**THE ROLE OF EXTERNAL AND INTERNAL FACTORS IN PATHOLOGY. PATHOPHYSIOLOGY OF HEREDITARY, REACTIVITY , CONSTITUTION.**

*Mechanical factors may be not only of exogenous but also endogenous origin(pressure of hemorrhage or growing tumor on the surrounding tissue).*

The number of disease caused by mechanical trauma is especially great in the war. Therefore, N.I. Pirogov called wars “epidemic of traumata”. The main causes of traumata in the time of peace are occupational and transport accidents.

In the damaging action of the mechanical energy the most different combinations of the powers are observed which cause strain, compression, bend . When the loading exceeds the limit of solidity of corresponding structures their destruction (fracture of bones, rupture of muscles and ligaments), dislocation of bones in joints, damage of skin occur.

Resistance to rupture of combination of tissues which form the structure of the organ is more than that of the separate tissues. For instance, more power is required to pull out thighbone from the hip joint of the corpse than to rupture the bone and tendon separately.

Repeated influences are more pathogenic. They weaken ligamentous apparatus, work joints loose, cause habitual dislocation.

Contusions are inflicted by blunt instruments, wounds are made by cutting or pointed instruments.

*The wounds cause in the organism, besides the local changes, also the general changes.*

In general reactions caused by wounds in the organism 2 stages are distinguished. In the first stage (1-4 days) the sympathetic nervous system is activated and a great amounts of adrenaline enters the blood. Simultaneously production of glucocorticoids in the adrenal cortex is increased. For the second stage (4-10 days) activation of the parasympathetic nervous system, increase of secretion of mineralocorticoids and hormones that intensify the regeneration, is characteristic. All of these changes accelerate healing of the wounds.

Blows to the epigastric region, extensive wounds, fracture, crushing of tissues may give rise to the most severe general morbid phenomena-traumatic shock. This is a special state of organism produced in neuroreflex way by the action of an extraordinary stimulus and manifested in an acute circulatory disturbance with a sharp drop in blood pressure, respiration, metabolism, etc. The traumatic shock may result in death.

The traumatic shock may develop at the moment of injury or soon afterwards, more frequently- within 4-6 hours and later. Its pathogenesis is based on disturbances in the function of the central nervous system (excessive stimulation of the extero- and interoceptors evokes strong excitation with subsequent protective inhibition in the cerebral cortex).

Overload causes the sensation of weight in all the body , sense of pain, difficulty and then complete absence of possibility of voluntary movements, displacement of soft tissues and some internal organs in the direction of action of overload.

For craniocaudal overload visual disorders(weakening of the peripheral vision, then weakening and even loss of the central vision) are characteristic; they are caused by the disorders in the hemodynamics of brain and retina. The caudocranial overload causes intense sensation of pain in head and eyes, hemorrhage into sclera and eyelids. For the transverse overload difficulty in breathing and sensation of pain in epigastric region are characteristic.

Disturbances of hemodynamics and respiration play the leading role in the mechanism of disorders of organism’s functions during overload.

The influence on the organism of more or less protracted and changing accelerations causes kinetosis, that is, motion sickness (sea sickness, air sickness, automobile sickness, etc.). So, kinetosis is complex of pathological processes emerging as a result of slight and continuously repeated concussions and accelerations which cause irregular movements and changes in the position of the body. In kinetosis the disorders are manifested in disturbed functioning of the nervous system, especially in stimulation of the vestibular apparatus. At the same time the interoceptors of the internal organs (especially those of the stomach) are stimulated. This gives rise to general weakness, disturbances in neuromuscular coordinations, dizziness, nausea, vomiting, excessive sweating, slow heart action, drop in blood pressure. In severe cases depression, asthenia, disturbance of consciousness are observed.

*Kinetosis develops in persons with the hypersensitivity of vestibular apparatus and an easily excitable vegetative nervous system.*

The pathogenic action of the weightlessness (zero-gravity) on the organism is less than that of overload. It causes the sensory (disorientation, sensation of heel, dizziness), motor (reduction of exactness of movements, disturbance of precise coordinated acts, reduction of muscular strength of hand) and vegetative (changeability of physiological indices, more frequently- decreased blood pressure, tachycardia and then bradycardia, rapid, normal and then slowed - up breathing, concentrated diuresis) changes in the organism.

On the ground the blood pressure in the feet is 100 mm Hg higher than on the level of heart and in the blood vessels of the brain it is 30-40 mm Hg lower .In the conditions of weightlessness the hydrostatic pressure of blood in vessels disappears and this difference is smoothed. The blood is distributed evenly in all vascular areas and more blood is accumulated on the upper part of the body than on the ground; the sensation of heaviness in the head and swelling in the face come into being.

The organism loses more sodium , potassium, calcium, etc. The destructive changes in muscular system and bones (osteoporosis ) develop. Capacity for work and endurance of the organism against the physical load are diminished.

Man gets used to the weightlessness gradually during 3-7 days.

When the cosmonauts come back on the Earth after being accustomed to the conditions of weightlessness they fell excessive heaviness in the body and find it difficult to take the vertical position .They are quickly tired even during the easy physical work. The disturbance in the coordination of movements is observed.

The sound vibrations that are perceived by the human ear (16-20000 cycles per second) may become pathogenic and cause an acoustic trauma only when being excessively intense and acting for a very long period of time. Disorderly combinations of sounds of different pitch and frequency , that is , intense noises are especially harmful to the organism.

The sound stimuli of 120 decibel cause pain in the organ of hearing ,those of 140 decibel- pathological changes in the middle and internal ear. More intensive sounds cause sensations that are not connected with the acoustic analyzer (cramp, paralysis, complete loss of consciousness).

The regular action of noise during a long time causes deafness. The intensive (100 decibel and more) noises disturb the higher nervous system (rapid fatiguability, aggravation of memory, reduction of attention, capacity for work, increased irritability, etc.). The noises of large intensity and high frequency cause the functional disorders in cardiovascular system, instability of blood pressure, changes in ECG, increased lability of the nervous system, etc.

Since ultrasound (sound waves above the audible limit of 16000- 20000 cycles per second) is widely used in industry and medicine, it is particularly important to study its pathogenic influence on the organism.

Employment of ultrasound in diagnosis is based on the fact that these waves are absorbed and reflected differently in different biological mediums and structures. Ultrasonic therapy is based on the thermal and mechanical actions of the ultrasound. The ultrasound of insignificant power increases permeability of cell membrane, activates the processes of tissue metabolism. It has also the bactericidal action.

Intense ultrasonic waves cause pathological changes in tissues. Ultrasound influences tissues by the mechanical, thermal and chemical ways.

The mechanical influence of ultrasound is connected with spreading of acoustic waves which cause the formation of many microscopic bubbles in the liquid mediums of the organism(cavitation). As a result of cavitation the tissues are demolished (cell membranes are destroyed, nuclei are damaged, chromosomes are crushed, protoplasm is vacuolized).

As the ultrasound accelerates vibration of molecules, much thermal energy is formed in tissues and they are warmed up.

Ultrasound causes ionization and formation of chemically active and toxic substances (free radicals, cyanide, ammonia, etc.) which cause disturbance in the colloid systems, denaturation of proteins, increased permeability of the biological barriers, etc. The pathogenic influence of the ultrasounds is connected also with the reflex reactions.

The nervous system, endocrine glands, cardiovascular system, organ of hearing are particularly sensitive to the influence of the ultrasound. In specialists that work with ultrasound for a long time and persons that were exposed to the influence of powerful ultrasound disturbances in the nervous and cardiovascular systems, fatiguability, headache, insomnia, increased irritability, emaciation, trembling of hands, increased sweating, disturbances of the thermoregulation are observed.

Considerable changes of the external temperature may damage the organism. Both heat and cold cause general and local changes in it.

*General action of heat on the organism may cause overheating (hyperthermia) . Under conditions facilitating heat loss man can tolerate the surrounding temperature of 50- 60o C, whereas under conditions making heat loss difficult (in humid air or when physical work is done in warm clothes) overheating may take place at 30 –35 o C.*

Since the thermoregulatory mechanisms of infantile organism is not yet completely developed, the babies are subjected to overheating more easily.

Two stages of hyperthermia are distinguished: compensated and decompensated . If the thermoregulatory mechanisms cannot ensure maintenance of the constant body temperature, then decompensation occurs.

Under conditions of overheating the blood vessels of skin dilate, the blood flow in them is accelerated, increased respiration, tachycardia are observed. As a result of excessive sweating organism loses much water and mineral substances. Thickening of the blood (pachyhemia) and increase of its viscosity make difficult the blood circulation and lead to heart failure.

Overheating is accompanied at first by excitation and then- by depression of the functions of the nervous system , general weakness. In 39-39.5 o C reversible changes are observed in the organism (loss of consciousness, cramp, respiratory and circulatory disorders). Hypoxia develops in tissues. When the body temperature reaches 42 o C the metabolism in cerebral tissue is sharply disturbed.

In severe cases reflexes are lost, comatose condition develops, the end is paralysis of the heart and death.

The acute hypothermia which is accompanied by the rapid increase of temperature (sometimes up to 42-43 o C) is called heat stroke (heat apoplexy).

