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Mathematical Modeling for the Development of a Multilevel "Electronic Physician Assistant" and Simplified Assignment of Corrective Therapy to Immunocompromised Patients

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Mathematical Modeling for the Development of a Multilevel "Electronic Physician Assistant" and Simplified Assignment of Corrective Therapy to Immunocompromised Patients

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I. Introduction

One of the achievements of modern medicine is the development of principles for prescribing immunotherapy to patients, consisting of assessing the immune status, verifying the diagnosis of the underlying disease, comparing the signaling mechanisms of pathology and targets of the modulator, and testing the correction option in practice. Considering the certain complexity of the implementation of the above technologies, permission was given to develop a simplified algorithm for identifying the main immunopathological syndromes by the questionnaire method, to carry out auxiliary corrective therapy with traditional drugs, and to simplify the appointment of targeted immunotherapy to patients based on a set of programs for the Electronic Computing Machine, taking into account the laboratory examination of patients.[1,2,3,4]

II. Pre-Laboratory Analysis

a) Identification of immunocompromised persons by the method of pre-laboratory analysis

Table 1 shows questionnaires for identifying 11 immunopathological syndromes, which include a predisposition to immune disorders, secondary immunodeficiency, infectious bacterial, viral, allergic, pseudo-allergic, metabolic, autoimmune and immunocomplex, lymphoproliferative, other syndromes, and concomitant chronic and combined diseases and conditions.[5]

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Table 1: Immunopathological syndromes

I. Immune Disorder Predisposition Syndrome
1. Professional harm. 2. Bad habits: smoking, alcohol, drug addiction, substance abuse, etc. 3. Frequent cooling, overheating, change of climatic zones. 4. Metabolic disorders, obesity. 5. Transfer in the last 3-6 months of great stress, burns, poisoning, physical exertion, radiation. 6. Risk groups - childhood, pregnancy, childbirth, menopause, old age. 7. Long-term stay in isolated spaces (prisons, submarines, spaceships). 8. Transplantation of foreign organs, tissues, implants.
II. Secondary Immunodeficiency Syndromes
1. Syndrome of immune deficiency in children 1 year of life, is manifested by frequent, chronic infectious lesions of opportunistic pathogens, low virulent flora, viruses, chlamydia. 2. The syndrome of immunodeficiency in the elderly is manifested by frequent viral, bacterial, fungal infections of the bronchopulmonary, digestive, and genitourinary systems. 3. Syndrome of general variable immunodeficiency, which implies protracted recurrent bacterial infections of the respiratory, intestinal tracts, paranasal sinuses. 4. Post-tonsillectomy syndrome, which is characterized by recurrent infections of the nasopharynx, upper respiratory tract, hyperplasia of the lymphoid tissue of the nasopharynx. 5. Post-splenectomy syndrome with increased sensitivity to a wide range of infections. 6. Post-appendicectomy syndrome, manifested by chronic infections of the intestinal tube, dysbiosis. 7. Medical factors, which include surgery, anesthesia, antibiotics, nitrofurans, alkylating derivatives, corticosteroids, antimetabolites, drugs.
III. Infectious Bacterial Syndrome
1. The frequency of infectious diseases is more than 3-4 times a year in adults, more than 6 times in children. 2. Atypical temperature reaction in case of an infectious disease. 3. Chronic pustular diseases of the skin, subcutaneous fatty tissue, soft tissues (furunculosis, sycosis, abscesses, lymphadenitis, phlegmons, proctitis, paraproctitis). 4. Gastrointestinal infections (gastroenteropathy, chronic diarrhea, dysbiosis, cholecystitis, pancreatitis). 5. Chronic lesions of the urogenital tract (pyelonephritis, cystitis, chlamydia, gardnerellas, mycoplasmosis, Reiter's syndrome). 6. Chronic infections of ENT organs (sinusitis, frontal sinusitis, gaymority, purulent otitis media). 7. Purulent keratoconjunctivitis. 8. Torpid to treatment recurrent aphthous stomatitis. 9. Specific infections tuberculosis, toxoplasmosis, brucellosis, leprosy, syphilis, malaria. 10. Sepsis, septicopyemia, peritonitis, abscesses of the lungs, and other organs.
IV. Infectious Viral Syndrome
1. Frequent relapses of viral infections. 2. Refractoriness, i.e. resistance of viral diseases to traditional therapy. 3. Prolonged low-grade fever, unmotivated lymphadenopathy, chronization of infectious processes. 4. Persistent viral infections - cytomegalovirus, herpes, caused by the Epstein-Barr virus, Dengue fever, chronic viral hepatitis (B and C). 5. Persistently recurrent clinical manifestations of papillomatosis and candilomatosis against the background of ongoing standard therapy. 6. Chronic fatigue syndrome, which occurs in young women and men. 7. Risk groups of ARVI. These include newborn babies, early age, with late-onset of reactivity, low body weight, and those born during pathological pregnancy. These are older children with chronic diseases of the heart, lungs, kidneys, etc.
V. Other Infectious Syndromes
1. Mycoses (superficial, subcutaneous, systemic, opportunistic). 2. Lesions with protozoa (trypanosomes, leishmania, lamblia, trichomonad, malaria plasmodium, toxoplasma, intestinal balantidia). 3. Defeats by intracellular parasites (chlamydia, gardnerella, mycoplasma, ureaplasma).

