disease (nosological entity). “Pathological process” is more general idea than “disease”. One and the same pathological process may occur under the influence of different factors, and in different diseases one and the same pathological process may be observed.

Pathological process is a constituent of the complex of phenomena characterizing a disease. For instance, increased arterial pressure in hypertensive disease is one of the pathological processes characteristic of this disease; there are also other changes in different organs and systems of the organism.

There are quantitative and qualitative differences between the pathological processes and diseases of the whole organism. For example, furuncle (inflammation of the hair follicle) is the pathological process, but a large number of furuncles is the severe general disease of organism (furunculosis) that is accompanied by the temperature, disturbance of the functions of the gastrointestinal tract, nervous system, etc.

***Pathological reaction or pathological function of the cell, tissue, organ is extraordinary reaction of short duration to unusual stimulation.*** For instance, lacrimation (secretion of tears) in answer to the chemical stimulation, the short-term changes of blood pressure under the negative emotions or stimulation of sensory nerves, secretion of mucus in answer to the painful stimulation, etc. The pathological reaction is the simplest form of the pathological process.

***Pathological state is long-term disturbance of the functions and structure of organs and tissues of the organism.***It is slowly developing pathological process or one of the stages (or a consequence) of the pathological process. For instance, inflammation of the skin and subcutaneous fat is pathological process. Frequently the outcome of the infammation is scar that remains for many years. In the cicatricial tissue as well as in any living tissue metabolism is proceeding, collagenous and elastic fibers are formed. So, the scar is slowly developing pathological process, that is, pathological state. Transition of the pathological process into the pathological state is observed in the change of the active progressive form or pulmonary tuberculosis to the fibroid form or when endocarditis causes disease of the heart valves. Pathological state develops after loss of some parts of the body. For example, after extraction of many teeth the alveolar process of jawbone is gradually atrophied. Pathological state may be the result of genetic defects or disturbances in the intrauterine development: bradydactilia, polydactilia, syndactilia, spina bifuda, etc. Blindess, lameness, ankylosis, pseudoarthrosis, scars, stumps after trauma, bony defects after rickets, hunchback after tuberculosis of bones and joints are also pathological states.

Pathological state is relatively stable. But different influences, disturbance in the adaptation of the organism to its environment (excessive functional load, infection, etc.) may cause conversion of pathological state into pathological process again. For instance, birthmark may be converted into melanosarcoma under the influence of the mechanical, chemical irritation or ultraviolet rays.

Often a number of pathological and defence reactions of cells and tissues are found in the form of permanent combinations. They are called the typical pathological processes. For example, inflammation, fever, tumor, allergy, shock, dropsy (edema), dystrophy, etc., are the typical pathological processes.

All of the typical pathological processes are formed in the process of evolutionary development. From the first days of its origin the concept of disease is the object of ideological struggle, and the views on the essence of disease develop inder conditions of the struggle of materialism and idealism. All the time throughout the history socio-economic formations and their prevailing philosophical doctrines influenced the concept of disease, and always some scientists yielded to the ideology of existing social system.

Some scientists applied the regularities of the animate nature to the human society and pointed out that the same laws dominate in nature as well as in society. They try to conceal the social factors causing diseases and replace them by the biological factors. They deny the connection of diseases with the conditions of labour and way of life, with poverty and assert that the human diseases are connected only with the natural and biological causes, with the constitution and heredity. So, they affirm that diseases are inevitable natural phenomena, and therefore, the prophylactic measures are not wanted.

The author of the theory of stress and general adaptation syndrome, the Canadian endocrinologist H.Selye (1907-1982) established that pituitary body and adrenal glands respond to the specific as well as non-specific (general) stimuli by changing their activity. He called such stimuli stressors. Selye considered that the adaptability of the organism depends on the activity of the pituitary body and adrenal glands, which secrete “adaptive hormones”. He connected a number of diseases with disturbances in the “system of hypophysis- adrenal glands”, that is, disturbances of adaptation, and called them the :diseases of adaptation”.

Looking for the parallelism between the reactions of the endocrine system and activity of the cerebral cortex, Selye regarded the endocrine system as the autonomous system and underestimated the significance of the central nervous system. Besides, he paid too much attention to the role of the non-specific reactions in pathology, underrating the specific factors.

The results obtained in the investigations of Selye were applied by some scientists (Francis, Libman) for the explanation of the social events. They regard the relations of stress nature (selfishness, the battle for survival between weak and strong individuals) among human beings as the main motive power of the development of society.

According to the theories of “diseases of civilization” and “social deadaptation” the absence of the harmony between the rhythms of the natural life and cultural and technical progress plays the role of the universal condition for the origin of diseases. The supporters of the theory of the social deadaptation regard these diseases as inevitable result of the scientific and technical progress.

Unlike all these theories, authors of the theories which are based on the principle of nervism, take a correct stand. According to the cortico-visceral theory of Bykov and Kurtsyn a number of diseases occur as a result of disturbance of interrelations between the cerebral cortex and internal organs. The disturbance of the relations between excitation and inhibition in the cerebral cortex leads to the formation of the dominant stagnant foci in subcortex which send continuous impulses to visceral organs. These impulses cause successively the disturbance of the innervation, trophicity, adaptive, functional, organic changes and at last, the disease of corresponding organ. By this principle of cortex-subcortex-visceral organ the corticovisceral diseases (stenocardia, bronchial asthma, hypertensive disease, peptic ulcer, etc.) develop.

*The knowledge of the signs of diseases is necessary for their diagnosis.* It is important also for choice of the tactics of treatment and determination of the prognosis. The science about symptoms (signs) of diseases and mechanisms of origination of the symptoms is called semiotics (Gr. semeiotikos-on the basis of the signs) or symptomatology.

The most frequent signs of diseases are pain, weakness, fever, swelling and reddening of the injured organ, change of the colour of the skin, etc.

Semiotics consists of two parts: 1) general semiotics, 2) special semiotics.

