Diseases of the Immune System

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Received October 29, 2021; revised November 29, 2021; accepted November 29, 2021

This review presents, in detail and from multiple angles, the classification of diseases of the immune system during different periods of a person’s life, including immune-associated and immune-dependent diseases, their phenomenology, disease triggers, and the mechanisms of regulation of immune reactivity.

Keywords: immune reactivity, immunosuppression and immunostimulation, factors of immune diseases, immunoregulation

DOI: 10.1134/S2079086422040107

INTRODUCTION

From a certain point of view, the human body can be presented as a target for external and internal pathogenic factors. The immune system is the body’s main shield against pathogenic agents of any origin. Like any part of the body, it can itself be exposed to pathogenic influences, as a result of which prenosological changes can form, and subsequently diseases of the immune system. This entails the inability of the body to recognize and eliminate foreign objects due to anatomical defects or functional insufficiency of lymphoid organs (Chereshnev and Schmagel, 2014; Zemskov et al., 2018b).

Of interest is the development of infections at different periods of the human lifespan and in certain functional states of the body.

Childhood. In child morbidity, infectious diseases account for 60–70% of deaths, with disability of about 600 thousand children. Recently, there has been an increase in: acute intestinal infections by 11.4%; cytomegalovirus, herpesvirus, chlamydia, and mycoplasma infections—by 24.4%; and hemorrhagic fevers and trichinosis—by 1.8–2 times (Zemskov et al., 2017, 2017a).

Old age. Age-related immunodeficiency is characterized by the frequent formation of infectious and autoimmune syndromes. At old age, chronic recurrent bacterial, viral, and fungal infections of the skin and mucous membranes develop (pyoderma, furunculosis, abscesses, herpes, candidiasis, conjunctivitis, and stomatitis), along with chronic bronchitis, pneumonia, urogenital lesions (vulvitis, pyelonephritis), gastroenteropathy with prolonged diarrhea, dysbacteriosis, and a subfebrile condition (Zemskov et al., 2018a, 2018b).

Pregnancy. Infectious and inflammatory diseases in pregnant women are dangerous both for the woman herself and for the fetus. During pregnancy, viral infections (poliomyelitis, hepatitis A and B, influenza, and genital herpes), cytomegalovirus, and Epstein–Barr virus can cause liver dystrophy, acute pancreatitis, pyelonephritis, encephalitis, anemia, and myocarditis. Typhoid fever, gonorrhea, listeriosis, tuberculosis, toxoplasmosis, amebiasis, giardiasis, chlamydia, mycoplasmosis, and Gardnerella occur more frequently and are more severe. Deficiency of sIgA, along with reduction of the absorptive, metabolic and chemotactic ability of phagocytes, and T-dependent reactions contribute to the development of vaginitis, cervicitis, parametritis, pelviperitonitis, and chlamydia, anaerobic bacteria, fungi, opportunistic flora, and trichinosis (Zemskov et al., 2017c, 2018b).

Childbirth. Postpartum infectious and inflammatory diseases occur in 13.3–54.3% of cases and occupy the second—fourth place among the causes of maternal death. Caesarean section increases the risk of endometritis and wound infection by 5–10 times. In the etiology of postpartum infectious diseases, the leading role is played by microbial associations (more than 80%), which have more pronounced pathogenic properties than monocultures. In the last 10—15 years, traditional infectious pathogens of obstetric infection have been replaced by chlamydia, cytomegalovirus, group B streptococci, Staphylococcus aureus, non-spore-forming anaerobes, etc. (Zemskov et al., 2021b).
CLASSIFICATIONS OF DISEASES OF THE IMMUNE SYSTEM

Pathogenetic Classification of Diseases

Immune dependent diseases. Immune dependent diseases can be classified as: primary immunodeficiencies, malignant neoplasms, and allergic diseases. Primary disorders of the immune system are the main pathogenetic mechanism. The main method of treatment is immunotropic therapy (Zemskov et al., 2014).

Immune associated diseases. Immune associated disease can be classified as: secondary immunodeficiencies, infections, somatic and other pathological processes, and allergic complications, which are based on the formation of secondary disorders of the immune system, requiring auxiliary immunotropic treatment (Zemskov et al., 2014).