4. Lesions by helminths- intestinal (ascariasis, trichinosis, trichocephalus), extraintestinal (opisthorchiasis, fascioliasis, paragonimiasis), larval (echinococcosis, cysticercosis, toxocariasis), tropical (strongyloidiasis, ankylostomids), schistosomiasis.
VI. Allergic Syndrome
1. Food intolerance. 2. Drug intolerance, vaccination reactions, iatrogenic diseases (serum sickness, D-penicillamine nephropathy, drug thrombocytopenia). 3. Transfer in anamnesis of anaphylactic shocks, Quincke's edema, Lyell's syndrome, Stephen-Johnson's, drug-disease, and other allergic reactions. 4. Allergic reactions to insect bites, contact with plants, odors, dyes, cosmetics, house dust, chemicals, bio-preparations, precious metals. 5. Helminthic invasion. 6. Cold allergy.
VII. Pseudo-allergic Syndrome
1. Violations of the diet (citrus fruits, fish, potatoes, cheese, chocolate).
2. Violations of histamine inactivation in the body.
3. Disorders of intestinal absorption.
4. Insufficiency of the hepatobiliary system (liver cirrhosis, cholecystitis, cholangitis).
5. Dysbacteriosis.
6. Activation of the complement system with accumulation (C3a, C2в, C4a, C5a).
7. Reaction to medications - local anesthetics, X-ray contrast agents, carrying out physiotherapy procedures (inhalation, electrophoresis).
VIII. Metabolic Syndrome
1. The actual metabolic syndrome (abdominal obesity, type 2 diabetes mellitus or impaired glucose tolerance, arterial hypertension, dyslipidemia). 2. Dysnucleotidosis. 3. Disorders of free radical oxidation of lipids and proteins. 4. Disorders of the antioxidant system.
IX. Autoimmune, Immunocomplex Syndrome
1. Diseases with an autoimmune component (hemolytic anemia, systemic lupus erythematosus, pernicious anemia, Sjogren's syndrome, Behcet's disease, Goodpasture's syndrome, systemic vasculitis, Wegener's granulomatosis). 2. Diseases with the presence of immune complexes (rheumatoid arthritis, ankylosing spondylitis, essential cryoglobulinemia, scleroderma, etc.) 3. Renal diseases (acute glomerulonephritis, Berger's disease, renal transplant). 4. Skin diseases (dermatitis herpetiformis, pemphigus, pemphigoid). 5. Diseases of the gastrointestinal tract (Crohn's disease, ulcerative colitis, active hepatitis, primary biliary cirrhosis). 6. Neurological diseases (subacute sclerosing panencephalitis, amyotrophic lateral sclerosis, multiple sclerosis, etc.). 7. Diseases of the endocrine system (chronic autoimmune thyroiditis).
X. Lymphoproliferative Syndrome
1. Symptomatic (secondary) lymphoproliferative syndrome. 2. Lymphadenopathy, chronic tonsillitis, hypoplasia of lymph nodes. 3. Thymomegaly, hyperplasia, or hypoplasia of the thymus in children. 4. Transferring a history of infectious mononucleosis. 5. Lymphogranulomatosis (Hodgkin's disease). 6. Non-Hodgkin's lymphomas. 7. Burkitt's lymphoma. 8. Sarcoidosis. 9. Macroglobulinemia, polyclonal hypergammaglobulinemia. 10. The presence of any malignant neoplasms.
XI. Syndrome of Concomitant Chronic, Combined Diseases, and Conditions
1. Exacerbation of any chronic diseases at least 2-3 times a year. 2. Combinations of diseases of the same type (ischemic heart disease + hypertensive disease,