The sunbeams failing on the bare head may cause sunstroke. First the activity of the central nervous system is disturbed and this results in respiratory and circulatory disorders, increased body temperature and so forth.

Ultra-red and ultra –violet rays penetrate inside and damagemeninges and nervous tissue.

The local changes caused by heat in the organism are burns. Beginning from 45 - 50o C the thermal factor (hot water, heated metal, fire, etc.) causes injury to the surface of the body.

Four degrees of burns are distinguished:

1 – erythema (reddening );

2 – formation of vesicles:

3 A- partial necrosis of skin (of superficial layers);

3 B – complete necrosis of skin (of all its thickness);

4 – necrosis embracing not only the skin , but also muscles, bones, etc.

The inflammatory edema in skin and subcutaneous fat protects more deep tissues from the damage. Therefore, burns caused by hot water and steam are superficial, and burn shock occurs rarely (vesicles and edema develop rapidly).

The general changes in the organism resulting from burns depend on the degree of the burn and size of the burned area. If one – third of the body surface (in the II degree burns ) and even less (in the III and the IV degree burns ) is damaged the organism perishes. In cases of vast and severe burns death occurs instantaneously or within 2-3 days. Early death is due to the burn shock.

The vast burns cause severe and prolonged disturbances in the general state of the organism, that is, the burn disease develops.

The general picture of burn is characterized by disturbances in nervous activity, change (rise and then drop) of blood pressure, respiratory disorders, hemoconcentration (passage of plasma through the capillaries into the injured tissue), relative increase of the number of erythrocytes, phenomena of hemolysis, accumulation of toxic products of tissue decomposition, rise of body temperature, development of infection (that has gained entrance into the wound). In protracted cases the kidneys are affected, urination is disturbed and anuria (arrest of urinary output ) develops.

*In the course of the burn disease the following phases are distinguished:*

1. *burn shock (in the first minutes or hours);*
2. *burn toxemia (in the first twenty four hours);*
3. *burn emaciation (in the late periods of the disease).*

The burn shock is caused by the pain sensation and excessive irritation of the nervous system. Pathogenesis of the burn toxemia is connected with poisoning of the organism by toxic products of tissue origin.

In the blood serum of persons that were recovered after the burn , autoantibodies were found which act against the burn .

The general effect of cold on the organism causes overcooling (hypothermia) . It develops as a result of drop in external temperature and inability of the organism to regulate its own temperature. Increased heat loss, diminished heat production and metabolism , poor nutrition, inadequate clothing promote development of hypothermia.

The utmost low temperature of the organism permitting restoration of functions when rendering the medical aid is called “the biological zero” . The temperature slightly higher than the biological zero causes the state of cold narcosis , that is , reversible suppression of movements and sensitivity . For man the biological zero is 24-26 o C , and 31-35 o C causes the cold narcosis.

The compensatory reactions under the influence of cold are chiefly of reflex character: constriction of peripheral vessels , decrease of respiration raye, shivering, etc. The further influence of cold causes decompensation: decrease of metabolism and body temperature , cessation of muscular shivering , dilation of peripheral vessels. Function of cerebral cortex is inhibited (the state of cold narcosis), then subcortical and bulbar centers are depressed , blood pressure is decreased , breathing is rare and sometimes –periodic . The death occurs as a result of respiratory standstill.

Sudden cooling of separate parts of the body surface or of the whole body underlies various chills which frequently lead to appearance or aggravation of inflammatory processes (bronchitis, endocarditis, nephritis, etc.) . In the mechanisms of development of diseases caused by chill the allergic reactions take part. Hypercryesthesia (hypersensitivity to the cold) in some persons is connected with formation of autoallergens under the influence of the cold and autoantibodies against them.

Alcoholic intoxication, wound, exhaustion, emaciation, alimentary dystrophy promote freezing.

To slow down metabolism with the purpose of operation on vital organs such as brain, heart lungs the artificial hypothermia (hibernation) is caused by the way of physical cooling on the background of pharmocological preparations blocking the nerve conduction ( myorelaxation drugs).

*The local disturbances caused by the action of cold are called frostbite. It is more frequently observed in fingers and toes , ears, nose, cheeks, jaw.*

*Four stages of frostbite are distinguished:*

*1 – superficial damage of epiderm;*

*2 – damage of the basal membrane of skin – formation of blisters;*

*3 – necrosis of skin and subcutaneous fat;*

*4 – necrosis of soft tissues and bones.*

The visible part of light rays does not cause pathological processes in organism. Only very strong rays when influencing the diencephalohypophyseal area (visual ceptors – visual center – vegetative centers of hypothalamus ) cause disturbances in the vegetative functions, temporary loss of vision.

The chemical and weak ionizing action of the ultra- violet rays (by the length of wave their place is between X- rays and visible rays) on the skin is of great significance for the organism. But excessive irradiation causes a number of pathological processes.

The ultra – violet rays take part in the formation of pigmental cover and in the vitamin D metabolism . Lipides that are in the cell membrane , are oxidized under the influence of ultra – violet rays , and their functional properties are disturbed. Antioxidants that are in cell protect the lipides of biological membranes from the processes of photooxidation.

When the dose of irradiation is high, a large amount of histamine is formed in the cells of skin which causes erythema. Ultra- violet rays have bactericidal action , they stimulate the immunogenic reactivity.

Action of ultra – violet rays on the eyes (welders, medical workers of quartz cabinets, mountain climbers) cause pathological changes in the sclera ( photo – ophthalmia): pain in the eyes, hyperemia and edema in vision. These local changes are accompanied by general ones: headache, malaise, insomnia, tachycardia.

Mechanism of changes caused by ultra – violet rays are based on humoral and neurogenic reactions.

Under the influence of high doses of ultra –violet rays on the skin the erythrocytes are hemolysed. Some substances (photosensibilizers ) such as fluorescein, porphyrin , cholesterol, lecithin – strengthen this effect (photohemolysis ) as well as burning effect of ultra –violet rays on the skin. The changes of skin in porphyrya (a hereditary disease ) is connected with photosensitization. These persons are sensitive to sunbeams which cause formation of erythema and vesicles on the skin and then – deformation , ulcer, cicatrization.

Some ultra –violet rays (290-380 nm long waves) has cancerogenic action.

Infrared rays exercise on the organism mainly warming and burning influences. Their action may be local (increase of vascular wall permeability , dilation of vessels , exudation) and general (acceleration of metabolism , increase of temperature , disturbance of thermoregulation and heat stroke).

The X-rays , streams of neutrons and protons , α, β, γ particles penetrate into any object, and therefore, they influence the organism from the external as well as internal sources of radiation (they enter the body with food and water , through the skin).

Since the same amount of ionizing radiation of different kinds cause different biological effects, to evaluate the degree of damaging effect of ionizing radiation on the biological objects the coefficient of relative biological effectiveness is used. The damaging dose of α - radiation , neutrons and protons is 10-20 times more than that of X –rays , the biological action of which is taken as 1. The lethal dose (LD-50 ) of the ionizing radiation for man is 400R.

Ionizing radiation causes physical , physicochemical and chemical changes in biological substrata. The ionizing radiation causes formation of a whole complex of radiotoxins (free radicals , peroxides, ketones) which stimulate formation of other biologically active substances (quinones, histamine) and cause concentrated disintegration of proteins (albuminolysis).

Disturbances of ultrastructures of cell organoids and metabolic changes connected with them form the base of radiative injury of the cells.

Ionizing radiation causes in the organism local (cataract, burns, breach of mucous membrane) and general changes. Severity of the general changes depends on the dose of the radiation. The dose more than 10000 R causes mass scale death of cells and tissues, and death of organism within several minutes to several hours. 600R leads to death during 10 days. The dose of radiation less than 600R causes the development of radiation illness.

Acute and chronic forms of the radiation sickness are distinguished . Acute radiation sickness results from single exposure of the organism to large doses of radiation, whereas repeated small doses cause chronic form of the sickness.

*In the clinical course of the acute radiation sickness four periods (not strictly defined) are distinguished:*

*I - initial period (1-2 days);*

*II - latent period (1-2 weeks);*

*III - period of marked manifestations (from several days to 2-3 weeks);*

*IV - outcome.*

So, as distinct from other diseases , in radiation sickness the prodromal (initial) period comes first, and then – the latent period. The initial period begins a few hours after irradiation, then the morbid phenomena (overexcitation of the nervous system, general intoxication, intense headache, dizziness, quickening of the pulse, dyspnea, nausea, vomiting, high temperature, lymphopenia) disappear and the latent period begins, in which lymphopenia and trombocytopenia may develop and reticulocytes may diminish. In severe cases the first period may be directly followed by the third period in which the main disturbances are most strongly pronounced: the high temperature, headache, nausea, vomiting, signs of circulatory disturbances in the brain , inflammation and ulcerations of the mucous membranes, disturbance of the function of the gastrointestinal tract and metabolism, protein decomposition, depression of hematopoiesis, leukopenia, thrombocytopenia, sometimes agranulocytosis, progressive anemia, signs of bone marrow cachexia, hemorrhages into internal organs. The sputum, urine, feces, vomit are stained with blood. Affections of the central nervous system are observed very early: disturbances in the intensity , mobility and balance of the excitatory and inhibitory processes, depression of reflex activity, neurovascular and neurotrophic disorders (especially those of the skin) in the form of alopecia and ulcerations, and dysfunction of the hypohpysis, adrenals and gonads.