Phenomenological Classification of Diseases

Hyporeactivity of the immune system. Acute immune deficiency develops with acute infections, subacute immune deficiency with convalescence, and chronic immune deficiency with a chronic process. Primary immunodeficiencies are congenital, they are genetically determined by a deficiency of the immune system (0.05%), and can be B-dependent (50%), T-dependent (30%), combined (10%), or phagocytic (8%). Secondary immunodeficiencies are phenotypic immunodeficiencies after infection, somatic disease, radiation, metabolic disorder, etc. In addition, there are immunoproliferative and malignant neoplasms, that are also referred to as secondary immunodeficiencies (Zemskov et al., 2021a).

Hyperreactivity of the immune system. This category includes exorbitant humoral or cellular immune responses to low immunogenic agents against the background of immunodeficiency, or reactions due to the small size of allergen molecules. Immediate-type hypersensitivity (IHT), delayed-type hypersensitivity (DTH), and atopy, have been identified. These types of reactions carry both protective and pathogenic potentials. IHT and specific IgE provide protection against parasites, and DTH provides protection against antibiotic-resistant pathogens, which is undoubtedly a positive phenomenon. Atopy is a response to mild allergens, and there are three variants of it: (1) with a predominance of specific reactions; (2) parity non-specific specific reactions; (3) pseudo-allergic reactions, these are all pathological reactions.

One of the manifestations of hyperreactivity of the immune system is autoimmune disease that develops when trans-barrier antigens or microbial mimicry antigens appear in the bloodstream. Organ-specific reactions (for example, Hashimoto’s thyroiditis, and thyrotoxicosis) develop in response to autoantigens of one trans-barrier organ. Non-organ-specific reactions (in particular, rheumatoid arthritis, dermatomyositis) are directed against antigens of different tissues. Mixed reactions are realized by both mechanisms. Immune complex diseases (ankylosing spondylitis) are caused by medium-molecular or large circulating immune complexes that thrombose the capillaries of the kidneys, alveoli and other organs or cause the destruction of phagocytic macrophages with the release of aggressive digestive enzymes (Klinicheskaya..., 2016; Zemskov et al., 2021a).

Unclassified Diseases

These include: virus-induced immunodeficiencies (HIV/AIDS), transplantation disease, graft-versus-host disease, and reproductive immunopathology.

FACTORS CONTRIBUTING TO THE DEVELOPMENT OF IMMUNE SYSTEM DISEASES

The microenvironment has helminths, protozoa, fungi, 100 000 types of bacteria, 300 000 types of viruses, prions, and 1400 anthropogenic infections. The origins of pathogens (and corresponding diseases) are: abiotic components of the environment — the soil, water, and air (sapronoses); infected animals and people (zooanthroponoses, in particular glanders, anthrax); sick people (anthroponoses, which include, in particular, venereal diseases); contaminated food products (salmonellosis, paratyphoid); and plant microflora, including medicinal plants (Zemskov et al., 2018b, 2021b; Mikrobiologiya dlya..., 2020).

Diseases of the microbiota constitute dysbacteriosis. Note that absolute normocenosis is the normal state of microflora and is extremely rare. There are four types of dysbiotic disorders of the normal human microflora, type I—conditional normocenosis, type II—intermediate, type III—dysbiosis, and type IV—a pronounced inflammatory process. There are several options for linking the level of immune reactivity of patients with the microbiota: (1) in a healthy state, there is a balance between commensals and opportunistic pathogens; (2) in the case of immune compromise of patients (AIDS), weakly virulent and saprophytic microflora of the skin and mucous membranes can cause infectious lesions; (3) with the accumulation of antibacterial factors in the epithelium of the host in microorganisms, a response activation of aggression enzymes occurs; and (4) pathological conditions caused by highly virulent pathogens may not depend on the state of immunity (Zemskov et al., 2017b, 2019).

Changes in the nature of the course of infections at the present time. The causative agents of HIV, hemorrhagic fevers of Marburg, Lass, Lyme, atypical pneumonia, and coronavirus infection-19 have been discovered, the pathogenicity of Helicobacter pylori has increased, and cholera vibrio has been lowered, which significantly changing the manifestation of infections.
The participation in cervical cancer of papillomaviruses 16, 18, 48 and 56, and herpes I and II has been proven; in Burkitt’s lymphoma and nasopharyngeal carcinoma, Epstein–Barr virus participation has been shown; viral hepatitis B and C are involved in primary liver cancer; and lymphotropic viruses BVI and BII are involved in cellular lymphosarcoma.