bronchial asthma + chronic pneumonia), or different genesis (autoimmune thyroiditis + obstructive pulmonary disease).
3. Combinations of immunopathological syndromes (infectious + allergic, immunodeficient + infectious).
4. Medicinal complications (dysbacteriosis, toxicosis, allergization, immune disorders).

b) Interpretation of the results of the analysis of the pre-laboratory examination of patients

It concerns the syndrome of susceptibility to immune disorders, displayed when there are three positive answers to any question in the questionnaire. This also includes immunodeficiency, infectious, pseudo-allergic syndromes, and a syndrome of combined and accompanying diseases, presented with a positive answer to two questions of the questionnaire. And, finally, autoimmune, lymphoproliferative, allergic, and metabolic syndromes, which are displayed with a positive answer to one question of the corresponding questionnaires.

c) Options for the conclusion based on the results of the survey

According to these results, the patient belongs to a risk group for predisposition or immunodeficiency syndromes and a high-risk group for allergic, autoimmune, lymphoproliferative, or the same, with a combination of several immunopathological syndromes.

III. Syndromic Appointment of Auxiliary Immunotherapy

Auxiliary immunotherapy involves the use of traditional medicines with an immunotropic effect in the treatment of patients.[6,7]

a) Risk group

Patients from this group, in addition to the basic treatment, receive "small" immune correctors. These include adaptogens (Manchurian aralia, Roseola Rosea, extracts from ginseng, Pantocrine, Eleutherococcus, Esberitox, tincture of Chinese magnolia vine) and metabolites, antioxidants, and vitamins (Riboxin, Potassium orotate, Hypoxenes, Reamberin, Tramelan, Pentoxyl, Methyluracil, Mildronate, Pantholex, vitamins of group B, C, A, E, Quercetin, Pangamic acid, Lipoic acid, Asparkam, brewer's yeast, Sodium nucleinate). The group of other drugs includes Piracetam, Polistim, Bendazole, Glutamic acid, Curantil, Apilac, Splenin, Leucogen, interferon, Cinnarizine, Zaditen. Finally, the eubiotics group consists of Acipol, Acylact, Bactisubtil, Bactobacterin, Bifacid, Bifibin, Bifilong, Bifidumbacterin, Bificol, Colibacterin, Biphilis, Lactobacterin, Vitanar, Linex, Narine, Sporobacterin.

b) High-risk group

Patients of this group, in addition to traditional therapy, receive a combination of two or three small immunocorrectors or broad-spectrum modulators. The latter include Sodium nucleinate, Isoprinosine, thymus drugs, Myelopid, Levamisole, Hemodez, Reamberin, Splenin, Sanaviron, Leukinferon, Polyelectrolytes, Diucifon, etc.

c) Infectious bacterial syndrome

In this syndrome, combinations of the following drugs are recommended: (1) Eleutherococcus + Interferon, (2) Vitamin B6 + Riboxin, (3) Apilak+ lipoic acid, (4) Vitamin B6 + Riboxin+ Panangin, (5) Dibazol + Eleutherococcus+ Asparkam,(6) Dibazol + Glutamic acid + Pantocrine, (7) Potassium orotate + Duovit+ Methyluracil, (8) Vitamin B15 + Quercetin, (9) Sodium nucleinate + Panangin+ Duovit, (10) Dry brewer's yeast + Kurantil+ multivitamins+ Asparkam, (11) Riboxin + Potassium orotate + Methyluracyl.

