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Учреждение образования
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии
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МЕТОДИЧЕСКАЯ РАЗРАБОТКА
Для проведения занятия со студентами
3 курса ФПСЗС, обучающихся на английском языке
по патологической физиологии

Тема: **Введение в дисциплину «Патологическая физиология». Общие вопросы учения о болезни. Общая этиология и патогенез**

Theme: **Introduction to the discipline "pathological physiology". General doctrine about disease. General etiology and pathogenesis**

Время 3 ак. часа

Actuality of the theme. In everyday practical activity doctor always takes into account of illness nature and peculiarities of it course. This is important for planning of prophylactic arrangements, diagnosis rising, selection of medical drugs. In illness is distinguished two process: a) damage property illness; b) physiological measure against illness that is complex of protective compensatory-adaptation reactions. The protective reactions perform with nervous, endocrine, immune and other systems. With their help an organism resists to pathogenic factors and restores broken functions. Aim of such arrangements is rising of individual organism resistance to effect of harmful agents.

Learning goals of the lesson: to study a subject and tasks of pathological physiology, basic concepts of general nosology and their characteristics.

Educational goals of the lesson: formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

Objectives of the lesson:

1. To know a definition of "pathological physiology", subject, tasks and methods of its study, importance for medicine.
2. Be able to define a concept of "disease" and "pathological process."
3. To know contribution of domestic and foreign scientists to development of pathophysiology.
4. To know mechanisms of onset and development of disease.

To repeat the following questions from related disciplines to ensure absolute mastery of the material:

1. Structure of cells (histology, cytology, embryology disciplines).
2. Definition a "health". Physiological regulation of the organism functions (physiology discipline).

Control questions of the lesson:

1. Pathophysiology: subject, content, tasks and methods. A concept of clinical pathological physiology.
2. Basic concepts of general nosology. A dual nature of disease.
3. Typical pathological processes: their characteristic, features and clinical significance.
4. Role and place of an etiological factor in pathogenesis of diseases. Critical analysis of concepts of general nosology.
5. General pathogenesis: definition, role of damage in pathogenesis, types of damage, manifestation of damage at different body levels.
6. Causal relationships in pathogenesis; leading link of pathogenesis and "vicious circles".
7. Types and mechanisms of sanogenesis, their role in development of disease. A phenomenon of decompensation.
8. Etiotropic and pathogenetic principles of disease therapy.

Calculation of study time

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes

Additional materials:

Pathophysiology (from the Greek: *pathos* – illness, suffering; *physis* – nature and *logos* – teaching, science) – the basic fundamental integrative biomedical science that studies the most common patterns of occurrence, development and outcome of the disease.

The main subjects of pathophysiology study are:

- 1) the causes and mechanisms of the functional and biochemical abnormalities underlying the disease;
- 2) mechanisms of adaptation and restoration of disturbed functions in disease (recovery mechanisms).

Object of the pathophysiology study includes three components:

- illness and disease states;
- typical pathological processes;
- typical forms of pathology of organs, tissues and systems.

As a theoretical foundation of medicine, pathophysiology binds the basic theoretical disciplines (biology, biochemistry, biophysics, physiology, genetics, etc.) to the disciplines of clinical profile:

- *biology* – pathological processes often begin at the cell level;
- *biochemistry* – the changes in biochemical processes underlie in the pathological condition
- *biophysics* – reveals the connection between the physical mechanisms underlying the organization of living objects and biological characteristics of their life;
- *physiology* – to be able to find the pathological functions needs to understand the functions of the healthy tissues, organs and systems of the body.

Pathophysiology is closely related to the morphological sciences (anatomy, histology, pathological anatomy), as it cannot be dysfunction without disturbing the structure.

The main task of the pathophysiology as a fundamental medicobiological science – to provide new knowledge about the nature of disease and pathogenetic mechanisms of recovery (sanogenesis)

History of pathophysiology

In one of the earliest printed medical publications «De naturali parte medicinae» («On natural part of medicine», 1542, J. Fernely) indicates that the occurrence of the disease is accompanied by the transition of the body to the world of qualitatively new, peculiar laws. In this regard, the field of medicine that studies the life features of a sick organism, the author has designated as pathology.

Term and content of the pathophysiology foundations were formed by the beginning of the XVIII century.

Claude Bernard (1813-1878 yy.) researched the processes of internal secretion, the founder in endocrinology; introduced the concept of «internal environment» of the body. Find out the blood and lymph as «internal environment» for all cells are the source from which cells receive nutrients and to which they give the products of their metabolism.

Development of experimental physiological direction in the pathology is inextricably linked with the name of a prominent Russian scientist V.V. Pashutin, widely regarded as the father of Russian pathophysiology. **Viktor Vasilyevich Pashutin** (1845–1901 yy.) created the first pathophysiology schools. He had the first in Russia scientific works of endocrine glands activity and studied the problems of metabolism impairments.