The possibility of chronic viral, chlamydia, and other infections as the cause of atherosclerosis, Alzheimer’s disease, diabetes, stroke, and multiple sclerosis has been shown.

The transformation of zooanthroponoses (plague, yellow fever) into anthroponoses is noted. In some cases, there is a change in the typical place of residence: for example, the migration of Pseudomonas aeruginosa from the intestine to other organs with the development of pleural empyema, arthritis, enterocolitis, and sepsis.

It has been established that a mitigation of the nature of a number of diseases is formed as subclinical infections with early or late recurrence (typhoid, brucellosis, and ornithosis). The risk of asymptomatic carriage, persistence, dysbacteriosis, immunodeficiencies, allergization, and autoimmune lesions is high.

**Anthropogenic Factors of Diseases of the Immune System**

There are factors associated with the modern world order, these are the welfare of the population, the features of modern transport systems, animal husbandry and, in particular, veterinary medicine in animal husbandry, which indirectly affect humans (Zemskov et al., 2018b, 2021a; Mikrobiologiya dlya..., 2020).

**Improving the welfare of the population** provokes allergies to precious metals (gold, silver bronchial asthma, dermatitis), cosmetics, perfumes, and adjuvant disease to transplants.

**The modern network of transport communications** ensures the rapid spread of pathogens from endemic foci, and ensures pandemics and imported infections. In 1999, more than 4000 people were infected with the West Nile virus in the United States due to migrants from Africa. In the Faroe Islands, the introduction of the measles virus has led to high mortality in Aboriginal children who do not have resistance to the pathogen. Added to this is geographic stress, which causes suppression of immune reactivity when changing the place of residence, especially in the older contingents.

**Domestication of wild animals by humans** led to the development of zooanthroponotic, then anthropotonic, especially viral infections, which are directly related to the reactivity of the immune system.

**The development of animal husbandry, crop production, and fish farming** due to the uncontrolled use of medicines used for the treatment and prevention of diseases of animals and plants, led to the development of drug complications in the population.

The group of anthropogenic factors associated with medicine is heterogeneous.

Some of them involve a direct impact on a person, the purpose of which has always been to improve the quality and increase life expectancy. But this, paradoxically, may not lead to a decrease in morbidity, but may cause either an increase in the number of new diseases or the transformation of known diseases.

**Diagnostic and therapeutic aggression.** In modern medicine, more than 3000 types of various traumatic interventions are used that contribute to the development of infectious diseases. These include (1) infections associated with devices of artificial lung ventilation, bladder catheterization, vascular catheterization, etc.; (2) infections caused by medical procedures: blood transfusions, injections, etc., as well as surgical interventions (Kalinina et al., 2008).

**Medications.** All drugs are immunotropic, although their effect is not unidirectional: antibiotics, antihistamines, anesthetics, corticosteroids, and cytostatics suppress the immune system, while metabolic agents, vitamins, plasma-substituting solutions, antioxidants, and modulators, on the contrary, stimulate it.

**Vaccine-serum prosthetics of the immune system.** In the Russian Federation, 150—200 million people annually undergo active/passive immunotherapy and prophylaxis. However, drugs have reactogenicity, vaccination reactions, complications, and vaccine incidents. Complications are formed in case of violation of the prescription, administration, and storage of drugs, as well as in risk groups, which include alcoholics, drug addicts, the immunocompromised, allergic patients, including against the background of an excess of antibodies, and those taking antihistamines, antibacterial drugs, cytostatics, modulators and others.

**The creation of antibacterial drugs** induced the ESCAPE phenomenon (ESCAPE—abbreviation for *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* bacteria, representatives of Enterobacteriaceae family), which means the formation of total antibiotic resistance of bacteria with the risk of planetary bacterial resistance in 20—25 years, which certainly will have a negative impact on the human immune system.