The general semiotics studies the signs that are related with the general characterization of patient (sex, age, heredity, profession, bad habits, the past diseases and intoxications), his general state (expression of face, colour of skin, posture of body), as well as the functional and morphological changes which manifest themselves as signs of diseases and examination of laboratory materials (blood count, analysis of gastric juice etc.). Each of above- mentioned factors is significant for diagnosis to a certain extent. For instance, in women A and B hemophilias are not observed, whereas lupus erythematosus is more often found in young women than in men. Each age has its more frequent diseases (measles and pertussis in children, atherosclerosis in elderly persons).

Some diseases are connected to a certain degree with the heredity (schizophrenia, diabetes mellitus), profession (vibratory disease, silicosis), bad habits (the higher frequency of coronary disease and carcinoma of the lip in smokers, hepatocirrhosis and psychic diseases in drunkards). Yellowness of the skin and mucous membranes is characteristic of jaundice, whereas in chronic adrenal insufficiency (Addison’s disease) the skin of body is tinged bronze. The special semiotics studies the separate signs of diseases, the mechanisms of their origin and development and their diagnostic significance.

Symptoms of diseases may be objective or subjective, latent or overt, early or late, specific or non-specific. From the diagnostic point of view the most significant are the pathognomonic symptoms, that is, the symptoms which are characteristic of only one disease. The groups of symptoms that are constant and characteristic of separate diseases one way or another, are called syndromes (adiposogenital syndrome, Brown-Sequard’s syndrome, Icenko- Cushing syndrome, etc.). All the changes that are observed in the initial periods of the disease form symptom-complex.

*To classify the diseases, that is, to group them by similar signs, different principles were used.* The first scientifically grounded classification of diseases was made in 1761 by Morgagni on the topographic anatomical principle. According to this principle the diseases of heart, lungs, liver, eyes and other organs are distinguished. But according to modern scientific ideas there are no diseases of separate organs. Therefore, it is more reasonable to classify the diseases by the functional systems (the diseases of blood system, cardiovascular system, digestive system, nervous system and so forth).

In pathoanatomical classification the localization of the damages is taken as a basis, whereas the public health organizers are more interested in the etiology and clinicians – in the concrete manifestations of diseases.

According to their clinical course (duration, intensity of symptoms) diseases are divided into acute, subacute and chronic ones.

From the etiologic point of view hereditary, infectious diseases, radiation sickness, drug disease, intoxications, traumata, kinetosis, etc. are distinguished.

According to pathogenesis there are metabolic, allergic diseases, tumors, shock, etc. The diseases are classified also by the principles of age and sex. Different fields of the medicine are engaged in the treatment and prophylaxis of children’s diseases (pediatry), diseases of newborns (neonatology), long-livers (geriatrics), diseases of female genital organs (gynecology), male genital organs (andrology).

The diseases connected with the ecological factors are also distinguished. From this point of view the pathogenic influence of the conditions of work are especially important (occupational diseases). The medical genetics is engaged by the treatment of the hereditary diseases. Some diseases that are connected with the intensive rhythm of life in the big cities, hypodynamia, overeating ( diabetes mellitus, obesity, etc.) lately are regarded as the result of the cultural and technical progress and are classifild under the group of the “diseases of the civilization”.

So, it is impossible to make a perfect and full – bodied classification of all diseases using only one principle. According to the international classification of diseases which was approved by the conference of World Health Organization in 1975 (in Geneva), all the diseases are divided into 17 classes:

***In the course of disease four principal periods may be distinguished:***

1. ***latent period;***
2. ***prodromal period;***
3. ***period of marked manifestations;***
4. ***outcome.***

These periods are especially marked in acute infectious diseases. It is difficult to distinguish them in some diseases (metabolic, blood, hereditary, endocrine, nervous, psychical diseases) and practically impossible in the course of traumata. In radiation sickness the prodromal period comes first and then the latent period follows.

The latent period lasts from the beginning of action or entrance of pathogenic agent to the manifestation of the organism’s reactions (the first clinical manifestations of the disease). In infectious diseases this period is called the incubation period.

In the latent period the defence-adaptative strengths of the organism are mobilized to fight against the disease. In this period no changes are revealed in the general state of the patient. But modern methods of examination allow to reveal some latent pathological changes. Duration of the latent period depends on the peculiarities of the causative agent, the organism’s reaction to its action and ability of the organism to overcome the resultant disturbances by means of its defence mechanisms. For example, intoxication occurs almost instantly (within several seconds or minutes) after the action of powerful poisons (cyanides), whereas duration of the latent period of leprosy is several years.

The prodromal period lasts from discovery of the first sign of the disease to complete manifestation of its all symptoms. Frequently in the prodromal period only indefinite manifestations of the general nature are observed (general indisposition and weakness, chills, headache, inappetence, rise in temperature, etc.) Some diseases have the symptoms that are characteristic of this period (Filatov’s and Koplik’s spots in the internal surface of cheek in measles).

In some diseases (croupous pneumonia, dysenteria, cholera, plague) the latent period is immediately followed by rapid development of clinic manifestations. Often the prodromal period of the chronic diseases is also impossimple to distinguish.

The period of marked manifestations is the period of development of all the principal morbid phenomena. This period may last from several days to several years. Some (particularly infectious) diseases run a rather definite course (typhus – 13-16 days, measles- 8-10 days), whereas other (especially chronic) diseases do not have a definite duration.

Duration of disease depends on the characteristics of the pathogenic agent, the intensity and duration of its action on the given organism, as well as properties of the organism itself. According to their duration diseases are divided into very acute (to 4 days), acute (5-14 days), subacute (15-40 days), chronic (more than 40 days, that is, 6 weeks). Chronic diseases are often results of acute diseases and last during months and years.

In the period of marked manifestations the typical features of the disease are clearly expressed. But they manifest themselves in different extent depending on the type of the disease and reactivity of the organism. In some cases rapid course of illness is observed (the lightning – like form), whereas in other cases the signs of the disease are weakly expressed and scarcely may be distinguished (the distorted form). In such cases it is comparatively difficult to diagnose the disease. Sometimes the mild course of disease and rapid recovery is observed (the abortive form).

Joining of the additional signs that are not connected with the main signs of the disease by the mechanism of development, is called complication of the disease. Complications may be found in all diseases, but there are complications that are characteristic of each disease. Complications aggravate the course of the disease and frequently cause undesirable result. For instance, successfully operated patient may suddenly die owing to thrombosis and embolism.