The founder of the second school was Russian pathophysiologists **A.B. Fokht**. Was one of the greatest experimenters. The range of scientific interests A.B. Fokht was extremely wide: problems of pathology of the cardiovascular system, kidneys, respiratory system, digestive system. He was one of the first Russian scientists have raised questions about the need for extensive study of the endocrine glands.

Founder of comparative pathology is **I.I. Mechnikov**. He initiated the comparative pathology of inflammation, the theory of cellular and humoral immunity, the doctrine of phagocytosis and formulated biological (phagocytic) theory of inflammation. The first time established a link of inflammation with immunity, in mechanisms of which phagocytosis also plays a significant role.

Cohnheim J. was a creator of the theory of vascular inflammation. The first time described in detail the entire set of changes in vascular tone and blood flow with exudation and emigration.

Scientific interests of **G.N. Sakharov** focused mainly on problems of immunity, allergies, cytotoxins, endocrinology, constitution, infectious diseases, etc.. In 1904, discovered the phenomenon of serum anaphylaxis and described the tissue changes characteristic of hyperergic inflammation (phenomenon Arthus-Sakharov).

A.A. Bogomolets (1881-1960 yy.) developed and introduced into clinical practice antireticuloendothelial cytotoxic serum. He had research in the field of endocrine pathology pathophysiology of tumor growth, circulation, physiology of aging, immunology.

N.N. Anichkov (1885–1965 yy.) first in Russia introduced the practical lessons in pathophysiology. Main areas: pathology of cardiovascular system, physiology and pathology of the RES, anoxia, gastrointestinal pathology.

Andrei Dmitrievich Ado had fundamental studies in the mechanisms of allergic reactions, the pathogenesis of inflammation and immunity; studies of autoimmune process; selected a new class of virus-induced "intermediate" antigens.

Rudolf Virchow introduces term «pathological physiology» to medical terminology; study the nature of the disease; create the theory of cellular pathology, cellular theory of inflammation.

S.S. Khalatov (1884-1951 yy.) first pointed to the importance of local deposits of cholesterol in the origin of a number of pathological processes; proved the role of disorders of cholesterol metabolism in the development of atherosclerosis.

P.N. Vesvolkin created the doctrine of fever, pathogenesis of hemotransfusion complications and traumatic shock. He studied the pathophysiology of the heat exchange disorders.

Research activities **I.R. Petrov** was devoted to the study of mechanisms of the damaging effect of electric current, oxygen deficiency, pathogenesis of shock (trauma, burns, electric) and radiation sickness.

N.N. Sirotinin had experimental studies of anaphylaxis research on the problem of oxygen starvation and adaptation to hypoxia; studied in comparative evolutionary pathology of infection, immunity and allergy

A.M. Chernuh studied common problems of nosology, sanogenesis, theory of inflammation and microcirculation, experimental therapy; created the original doctrine of the neurovascular regulation of cell activity in various pathological processes (inflammation).

U. Kennon formulated the principle of homeostasis.

P.D. Gorizontov had fundamental research on the pathogenesis of radiation sickness; classic work on the problem of stress and the regulation of hematopoiesis.

A.D. Speranskii developed the doctrine of decisive role of the nervous system (trophic function) in the mechanisms of origin, development and outcome of disease.

G.N. Kryzhanovsky was a creator the theory of generating mechanisms of neuro-pathological syndromes. Was the founder of study of determinant.

L.A. Orbely formulated the position of the adaptive-trophic role of the sympathetic nervous system, that under the damaging effects activates the higher parts of the central nervous system, mobilizes energy, stimulates the cardiovascular system, enhances muscle performance, activates immunological mechanisms and other processes.

Hans Selye identifying the term "stress"; was at the forefront of modern concepts of unified neuroimmune-endocrine regulation of body functions in health and disease.

V.V. Parin founder of new scientific trends in physiology, medicine and biology, and one of the founders of space biology and medicine.

Basic studies of **F. Burnet** are devoted ecology of viruses, their relationship with "host", mechanism of viral replication, their variability. Is the author of clonal-selection theory of immunity and discoverer of immune tolerance phenomenon; for the latest discovery received the Nobel Prize (1960).

The methods of pathophysiology

Scientific facts and positions obtained using different methods, are the basis for the development of specific and general concepts and theories of pathology in humans. The results of these developments

consider and used in solving actual fundamental and applied problems in medicine and biology. The main methods are:

1. modeling:
 - physical:
 - ✓ on biological objects
 - ✓ on artificial systems
 - formalized:
 - ✓ intellectual
 - ✓ mathematical
 - ✓ computer
2. clinical examination;
3. theoretical analysis;
4. medical thinking.