In the fourth period gradual restoration of the functions impaired by the sickness takes place or the disease takes a protracted course and becomes chronic.

Chronic radiation sickness is characterized by disorders of the functions of the nervous system and especially disturbances in hematopoiesis (leukopenia) , appearance of megalocytes, megaloblasts , myelocytes).

Eventually ionizing radiation may have a cancerogenic effect and cause disturbances in the chromosomes of the germ cells.

Monochromatic light – pencils of extraordinary intensity and with a small angle of divergence that are given off by optical maser (laser rays ) are applied as means of treatment . But if their dosage is broken they exercise damaging action on the living structures. The laser rays penetrate 20 – 25 mm into the organism and act during one hundred thousandth of second. Therefore, the pain is not felt.

The mechanism of damaging influence of laser rays depends on their thermic, mechanical (explosive effect causes cavitation), biological (formation of toxic substances in tissues that probably cause necrosis) effects and inactivation of tissue enzymes. Tumors are more sensitive to the action of laser rays.

The phenomena resulting from contact with electric energy depend on the properties of the current (tension , strength, frequency, direction, duration of action) and the functional state of the organism. Direct current acts faster , but alternating current is more dangerous at a relatively low tension and low frequency. Because tissues offer less resistanse to alternating than to direct current. The complete resistence of human body against alternating electric current (impedance) is formed of active (ohmic) and reactive (capacity) resistances.

Electric current of 40V with a frequency 40- 60 cps is not dangerous for human organism. Tension up to 100 V is conditionally pathogenic, 200 – 500 V absolute pathogenic and relatively lethal, above 500 V – absolute lethal.

Alternating current with a frequency of 40 – 60 c p s is the most dangerous to life. Increase in the frequency diminishes the harmful effects of the current. High frequency currents are not dangerous and are even used for therapeutic purposes (for example, d’ Arsonval current).

The harmful influence of current will be much greater when exerted on moist skin (dry human skin offers greater resistance to electric current). Electric current causes death sooner if it passes through head or heart.

The mechanism of damaging action of electric current is connected with its biological (excitation of muscles, glands, receptors, etc.), electrochemical (electrolysis), thermal (burns) , mechanical (tearing off parts of body) influences.

Electric current causes local and general changes in the organism.

Action of electric current on the body surface produces a burn which oftenly is shaped like the conductor that made contanct with the body. Wounds resembling those resulting from a gunshot are formed at the sites of entrance and exit of current . The branchy redness (caused by the paralysis of blood vessels) around the damaged tissues (“electrical burn”) is characteristic. In some cases after the action of the electric current necrosis of the affected portions of the skin and underlying tissue may develop.

An ultra – high frequency alternating electric field (short and ultra- short waves) produces mainly electrothermal effect and causes some electrochemical reactions. It intensifies protein metabolism and phagocytosis, produces bactericidal effect. Law – tension ultra – short waves are for therapeutic purposes in various inflammatory processes.

Under experimental conditons high tension decimetre and centimetre waves caused disorders of the nervous system function with subsequent circulatory disturbances and even death.

Changes in the organism are observed in cases of both lowered and elevated atmospheric pressure.

The disease developing as a result of lowered atmospheric pressure (hypobarism) affects persons climbing high mountains (mountain sickness), pilots flying at high altitudes without oxygen masks (altitude sickness), etc.

The pathogenic influence of altitude on the organism is connected with hypoxia, that is, decrease of oxygen’s partial pressure.

Lowered atmospheric pressure (beginning from the altitude of 4000- 5000 m ) gives rise to various functional disorders: fatigue, dizziness, headache, tinnitus, dyspnea, tachycardia, diminished conditioned reflex activity, metabolic disturbances. Prolonged staying at an altitude of 7000 – 8000 m results in unconsciousness and even death. All these phenomena are intensified by increased oxygen requirements connected with muscular work ( mountain climbing) and increased rate of ascent.

The decompression disturbances are observed : meteorism, pain in abdomen , antrum of Higmore , middle ear. At the altitude of more than 9000m gas embolism is possible by the vesicles of gas that are going out of tissues as a result of decreased solubility of gases.

The action of rarefied air on the organism develops a number of adaptive phenomena: reflex acceleration of respiration and increase in pulmonary ventilation, acceleration of the blood flow, contraction of the spleen and stimulation of the hematopoetic apparatus (leading to increase in the erythrocytes of the blood and of its oxygen capacity).

Elevated atmospheric pressure (in deep-sea diving, caisson work, etc.) also causes pathological states in the organism (hyperbarism).

By each 10 m of depth the pressure on the body surface increases on 1 atmosphere. So, at a depth of 20 – 25 m under water the pressure on diver’s body is 3 – 3.5 atmospheres. Morbitic effect of elevated atmospheric pressure may appear after a few hour’s stay under a pressure of 2 – 3 atmospheres : the pulse and respiration slow down , the blood pressure rises and internal organs overfill with blood.

In conditions of elevated atmospheric pressure a large amounts of gases ( especially nitrogen and oxygen ) are dissolved in the blood and colloidal solutions of tissues (saturation) .

In cases of rapid return from elevated to normal atmospheric pressure (decompression ) the gases formerly dissolved in the blood ( chiefly nitrogen ) are liberated in the form of bubbles ( desaturation ) and obstruct small vessels, the state called caisson disease. Pains in the muscles and joints develop, the skin itches, respiration and circulation are disturbed. Severe cases are accompainied by paralyses, convulsions, unconsciousness. Owing to resorption of the gases these phenomena often disappear.

The person must be rapidly returned into the condition of elevated atmospheric pressure and then slowly lifted.

To prevent the development of decompression illness (caisson disease) the mixture of helium with oxygen is applied and the maximum speed of lifting is established.

Chemical substances may produce various effects on the organism. Frequently they cause poisoning. Depending on the dose, the same chemical substance may produce therapeutic or toxic effect, or even cause death.

Exogenous and endogenous poisons are distinguished. Food poisoning, occupational poisoning, drug poisoning, poison gas are of exogenous nature. Poisoning with endogenous substances (metabolites and products of tissue decomposition) is called autointoxication (self – poisoning). This may develop as a result of dysfunction of excretory organs, abnormal processes of absorption from intestines, metabolic disorders (for instance, in diabetes mellitus, liver pathology, infectious diseases).

Toxic substances may be inorganic (acids, alkalis, salts of lead, mercury, arsenic and copper) and organic (cyanide compounds, phenol, chloroform). Among the organic poisons there are substances of vegetable origin (alkaloids, glycosides) and animal origin (animal alkaloids, snake venom, ptomaines, products of putrefaction).

Chemical substances producing general toxic effect (cyanide compounds, narcotics), affecting the blood (potassium chlorate, pyrogallol, carbon monoxide), affecting the liver (carbon tetrachloride, phlorhizin), asphyxiating (chlorine, phosgene), affecting the nervous system (strychnine, arsenic) may be distinguished. But all of them affect the nervous system, which is particularly sensitive to many poisons.

The neurotropic drugs (narcotics, hypnotic, and neuroleptics) influence different parts of the nervous system. Poisons affect synaptic contacts. Prussic acid paralyzes the cell respiration by the way of blocking the respiratory enzyme cytochrome oxidase. The action of compounds of arsenic and heavy metals is explained by their interaction with sulfhydryl groups of enzymes.

The chemical pathogenic factors include also the cancerogenic substances and allergens. Some of them cause mutations and congenital malformation (teratogenesis).

Nutritional factors (underfeeding, malnutrition, overfeeding, vitamin deficiency, lack or excess of salts, altered composition of water) as factors of the external environment are causes or conducive to appearance and development of diseases.

Action of biological factors on the organism is extremely diverse.

Plants may exercise on the organism the following actions:

1. fruits and juices of some plants (ergot, henbane, poppy, poisonous fungi) exert toxic influence;
2. some plants (nettle) secrete poisonous liquid which causes inflammation in skin and mucous membranes;
3. thorns of some plants damage the human body;
4. some plants cause allergic reactions.

The principal group of pathogenic biological factors include microorganisms (bacteria, viruses, rickettsia, fungi, protozoa).

Animals exercise the following influences on the human organism:

1. mechanical traumata (bite, sting, blow);
2. zoonozes, that is, the infections which are infected by animals (plague, brucellosis, lyssa);
3. helminthic invasion (ascariasis);
4. action of poisonous excreta of animals (snake, scorpion, phalanx, bee, some poisonous insects, fish).

Since human beings possess the second signaling system (speech) and well-developed higher nervous activity, the mental (psychical) factors acquire a great significance in the diseases of man.

Overstraining of higher nervous activity and a clash between the processes of excitation and inhibition in the cerebral cortex may lead to disturbances in corticosubcortical interrelations and cause vegetative disturbances (respiratory and cardiac dysfunctions, rise in blood pressure, spasm of coronary vessels, etc.).