**The increase in life expectancy and the decline in the birth rate in developed countries has led to demographic aging.** Thus, according to world statistics, currently people over 65 account for 10% of the population while in 10—15 years it will be 25%, it is expected that by 2100 the number of people aged 80 years and over will reach 881 million. At the same time, the frequency of diagnoses in 60-year-olds is 3—5%, and in 70-year-olds is more than 10% (Zemskov et al., 2018b).

**Pathological pregnancy.** Excessive obstetric manipulative activity, and the reduction of child mortality at any cost causes the formation of a population of disabled children with subsequent reproduction of defective offspring.
Some of the factors associated with medicine relate to the organizational problems of modern medical care.

Violation of the logistics of creation medical institutions led to the accumulation of hospitals on a total area of 15 km² with three million beds accounting for more than 1 billion bed-days/year 50 million patients and medical personnel. It would be more logical to separate hospital departments, for example, into purulent gynecology, clean gynecology, etc., into isolated rooms with periodic visits by attendants, and not with their permanent residence in the general structures of these departments.

The creation of unified air conditioning, ventilation, sewerage, and oxygen supply systems, and the creation of common catering units, and cleaning services contributes to the spread of sapronose and other infections, such as legionnaires’ disease in crowded places including accommodation and treatment areas.

Special properties of hospital strains cause: (1) drug multiresistance; (2) low virulence with high resistance to external factors; (3) slowed and perverted metabolism with growth of infectious agents; (4) changes in membrane receptors of pathogens and macroorganisms; (5) the formation of mixed associations of virulent, opportunistic pathogens, chlamydia, viruses, prions, myco- and ureaplasmas, gardnerella, rickettsia, fungi, protozoa, and helminths.

Failure of Immune Responses

Lack of reactions. The defeat of the cellular link of immunity causes viral and fungal infections, humoral links are bacterial, and combined lesions of the immune system contribute to the disruption of the intercellular interactions of T- and B-lymphocytes; defeat of the phagocytic link determines severe bacterial infections, and defeat of components of the complement system leads to recurrent infections. Purine metabolism disorders contribute to the development of T-immunodeficiencies, and suppression of the migration and cooperation of immunocompetent cells—immunodeficiency. Immunity blocking develops in malignant neoplasms. The “slip phenomenon” causes the development of protective mechanisms on the average number of malignant cells, and small and large concentrations of cells are difficult to recognize. The “blocking phenomenon” consists of the loss of cytotoxicity of anti-cancer antibodies in the absence of complement, and the concept of the “parity phenomenon” implies a stable quantitative balance of malignant and specific killer T cells.

Features of antiviral immunity. The mimicry of viruses of biologically active compounds necessary for cells causes the potential danger of an immune response (Zemskov et al., 2020). Location of the virion antireceptor in narrow recesses (crevices, canyons) inaccessible to the active centers of antiviral antibodies, reduces the effectiveness of humoral protection. The cellular factor, which is natural killers that lyse targets infected with viruses, is inactivated during fever, stress, and the administration of corticosteroids. Interferons (α-, β-, γ-), blocking the affected cells, induce intestinal, cardiovascular, and urinary syndromes. In some cases, the SARS-CoV-2 virus suppresses the synthesis of type I, II, III interferons in infected human lung tissues, which is combined with the release of pro-inflammatory cytokines against the background of a deficiency of circulating T-lymphocytes.

Reaction activation. Mediator (type I), cytotoxic (type II), immunocomplex (type III), and cellular (type IV) reactions accompany worm infestations, fungal infections, protozoan lesions, etc. Selective hypersensitivity of the immune system to drugs can induce anaphylactic shock, Stevenson’s disease, or Lyell’s disease.

Pathogenicity of reactions. With the release of endotoxins, bacteria in a sensitized organism cause endotoxin shock, under the influence of pathogens, autoantigens are modified, mimicry antigens are formed on the cells of the host and infect them, and due to the integration of viral RNA into the genome, the cell receptors change. With the formation of medium- and large-molecular complexes, autoimmune diseases develop, and with a slowdown in the excretion of circulating immune complexes from the body due to the breakdown of IgG, associated pathogens, toxins with relapse of diseases (for example, diphtheria), etc. are released. Graft-versus-host reaction occurs due to aggressive immune reactions of the graft against the host with the manifestation of Runt disease (dwarf disease), Simonsen’s phenomenon (the key manifestation is splenomegaly), and homologous disease in adults without growth retardation, among others.