Modeling.

The main method of pathophysiology is to model of diseases, pathological processes, states and reactions. This method is used for creating theoretical (logical) models of pathogenesis, carry out mathematical and computer modeling of diseases.

Physical or material modeling on real physical objects (animals, their organs, cells, etc.). Models of pathological processes, conditions, reactions and diseases imitable in animals are used to study the etiology and pathogenesis of human diseases, the development of methods of diagnosis, treatment and prevention. Experiment on animals made under strictly justified need; using optimal species and number of animals; with the use of painkillers. To study the pathological processes in living subjects use the following methods of the experiment:

- a) the method of removal or damage (off) of any organ with subsequent analysis showed symptoms compared with the clinical picture of the humans disease in which detected the lesion of corresponding organ.
- b) the method of inclusion (on) – introduction of various substances, the excess of which leads to the development of a disease (for example, to study hyperthyroidism the introduce the thyroid hormones);
- c) the method of stimulation (for example, stimulation of the vagus nerve occurs bradycardia);
- d) the method of isolated organs - the nature and extent of damage of a particular organ (heart, lungs, liver, and others.) and its contribution to the development of circulatory failure, respiratory, digestive, etc .;
- e) the method of parabiosis - connection of two animals (parabiont) through the bloodstream and lymphatic system to study the mutual humoral influences (hormones and other metabolites);
- f) the method of tissue culture - isolation and fractionation the cellular elements of the various organs and tissues to study their role in the regulation of hematopoiesis and immunopoiesis, mechanisms of cells malignization, the establishment of mechanisms damaging effect on cells of various pharmacological agents, etc .;
- g) the method of comparative pathology - the study of the evolutionary aspect of the development features and course of various pathological processes (inflammation, hypoxia, fever, etc.).

Modeling of pathological processes of human in animals has a number of shortcomings due to significant species differences of vital processes in animals and humans, as well as important role of social factors in the occurrence, development and outcome of human diseases. Also used modeling of human pathology using artificial physical systems - artificial heart, kidney, blood, lung ventilation apparatus, cardiopulmonary bypass, etc.

Formalized (non-material, virtual) modeling of diseases. It is realized as logical, mathematical, computer, etc. Logic modeling is used in learning process of future specialists. Logical modeling of diseases and pathological processes, as well as the patient followed by actual confirmation of the assumptions made are widely used in clinical practice and research.

The formation at students the basics of medical thinking is achieved in the course of their analysis of specific pathophysiological experimental or clinical data, in solving professional medical problems (situation tasks) in the classroom. This simulates behavior of the doctor, modeling the disease and patient

as a whole to develop methods of diagnosis of the disease, as well as the strategy and the specific treatment regimens of the patient.

Computer modeling (e.g., pathological processes or effects of therapeutic interventions) is often carried out by modern computers and programs.

Methods of clinical examination

The availability of modern equipment and the latest examination technology allows in a human patient focused study the dynamics of the state of various organs and systems, structural changes in them, biochemical and electrophysiological parameters of functioning the body as a whole.

Obligatory conditions for the implementation of such studies are their safety for the patient and the well-reasoned need.

Obtained from the direct study of patient data allow:

1. to make the accurate diagnosis of the disease;
2. to evaluate the effectiveness (or ineffectiveness) of treatment;
3. examine the characteristics and patterns of occurrence, development and outcome of disease in humans;
4. provide material for a scientific explanation of the etiology and pathogenesis of diseases and pathological processes.

Methods of theoretical analysis

Theoretical analysis and development on this basis of scientific ideas, concepts, hypotheses and theories related to the solution of fundamental and applied problems in medicine and biology - the most important method of pathophysiology.

The result is the formation of a system based views on the causes and mechanisms of the origin, development and outcome of disease, disease states and pathological processes, principles and methods for their detection, treatment and prevention the theoretical propositions in medicine and biology.

Medical thinking

Medical thinking is one of the most delicate and difficult types of modeling in medicine: predictive modeling of the patient and his disease.

Having examined and listening to the sick person, examining results of various studies (biochemical, functional etc.) the doctor creates a model of the patient and his disease. With this in mind, it models the scheme of further diagnostic search methods (strategy, algorithm) of treatment and prevention disease in individual patients.

Part of pathophysiology

Pathophysiology as an academic discipline includes three main sections:

1. **general nosology;**
2. doctrine about **typical pathological process;**
3. doctrine about **typical form of tissue, organs and system pathology.**

First two are the part of general pathophysiology, last – systemic pathophysiology.

General nosology

Norm — it is the **biologic optimum** of functioning and developing of the organism.