***Heredity is the property of living organisms to develop the morphological,physiological , biochemical peculiarities determining the specificity of the individual development of their parents or more remote ancestors.Being inseparably connected with reproduction,heredity ensures the continuity of generation.***

In spite of the elegance and precision of mitosis and meyosis,these processes sometimes fail to deliver a diploid complement of chromosomes to a gamete resulting in what is called an unbalanced chromosomal abnormality.Such chromosomal abnormalities can be either germinal or somatic.Any alterations in genes cause corresponding changes in the hereditary signs which may be inherited.

Spasmodic changing of hereditary signs is called mutation. Germinal mutations are hereditary, whereas somatic mutations influence only the organism in which they arise.

Pathological mutations form the basis of hereditary diseases.

The diseases conditioned by heredity must be distinguished from pathological phenomena arising as a result of influences exerted on the fetus during its intrauterine development,for instance,infection of the fetus with syphilis through the placenta,intoxication of the fetus with alcohol,transplacental transmission of certain characteristics of the maternal blood,as inherited thrombocytopenic purpura and intrauterine deformation of the fetus,The latter may be caused by changes in the egg membranes,diminution in amniotic fluid or pressure on the gravid uterus.These pathological phenomena are called congenital and are diseases acquired in uterus.

On the other hand,the first signs of a number of hereditary diseases manifest themselves much later after the birth of the child (for instance,Friedreich’s disease-at 6-12 years,cerebellar ataxia at 20-30 years).

Also, hereditary diseases and familial diseases must be distinguished. Because familial diseases include, besides the hereditary diseases, also the diseases that develop in several members of one family as a result of the identity of the external environment (for instance, tuberculosis in several members of one family).

Mutations occur as a result of the action on the organism and its hereditary apparatus of different physical,chemical,biological factors of the external environment which are called mutagenous factors: radioactive, Roentgen,ultroviolet rays,free radicals,formaldehyde,phenol, derivatives of purine and pyramidine,steroid hormones,drugs of cytostatic action (such as theobromine,caffeine) , some viruses (measles, rubella, infectious hepatitis) etc.

As all the ordinary genes, the mutant genes also may be dominant and recessive. The sign belonging to the dominant gene in all cases manifests itself in the phenotype of the organism, whereas recessive sign is distinctly manifested in the phenotype only when it is in the homozygous state (that is, when allele genes located in both pairs of the chromosomes are changed).

By their action on the morphological and functional properties of the organism mutations may be useful,neutral and harmful.As a decisive factor of the natural selection the useful mutations form the basis of evolution of the living world.

According to their influence on the viability ( vitality ) of the organism the lethal and non-lethal mutations are distinguished.Most of lethal mutations are inherited as recessive characteristics. Because lethal mutations of dominant characteristics cause death of the first generation.

Mutations may embrace different levels of the genetic apparatus of cells: genes, chromosomes and genome.

Genic mutations are connected with the changes in the chemical structure of genes, that is, one or several nucleotides are replaced by others. In most cases the developmental anomalies arise from genic mutations.

Chromosomal mutations may be of four types which result from breakage and rearrangement of specific chromosomes:

1) translocation-transference of part of the chromosome to the other chromosome;

2) deletion – crushing and loss of part of the chromosome ;

3) duplication – lengthening of the chromosome as a result of the repetition (doubling ) of some segment;

4) inversion – overturn of some segment of chromosome.

Some structural changes (aberrations) may take place in one chromosome.

The chromosomal mutations manifest themselves as developmental anomalies of different character in the phenotype of the organism.

Genome mutations are the changes of the number of chromosomes in the karyotype.Frequently they include trisomy (existence of 3 homologous chromosomes instead of 2) and monosomy (absence of one of the twin chromosomes).

Genome mutations terminate in spontaneous abortion or cause chromosomal diseases.

So, trisomy refers to the presence of a single additional chromosome in the cell and trisomic cells contain 47 rather than 46 chromosomes while monosomy refers to the absence of a single chromosome and monosomic cells contain only 45 chromosomes.

The karyotype of a male cell trisomic for chromosome 21 is written 47 XY,+21,while a female cell trisomic for chromosome 13 would be designated 47 XX,+13. Similarly,a male cell monosomic for chromosome 21 would be designated as 45 XY,-21.

In addition to trisomy and monosomy, other rarer types of numerical chromosome abnormalities include triploidy (3n), in which each cell contains three copies of every chromosome or 69 total chromosomes, and tetraploidy (4n ), in which each cell contains four copies of every chromosome or 92 total chromosomes.

Approximately one in 200 liveborn babies has a detectible chromosomal aberration. Of these, about one third are trisomic for either chromosome 21 , chromosome 18 , or chromosome 13. Another one third have numerous abnormalities of the sex chromosomes, the most common of which are 47 XXY ( Klinefelter ‘s syndrome), 47 XYY syndrome, 47 XXX (triple X syndrome), 45 X (Turner’s syndrome or Shereshevsky – Turner syndrome). The remaining one third of newborns with chromosomal abnormalities have structural rearrangements of chromosomes, most of which are balanced reciprocal translocations, and which do not lead to clinical abnormalities.

The incidence of chromosomal abnormalities in spontaneous abortuses is remarkably higher than that in live births.

Diverse methods are used to study the hereditary diseases:

1. Spreading of the hereditary diseases in different geographical zones is studied by the help of the statistical method.

2. The genealogical method consists of learning the family – tree in the families where the hereditary diseases are spread. This method allows to ascertain the types of inheritance of hereditary diseases and to distinguish them from similar non – hereditary diseases.

3. The karyologic method consists of studying the number and structure of chromosomes which are included in karyotype.

4. The method of twins permits to study the role of the heredity and factors of the external environment in the origin of diseases.

5. The method of experiment allows to study the hereditary diseases on the animals. By this method hemophilia (on dogs), muscular dystrophy (on hens) ,achondroplasia (on rabbits), hypophyseal dwarfness (on mice) were investigated.

6. Determination of the sex chromatin is used in the diagnosis of Shereshevsky – Turner’s syndrome, triple X syndrome, Klinefelter’s syndrome. The sex chromatin is observed in the cells in the nucleus of which there are no less than two X chromosomes. If there are several X chromosomes the number of sex chromatins is one less than their number.

7. The immunogenetic method is applied to establish the antigenic incompatibility between the maternal organism and fetus in the diagnosis of the diseases connected with the immune system pathology.

8. Methods of biochemical analysis are used because the principal pathogenetic factor of most diseases which originate as a result of genic mutations, consists in disturbance of the biosynthesis of certain protein molecule (enzyme).

9. Dermatoglyfics is used in the diagnosis of Down’s syndrome. It is based on the study of the structure of the skin in the palm of the hand . In 40 per cent of cases of Down’s syndrome “the monkey furrow “ (the deep transverse furrow in the palm) and in 20 – 25 per cent of cases only one fold in the internal surface of the little finger are observed (in general population these signs are found in 1 per cent and 2 per cent of cases accordingly).

The following methods of prenatal diagnosis of hereditary diseases are applied :

Amniosentesis – amniotic fluid can be aspirated transabdominally from the uterus at 16 weeks of gestation.

Direct analysis of abnormal gene structure – since not all genes are expressed in amniotic fluid cells.

3. Restriction fragment length polymorphisms – random , single – copy human DNA

sequences are used as probes to detect RFLPs tightly linked to genes that resulted in human disease.

4. Visualization of the fetus – ultrasonography allows direct visualization of the fetus.

5. Fetal chorionic biopsy – amniosentesis has to be performed in the second trimester, the technique of fetal chorionic biopsy allows to obtain fetal tissue samples in the first trimester of pregnancy .

According to clinical manifestations the hereditary forms of pathology are divided into 3 groups:

1 ) Hereditary predispositions ( for example , heightened sensibility to the antimalarial preparation primaquine);

2 ) Hereditary diseases ;

3 ) Malformations (monstrosities, teratisms), that is, the special form of the hereditary diseases (polydactylism , syndactyly – symphysodactylia , brachydactylia ,arachnodactyly – spider fingers, etc.)

According to the number of mutant genes monogenous and polygenous hereditary diseases are distinguished . The diseases caused by genic mutations are called genic (monogenous) diseases. These are inherited by Mendel’s laws. The polygenous diseases include, in the first place, those connected with the hereditary predisposition .

The diseases caused by chromosomal and genome mutations are united in the group of chromosomal diseases.

According to the way of inheritance , the genic diseases are divided into three groups:

1 ) autosomal dominant diseases ;

2 ) autosomal recessive diseases ;

3 ) X – linked diseases.

When mutation of only one of the two alleles at a particular autosomal genetic locus is sufficient to result in a characterictic disease , that disease is called an autosomal dominant disorder. So , the hereditary diseases of this type are manifested in the organisms which are heterozygous carriers of the pathological gene .

On the average 50 per cent of the offspring of a person with an autosomal dominant disease married to a normal individual will have the same disease, while 50 per cent will be normal and not carry the mutant allele.

Usually the autosomal dominant diseases do not influence the reproductive function of the organism and do not shorten the life – span. Therefore, they may be inherited for a long time from generation to generation.

The following diseases are inherited by the autosomal dominant way : polydactylia, syndactylia , brachydactylia, achondroplasia, Huntington’s chorea, Recklinghausen’s disease (neurofibromatosis), congenital hemeralopia, cerebellar ataxia, etc.