Reaction competition. Simultaneous deployment of cellular (antiviral) and humoral (antibacterial) immune responses inhibits both defense mechanisms. Allergy prevails over immune deficiency. DTH slows down ITH, and vice versa. Allergy and autoimmune pathology modify immune deficiency. Excess antibodies inhibit cellular immunity. Antigen-free revaccination with modulators depletes immune memory. Vaccine immunity suppresses natural resistance, stimulating the formation of anamnestic antibodies, and reducing the number of uncommitted lymphocytes.

MECHANISMS (LEVEL) OF REGULATION OF IMMUNE REACTIVITY

An important mechanism for preventing, forming and eliminating diseases of the immune system is maintaining the balance of various mechanisms for regulating the reactivity of the body (Mikrobiologiya dyya..., 2020).

The levels of natural regulation of immune reactivity are determined by natural compensatory mecha-
isms before the development of diseases of the immune system in the patient.

The organism level: the joint functioning of regulatory systems: central nervous, endocrine, immunometabolic, hematological, etc. (Zemskov et al., 2008, 2018b).

The phenomenological level consists of natural resistance, tachyphylaxis, innate, species immunity, and adaptive immunity (Petrov et al., 2017). These mechanisms can be corrected by various modulators: thymopeptides, myelopeptides, interferons, nucleic acids, synthetic modulators, etc. (Zemskov et al., 2018b).

The system level is based on associated variations in immune, biochemical-metabolic, hematological, bacteriological, specific clinical status, etc. (Zemskov et al., 2017).

The grouped by immunity level is determined by the state of cellular (T-dependent), humoral (B-dependent), phagocytic (non-specific), cytokine (inflammatory), metabolic and other indicators (Zemskov et al., 2018b). The development of disease occurs in cases when the damaged link of reactivity is in demand during the pathological process.

The specialized level includes antibody formation, ITH and DTH, immune memory and tolerance, the ratio of parameters of free radical oxidation of lipids and proteins, and mechanisms of the antioxidant system (Zemskov et al., 2008, 2018b, 2020).

The detailed to signal targets level can be characterized by sets of key tests, the results of which specify the model ISDF and MDF formulas (Immune System Disorder Formula and Metabolic Disorder Formula). So, for example, in the acute period of pyelonephritis in patients, according to the ISDF (B^2 MMM^3 NSTSp^2), there is an accumulation of the third degree of both B-cells and a marker of autoaggression of medium-mass molecules (MMM) against the background of an insufficient level of superoxide dismutase of the antioxidant system (Zemskov et al., 2018b).

The level of genetic regulation of immune reactivity regulates infectious and somatic morbidity, is active in the deployment of protective and immunopathological reactions, the vaccine response, and the effectiveness of correction. Specific regulation of processes is carried out by the genes of the human major histocompatibility complex (MHC), the HLA system, antigens of the AB0 system, Rh factor, serum haptoglobins, etc. A distinctive feature of this level is that the listed genetic systems are located on different chromosomes: on chromosome 6—the HLA system, on chromosome 9—the AB0 system, on chromosome 1—the Rh factor, and at the same time they function as a single whole (Vasilyeva, 1992; Zaretskaya et al., 2002; Zemskov et al., 2008).

Pathological Regulation of Immune Reactivity

Pathological endogenous lymphoid regulation of immune reactivity occurs due to the immune system reaching the limit of competence, which contributes to the development of immune-dependent, immune-associated and other diseases (Khaitov et al., 2010; Zemskov et al., 2015).

Pathological endogenous metabolic regulation of immune reactivity is realized due to the accumulation of acute phase proteins, low molecular weight nucleic acids in the body, the formation of an imbalance of the free radical oxidation/antioxidant system, the induction of the metabolic syndrome (abdominal obesity, type 2 diabetes mellitus, arterial hypertension and dyslipidemia), which causes immunodeficiency states (Prokopenko and Brovkina, 2003; Lutsky et al., 2016; Zemskov et al., 2020).