Health — is a condition of total physical, spiritual and social well-doing, but not only the absence of disease and physical defects (World Health Organization, 1946). The health is the life of the human, who is able to work and adapted to the changes of environment (I. Petrov). By N. Zaiko — the health is the normal condition of organism, its structure and functions correspond to each other and its regulatory systems are able to support the homeostasis.

Pre-disease —condition of the body with the **weakening of some sanogenetic mechanisms** and their complexes **preceding and promotes the development of the disease.**

Disease – it is a **qualitatively new process** of life with **disturbance of normal activity** of the human organism **under the influence of injurious agents** accompanied by structural, metabolic and functional changes **with limitation of adaptation, ability to work.**

Table 1. Differences between health and disease

Health	Disease
Wide range of variation of functions	Narrowing range of variation of functions
Sufficient amount of functional reserves	Reducing the amount of functional reserves
Lack of strong linkages between functions	Presence of hard linkages between functions
Optimum adaptation to changing conditions of functioning	Reduced adaptation to changing conditions of functioning

There are subjective criteria of the disease (patient complaints of malaise, pain, various functional impairment, etc.) and objective (results of a study with laboratory and instrumental methods), allowing to identify abnormalities and to establish the typical symptoms (signs) of the disease.

Semiology (sémeion = sign, symptom) — the study of symptoms and signs of diseases.

Symptoms – subjective feeling of disease.

Signs – objective parameters of changed functions and structures of body systems.

Classification of diseases

Classification may follow various principles: cause, localization, mechanisms of development, age, sex, type of dysmetabolism, professional aspects, clinic duration and others.

Clinical classification of the diseases is based on the clinical forms, localization, duration of processes, types of diseases current (acyclic, cyclic).

According to duration:

- ✓ flash-like (several minutes – several hours);
- ✓ acutest (several hours – 3–4 days);
- ✓ acute (5–14 days);
- ✓ sub acute (15–35–40 days);
- ✓ chronic (several months and years).

Etiological classification is based on a cause: heredity or acquired, infectious noninfectious, traumatic, toxic etc.

Topography-anatomic classification of the diseases corresponds with the main physiological systems (pulmonary, cardiac, renal diseases etc.).

The International Classification of Diseases (ICD) applied the following criteria:

- reason (hereditary, infectious etc.);
- main link in the pathogenesis of the disease (degeneration, hypertension, immunopathological condition, endocrinopathy, etc.);
- main localization of the diseases (diseases of blood, respiratory system, heart, liver, etc.);
- patient's age (newborn illness, childhood diseases, diseases elderly and senile age);
- basic principles of treatment (surgical, therapeutic disease).

There are four stages of disease:

1. **Latent period** (incubation period for infectious diseases). It lasts from the moment of impact disease agent on the body until the first signs of the disease. During this period start numerous protective reactions aimed at removing the causes of diseases and compensation of the damages. The initial period for different types of the disease may be very short (eg, mechanical trauma, acute intoxications) or very long (metabolic diseases, tumors, certain infections).
2. **Prodromal period.** The first signs of the disease are appear (initially non-specific), followed by the deployment of clinical manifestations characteristic of this disease.
3. **Period of expressed manifestations** (specific signs of the disease).
4. **Outcome of the disease.**

Outcome of the disease may be:

- recovering;
- transition in chronic form;
- relapses;
- complication;

- death.

Recovering may be complete and incomplete

Complete recovering — is characterized by the absence of symptoms and normalization of impaired functions.

Incomplete recovering — persist dysfunction (in varying degrees of severity) of individual organs and their regulation. One expression of incomplete recovery is a relapse (return) of the disease, as well as its transition a chronic state.

The study of **mechanisms involved in recovery from disease to health is sanogenesis** (sanos - health).

Classification of sanogenetic mechanisms:

1. Primary:

- ✓ adaptive
- ✓ protective
- ✓ compensatory

2. Secondary:

- ✓ protective
- ✓ compensatory
- ✓ terminal

Adaptation — changes in the structure and metabolism, conducive to the optimal functioning of the body in the new environment (in case of damage). **Maintains the homeostasis and prevents damage under the action of environmental factors.**

Compensation — restructuring of the relationship between the elements of the system, aimed at ensuring full (sufficient) function, at damage of specific structures responsible for the implementation of this function in norm. Compensation **eliminates the consequences of the damage.**

Distinguish 3 main ways of sanogenesis:

1. **Immediate** (unstable, "alarm") protective compensatory reactions that occur in the first few seconds and minutes after exposure (protective reflexes - vomiting, coughing, sneezing, etc. ; release of adrenaline and glucocorticoids in stress reactions etc.);
2. **Relatively stable protective and compensatory mechanisms** act throughout the disease (initiation of reserve capabilities, including regulatory systems (eg switching to a high level of thermoregulation, increasing the number of red blood cells, etc..); processes of neutralization of poisons; reaction from the system of active connective tissue);
3. **Stable protective compensatory reactions**: immunity, compensatory hypertrophy, reparative regeneration and other structural compensation persist for many months or years after undergoing the disease.