The autosomal – recessive diseases manifest themselves only in homozygous carriers of the pathological gene, that is, mutation of both alleles (in both parents) at a particular autosomal genetic locus is required to result in a disease, while the same mutation at only one allele leads to no clinical abnormality. Such diseases are more frequently observed in persons the parents of which are in blood relationship. Because it is more probable for genetically close persons to be carriers of the same recessive mutation.

When both of parents are recessive carriers of disease, on an average 25 per cent of children become ill , 50 per cent – recessive carriers and 25 per cent – healthy ( 1:2:1 ). If both parents are ill,theoretically the signs of disease may be found in all children. But in some cases in children of parents with albinism the signs of this disease are not found. When one of parents is heterozygous (phenotypically healthy) and other – homozygous (phenotypically ill ), then in 50% of children the signs of disease are observed while are healthy (but are recessive carriers of the same disease).

The following diseases are inherited by the autosomal recessive way : congenital dea-mutism, cystic fibrosis of pancreas, albinism,Tay – Sachs disease ( amaurotic idiocy ), other inborn errors of metabolism (phenylketonuria, alkaptonuria, fructosuria, histidinuria), ect.

Since many more genes are present on the autosomal chromosomes , most dominant and recessive diseases are autosomal rather than X – linked.

Sex – linked (or X – linked ) diseases are due to mutation at a locus on the X chromosome (genes on Y chromosome are not known to cause any sex – linked disorder and therefore, all sex – linked disorders are, in fact , X – linked disorders).

Up to 60 human disorders are revealed which are inherited through X chromosome.

X – linked recessive diseases also may be either dominant or recessive.

X – linked recessive diseases are: hemophilia, Duchenne’s muscular dystrophy,daltonism (colour blindness), etc. Since women’s cells possess two X chromosomes,and homozygous forms of these mutations in most cases are lethal,these diseases are found chiefly in men, and only women may be carriers.

If the father is healthy and the mother is heterozygous carrier of X – linked recessive disease,then 50 per cent of sons are ill and 50 per cent – healthy, whereas 50 per cent of daughters are heterozygous carriers of disease and 50 per cent – genotypically healthy.

X- linked dominant diseases are rare among human beings. One of them is hypophosphatemic (resistant against vitamin D) rickets. The signs of this disease may be manifested in heterozygous as well as in homozygous carriers. It is found in all doughters of diseased man with healthy woman, whereas their sons are healthy . Because father’s X chromosome may be inherited only by daughter.

Most of chromosomal diseases arise as a result of mutations originated in the process of gametogenesis ( development of sex cells), and they are observed in children of healthy parents . Some of these diseases cause infertility, and the persons with some chromosomal mutations do not live up to the reproductive period . Therefore, such diseases are not found in several members of one family .

Up to now more than 750 types of chromosomal anomalies were informed . Most of them are accompanied by anomalies of skeleton and internal organs .

Different forms of chromosomal diseases have a number of similar aspects. In most of them deformities of skeleton ,mental disorders, congenital defects of internal organs, pathological changes of nervous and endocrine systems are revealed, life – span of patients is shortened and reproductive ability is absent.

The chromosomal diseases are divided into two groups :

1) abnormalities of autosomal chromosomes (Down’s syndrome, Edwards’ syndrome (trisomy 18), trisomy 22, Patau’s syndrome, cat cry syndrome, etc.) ;

2) abnormalities of sex chromosomes (Shereshevsky – Turner syndrome, triple X syndrome, Klinefelter’s syndrome, XYY syndrome, etc) .

In anomalies of autosomal chromosomes the higher nervous activity is subjected to deeper changes and the clinical signs of diseases are especially severe.Life – span of persons with anomalies of sex chromosomes is comparatively long.

Trisomy 21 or Down’s syndrome is the most common chromosomal abnormality in humans.The disease occurs in the following variants: trisomy 21 (47XY ,+ 21); translocation of the long arm of chromosome 21 to chromosome 22 or 14 (46XY ) .

Down’s syndrome is characterized clinically by a regular pattern of dysmorphic facial features, mental retardation , congenital heart disease,hypotonia ,an increased incidence of infection , leukemia and presenile dementia,premature aging in older individuals .They are short, with different physical defects ,little head,flat back of the head,oblique eyelids ,flat and wide nose , little and deformed ears, short fingers and toes .The mouth is always half – open and the tongue is hanging out.

Thanks to modern medical aid the persons with Down’s syndrome may live up to 30 years of age and more.

The characteristic features of trisomy 18 (Edwards’ syndrome) are severe failure to thrive and mental retardation, prominent occiput, micrognathia,congenital heart disease and multiple additional malformations.

In trisomy 22 severe myopia, subnormal intellect, aggressiveness, etc. are observed.

Trisomy 13 (Patau’s syndrome ) is characterized by severe mental retardation and failure to thrive, abnormal development of eyes,cleft lip and palate, extra digits and congenital heart disease.The majority of children with trisomy 18 (Edwards’ syndrome) or 13 die by one year of age.

In children with cat cry syndrome one of analogs of the chromosome 5 is shorter than other one. The disease is characterized by short stature ,developmental anomalies of skeleton and different organs,round face, squint,micrognathia ,deformed floor of the auricle, syndactylia of lower extremities, congenital defects of heart and genital organs, anomalies of kidneys. The voice of diseased child ( cat cry ) and cytogenetic methods of examination are decesive in the diagnosis. The life – span is short.

The abnormalities of sex chromosomes in most cases are in the form of mosaicism , that is, the number of sex chromosomes in different cells of the same organism differ from one another.

Females with Shereshevsky – Turner syndrome ( 45 X) have short stature ( 125-140 cm in adult women), ovarian dysgenesis, failure of the secondary sexual development , occasional difficulties with spatial – perceptual tasks. Approximately 20 per cent have coarctation of the aorta, and renal anomalies are fairly common. Often there are wing – shaped folds in the region of the neck. The patient differ from normal women by absence of sex chromatin in epithelial cells of internal surface of cheek and in leukocytes.

Females with the triple X syndrome (47 XXX) occasionally have mild mental retardation and learning disabilities as well as abnormal ovarian function , but otherwise are normal.

Males with Klinefelter’s syndrome (47 XXY) are tall , with disproportionately long extremities, testicular atrophy and infertility, slightly feminized body habitus , and occasionally have behavioural problems and a mildly impaired intelligence. In mucous membrane ephithelial cells of internal surface of cheek sex chromatin is revealed , whereas in normal men the sex chromatin is absent.

Males with the XYY syndrome (47XYY) are quite tall and occasionally have behavioural abnormalities, but are generally normal. As in Klinefelter’s syndrome, infertility, pathology of endocrine system, hypoplasia of sexual glands are observed.

Methods of treatment of the hereditary diseaser are: etiologic, pathogenetic and symptomatic.

The perfect method of treatmant of the hereditary diseases would be the etiologic therapy. Because the methods of the pathogenetic and symptomatic therapy do not completely eliminate the signs of the disease. The essence of gene engineering is to influence the mutant gene and make corrections in it . But for the present these methods are studied under the conditions of experiment. Therefore, in our times the methods of treatment of hereditary diseases are based on the principles of the pathogenetic therapy.

***Reactivity (Lat. reactia - counteraction) is ability of organism to respond to the action of ordinary and pathogenic stimuli in a definite manner corresponding to each concrete condition.***

The reactivity is important aspect of organism's adaptation to the external environment which has been developed in the course of its evolution. It is also one of the principal characteristics of the living organism as well as growth, reproduction, feeding, metabolism, etc.

Each organ, tissue, cell and even cellular organoid have their own peculiarities of reactivity. But the reactivity of the organism as the whole is determined, in the first place, by functional state of nervous, endocrine and immune systems.

The reactivity is more extensive and complicated idea than irritability, excitability, etc. These can be regarded as the indices of reactivity. For instance, irritability is the ability of any living tissue to respond to stimuli, excitability is the ability of only excitable tissues to specific response, whereas reactivity characterizes the response of the whole organism to the action of stimuli in every concrete situation.

To understand the essence of reactivity let us consider such a simple (maybe somewhat rough) example. To a man in wonderful spirits comes his friend and relates a funny story. The man laughs with all his heart. Next time the same friend comes and begins to relate more funny story. But the man sends him to hell angrily. The friend is extremely surprised. Because he does not know that this time his host is hungry and in a bad mood after some unpleasant incident.

Reactivity underlies the organism's ability to resist influences of pathogenic agents. For example, not all people are equally susceptible to the same infection. The course of an infectious disease also depends on the organism's reactivity and therefore it runs differently in different people. All other conditions being equal, wounds heal differently in different people. In cases of higher reactivity wounds heal relatively fast, whereas in cases of low reactivity they heal slowly.

So, to understand the pathogenesis of diseases and be able to exert purposeful influences on the affected organism, it is important to study reactivity and its changes.

Reactivity of the organism is closely connected with its resistance and defence-adaptative reactions. As a matter of fact, all defence-adaptative reactions of the organism (beginning with such simple ones as drawing away the hand from hot objects and up to such complex mechanisms as inflammation, allergy, etc.) belong to reactivity.