The outcome of disease depends on many factors (peculiarities of the pathogenic agent and organism, correctness of the treatment, observance of the regimen by the patient and so forth).

***The outcome of disease may be the following:***

1. ***transition to the chronic form;***
2. ***relapse (recurrence or recidivation);***
3. ***recovery;***
4. ***death.***

If the pathogenic agent is not eliminated completely, acute disease may develop into chronic state. Alternation of periodical relief of patient’s state with the periods of acute attack of the disease is characteristic of the chronic course of disease.

As a result of the disease irreversible changes may occur in different organs, and sometimes they cause the new diseased state. For example, endocarditis often results in valvular defect or after the tuberculosis of bones and joints ankylosis is observed in joints.

Repetition of the signs of the disease after the period of temporary outward recovery is called recidivation (replase or recurrence) of the disease (lat. recidivus-renewal). In these cases the patient is outwardly as if healthy, but when the conditions are unsatisfactory, the pathogenetic processes which are characteristic of the same disease, manifest themselves once again. The periods of relative health between relapses are called remissions (remittences). Duration of remissions may be from several days (infectious diseases) to several months and even years (especially non-infectious diseases).

Relapses are particularly characteristic of recurrent endocarditis, recurring fever, chronic bronchitis, chronic pancreatitis, peptic ulcer, dysentery, rheumatism, gout, erysipelas, schizophrenia, etc. Besides the persisting focus of infection, often changes in the functional state of the central nervous system take part in the mechanism of recidivations.

Recovery (convalescence) is the active process of restoration of disturbed functions and adaptation of the diseased organism to the external environment. For man as social being the main criterion of the recovery is return to the labour activity and in this sense of the word the recovery is called rehabilitation (he may return to his former work or requalify in connection with the alteration in the state of health).

The recovery may be complete or incomplete.

During incomplete recovery traces of disease (disturbances of functions of different organs and their regulation) remain in the organism, and the activity of organs and systems, as well as the whole organism, cannot ensure its adaptation to the external environment. Sometimes the man’s ability to work is reduced.

During the complete recovery residual effects are not observed in the organism, and the man’s ability to work is fully restored. Formerly the complete recovery was called “restitutio ad integram” (restoration to the whole-intact). But complete restoration may be only imaginary. Because after any disease the new processes of the vital activity and regulation of functions occur in the organism. For example, after infection the organism acquires a state of imminity to the given infection or becomes more susceptible to it; after inflammation scar remains, etc.

Recovery is more than regression of disease. The recovery after each disease is qualitatively new state of the organism and creates new forms of its interrelations with the external environment. Also, recovery is not only the expression of the last stage of the disease. The processes leading to recovery begin right from the start of the disease. They are the totality of diseased organism’s reactions to the damage of its cells, organs and systems.The mechanisms of restoration of disturbed self-regulation of the organism throughout the disease is called sanogenesis (lat. sanus-healthy, genesis-origin, development). Otherwise, the sanogenesis is complex of defence-adaptative processes directed to conservation of the normal and restoration of the disturbed homeostasis of the organism.

So, it is impossible to separate the process of recovery from the disease. The disease is just the unity of two processes - the pathological disturbances and the adaptative reactions directed to their restoration. These processes are interconnected. For instance, inflammation develops as the reaction of the organism to damage of tissues, and it serves the recovery of the organism.The mechanisms of recovery may include also the components that are injurious for the organism. The harmful sides of the defence – adaptative processes consist, first of all, in the fact, that they are uneconomical and go on with considerable expenditure of energy and substances (for instance, in fever, inflammation, stress, shock).

***In the development of the defence – adaptative reactions that take part in the process of recovery great is significance of the nervous, endocrine and reticuloendothelial systems. These reactions are divided into 3 groups:***

1. Defence reactions of the organism- ensure the endurance of the organism against different pathogenic agents in ordinary conditions and continue their activity in the premorbid period and during the disease. If the pathogenic agent is weak or influences the organism during short time, thanks to these reactions, development of the disease may be prevented. Sport and physical training of the organism intensifies its defence reactions, whereas bad habits (smoking, alcoholic drinks) weaken them.

2. Early reactions of recovery – function in the latent and overt periods of the disease. After entry of the pathogenic agents into organism and beginning of the disease, mechanisms of restoration and compensation join up with the defence reactions and they compensate disturbed functions of the organism one way or another (compensation of the hemodynamical disturbances by hypertrophy of left ventricle in aortic stenosis).

3. The late reactions of recovery – promote restoration of organic disturbances. They are especially significant in the recovery of diseases of infammatory and necrotic type: abolition of products of destruction of tissues by the reaction of phagocytosis, formation of new tissues in place of damaged areas by the way of regeneration, etc.

Death is cessation (stopping) of the life of organism. The natural (physiological) death and untimely (pathological) death are distinguished.

The natural death is inevitable end of the life. It occurs as a result of wear of the organism and extinction of its functions.

Untimely death is divided into two groups:

1. death by violence (murder, suicide),
2. death in consequence of disease.

The death that sets in suddenly, is called sudden death (cardiorrhexis after myocardial infarction, rupture of uterine tube in extrauterine pregnancy).

The death ensues when the organism cannot adjust itself to the altered conditions of existence, its adaptation mechanisms become exhausted and further vital activity becomes impossible.

The direct causes of death are usually cardiac arrest and respiratory arrest. The cardiac arrest may be provoked by damage of the heart (coronary thrombosis, heart failure) or the cerebral centers regulating the function of the cardiovascular system. The respiratory arrest is observed in paralysis of the respiratory center in the medulla oblongata (as a result of hemorrhage or anemia, compression by tumor, intoxication with certain poisons). The clinical death and the biological death are distinguished. The clinical death is characterized by the deepest depression of the functions of the central nervous system. Breathing and blood circulation stop, all the reflexes disappear. The clinical death lasts 5-6 minutes. Although the metabolic processes are noticeably disturbed and the energy reserves become depleted, but the changes in the tissues are still reversible. Therefore, restoration of the vital functions of the organism is sometimes possible during clinical death. With the appearance of irreversible changes in the tissues a state of biological or true death sets in.