Main features of sanogenesis:

- ✓ it's a dynamic complex of mechanisms;
- ✓ it's a complex of physiological and pathophysiological mechanisms;
- ✓ it's develop in action to the organism extreme stimulant;
- ✓ mechanism of sanogenesis are affected during all pathological process;
- ✓ it's direct to repairing autoregulation of organism.

The transition to a chronic form means that the disease progresses slowly, with long periods of remission (months or even years). Such a course of the disease is determined by the virulence of the pathogen and mainly reactivity of organism. So, in old age, many diseases become chronic (chronic pneumonia, chronic colitis).

Relapse (in roman recidivus) — is a **renewed or aggravation the symptoms of disease after their elimination or easing.**

Remission (in roman reduction, easing) — is a **temporary easing** (for incomplete remission) **or an elimination** (for complete remission) of the manifestations of disease.

Complication — is **pathological process, condition or reaction, developing on the basic disease background, but it is not obligatory for disease** (appendicitis can be complicated by peritonitis, myocardial infarction – arrhythmia).

Death may be:

- natural;

- premature:
 - the violent death,
 - death as a result of disease.

Tanatogenesis (thanatos – death) — study of signs, conditions, causes and nature of death.

The dying process is divided into a series of successive stages called terminal condition.

Terminal conditions — is a reversible decrement of organism function that preceding the biological death, when the protectively-adaptive complex of mechanisms are insufficient to eliminate the consequences action of the pathogenic factor on organism.

The characteristic features: an inability of the dying organism to revert to the normal state independently, without help from the outside even if the etiologic factor action has stopped

The leading mechanism: hypoxia

The main steps of dying are:

- preagony
- terminal pause
- agony
- clinical death

Preagony

- characterize by the higher nervous system structures inhibition, it manifestates by the twilight state, sometimes with the medullary vasomotor centre excitation
 - decrease in reflex activity, the alive eye reflexes
 - the arterial blood pressure is decreased, the peripheral arteries pulse is weak filling or it is not probed at all.
 - the aerobic exchange prevails

Terminal pause

- the respiratory termination, the acute cardiac activity to the temporary asystole
- apnea has temporary character (from several minutes till 3–4 hours).
- terminal pause can be absent (in case of the electric current injury).
- terminal pause is distinctly expressed in case of the dying because of the blood loss and asphyxia.

Agony (in greek *agonia* is a struggle):

- main agony sign is the first inhale occurrence after the terminal pause period;
- at the beginning –respiration is weak, then it increases in depth, reaches the maximum, gradually weakens and absolutely stops; may appear terminal type of breathing;
- bradycardia, temporary asystoly, decrease in the arterial blood pressure may be short-term increase in the arterial blood pressure;
- in metabolism – a prevalence catabolism;
- deep dysfunctions of higher nervous system with simultaneous excitation of the medulla oblongata;
 - consciousness is absent, sometimes it quickly clears up;
 - eye reflexes and external irritants reaction are disappear;
 - sphincter relaxation.

Clinical death

- consciousness is absent
- absence of pulse and blood pressure;
- absence of breathing;
- widely dilated pupils;
- completely unresponsive to the painful stimulus;
- recovery can occur only with resuscitation.

Postresuscitation disease

This is not a complication of intensive care, it is a form of pathology, with pathogenetic base on fundamentally new totality pathological processes and reactions, whose interaction and characteristic sequence of development define specific features of the clinical course of postresuscitation.

In the postresuscitation period are identified:

- violations of systemic and peripheral hemodynamics, hemostasis disorders, rough disorders of all kinds of metabolism;
- violation of gas exchange function of the respiratory system;
- failure of the liver and kidneys;
- brain dysfunction (encephalopathy).

I period – early postresuscitative (in the experiment, it takes the first 6-8 h in the clinic - 10-12 h), is characterized by rapid dynamics of the restore the functioning of vital organs and systems in combination with the instability of many body functions. Cardiac output first increases and then decreases, develops hypovolemia, increases the total peripheral vascular resistance, instability in blood pressure; violations of regional circulation and microcirculation in the form of blood flow shunt, increased blood viscosity, blood circulation centralization of on the background of hypoperfusion of the peripheral tissues; growing oxygen consumption to vital organs; stored oxygen debt of the body. Oxidized products of metabolism are accumulated (due to ongoing hypoxia), that deepens metabolic acidosis, which further goes into respiratory alkalosis. Identified hyperenzymemia, hormone imbalance, hypercatecholaminemia, endotoxemia, expressed hemostatic disorders (bleeding, microthrombosis), water and electrolytes imbalances. Death can occur from repeated circulatory disorders, heart failure, coagulopathic bleeding, pulmonary and brain edema.