Organisms’ reactivity at different stages of evolution gradually developed in the struggle against pathogenic agents. For instance, reactivity to inflammatory agents grows more complex with the development of organisms and differentiation of their nervous system. In cold-blooded animals inflammation is less clearly marked than it is in warm-blooded animals. The same is observed in experiments aimed at developing increased sensitivity to protein. In warm-blooded animals it develops relatively easily, whereas cold-blooded animals either react to protein very feebly or do not react at all.

Reactivity of the human organism is the most complicated and diverse. It depends on social factors largely, that is, the human reactivity is socially mediated. In our epoch of scientific and technical progress vivid examples of the social madiation of human organism’s reactivity are different systems of “man-machine” (“man-bicycle”, “man-car”, “man-lathe”, etc.). For instance, at a factory frequently the man becomes as if a part of the machine and they run together in the course of this or another productional operation. Breach in the work of this system may cause traumatism, disturbances in analyzers, psychical disfunctions. The second signaling system is of particular importance in the human reactivity. Changing the reactivity differently, a word may exert medicinal or pathogenic influence on the man.

The basic form of reactivity is the biological reactivity which is divided into group reactivity and individual reactivity.

The biological (specific) reactivity is the most common form of reactivity of healthy and sick human organisms. The characteristic for each species of living beings forms of defence – adaptative reactions which occur in the organism under the influence of all ordinary (adequate) and pathogenic stimuli, is called biological reactivity. It is determined by the hereditary and variability within the limits of species. The biological reactivity is directed to preservation of the species on the whole as well as each individual separately.

Taxis (movement to the stimulus or in the opposite direction) of protozoa, instincts (complex unconditioned reflexes) of invertebrates (bees, ants), seasonal migration of birds, hibernation of some animals, etc. belong to the biological reactivity. All of these processes are accompanied by thorough changes in metabolism, resistibility and other peculiarities of organism. For instance, excitability of frog’s nervous system in summer is higher than in winter.

Although resistance of the organism is also manifestation of its reactivity, but they can change in opposite directions. For example, in response to low temperature of external environment and bad conditions of feeding in winter, some animals sink into deep sleep (hibernation) during which organism’s reactivity becomes lower. In the central nervous system diffuse protective inhibition is developed and its reflex activity becomes weaker, the rate of metabolism and organism’s need for oxygen are decreased, body temperature falls. In this period it is impossible to cause local allergic reactions and anaphylactic shock in animals. Reaction of phagocytosis is weakened. But organism’s resistance against infections (plague, kala azar, tuberculosis, etc.) and intoxications (strychnine, toxins of diphtheria, tetanus, etc.) is sharply increased. However, the microorganisms remain in the organism and infected animals fall ill soon after waking up.

Specific immunity of the organism to infectious diseases is connected with the biological reactivity.

In group reactivity the reactivity peculiarities of the species where the group is included in and those of different individuals forming the group, are taken into consideration. The peculiarities of reactivity of the people differing by the type of the higher nervous activity, blood groups, types of the vegetative nervous system (vagotonics and sympaticotonics), constitutional types, systems of “man-machine” may be characterized as the group reactivity.

Danish artist – caricaturist Bidstrup in his well-known picture with a profound comprehension (I should say – with a simplicity of genius) demonstrated the group reactivity. He describes the response of persons belonging to different types of the higher nervous activity to one and the same incident. An old man sat on the bench and put his hat besides him. Another old man (apparently, absent-minded) came and sat on the hat. Seeing this sanguine ironically smiles, understanding that this was not done intentionally.

Phlegmatic does not react at all, as if this is not his hat. Choleric vehemantly attacks the guilty man, whereas melancholic begins to weep.

Also, the blood belonging to the IV group may be transfused to the recipient of the same group with best results, whereas the same blood when transfused to the recipient of any other group will cause death.

The individual reactivity of the organism depends on its hereditary and constitutional peculiarities, age, sex and influence of external environmental factors. The type of higher nervous activity, functional properties of the vegetative nervous system, endocrine glands, etc. are the factors determining the individual reactivity of the organism.

Two types of individual reactivity are distinguished: physiological reactivity and pathological reactivity.

Immune reactivity of individual is determined by his physiological and pathological reactivity and manifests itself in the form of immunity or allergy.

Reactivity of the organism may be increased or decreased. Changing of reactivity is regarded as positive if it is conducive to mobilization of defence- adaptative reactions of the organism and negative-if it disturbs this process. For instance, increase of reactivity in allergy as well as its decrease in shock, collapse, faint and on the severe stages of many diseases are negative (pathological) phenomena, whereas increase of reactivity in immunity and its decrease in protective inhibition, narcosis, sleep are appraised as positive (defensive) phenomena.

According to its intensity the following forms of reactivity are distinguished:

1) hyperergy (increased);

2) hypergy (decreased);

3) dysergy (distorted).

The pathological reactivity is characterized by limitation of organism’s adaptative possibilities. For instance, the animals subjected to powerful mechanical trauma, hyperthermia or hypothermia perish after loss of 15-20 per cent of their blood, whereas in ordinary conditions thanks to compensatory-adaptative reactions the organism may survive after loss of up to 50 per cent of its blood.

Usually the changes connected with the pathological reactivity limit the vital activity of diseased organism and decrease ability to work. But some functions may be strengthened. Some reactions characteristic of the pathological reactivity (formation of antibodies, phagocytosis, inflammation, etc.) are of protective significance for organism.

Both physiological and pathological reactivities are characterized by specific and non-specific reactions occurring in the organism. By the participation of the specific reactions the signs originate which are characteristic of any concrete disease (spasm of arterioles in hypertensive disease, damage of upper respiratory tracts in grippe, etc.) . Manifestations of non-specific reactivity are the reactions which are characteristic of different diseases, such as fever, phagocytosis, general adaptation syndrome, etc.

The reactivity depends on a number of external and internal factors.

One-sided nutrition and various forms of starvation noticeably weaken organism’s reaction to pathogenic agents. Organism’s resistance to infections diminishes in cases where the food is deficient in vitamins. Protein starvation weakens inflammatory reactions and greatly reduces the organism’s resistance to infections (abscess, typhus, typhoid fever, etc.).

Overheating and overcooling of organism produce a reflex reorganization of its reactivity to all stimuli. For instance, sudden cooling reduces man’s resistance to influenza and pneumonia. Experimental cooling of chickens make them susceptible to anthrax which normally does not affect them. Overheating lowers the sensitivity of sensitized guinea pigs to foreign protein.

Poisoning with war gases, alcohol, carbon monoxide, mercury, lead and hydrocyanic acid reduces the processes of inhibition in the cerebral cortex and organism’s resistance to pathogenic agents. For instance, chronic alcoholism considerably weakens man’s general reactivity. Pigeons poisoned with alcohol become susceptible to anthrax.

Radiant energy (ultraviolet rays) in some doses increases the organism’s resistance to infections and in others lowers it. Reactivity is particularly harmfully affected by prolonged exposure to roentgen and gamma rays.

Reactivity is affected also by other factors (atmospheric pressure, trauma). It depends on psychological and social factors. This shows that reactivity varies depending on environmental conditions and that the environment can be used to exert purposeful influences on it. For instance, frequently positive emotions play decisive role in the recovery of patient.

Great is also the influence of internal factors on reactivity. First of all, the biological reactivity is determined by hereditary factors.

The role of ontogenesis is confirmed by the fact that in different ages reactivity is subjected to different changes. In childhood, period of puberty and in old age the organism may react differently to one and the same stimulus. Organism’s sensitivity to pathogenic agents and character of its defence-adaptative reactions during disease depend on its age. Therefore, there are characteristic diseases of every period of age.

In the first stages of embryonal period of development organism does not possess reactivity, and development of tissues is realized by the genetic mechanisms of regulation. Then the nervous system and hormonal receptors in cell membranes are formed.

In newborns the nervous system is not completely developed, and the reactivity is low. But organism’s resistance to some infectious diseases (diphtheria, scarlet fever, measles) is high, and in the first six months of life they rarely catch these diseases. Because the fetus receives ready antibodies from mother’s blood through the placenta.

Depending on the reactivity of children’s organism the younger the child, weaker are manifested the specific signs of diseases and stronger are non-specific signs. Therefore, the general signs of the diseases are stronger than the local signs.

In the first 6-12 months of their life the infants lose the antibodies that were received from mother and their own ability to form antibodies is weak. Therefore, during two years of their life they catch easily different infectious diseases.

Some diseases (rickets, scarlet fever, diphtheria, wooping cough, poliomyelitis, etc.) occur, usually in childhood. Since the mechanisms of thermoregulation are not yet fully developed, they adapt to the changes of external environment’s temperature with difficulty.

For adolescents instability of the neuro-endocrine system is characteristic, and in this period some psychic and somatic diseases are frequent.

In the period of puberty and middle age organism’s reactivity and resistance are comparatively high.