In the process of dying the function of the central nervous system becomes extinct in the first place. The extinction begins with cessation of the activity of the cerebral cortex followed successively by that of interbrain, midbrain, medulla oblongata and the spinal cord. So, the older the parts of the central nervous system in their development the later they become extinguished. Next the functions of endocrine glands, parenchymatous organs and other tissues die away. In skin, kidneys, cardiac muscle, lungs and other organs the process of autolysis may begin several hours or even days later after the clinical death. During several days after the death nails and hair of the dead body grow, the cells of epidern and mucous membranes multiply. In autopsy instantly after the death one may observe intestinal peristalsis. After being extracted from the dead body separate organs (heart, liver, kidneys, etc.) may be resuscitated (reanimated), and some cells (of epithelial, connective and other tissues) may be cultivated outside the organism. This is very important for transplantation of organs and tissues taken from the dead body (blood, blood vessels, skin, bone, cornea, kidneys, heart, liver, etc.). After the biological death in the body some characteristic changes take place (cooling, rigor mortis, livores mortis, imbibition, putrefaction, etc.).

***The state of organism between life and death is called terminal state. It consists of several successive stages:***

1. ***preagonal state;***
2. ***terminal pause;***
3. ***agony;***
4. ***clinical death.***

During the preagonal state usually the patient does not lose consciousness, but gradually functions of the cerebral cortex and subcortical centers, as well as brain stem, become weaker. At first heart rate, respiration rate and arterial pressure increase, general motor excitement happens, then all these indices decrease, and patient may lose consciousness. The preagonal state as a result of the acute disturbance of coronary circulation or electric trauma lasts during a short time, whereas it continues several hours in the case of loss of blood.

The terminal pause lasts from several seconds to 4 minutes. In this period breathing stops, heart rate decreases (sometimes asystolia occurs), pupillary and corneal reflexes disappear, the pupils dilate. In the cases of prolonged agony and in patients under narcosis the terminal pause is not observed.

For the state of agony loss of consciousness and increased activity of bulbar parts of the brain are characteristic. One of the main signs of this period is the agonal breathing (deep convulsive respiration). It beging by the weak inhalation movements which gradually intensify and reaching the maximal level, become weaker once again. In agonal breathing the respiratory muscles become more taut than in ordinary breathing. Besides, some muscles that do not take part in ordinary respiration (the muscles of mouth, neck etc.) participate in the agonal breathing. The transition period from the agony to the clinical death is characterized by stopping of blood circulation.

One of the main causes of the terminal state is hypoxia that frequently develops as a result of disturbance of blood circulation (circulatory hypoxia).

The vital functions may be restored during agony or clinical death (in severe shock, loss of blood, asphyxia, etc.). **Complex of measures aimed at restoring the vital functions of the organism is called resuscitation or reanimation (renewal of life).** But resuscitation is impossiple when death is the result of severe and protracted disease causing deep, irreparable damage to the vitally important organs (brain, heart, lungs).

To restore the vital functions of a dying organism usually different methods or their combinations were applied: injection of adrenalin into the heart or into the myocardium; administration of blood under certain pressure into large arteries in the direction to the heart; creation of the artificial circulation with the aid of special apparatuses, closed or open chest massage; defibrillation by the electric current with the aid of defibrillator, etc. The method of resuscitation elaborated by V.A.Negovsky during the II world war includes complex of measures:

1. Blood with glucose, adrenalin and hydrogen peroxide warmed up to 38o C under certain pressure is pumped into peripheral artery (for example, brachial artery) in the direction of the heart. This produces double effect: a) blood penetrates into the coronary arteries and supplies myocardium; b) intra-arterial pumping of the blood stimulates receptors of the walls of blood vessels and heart.
2. In 30-40 seconds after pumping the blood, when the heart begins to contract, blood is introduced into vein. In this way sufficient diastolic filling of the right heart and its stimulation to more powerful contraction is secured.
3. Simultaneously artificial respiration is applied, that is, through the tube, introduced into the larynx, air is blown into lungs under certain pressure.

Since in 5-6 minutes the clinical death is replaced by the biological death, the resuscitation measures must begin instantly. This is very difficult and in a number of cases, even impossible. Therefore, the duration of the clinical death must be prolonged. This is achieved mainly by two ways:

1. Creation of the artificial circulation. The most simple method to create the artificial circulation is the cardiac (chest) massage which not only prolongs duration of the clinical death, but sometimes leads to the restoration of heart activity. Massage is made through the thoracic wall (indirect or closed chest massage) or the chest is opened by the operative way (direct or open chest massage).
2. Reduction of the organism’s need of oxygen by the way of weakening of metabolism. This is achieved by the way of artificial cooling of the body or creation of artificial hibernation by the way of influence on the nervous system by the pharmacological substances.

The totality of the pathological changes in the tissues and organs in the post-reanimation period is called post-reanimation disease. The disease of the organism that was reanimated with the aid of the resuscitation measures, is regarded as a form of the terminal state.

The post-reanimation disease is due to the disturbances that result from the severe hypoxia in the period of agony, as well as to the changes in consequence of repeated oxygen supply of tissues.

Three stages are distinguished in the course of the post-reanimation disease:

1. temporary stabilization of the organism’s functions (up to 24 hours);
2. repeated aggravation of the patient’s state (2-5 days);

normalization of functions (from 1 month to several months).

***Etiology (gr. aitia- cause, logos- science, teaching) is the teaching about causes of diseases and conditions under which diseases arise.*** General etiology establishes general regularities of the origin of various deseases, and special etiology studies the causes of separate deseases.

Since specific peculiarities of any pathological process depends, in the first place, on the etiologic factors, elucidation of the pathogenic factors and the conditions under which diseases arise is significant for elaboration of the methods of treatment and prophylaxis.

The factor which causes the disease and imparts to it the specific features, is called the cause of the disease. For instance, the cause of radiation sickness is ionizing radiation, that of infectious disease- pathogenic microbes.

Frequently the origin of the disease is connected with several factors. For example, croupous pneumonia arises not only under the influence of the infection by pneumococcus. Chill, fatigue, negative emotions, underfeeding and other predisposing factors also promote the disease. However, without infection by pneumococcus all above – mentioned factors cannot cause the croupous pnevmonia. So, the cause of the disease is such an influence, without which the development of given disease is impossible. The rest of the factors are conditions for the onset of the disease.