II period (lasting several hours) – the period of temporary and relative stabilization of the main body functions and improve the general condition of the patient. Notes the temporary stabilization of basic functions, but microcirculatory disorders are not fully eliminated. Save metabolic disorders (hypokalaemia, slow fibrinolysis, increased lipolysis, tendency to hypercoagulability), blood volume deficit and widespread violations of acid-base status.

III period (from the end of first – to the beginning of second day) – is the stage of repeated deterioration. To circulatory and anemic hypoxia bind respiratory (caused by microthrombosis of pulmonary vessels, shunt in the pulmonary circulation). Noted persistent and progressive arterial hypoxemia. Observed recurrence of hypovolemia, deterioration of peripheral circulation, oliguria, metabolic acidosis, increase of catabolic processes, development of severe hypercoagulation and slowing of fibrinolysis. Critical expression reaches damage of parenchymal organs.

IV period – is end stage (2-3 day after resuscitation). During this period, perhaps as improvement, followed by recovery as well as deepening of functional metabolic disorders and structural abnormalities. Appear purulent-septic complications on the background immunosuppression; again grow disorders of peripheral circulation; reduces the blood oxygen capacity due to deepening of anemia; increases the excretion of potassium with urine (due to hypoxic cell damage). Usually develops complete failure of spontaneous breathing occurs or deepening coma.

In the case of a favorable course of the recovery period the consequences of suffering from terminal condition can be observed for a long time (autoimmune brain damage, encephalopathy, etc.), so the patient must be in a year or more to be under a doctor's supervision.

Biological death

Soon after **biological death** a number of **signs** of death and postmortem changes appears. They are the followings:

- **algor mortis** (cooling) – result of heart production stopping in the body and body temperature equal to environment;
- **rigor mortis** – complete loss of ATP which required to cause separation of myosin and active during relaxation, and muscle is unable to relax until further enzyme activity complete degrades. Usually develops in 2-5 hours after death and kept during 2-3 days;
- **livor mortis** (Latin: livor – bluish color, mortis – death), postmortem lividity, due to heart stops functioning, heavy red blood cells sink through the serum by action of gravity (starts twenty minutes to three hours after death);
- **decomposition** – caused by autolysis (breaking down of tissues by the body's own internal chemicals and enzymes) and putrefaction (by bacteria).

The basis of the disease is the pathological process

Pathological process – is a complex of morphological, biochemical and functional changes developing in tissues at infringement of realization of the genetic program or interaction with the sickly factor of environment.

Differences between the pathological process from the disease:

1. disease is always one main reason (producing a specific etiological factor), the pathological process always polyetiological;
2. same pathological process may cause the different picture of the disease in depending on the location (inflammation of lung – pneumonia, heart muscle inflammation – myocarditis, etc.).
3. disease usually is a combination of several pathological processes (pneumonia has a combination of pathologic processes such as inflammation, fever, etc.).
4. local pathological process can exist without disease (callus).

Slowly current pathological process is a pathological condition.

Pathological condition – is a stable deviation of the structural, functional, biochemical properties of tissues, organs and systems from norm, arising under the injuring factor action and poorly varying in time.

In some cases, the pathological condition may go back in the pathological process, disease (eg, pigmented skin area under the influence of mechanical, chemical and physical factors can be transformed into a malignant tumor melanosarcoma).

Pathological reaction (function) is inadequate (quantitatively or qualitatively) answer of alive system on physiological irritation. It is an external display of pathological process, symptom of disease, an attribute of presence in the organism of pathological process. Examples: dilation of skin vessels under the influence adrenaline, allergic reactions, inadequate psycho-emotional and behavioral reactions, abnormal reflexes (reflexes Rossolimo, Babinski) etc.).

Within the general nosology develop three important categories of doctrines:

- nosology
- general etiology
- general pathogenesis

Nosology (from Greek: nosos – disease; logos – science) – the doctrine of the disease in the strict, narrow sense of the term or private nosology.

General etiology (from Greek: aitia - reason, logos - science) – the doctrine of causes and conditions of occurrence and development pathological processes, states, reactions, disease.

Etiological factors are divided into exogenous and endogenous; acquired, congenital, heredity; according nature –physical (mechanical, thermal, radiation, etc.), chemical (poisons, toxic metabolites, side-effect of medical drugs) and biological (microbes, viruses, parasites, immune), psycho-emotional, social causes.