Pathological exogenous ecological regulation of immune reactivity is carried out by abiotic and biotic environmental factors. Natural factors include temperature, radiation, humidity, daylight hours, magnetic field disturbance, chemical composition of air, soil, water, etc., and biotic factors include microflora, flora and fauna. These factors have a soft/hard, direct/indirect, regulated/unregulated, short/long-term, local/global, accumulating/non-accumulating effect (Zemskov et al., 2018b).

Clinical regulation of immune reactivity has an impact on localization, pathogenesis, etiology, stage, combination, and allergization of diseases (Zemskov et al., 2017, 2018b; Mikrobiologiya dlya..., 2020).

Influence of localization of diseases on immunopathology. In quantitative terms, in the acute period in patients with ophthalmic chlamydia, significant differences in immune markers from the norm were established in 36%, with urogenital chlamydia—in 68%, and with Reiter’s syndrome—in 80%. Qualitatively, in ophthalmic chlamydia, there are minimal changes in hemograms with a deficiency of T- and B-cells, while dysimmunoglobulinemia, inhibition of neutrophil metabolism, and stimulation of the level of pro-inflammatory cytokines were found. In urogenital chlamydia, the severity of inflammation and sensitization increases against the background of inhibition of T- and phagocytic immunity, imbalance of humoral protection, and accumulation of pro-inflammatory interleukins. Reiter’s syndrome is characterized by stimulation of the white blood cells, and disproportionate T- and B-mediated cytokine reactions with suppression of phagocytic immunity (Novikov, D.K. and Novikov, P.D., 2009).

Influence of the pathogenesis of diseases on immunopathology. In the period of exacerbation of exoge-
nous and endogenous bronchial asthma, the formation of immunopathology is noted in 58 and 85% of cases, respectively. At the same time, in exogenous bronchial asthma, significant variations in the cellular component are observed, that make up more than 66%, and the remaining variations (hematological, immune humoral, phagocytic, cytokine) which can be considered average, make up 33–66%. In endogenous bronchial asthma, the severity of changes is significantly higher, it is maximum for all markers, except for cytokines.

Influence of the etiology of diseases on immunopathology. Quantitative and qualitative differences in laboratory markers in patients suffering from secretory viral and purulent bacterial otitis were expressed as a decrease of 42 and 77% of marker values, respectively. Qualitatively, in the first case, the changes concerned T- and B-cells, their regulatory subpopulations, and in the second case, the main populations of lymphocytes, natural killers, and phagocytosis.

Influence of disease stage on immunopathology. In patients with primary acute and exacerbation of chronic adenitis, an unambiguous reaction was formed in as inflammation, sensitization, suppression of T- and phagocytic links and activation of the B-link of immunity, with accumulation of circulating immune complexes. At the same time, in chronic inflammation, an imbalance of pro- and anti-inflammatory cytokines, leukocytosis, and eosinophilia were also observed. In general, in these diseases, the number of “perverted” laboratory parameters was 49 and 78%, respectively.

Influence of combinations of diseases on immunopathology. In patients with chronic autoimmune thyroiditis, an imbalance of thyroid hormones, an increase in antithyroid antibodies and circulating immune complexes, suppression of the T-suppressor, and irritation of the humoral immunity were observed. In chronic bronchitis, lymphopenia, accumulation of granulocytes, suppression of cellular immunity, accumulation of killers, and accumulation of IL-4 developed. With a combination of both diseases pathogenesis clusters of the two diseases were noted.

The influence of allergization on immunopathology. In the acute period of purulent infection of soft tissues in patients, a decrease in 42% of immune parameters is recorded. After additional development in patients with allergic dermatitis, the number of altered indicators reaches 81%. Qualitatively, there is suppression of cellular defense reactions, imbalance of B-lymphocytes and IgG, induction of auto-aggressive and toxic reactions, and total suppression of the absorptive and metabolic capacity of phagocytes against the background of accumulation of pro-inflammatory cytokines and cells with a tendency to apoptosis.