The cause of disease cannot always be disclosed. For example, the origin of cancer is put in touch with a number of physical, chemical and biological agents. The rough food, vegetative and endocrine disorders, neurosis and other factors are mentioned as causes of the gastric ulcer. But such polyetiologic theories are wrong. Because every disease is caused by one factor which will be revealed by the progress of the science.

Diseases may be caused by pathogenic agents which act on the organism from the external environment (external or exogenic factors) or by those that arise within the organism itself (internal or endogenic factors). The external causes of diseases include the mechanical, physical, chemical, biological, psychical, social and other factors, and the main internal causes are the pathological heredity, constitution, sex, age.

But external and internal factors in the etiology of pathological processes must not be opposed to each other. The external pathogenic agents cause disorders in the internal environment of the organism which may provoke a new pathological process. So, the internal factors are actually a result of the action of the external factors. For instance, obesity caused by disturbances in nutrition may become the cause of circulatory disorders. Or genic mutations causing hereditary diseases, are resulted by environmental mutagenous factors that influence the mother of the child during pregnancy or his ancestors. In this connection remarkable is **S.P.Botkin’s** following statement: “The idea of disease is inseparably connected with pathogenic cause which always depends exceptionally on the environment and influences the organism either directly or through parents or ancestors”. The conditions may lower the resistance of the cause (unfavourable conditions) or raise the resistance of the organism and diminish the effect of the cause (favourable conditions). Both unfavourable and favourable conditions may be external or internal. The external unfavourable conditions are: disturbances in feeding, exhaustion, nervousness, the diseases that the patient had suffered earlier, the bad care of the patient, etc. The internal unfavourable conditions include: the hereditory predisposition to the disease, the pathological constitution (diathesis), the early childhood or old age, etc. The external favourable conditions are: the rational diet, the correct time-table of working day, physical culture, the good care of patient, etc. The internal favourable conditions include: the hereditary, racial, constitutional factors. For instance, man does not catch many infectious diseases of animals (distemper, plague of cats, pneumonia of cattle, etc.). The persons with sickle-cell anemia (drepanocytosis) do not get malaria.

The wrong interpretation of interrelations between the causes of diseases and the conditions under which diseases arise, led to some misconceptions: monocausality, conditionality, the theory of factors, constitutionalism, etc.

The correct concept of etiology is based on dialectic materialist determinism which affirms that all the natural phenomena have the objective causes and there is no phenomenon without the cause. Monocausality is the expression of mechanical determinism and conditionality - that of indeterminism.

The discovery of the causes of a number of infectious diseases struck a crushing blow at the vitalistic conceptions of etiology of diseases. But on the other hand, it gave rise to the erroneous idea that penetration of the pathogenic agent or contact with it was alone enough to cause disease (monocausality). Monocausality is essencially mechanistic theory because the cause is considered in its simple relation to the effect; the complexity of interrelations between the organism and its environment, the unity of the organism and the conditions of its existence are not taken into account. Meanwhile, for the disease to develop, besides the pathogenic factor, corresponding conditions are also necessary. For instance, often in the organism of the healthy people agents of some diseases (tuberculosis, pneumonia, enteric fever, diphtheria, dysentery, cholera, etc.) are found. But in the weakened organisms (cooling, starvation, fatigue, etc.) the conditions arise for the development of these diseases. In ordinary conditions pigeons do not catch kala azar (visceral leishmaniasis). But if the agent of this disease is administered into the organism of the starving pigeons, kala azar develops.

Conditionality is the opposite trend. The conditionalists (**M.Fervorn,** D.Hanzeman) reduce etiology to conditions whose aggregate they believe capable of causing disease, that is, they consider that conditions alone suffice to produce disease. So, conditionalists are content with an external description of the agents taking part in the onset of the disease and are unable to single out the leading, determining factor and to establish its causal relation with the development of the given pathological process. For example, in the onset and development of tuberculosis, besides penetration of tubercle bacilli, a certain part is also played by a number of conditions (inadequate nutrition, poor housing conditions, preceding infections, etc.). Conditionalists completely disregard the fact that none of these conditions alone, nor all of them combined can account for specificity of the pathological reaction arising in organism only in response to the action of the tubercle bacillus. They draw the erroneous conclusion that there is no single causal factor in the onset of tuberculosis and its development is determined only by above – mentioned conditions. Failing to uncover the objective regularities of pathological phenomena, conditionalists believe them to be unknowable. So, this trend disarms the physician in his prophylactic and therapeutic activity.

One of the modern forms of conditionality is the theory of factors. According to this theory, the diseases originate from the combined influence on the organism of a number of equivalent factors (poor housing conditions, poor nutrition, infections, negative emotions, etc.). The sick person cannot work well and earns not much money. So, “the people fall ill because they are poor, and they are poor because they are ill”. This theory diverts the attention from the principal causes of diseases.

The constitutionalism arose at the period when the monocausality was critisized. The constitutionalists regard the constitution as immutable and hereditary sign of the organism and affirm that the unsound constitution is decisive in the origin of diseases.

Undoubtedly the constitution of the organism is significant in the origin of a number of diseases. But it is wrong to put all diseases in touch with it. Such an attitude to the origin of diseases compels to decline the preventive measures.

***Pathogenesis (gr. pathos-suffering, genesis-origin) is the teaching about the mechanisms of development, course and outcome of diseases.*** General pathogenesis studies the general regularities of development and course of the most typic variants of diseases and pathological processes. The special pathogenesis studies the mechanisms of development of separate diseases. Knowledge of pathogenesis is necessary for elaboration of the pathogenetic therapeutic measures.

The etiologic factors of some diseases act during a short time (the mechanical damage, burn, ionizing radiation). Then the disease develops under the influence of the pathological changes in the organism caused by the etiologic factors. These changes are called the pathogenetic agents. Besides, the etiology of some diseases is not clear yet. In all these cases the disease may be treated only taking the mechanisms of their development as a basis and using the pathogenetic remedies.

The principal task of the pathogenetic therapy is to reveal the methods and remedies that weaken the main link and decisive factors of pathogenesis of the disease and strengthen the defence-adaptative processes of the organism.