Factors which increase morbidity are **risk factors** (for example, hereditary factors, obesity, arterial hypertension are the risk factors for atherosclerosis).

Condition is a factor promoting, interfering or modifying action of the etiologic factor. The condition cannot cause disease. The difference between conditions and cause is that the cause is one and a lot of conditions. Conditions are not necessary for the disease occurrence and do not give it specificity.

According to origin conditions may be classified as exogenous (ecological, social), endogenous (sex, age, constitution, type of higher nervous activity). They may be formed during prenatal or postnatal period. Distinguish the conditions conducive to effect of cause and preventing it.

The idealistic and metaphysical theories of the disease etiology

1) **Monocausalism** (in roman mono – one, causa – cause) – is a mechanic study. It admits only the role of cause and refutes the role of condition in disease occurrence.

2) **Conditionalism** (in roman condition — condition) – is a study, which refutes causality in disease occurrence. It substitutes the categorion of cause for the sum of equivalent conditions (equivalent according to the role).

3) **Constitutionalism** – is a study, which admits the role of the body constitution in disease occurrence.

4) **Polyetiologism** – is an etiology school according to which the organism body constitution features have the crucial importance for the disease occurrence and current.

5) **The factors theory** — is a theory recognizing the plurality of reasons and conditions, their mutual influence.

6) **The civilization diseases** — the universal value attribute to the social factors in the development of pathological processes.

7) **Holism** (in greek holos – whole, everything) – is a doctrine according to which human life is controlled by some «integrity factor» on which health and disease depend.

General pathogenesis (pathos– pain, suffering, distress, genesis – origin) – the doctrine of the mechanisms of development and completion of pathological processes, states, reactions and diseases, the principles of pathogenetic therapy and prevention.

Pathogenesis — mechanisms involved in disease onset and diseases development (pathomechanisms).

Pathogenesis of illness always includes 2 processes: damage (pathological changes) and protective reactions and processes (adaptation and compensation).

All events, which are observed in pathogenesis of any disease, are called the links of pathogenesis. Pathogenesis of disease has **main** (leading, keyword, organizing) **link** or many links. As a rule, it (they) act from the beginning to the completion of the process. Identify key link or links of pathogenesis provides carrying out effective pathogenetic therapy and prevention of pathological processes and disease.

In the pathogenesis of diseases and pathological processes is always a start, initial, trigger, **releaser**. This mechanism is largely determines the specificity of disease regardless of act it throughout all disease or starts it. For example knowing that an initial link in the pathogenesis of ischemic renal hypertension is the activation of the renin-angiotensin-aldosterone system allows the physician to block this link using drugs and effectively treat the patient. But after the activation of other links of hypertension pathogenesis of releaser factor may lose the trigger value.

In the pathogenesis of disease can be identified a number of stages or links which are linked by causal-effect relationships. This means that the changes arising in the course of disease are becoming the causes of further violations. Distinguish the followings types of causal-effect relationships:

- 1) "straight line" (one event is a consequence of the previous and the cause of next);
- 2) Branched types (include the divergence and convergence): divergence – certain events of pathogenesis have many consequences; convergence – different events of pathogenesis lead to the same consequence;
- 3) "**vicious circle**" – certain phenomena of pathogenesis through a certain sequence events lead to increased themselves, **etiological factor causes the pathologic reactions (process) and then these reactions return to the etiological factor (first agent) and intensify it.** This type of causal-effect relationship self-sustained the pathogenesis of disease and worsens its course.

For example, a sharp deterioration in the transport of oxygen in blood loss leads to heart failure, which further impairs the transport of oxygen. There is a "vicious circle"

In the complex chain of causal-effect relationships in the development of disease distinguish local and general changes. There are 4 variants of relationships of local and general processes in the pathogenesis:

1. In response to the local damage to organ or tissue as a result of the general reactions of the organism are mobilized tissue adaptive mechanisms to delimitation of the lesion (eg, granulation shaft during inflammation, the barrier function of the lymph nodes). Consequently, the main parameters of homeostasis (body temperature, leukocyte count and leukocytic formula, erythrocyte sedimentation rate, metabolism) may not be changed.
2. Local process through the receptor system and entry of biologically active substances into the blood and lymph systems causes the development of generalized reactions, and certain changes in the main parameters of homeostasis. In this case, activates adaptive response aimed at preventing the development of common pathological changes in the body.
3. Generalization of the local process in severe cases can lead to failure of adaptive and protective reactions, and ultimately – to the general intoxication, sepsis, or death.
4. Local pathological changes in organs and tissues may develop secondarily on the basis of primary generalized process (eg skin leukemids in some types of leukemia, etc.).

In the development of almost any of disease can be distinguished specific and nonspecific mechanisms of its formation.