When choosing antibacterial drugs, in addition to their antibiotic sensitivity to pathognomonic microflora, it is recommended to take into account their immunosuppressive effect, for example, in Abactal, Ampicillin, Isoniazid, Kanamycin, Chloramphenicol, Monomycin, PASK, Pyrazinamide, Rifampicin, Streptomycin, Tetracycline, Furacillin, Furagin, and immunostimulating activity, as in the case of Erythromycin, Miramistin, Nizoral, Nystatin, Levin, Roxithromycin, Amphotericin, Metacyclin, Bactrim, Macropen, Isoniazid, and Clindamycin. [8,9]

d) Infectious viral syndrome

In this case, it is permissible to use a combination of two or three drugs. The list includes Dibazol, Interferon, Kurantil, Quercitin, Leukinferon, Levamisole, Myelopid, Methyluracil, Pentoxil, Prodigiosan, Remantadin, Arbidol, Vitamin A, Diucifon, Acyclovir. For persistent viral hepatitis, respectively, Katergen, Piracetam, Leukinferon, Sodium nucleinate, Lipoic acid, Acyclovir, Ribamidil, Sirepar, Cycloferon, human α-interferon, or recombinant genetically engineered human interferon Reaferon.

e) Metabolic syndrome

f) Dysnucleotidosis

In this condition, Derinat, Ridostin, Sodium nucleinate, Riboxin, Potassium orotate, Methyluracil, Pentoxil, Asparkam (Panangin), Vitamin B6, Glycerophosphate, Folic acid, Hypoxene, Cygapan, Lemont, and Tikveol are quite effective.

g) Elimination of metabolic disorders

It is carried out by energizers Riboflavin and Nicotinamide, glycolysis activators Thiamine and Riboxin, and the tricarboxylic acid cycle Biotin Lipoat.

h) Stimulates antioxidant defenses

These drugs include antioxidant defense stimulants β-carotene, Retinol, α-tocopherol, Ascorbic acid, Hypoxene, Limontar, hepatoprotectors Essentiale, Carsil, Lipostabil, Phosphoglyph, Tikveol, Bemitil, Katergen, and Flacoside, adaptogens Aralia Manchu, Roseola pink, Ginseng, Pantocrine, Eleutherococcus, Esberitox, tincture of Chinensis magnolia vine, metabolism activators Potassium orotate, Hypoxene, Tramelan, Pentoxil, Methyluracil, Mildronate, eubiotics Acipol, Acylact, Bactisubtil, Bactobacterin, Bifacid, Colibacterin, Biphilis, Lactobacterin.

i) Allergic syndrome

j) Treatment principles

They consist of (1) elimination of the allergen, (2) the use of agents that nonspecifically suppress allergic reactions, (3) nonspecific immunosuppressive therapy, (4) specific immunotherapy, (5) targeted immunomodulation, (6) non-drug immune correction. In practice, one principle of treatment is rarely used, mainly combinations of them are used. The tactics of treating patients significantly depend on the stage of the disease. So, in the period of exacerbation, therapy is aimed at eliminating acute clinical manifestations of an allergic reaction, and in the period of remission at preventing its progression.

k) Pseudoallergic syndrome

A variety of medications are used to relieve this condition.

i. *Antihistamines*

There are six groups of antihistamine compounds. These include (1) ethylenediamine, Suprastin, (2) ethanolamines, Diphenhydramine, (3) alkylamines, Dimethindene, (4) phenothiazine derivatives, Pipolfen, (5) piperazine derivatives, Cinnarizine, (6) antihistamines of various origins Tavegil, Fenkarol, Bicarfen, Peritol, Pernovin, Diazolin, Ketotyphene.

l) H1 - 2nd generation antihistamines

These include Teldan, Claritin, Gismanal, Zirtek, Semprex, Avastin, Terfenadine, Astemizole, Cimetidine, etc.

m) Hepatoprotectors

This group includes Legalon, Silibor, Katergen, Zixorin, LIF-52, and Essentiale.

n) Choleretic drugs

Which are Alcohol, Lyobil, Cholenzyme, decoctions of the sandy immortelle flower, immortelle extract, corn silk, Tanacehol, Konvaflavin, Flacumin, Oxyphenamide, and Tsikvalone.

o) Enteral sorbents

Polysorb, Polyphepan, Carboline, Enterosgel, Enterodesis are quite active.