In old age organism’s sensibility to infections is once more increased, but the activity of barrier systems is weakened. Atherosclerosis, disorders in blood circulation, decrease of endocrine glands activity, atrophy of tissues are observed. Phagocytic ability is decreased. The old people often and easily fall ill (infectious diseases, pneumonia, malignant neoplasms). But the organism’s resistance against the diseases connected with hyperactivity (allergy) is increased. They endure hunger and thirst comparatively easily (metabolism is low).

Some peculiarities of reactivity are connected with sex. The menstrual rhythms influence thoroughly reactivity and resistance of the female organism.

The biological reactivity depends considerably on the development of the nervous system and types of the higher nervous activity. The weakening of the higher nervous activity as a result of overstrain sharply decreases resistance of the organism against bacteria, bacterial and chemical toxins. The people subjected to high emotional overstrain easily catch eczema, gastroenteritis, pneumonia, etc.

The subcortical area plays significant role in reactivity. The limbic system and hypothalamus are the important apparatuses of reactivity and behaviour.

There is a great deal of evidence proving importance of the vegetative nervous system in the mechanism of reactivity. For instance, stimulation of the parasympathetic nervous system increases production of antibodies, whereas stimulation of the sympathetic nerves intensifies reaction of phagocytosis.

Humoral factors (hormones, mediators) and other physiologically active substances also play an important role in reactivity.

In pathology certain physiologically active substances are liberated and accumulated in the organism in accordance with the processes of excitation and inhibition operating in the nervous system. These substances are, in the first place, cholinergic and adrenergic substances. For instance, cholinergic reactions prevail in cases of ulcers and bronchial asthma, whereas adrenergic reactions predominate in spontaneous gangrene and hypertensive vascular disease.

Walter B. Cannon established the significance of sympathico-adrenal system in the organism's adjustments to the changing conditions of its surroundings (homeostasis). This system's reactions are evident when the organism is acted upon by various stimuli; for example, in cases of traumata or excessive cooling. Thermoregulation, redistribution of the blood and increased glycogenolysis in the cases of diminished blood sugar cannot be normally effected during dysfunction of the sympathetic nervous system.

Disturbances in the organism's reactivity arise in connection with endocrine disorders. For instance, resistance of the organism to certain infections diminishes in hypothyroidism and in insufficiency of the islets of Langerhans.

Pituitary body influences the reactivity through other endocrine glands. Hypersecretion of adrenocorticotropic and somatotropic hormones cause weakening of immunity.

Role of connective tissue's functional state in the reactivity is great. Thorough investigations of Bogomolets and his followers proved plastic, protective, trophic, barrier functions of the connective tissue. To stimulate activity of connective tissue Bogomolets offered to use antireticular cytotoxic serum (ACS) which was got from the blood serum of animals sensitized by the human tissues (spleen, bone marrow). In the blood of such animals specific antibodies are formed which act against human connective tissue. In large doses ACS exercises cytotoxic influence and destroyes connective tissue elements. But its small doses stimulate activity and development of these elements. So, ACS is successfully used in the treatment of diseases accompanied by decreased reactivity (to accelerate healing of wounds, knitting consolidation, prevent presenilation, etc.).

Most cells that belong to connective tissue closely participate in reactivity. Physiologically active substances such as heparin, histamine, serotonine are accumulated in their granules, and then going out of most cells, cause development of some pathophysiological reactions (for instance, in allergy).

The connective tissue takes part also in the formation of the organism's specific reactivity. The plasma cells or plasmacytes (the cells that synthesize the immunoglobulins), take part in the synthesis of antibodies.

Reactivity of the organism is closely connected with its resistance, and frequently these ideas are discussed together. Organism's resistance is its ability to resist against the action of different damaging factors. The fight of the organism against pathogenetic agents is connected with its response reactions to the action of the external environment. So, organism's resistance is actually one of the principal manifestations of its reactivity. Resistance, as well as reactivity, is one of the properties of the biological being which is acquired in the process of phylogenetic development.

True, sometimes organism's reactivity and resistance may change in opposite directions. For instance, in allergic diseases which are connected with increased reactivity to the substances of antigenic character, resistance of the organism to these substances is decreased; during the hibernation reactivity of animal's organism is decreased , but its resistance to infectious diseases is increased.

Resistance of some organs and systems is not connected with active reactions. For instance, barrier function of skin and mucous membranes is connected with their anatomic structure; subcutaneous fat takes part in the mechanism of organism's resistance against cold because it is bad conductor of heat; bones and tendons posses considerable resistance against deformation under the mechanical forces (bones of skull protect the brain from trauma).

But there are also active mechanisms of the resistance. The most important of active reactions of resistance are the adaptative mechanisms of the organism which ensure homeostasis in condition of influence of pathogenic factors.

Similar to reactivity, some reactions forming the mechanism of resistance are characteristic of only certain species of animals, that is, specific resistance exists.

The individual resistance of different organisms is connected with hereditary and congenital factors, as well as acquired peculiarities of the organism. For instance, during epidemics not all of the people fall ill, and the severity of disease is not the same in all of the diseased persons.

Factors of the external environment influence organism's individual resistance powerfully. For example, as a result of starvation or malnutrition organism's resistance becomes weaker. But overeating may exert also negative influence on the resistance. Hypokinesia, alcoholism, narcomania, smoking decrease organism's resistance, whereas observance of correct regimen, normal living and working conditions influence the resistance favourably.

According to its mechanisms, specific and non-specific types of resistance are distinguished. Specific resistance means resistance of the organism against one certain factor. The immunity that arises after the infectious disease or is caused by special vaccines, may be an example of the specific resistance. Immune reactivity consists of specific reactions. Non-specific resistance means resistance of the organism against different harmful factors. The mechanisms of non-specific resistance are extremely diverse.

There are mechanisms in organism that occupy the middle position between the specific and non-specific defence factors (phagocytosis, the system of complement).

In some cases in spite of high non-specific resistance of organism, its resistance against one concrete factor (specific resistance) may be weak. For instance, some people possessing enormous physical strength cannot endure the influence of alcohol. This is explained by low activity of the enzyme alcohol dehydrogenase in their liver.

Non-specific defence factors of organism include body temperature, oxygen content of tissues, concentration of hydrogen ions, biological barriers, some hormones, etc.

The biological barriers are organs, tissues or anatomic-physiological structures which prevent cells, high-molecular and low-molecular substances to diffuse from external environment into organism.

External and internal defence mechanisms (barriers) are distinguished. The external mechanisms include the skin with its adnexa and mucous membranes with the glands imbedded in them. Inpairment of these mechanisms facilitates penetration of infectious agents into the organism.

The internal defence mechanisms include the lymph nodes, the reticuloendothelial elements of various organs (spleen, bone marrow, liver, etc.), the kidneys (which eliminate toxic substances and certain microbes from the organism), hematoencephalic (cerebrospinal) barrier, the biochemical and physicochemical properties of tissues that impede the development and vital activity of infectious agents, etc.

The high body temperature is mortal for some microorganisms. Therefore, pigeons, the body temperature of which is 41.5-42.5o C do not catch anthrax. But when artifitially cooled, they fall ill.

When the oxygen content of tissues is sufficiently high, development and reproduction of microorganisms is delayed. Agents of tetanus and gas gangrene reproduce only in anaerobe conditions.

In the areas of normal organism which are frequently contacting with infectious factors, the concentration of hydrogen ions is high enough (gastric juice, sweat, etc.). In inflammatory foci also the acid medium appears. In acid medium the most of microorganisms perish.

Skin is, in the first place, mechanical barrier for microorganisms. It is impermeable to most of pathogenic and non-pathogenic microorganisms. Skin is covered with stratified cornifying epithelium. Gradual desquamation of the superficial layer of the skin helps in eliminating the microbes. Infectious agents (streptococci, anthrax and plague bacilli) easily penetrate into the organism through damaged skin.

Bacteria may enter the organism also through the opening of the excretory ducts of sweat and sebaceous glands. At the same time the sweat and sebaceous glands play an important part in the barrier function of the skin. The substances secreted by these glands on the surface of the skin wash off the microbes and prevent infectious agents from penetrating into the organism. Thanks to acidity of the sweat and composition of the secretion of the sebaceous glands and the secretion of antiseptic metabolites (certain lipides) skin has also bactericidal properties.

The barrier function of conjunctiva and cornea, mucous membranes lining the nasopharynx, respiratory, digestive, urogenital tracts is connected with their permeability and lysozyme. Owing to existence of hydrochloric acid and pepsin gastric juice possesses considerable sterilizing action. The intestinal juice also produces a bactericidal effect.

Barrier function of the liver is connected with activity of macrophages (Kupffer cells). Bile also exercises the bactericidal action.

Hematoencephalic, hemato-ophthalmic, hemato-labyrinth, hemato-testicular and other histo-hematic barriers ensure constancy of internal environment and take part in the regulation of the metabolism (by the way of controlling the entrance of substances into cells and tissues).

Physiological, biochemical, physicochemical peculiarities of tissues also play a certain role in non-sprecific resistance of the organism. In the blood, lymph and tissue extract some physiologically active substances of bactericidal action (lysozyme, properdin, complement, etc.) were found.

Interferon (in blood serum and tissues) is also non-specific defence factor of antiviral action.