Nonspecific mechanisms include typical pathologic processes such as inflammation, disorder of lymphocirculation, fever, thrombosis, the generation of reactive oxygen species, increase membrane permeability etc..

Specific mechanisms include activation the systems of cellular and humoral immunity, which provides specific protection in the fight against foreign objects in the body.

Pathological system – it is a **functional summation** of reactions single cells, organs, tissues, systems and organism, which **appear in the action to organism a pathogenic factor**.

Pathological system characterized by:

- ✓ long-term self-sustained activity
- ✓ depression adaptation and protective mechanisms
- ✓ based on disorders of information process
- ✓ lead (in case of long-term existence) to increasing a disbalance by sick organism and environment
- ✓ many PS are developed on the basis of the vicious circles or pathological dominant

Typical pathological processes

Typical pathological process (TPP) is a standard, answer of the organism, generated during evolution, on action of the damaging (injuring) agents with distinct prevalence of a protective component.

The basis of each TPP is logically developing complex of reactions and processes of damage, destruction, protection, compensation, reparation and adaptations that occur in response to the pathogenic agent. TPP have characteristic features:

- **Polyetiology.** TPP caused by a large number of causes of different nature (physical, chemical, biological) and origin (exogenous and endogenous, infectious and non-infectious), realizing their pathogenic effect in a variety of environments. For example, inflammation may be caused by mechanical trauma and various chemical agents; microorganisms; excess in the blood and tissues of metabolites (lactic salts, uric acid)etc.

- **Monopathogenetic.** TPP have standard, stereotypical, common mechanisms of development. For example, inflammation, regardless of its cause, features of development and localization in the body, in the pathogenesis involves complex of mechanisms of typical alterations, vascular reactions and changes in local blood circulation, fluid exudation and emigration of leukocytes, phagocytosis and cell proliferation.

- **Complexity.** The mechanism of the development of TPP – a complex of interconnected changes: damage and simultaneously developing protection processes, compensation, reparation and adaptation (adaptation).

- **Standardness of manifestations.** TPP are manifested typical for them standard features. Thus, the inflammatory process of any origin characterized by general (leukocytosis, fever, dysproteinemia et al.) and local (pain, redness, swelling of tissue, increasing its temperature and function disorder) signs. Standard manifestation of TPP due to the fact that it is based on the typical mechanisms of development.

Typical forms of pathology of organs, tissues and systems

Typical forms of pathology of organs, tissues and systems are also components of individual diseases.

Various typical forms of pathology developing in a particular tissue or organ, accompanied by a number of specific for tissues or organs, pathological and adaptive changes. Set of interrelated changes is referred to as the standard (typical) form of pathology of the tissue or organ.

Example. The typical form of pathology – anemia. A variety of reasons can cause hemolysis, violation of RBCs formation and maturation, their loss with bleeding and hemorrhage. But all these states are characterized by a necessary changes – decrease in the amount of hemoglobin per unit blood volume. Such typical, stereotyped form of RBCs pathology is referred to as "anemia." In turn, anemia as typical form of erythrocytes system pathology may be a component of various diseases (e.g., leukemia, kidney failure, radiation sickness, atrophic gastritis, etc.). Typical form of pathology organs and tissues also

include cardiac arrhythmias, respiratory failure, nephritic syndrome, uremia, liver failure, leukemia, hyperthyroid condition, syndromes of neurogenic disorders of movement and/or sensitivity, neuroses, and several others.

As a TPP the typical forms of pathologies of organs and tissues have a number of characteristic features of polyetiology, monopathogenetic, complex process of damage and adaptation, standardness of manifestations, including as a component in the pathogenesis of many concrete disease.

Questions for self-control of knowledge:

1. What study a general pathological physiology?
2. What is a significance of experiment in development of pathophysiology and clinical medicine?
3. What is a difference between categories of "normal" from "health"?
4. What is a pre-disease?
5. What is a difference between pathogenic and sanogenetic reactions during development of disease?
6. What is difference between disease from pathological reaction, pathological process and pathological state?
7. Named stages of disease. What is a "relapse" and "remission"?
8. What are referred to a terminal condition? What is characteristic of terminal conditions?
9. What are criteria for effectiveness of resuscitation?
10. What is a principle of etiotropic therapy and prevention of disease?
11. What is a unity of functional and structural changes in pathogenesis of disease?
12. What are concepts of "leading element on pathogenesis," "vicious circles" and "trigger"?
13. What are features of pathological system and its role in development of disease?
14. What are similarities and a differences between adaptation and compensation?
15. Role of genetical apparatus in formation of long-term reactions of adaptation and compensation?

Tasks for self-managed student work:

1. History of pathophysiology, main stages of its development.
2. Terminal states.
3. Postresuscitative disorders.

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