In the development of diseases besides the etiologic agent, the typical pathological processes are also of great significance. Therefore, to elaborate the measures of pathogenetic therapy, the principal regularities of typical pathological processes are also taken into consideration. In inflammatory processes to activate the arterial hyperemia and eliminate the main pathogenetic factors of the inflammation (venous hyperemia, stasis) the physiotherapeutic methods are widely applied. In a number of diseases connected with hypoxia oxygenotherapy is prescribed. When the course of disease is sluggish, to activate the feverish reactions and raise resistance of the organism the pyrogenic substances are applied. The combined application of methods of etiotropic and pathogenetic therapy ensures successful treatment of a number of diseases.

The development of disease depends on reactivity and resistance of the organism. Therefore, in different individuals one and the same etiologic factor may cause diseases that considerably differ from each other. The action mechanism of etiologic factor on organism may change in different stages of diseases. For example, in a number of infectious diseases immunity is formed against the pathogenic agent, and pathogenecity of microorganisms is gradually weakened, though they continue to remain in the organism. There is causal (cause and effect) relationship between etiologic and pathogenetic factors. Pathogenesis begins with primary damage or destructive process (“breakage”) of cells in some part of the body. In the course of development of disease the products of damage of tissues may become the source of new damage, that is, the etiologic factors of the II, III, IV order.

**To disclose the pathogenesis of diseases and understand their development it is necessary to investigate the following problems: the site of penetration of pathogenic agents into organism and the way of their spreading in the organism, the level of damage, interrelations between the local and general manifestations of pathological process and between the specific and non-specific mechanisms, the main link and vicious circles in the pathogenesis, restoration of functions impaired by disease, etc.**

*The gates of entrance of the pathogenic agents and site of their initial effect are very important in pathogenesis.* For instance, when gonococci penetrate to the urethral mucosa they give rise to gonorrheal urethritis, but their action on the mucosa of the eye produces blennorrhea (gonorrheal conjunctivitis)-the processes that greatly differ in their development.

In the process of evolution different pathogenetic agents has acquired the peculiarity to enter the organs and tissues with more favourable conditions for their development. This is called the specific localization. But at the same time the pathogenic agent influences the whole organism. Some (monotropic) pathogenic microorganisms parasitize only in one tissue, others (polytropic)-in different organs and tissues. When the same pharmacological substance (adrenalin, acetylcholine, calcium, etc.) is administered at different sites, effects differing in intensity, duration or character are observed.

The factors that determine the action mechanism of pathogenic stimuli, include the anatomic – physiological and biochemical properties of organs and tissues, their functional state and characteristics of their receptor fields.

Pathological processes predominantly affect particular organs also according to their physiological peculiarities. For instance, osteomyelitis (inflammation of bone marrow and bone) often begins in the metaphyses of tubular bones. Because the regulation of blood flow provides an abundant blood supply to this part of the bone, and the best conditions are created for contact of the tissue with the toxins or bacteria brought in by the blood flow. Injuries produce nutritional and metabolic disorders in tissues, reduce the general resistance of organism and facilitate the penetration and spread of the noxious agent in it. Therefore, the effect of the etiologic factor may be prodominantly manifested in the parts of organism which suffered injury. For example, an injury to limbs may stimulate development of tuberculosis of bones, an injury to lung - development of purulent inflammation in it.

**According to the duration of the action of the etiologic factors on the organism their 3 main types are distinguished:**

1. The etiologic factors that influence only at the beginning of the disease. In the further development of the disease that originate under the influence of such factors only the pathogenetic factors take place (traumata, burn, radiation sickness which is connected with single exposure to rays of large doses, some psychical and somatic diseases which begin under the influence of extraordinary strong stimuli and are connected with disorders in the nervous system).
2. The etiologic factors that influence equally throughout all the duration of the disease (some acute intoxications). They are especially important in the development and course of the disease.
3. The etiologic factors that influence throughout the disease, but change peculiarities of their action in different periods of the disease (the diseases that are caused by the pathogenic microbes). Since in the course of infectious disease the immunity is formed, sensibility of the organism to the pathogenic microbes weakens. If the etiologic factor takes part in the pathogenesis of the disease all the time, the pathological process may be wavy (diphtheria). Such diseases may once again become acute when the resistance of the organism is weakened.

For some infectious diseases the constant presence of the etiologic factor in the organism is characteristic, and non-sterile immunity is formed. This fact explains the positive Pirquet’s test in person in which the clinical manifestations of tuberculosis is not observed. Owing to the spreading of pathogenic agents in the organism after their penetration into its internal environment, the pathological process may involve the adjacent and often even distant organs and tissues.

**The principal ways of spreading of pathogenic agents are:**

1. By extension and contact. The spread by extension occurs when pathogenic agent affects one part of tissue and its action extends to the adjacent normal part (the spread of herpes over the skin or that of infection along the urinary tract). Intracanalicular spread (along bronchi or excretory gland ducts) closely resembles this route. For instance, infected masses spreading along bronchi from some tuberculous focus in the lungs cause pathological process in other parts of the lungs. The pathogenic agents may spread also by the way of contact of an affected surface with a healthy one: the spread of the cancer of the lower lip to the tissue of the upper lip or that of inflammation of the serous coat of stomach (perigastritis) in inflammation of the gallbladder (cholecystitis).
2. The humoral way (through the blood and lymph). Agents of infectious diseases, bacteria and toxins, poisons, cells of malignant tumors spread by this way. They spread more rapidly by the hematogenic route than by lymphogenic route.
3. Through the nervous system. The neurotropic pathogenic agents (the rabies virus, tetanus toxin) spread along nerve trunks.

Determination of the level of initial damage is important for elucidation of the interrelations of the damage and defence- adaptative reactions of the organism. The therapeutic measures must be directed to the strengthening of the defense- adaptative reactions and weakening of the pathological process.