Alternative Mechanisms (Phenomena) of Immune Responses

The phenomenon of the unity of specificity and non-specificity. Protection against internal and external antigenic intervention is based on primary non-specific and secondary specific mechanisms. A specific immune response is subject to non-specific regulation by thymimimetics, cytokines, fragments of the destruction of immune globulins, nucleic acids, endotoxins, etc. (Natsional’naya kontseptsiya..., 2012; Vaktsoy i vaktsinatsiya, 2014; Zemskov et al., 2017; Mikrobiologiya dlya..., 2020).

The preference phenomenon representing the ratio of hypersensitivity (allergy) and insufficiency (immunodeficiency). Allergy, as an extreme degree of manifestation of immune reactions, carries protective and pathogenic potentials. With simultaneous formation with immunodeficiency, it is predominant and at the same time aggravates its severity, and modifies and reduces the effectiveness of immunotherapy. At the same time, immune deficiency itself can show a positive potential in autoimmune and allergic diseases and a negative potential in many other conditions (Goryachkina and Kashkin, 2009; Zemskov et al., 2017).

Pendulum phenomenon (stimulation and suppression). In any pathological process in the immune system, reactions that are polar in relation to stimulation and suppression develop. At the level of individual nosoforms, the development of immune-dependent, allergic, auto-aggressive, immunocomplex diseases, primary and secondary deficiencies, and cancer is provoked. In immunosassociated processes, in which purulent infections of soft tissues, bronchopulmonary pathology, cerebrovascular lesions, etc. develop, an imbalance is recorded in various indicators. For example, in patients suffering from acute myocardial infarction, the general stimulation of reactivity in the acute period provokes a delayed pathology, such as aneurysms, Dressler’s disease, and the risk of complications decreases during inhibition (Zemskov et al., 2017, 2018b).

Web phenomenon (particular, intermediate, and general). To maintain the body’s homeostasis, several levels of protection develop: regional, subsystemic and systemic immunity. Regional immunity provides organ protection of the body, directly communicating with the external environment. Subsystemic immunity should be noted with is provided by the skin, and mucous membranes of the respiratory, digestive and genitourinary tracts (Zemskov et al., 2018b). The proof of existence systemic immunity is the formation of strong correlations between laboratory markers. For example, in autoimmune thyroiditis, there is formation of positive correlations between the level of thyroid hormones and insulin with IgG and circulating immune complexes and negative correlations with the T-link of immunity have been shown (Zemskov et al., 2017).
The phenomenon of harmonization (variability, normalization, synchronization). In the acute period of diseases, there is a high variability of hemato-immuno-metabolic, bacteriological, clinical, and other processes. In the remission/recovery stage, laboratory parameters normalize, which is combined with the synchronization of the functions of regulatory systems, namely the immune, endocrine, and central nervous systems (Petrov et al., 2017; Zemskov et al., 2018b).

The phenomenon of specificity and generality (personification and consistency). The induction of specific immune responses to an allergen in anaphylactic shock or Lyell’s syndrome is accompanied by instant involvement of the endocrine system in the pathological process, with the release of stress hormones, and involvement of the nervous system, with characteristic behavioral manifestations.

The phenomenon of disintegration and integration (dissimulation and assimilation). As a result of pathological and physiological destruction of somatic and microbial cells, biologically active substances are released: R-proteins, transfer factor, endotoxins, high- and low-molecular nucleic acids, acute phase microbinding proteins, C-reactive protein (CRP), etc., which initially promote the development of inflammation, and then cause compensatory activation and integration of immune functions (Zemskov et al., 2018b).

CONCLUSIONS

Thus, various diseases of the immune system have been considered in detail at various periods of a person’s life, with their dependence on external and internal factors of various nature, with detailed phenomenological characteristics, the influence of diseases of various nature on the development of diseases of the immune system, and many other important facets of this problem.

FUNDING

The work was carried out within the R&D Research Program at the Vishnevsky National Medical Research Center for Surgery (Moscow) and the Burdenko Voronezh State Medical University.

COMPLIANCE WITH ETHICAL STANDARDS

The authors declare they have no conflicts of interest.

All procedures performed in studies involving people comply with the ethical standards of the institutional and/or national committee for research ethics and the 1964 Helsinki Declaration and its subsequent changes or comparable ethical standards. Permission from each of the participants included in the studies and informed voluntary consent are not required, since the patients were subjected to research in terms of providing medical care provided by the Ministry of Health of Russia in an inpatient setting.

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