One of the defensive reactions of the organism is phagocytosis. Phagocytic ability is posessed by polymorphonuclear (microphages) and large mononuclear (monocytes) blood cells (macrophages). All the phagocytes are divided into two groups:

1)movable-granulocytes, monocytes;

2)immovable-macrophages of connective tissue, Kupffer cells of liver, macrophages of alveoli pulmonis, bone marrow, spleen, bone tissue, in peritoneal and pleural cavities, microglial cells in the central nervous system, etc.

The following stages are distinguished in the process of phagocytosis:

1. chemotaxis- approach of phagocyte to the object of phagocytosis (foreign body);
2. adhesion (contact)- sticking of the phagocyte to the foreign body;
3. endocytosis-engulfing of the foreign body by the phagocyte;;
4. intracellular digestion.

In the mechanism of chemotaxis physicochemical changes and especially decrease of surface tension (on the side of phagocyte directed to inflamed area) play certain role, but it is the active process which goes out with the consumption of energy (ATP).

Adhesion is realized with the participation of specific receptors of phagocytes, membrane of which carries negative charge. They join easily with positive particles. By the negative particles they join by means of membrane mucopolisaccharides and immunoglobulins.

In endocytosis the special glycoproteid of phagocyte's membrane takes part . The foreign body is embraced by the membrane and drawn into the phagocyte.

Intracellular digestion is realized with participation of lysosomic enzymes and proteins of bactericidal nature which decompose the foreign body. If the introcellular digestion is resulted in destruction of bacteria, it is called “completed phagocytosis.” But some bacteria do not perish. They continue to live in the leukocytes and even spread in them into different tissues of the organism. This is called “incomplete phagocytosis”.

Some factors stimulate and accelerate phagocytosis: antibodies (opsonins), complement (C3 fraction), calcium and magnesium salts, adrenalin, histamine, lymphokines, etc.

The following factors weaken and delay phagocytosis: avitominosis, acetylcholine, antihistaminic preparations, corticosteroids, special substances secreted by microorganisms (A protein and leukocidin in staphylococci, M protein in streptococci, proteins in capsules of some bacteria), etc.

There is certain connection between the activity of phagocytosis and organism’s resistance. More the rate of phagocytosis – higher is the resistance.

The immune system is one of the systems of the organism like respiratory, endocrine or nervous systems. But it differs from the organism’s any other system, because the cells of the immune system:

1. are spread in all organs and tissues of the organism;
2. circulate in the organism by the way of blood flow;
3. synthesize excessively specific antibodies (immunoglobulins).

The structural – morphological basis of the immune system is the lymphoid tissue, and its main figure is lymphocyte. All the lymphoid organs and tissues of the organism function as the “immune organ”. The total mass of all its components is 1.5-2 kg. The protein of the immune system comprise 20-25% of the total concentration of plasma proteins, and the cells that participate in this system constitute approximately 15% of body cells.

The central (thymus gland, bone marrow) and peripheral (spleen, lymph nodes, lymph follicles, faucial tonsils, lymphoid tissue of appendage, lymphocytes), also fixed (Kuppfer cells of liver, endothelial cells of intima) parts of the immune system are distinguished.

The human immune system encompasses the principal pathways by which individuals respond adaptively to foreign and endogenous challenges. It is activated especially when the pathogenic factors influence the organism.

Immunity (insusceptibility) is the totality of specific biological reactions (processes and mechanisms) serving for maintenance of the homeostasis and defence of the organism from genetically heterologous factors of infectious and non-infectious nature.

The immunogenic reactivity is the ability of the organism to produce the specific antibodies in response to the action of antigens and to respond by the complex of cellular reactions.

It was for a long time observed that in epidemics of plague, pox, cholera and other infectious diseases some of the healthy people that were in contact with the patients, were not taken ill. Also, the persons that get over some infectious diseases once, do not catch it repeatedly. In the XVIII – XIX centuries it became clear that the immunity was formed not only when the infectious diseases were got over, but also as a result of administration of dead microbes or products of their vital activity into the organism.

In 1796 E. Jenner elaborated the method of antivariolic vaccination. But actually vaccination was applied much earlier by Abu Bakr Muhammad ben Zakariya ar Razi (865-925), known as Razes in Europe.

In the organism the immunogenic reactions are observed also against the isoantigens, that is, proteins belonging to one species. A number of problems during hemotransfusion, transplantation of organs and tissues (rejection of transplant, etc.) are connected by these reactions. So, blood groups are attributed to the teaching about tissue isoantigens. Finally, when the antigen properties of cells are changed as a result of somatic mutations, the organism may manifest immune reactions against its own tissues. For instance, destruction of altered cells prevents development of the malignant tumors.

So, at present the immunity may be determined in the following way: “ Immunity is the way of defence of the organism from the foreign substances of infectious and non-infectious nature.”

The immune system is excessively sensitive to the heterologous substances. It can react even to the changing of one gene in the cells. When the immune system is suppressed, resistibility to diseases may decrease down to 300 times.

Immunity is the general defensive reaction which comes into being with the participation of the central and peripheral mechanisms of the organism’s immune system. But each infection has its organ which it damages in the first place, and each organ possesses its own immunity. So, besides the general immunity, the local immunity is also distinguished.

The local immunity against the microorganisms may be produced by the way of increasing of resistibility of the organs, and in this way it is possible to prevent penetration of the infectious agent into the organism (for instance, to increase resistance of the skin against the agents of anthrax.) The local immunity is closely connected with the general immunity and is one of its main indices.

In the classification of the immunity first of all congenital (specific) and acquired immunity are distinguished. Immunity is referred to as congenital when the insusceptibility of a given species of animal or man to a particular infection is an inborn property (man’s insusceptibility to cattle plague or the insusceptibility of animals to gonorrhea and leprosy).

The congenital immunity may be absolute or relative. The absolute immunity is not eliminated under the influence of the factors which weaken the general resistance of the organism (radiation, starvation, splenectomy, etc.) For instance, even high doses of influenza viruses which are pathogenic for man, do not cause disease in rabbits. The relative immunity may be weakened under the influence of the external environment. For example, chickens, although unsusceptible to anthrax, may catch it if cooled from 41-42º C (their natural body temperature) to 37ºC.

The acquired immunity is characterized by the high specificity. The immunity acquired as a result of an infectious disease is known as naturally acquired immunity. For instance, a person who has survived small pox usually becomes unsusceptible to this disease. People who have survived measles are unsusceptible to this disease for a number of years. Acquired immunity may be unstable to diphtheria, cholera and typhoid fever; it is temporary or does not develop at all to influenza and, especially, to rheumatism.

The immunity acquired as a result of immunization with bacterial preparations (vaccines) or administration of immune sera (taken from vaccinated animals or those who have survived the particular disease), is called artificially acquired immunity.

Acquired immunity (both naturally acquired and artificially acquired) may be active or passive. Immunity is active when the organism itself has elaborated it as a result of disease or inoculation with a vaccine prepared from attenuated or killed microbes (in small-pox or typhus vaccination). Immunity is passive if the organism has become unsusceptible to infection as a result of administration of immune sera. Passive immunity manifests itself very quickly but is unstable.

Passive immunity for purposes of prophylaxis or treatment may be produced to diphtheria and tetanus by administration of corresponding sera from immunized horses (antidiphtheritic and antimicrobic sera).

Acquired immunity may be of antimicrobic (bacteria, spirochaeta, rickettsia, viruses, fungi, protozoa) or antitoxic (toxins of pathogenic agents such as tetanus, botulism) character.

Sterile and non-sterile (infectious) immunity are also distinguished. The sterile immunity is characterized by the complete cleaning of the organism from the infectious agent (or carriage of bacilli remains for a short time), whereas non-sterile immunity exists while there is a focus of infection in the organism (if there is a focus of tuberculosis in the organism, it becomes insensitive to the repeated infection of this disease).

The cellular (Mechnicov) and humoral (Ehrlich) mechanisms of the immunity are distinguished which are closely connected.

The humoral immunity is connected with B lymphocytes, which are converted into plasma cells synthesizing the specific immunoglobulins, that is, antibodies (Ig A, Ig D, Ig G, Ig M). In the pathogenesis of the allergic reactions another type of immunoglobulins (Ig E or reagins) take place.

The cellular immunity is connected with T lymphocytes which participate in the preservation of the “immune memory”. They are able “to recognize” the substances which are heterologous for the organism. T lymphocytes easily pass from the lymphoid tissue into the blood and return back. In this way they transmit the information into lymphoid tissue about the immune homeostasis in the organism. T lymphocytes also dissolve the antigens in the specific reactions.

The following types of the T lymphocytes take part in the immune reactions:

1. T helpers – their receptors are able to “feel” corresponding antigens;
2. T killers – have cytotoxic action;
3. T suppressors – decreasing the activity of T helpers as well as B lymphocytes, take part in the regulation of immunogenesis.

Besides T and B cells, A cells (macrophages) also take part in immune reactions.

The immune reactions are connected with formation of the immune memory. Some part of T and B lymphocytes, after being in contact with the antigen, become sensitized. They may live in lymphoid tissue for a long time (month or years) and preserve the information about the specific signs of the antigen. When these sensitized cells meet their specific antigens repeatedly, they ensure the development of immune reactions (synthesis of specific antibodies by plasma cells that are in the organism’s immune system).