**The level of the initial damage may be different:**

1. In hereditary diseases the genetic apparatus of cells is damaged, that is, the initial damage is on the molecular level. The synthesis of proteins, their fermentative activity is disturbed, and changes occur in the course of the metabolism, in the structure and functions of organs and systems. In such damages the compensatory reactions of the organism serve the elimination of disturbances connected with the defect of the genetic apparatus. In the pathological processes that go on the molecular level besides the specific defense and compensatory reactions the non-specific reactions also develop.
2. In the damages on the cellular level the compensatory reactions manifest themselves as regeneration of the cells around the damaged area. The biologically active substances which accelerate reproduction of cells, take part in this process. The etiologic agent neutralized, the damaged cells are replaced by the cells of the same type or by the elements of the connective tissue.
3. When the initial damage is on the level of organs (valvular defects, pneumosclerosis, nephrosis, etc.), the compensatory reactions develop on the level of the organs, systems and the whole organism (cardiac hypertrophy in valvular defects). The general changes and the specific regulatory reactions that accompany them, ensure the compensation of the disturbed functions of the organism.
4. The initial damages on the level of anatomic functional systems (the diseases of the nervous system, endocrine disturbances) cause the extreme weakness of some functions of the organism, complicated changes in the metabolism and regulatory reactions of the organism.

Independent of the level of the initial damage, in all cases the changes occur in the cells and cellular organoids which lead to the disturbances of functions of cell organoids and biological membranes. But thanks to the large structural and functional reserve recources of organs and systems, cell injury not always leads to the functional disorders in them. For instance, hypofunction of liver is revealed only when 2/3 of all of its cells are injured. So, the initial damage of cells results the development of diseases only in presence of certain conditions.

The interrelations of destructive and compensatory processes in pathological conditions depend on the level of damage. But many specific peculiarities of pathogenesis as well as non-specific reactions caused by damage, depend considerably on the general state of the organism.

Usually adaptative reactions develop at the same time with the damaging and destructive processes, and some of them even may have a bad effect on the defence of organism. For instance, some of the reactions in the pathogenesis of inflammation (arterial hyperemia, acceleration of the metabolic processes in surrounding tissues, emigration of leucocytes, phagocytosis, regeneration of cellular elements) belong to the defence – compensatory processes, whereas others (alteration, stasis, metabolic disturbances and formation of toxic metabolites) are of damaging character.

The morphological bases of some (for instance, psychical) diseases are not yet revealed. But in due course the localization and morphological bases of majority of pathological processes are elucidated, and the number of diseases that up to now were regarded as functional ones, is gradually reduced. Thanks to the intensive development of molecular pathology the signal successes are achieved in the study of the morphological bases of diseases.

Although the morphological and functional disturbances that form the basis of diseases are closely connected, but sometimes insignificant morphological change may cause strong functional disturbances and vice versa (the morphological changes are compensated by mobilizing functional resources of the organism).

Every disease manifests itself as the damage of some organ (tissue) in a certain degree. But pathological processes are never strictly localized. Because the general peculiarities of the organism as a whole greatly influence the development of pathological process, and every local process, in its turn, exercises general influence on the organism. For instance, even such a limited inflammatory process as pulpitis causes the painful syndrome which, exciting the vital hypothalamic centers, leads to diverse changes in all processes that go in organism. Furunculosis, though a local disease, is often a result of nutritional and metabolic disorders as well as lowered immunity. Typhoid fever, being a disease of the entire organism, is characterized by peculiar changes in the small intestine. **There are following variants of interrelations between the local and general changes in the pathological processes:**

1. The pathological process begins by the local damage of organ or tissue, and the defense reactions which are directed to the restriction of the damage, join up to its course. The participation of whole organism in such pathological process is limited by the local adaptative mechanisms in tissues, and the principal indices of homeostasis (body temperature, blood count, ESR, intensity of the metabolism, etc.) do not change.
2. As a result of stimulation of receptors and entrance into the blood of biologically active substances that are formed in the focus of damage, the general reactions join up to the local process, and a number of indices of homeostasis are changed. Then the defense-adaptive reactions are activated which weaken the general pathological changes and influence of the focus of the damage on the organism.
3. As a result of the general changes in the organism caused by the local damage the defense-adaptive mechanisms are intensified and serious changes take place in the general state of the organism. In such cases the symptoms of the general intoxication and sepsis develop, the principal indices of the homeostasis change considerably.
4. The local changes develop on the background of the general disorders in the organism and sometimes after them.

The local character of the infectious diseases is connected with tropism of the microorganisms to certain tissues (damage of large intestine in dysentery, that of meninges in meningitis, etc.). In some intoxications the local disturbances that follow general disorders depend on the route of excretion of the poisonous substance from the organism (for instance, damage to kidneys in sublimate poisoning). Conversion of wide spread process into local is also connected with the functional properties of organs and tissues. For instance, ionizing radiation causes especially strong damage in the tissues, the proliferation of cellular elements of which is higher (the red bone marrow).

The interrelations between local and general changes in the pathological process depends on the area on which the pathogenic agent influences, on the way of the spread of pathogenic agent and the route of its excretion from the organism. The intensity of the general reactions of the organism depends also on the functional state of the regulatory (nervous and endocrine) systems.

Sometimes the local process may develop and spread causing severe disorders in the general state of the organism, or thanks to the defence reactions of the organism the general pathological process gradually weakens and is converted into the local process. In some cases structural disorder embracing the small area may cause the severe functional disturbance and even lead to death (especially when the respiratory center, vasomotor center and other vital areas are injured) or the damage to wide areas may be compensated owing to the hypertrophy of the surrounding healthy cells (hypertrophy of one of the pair organs when the other is injured).

**In the pathogenesis of all diseases the specific and non-specific mechanisms are observed.** Organism’s responses of the same type to all etiologic agents are regarded as non-specific mechanisms of pathogenesis (typical pathological processes – inflammation, fever, metabolic disturbances, etc.). The pathogenic agent causes, in the first place, the non-specific reactions after which the non-specific mechanisms develop. There is not sharp difference between these mechanisms: the change that is specific for one disease may take part in the pathogenesis of other disease as non-specific mechanism.

The principal change which causes development of all stages of the pathological process is called the main link of the pathogenesis. For instance, the main link in the pathogenesis of the arterial hypertension is constriction of arteriols. This is the cause of all other changes that are observed in this disease.

Disturbance of organ’s function itself may become the factor that causes this same disturbance, that is, cause and effect change places. This state is called vicious circle. For instance, sharp aggravation of transport of oxygen as a result of hemorrhage may cause acute cardiac insufficiency, which still more aggravates the transport of oxygen. So, the vicious circle comes into being.

Mechanisms of restoration of functions of damaged organs are closely connected with pathogenesis of diseases. The restoration of functions impaired by the pathogenic agent underlies recovery. Depending on type and properties of damage the defensive reactions of the organism manifest themselves variously: production of immunity (infectious diseases), elimination of the pathogenic agent (in the vomit, urine, feces, sweat, mucus), healing of the tissue defect (traumata, wounds), etc.

***The defensive reactions of the organism are closely connected with the adaptive and compensatory processes.***

Adaptation is extensive biological idea embracing all vital activity of the organism. Only owing to the adaptive mechanisms the organism ensures its life in the condition of influence of numerous ordinary and pathogenic environmental factors. In the process of evolution all the living beings have acquired adaptive reactions of different character ensuring the preservation of species which function in healthy organism as well as in the period of disease.

Compensation is ensuring of disturbed functions of tissues, organs, functional systems by the way of compensatory hyperfunction or qualitatively renewed activity of other tissues, organs or systems: hypertrophy of cardiac muscle (in valvular diseases of heart), replacement of one of the paired organs (in affection of a lung or kidney) or of one part of a single functioning system by another (replacement of renal activity by the functions of the skin, lungs and intestines in renal insufficiency), restoration of blood pressure by constriction of peripheral arteries and contraction of the spleen (after blood letting), change in the correlations of antagonistic factors (increased activity of cholinesterase in cases of acetylcholine accumulation).

If the adaptive – compensatory reactions can ensure the satisfactory activity of the injured organ, the state of compensation becomes established, and in severe cases the state of insufficiency, that is, decompensation takes place.

*The defence- compensatory reactions which develop in the course of disease are divided into 3 groups:*

1. the urgent, unstable, emergency reactions (seconds, minutes);
2. comparatively stable mechanisms of moderate duration (days, weeks);

3) protracted and stable processes (months, years).

All types of these processes are regulated by nervous and humoral mechanisms. The urgent defence – compensatory reactions are mainly the defensive reflexes with the help of which organism frees itself from harmful substances and removes them (vomiting, cough, sneezing, salivation, lacrimation, secretion of mucus). Secretion of adrenalin and glucocorticoid hormones of adrenal cortex in the state of stress and the reactions directed to preservation of “strict” constants (arterial blood pressure, osmotic pressure of blood and tissues, blood sugar, etc.).

Comparatively stable defensive and compensatory mechanisms act throughout all the disease. They include:

1. Mobilization of reserve resources of organs. For example, in sound organism only 20-25 per cent of respiratory surface of lungs is used. The surface that does not take part in breathing in resting state, joins in, for instance, in pneumonia, and this ensures the necessary gas exchange.
2. Inclusion of numerous apparatuses of regulatory systems (for instance, change over the higher level of thermoregulation).
3. The processes of neutralization of poisons (binding by proteins, oxidation, reduction, methylation, alkylation).
4. Defensive reactions of the system of active connective tissue the cells of which (reticular cells, endothelial cells of capillaries, Kupffer cells of liver, splenic cells, cells of lymphatic nodes, adrenal cortex, bone marrow, histiocytes of crumbly connective tissue) play an important role in the mechanisms of healing of wounds, in inflammation, immune and allergic reactions.

The protracted and stable defence- compensatory reactions include the compensatory hypertrophy, reparative regeneration (for instance, regeneration of blood after hemorrhage), immune reactions (production of antibodies, etc.) that last during months and years. Sometimes the defence reactions reach an intensity which may be even harmful to the organism. For instance, in many forms of intoxication vomiting helps to rid the organism of toxic products, whereas in toxemia of pregnancy intractable (pernicious) vomiting may imperil life.

Sometimes excessive exertion of adaptive mechanisms leads to the new disease, that is, the organism is adapted by the help of disease. For instance, hypertrophy of thyroid gland in iodine deficiency – endemic goiter.

The pathological regulation of functions is characterized by disturbance of some types of relations (nervous, humoral) and inclusion of new-emergency relations in the organism. The emergency regulation is uneconomical and unprofitable for organism, and with the purpose of self – preservation of the organism as a system, exhausts its power resources. For instance, abundant sweating in overheating, protective inhibition in cerebral cortex in the state of shock, abundant secretion of mucus in stomach in response to introduction of irritating substances.

The central nervous system (especially the cerebral hemispheres) plays an important role in the defensive physiological reactions of the organism. Its role in the processes of restoration of functions impaired by disease is observed in cases of deep anesthesia or cerebral trauma: efficiency of the organism is diminished, the compensatory reactions in cases of inflammation are reduced, proliferation and regeneration of damaged tissue noticeably decrease, after loss of blood the restoration of blood pressure is retarded, in disorders of cardiac activity hypertrophy of the heart muscle develops feebly and the blood circulation is impaired.

The numerous plastic reactions of the central nervous system which promote the activity directed to adaptation of the damaged organism to the existence in the environment, include the following mechanisms:

1. defensive plastic function of the central nervous system;
2. protective inhibition in the central nervous system;
3. unconditioned and conditioned defensive reflexes.

Cortical inhibition is a defensive reaction to exhaustion and great damage or destruction of nerve cells. It is conducive to restoration of cortical activity and is a safe-guard. In the course of various pathological processes (cerebral anemia, various forms of poisoning, infectious diseases) it is frequently a defence reaction to noxious agents and the damage caused by them. Production of defensive inhibition underlies the use of prolonged natural or artificial (caused by medication) sleep which is indicated in some cases of traumatic shock, hypertensive vascular disease, ulcers, etc.

One of important manifestations of the defensive activity of the central nervous system are the phonomena called “mechanical immunity”. Disorders in behaviour caused by removal of small areas of the cerebral cortex or damage of the spinal cord on different levels are compensated by the activity of non-damaged parts of the central nervous system. For instance, the dog after amputation of one limb acquires the ability to run on three extremities. These abilities are not revealed in animals deprived of the cerebral cortex.

Participation of higher nervous activity in pathogenesis of diseases is proved by the fact that it is possible to reproduce some diseases by conditioned reflex way.