p) Eubiotics

Various eubiotics, Acipol, Bactisubtil, Bactobacterin, Bifilong, Bifilis, Bifinormalizer, Bifidumbacterin, have also proved to be effective.

q) Autoimmune syndrome

i. *Correction principles*

They consist of (1) Elimination of "forbidden" clones of sensitized lymphocytes, (2) Removal of an immunogen or an adjuvant. (3) Plasmapheresis, (4) Immunosuppressive therapy, (5) Blockade of mediators of immune responses with antihistamines, (6) Replacement therapy for pernicious anemia with vitamin B12, for myxedema thyroxine, (7) Prescription of antiinflammatory drugs, nonsteroidal drugs and salicylates, corticosteroids, (8) Prescription of cyclosporin A, (9) Immunotherapy using causative allergens, (10) Immunocorrection of T-suppressor deficiency, (11) Use of gammaglobulins (immunoglobulins) for intravenous administration, (12) Application monoclonal antibodies against pro-inflammatory cytokines, (13) Autologous hematopoietic stem cell transplantation against the background of high-dose immunosuppression, (14) Gene therapy due to suppression of cytokine formation by genes transferred by viral vectors. It is essential to note that the effectiveness of the autoimmune syndrome correction is temporary and is expressed in remission.

r) Lymphoproliferative syndrome

i. *Correction principles*

The main types of treatment for lymphoproliferative and malignant neoplasms are surgical, radiation, and drug actions, which have a suppressive effect on the immune system, and this is the basis for the appointment of the thymus, polysaccharide, nucleic acid drugs, interferons, and interferon genes, synthetic polyoxidonium stimulants, Dapsone, Lycopid, Levamisole, vitamins, as well as blood plasma, etc.

IV. Simplified Purpose of Patients with Differentiated Immunotherapy based on the Software

a) Unified immunotherapy

This type of immunotherapy is implemented, taking into account the nature of the disease.[10,11,12] The choice of options is carried out according to the formulas of disorders of the immune system (FDIS is compiled by selecting the most significantly altered immune parameters from the normal level)[1] for specific diseases. The analysis of the immune status in patients may not be carried out because a verified clinical diagnosis of the disease, the key parameters of the previously defined typical FDIS for a specific isoform, and their coincidence with the passport targets of modulators are important (Table 2-4, 7).

Table 2: Targets of modulators grouped by immunity units

Preparations	C	H	N	Preparations	C	H	N
Adaptogens			+	Ozonized sodium chloride	+	+	+
Anabol	+			Lysozyme			+
Autohemotherapy	+	+	+	Methyluracil	+	+	+
Amixin	+			Myelopid	+	+	+
Acyclovir	+			Trace elements	+	+	+
Bronchomunal	+	+	+	Leukomax	+		
Vaccines		+		Likopid	+	+	+
Vitamin A	+		+	Sodium nucleinate	+	+	+
Vitamins B	+		+	Potassium orotate	+		+
Vitamin C			+	Polyoxidonium	+	+	+
Viusid	+		+	Synthetic polynucleotides	+	+	+
Gammaglobulin		+		Plasma	+		+
γ-interferon	+		+	Plasmapheresis	+		+
Gepon	+	+	+	Panavir	+		+
Hemodez	+	+	+	Piracetam	+		
Hypoxene	+	+	+	Plasmapheresis	+	+	+
Heparin	+	+		Polyelectrolytes	+	+	+
Glutoxim	+	+	+	Pentoxil	+	+	+
Dalargin	+	+	+	Pyrogenal	+	+	+
Derinat	+	+	+	Preventan	+	+	+
Dibazol	+	+	+	Prodigiosan	+	+	+
Diuciphon	+	+	+	Reaferon	+		
Diuciphon	+			Reopolyglyukin	+	+	+
Zixorin			+	Riboxin	+		+
Isoprenosine	+	+	+	Ridostin	+	+	+
Isoprenosine			+	Roncoleukin	+	+	+
Immunomax	+	+	+	Ruzam	+		+
Immunomax	+	+	+	Splenin	+	+	+
Indomethacin	+			Superlimph	+	+	+
Lysate of bacteria IRS-19			+	Tamerid	+	+	+
Katergen	+			Thymus preparations	+	+	+
Camedon		+		Trichopolus			
Combined immune drug	+	+	+	Body ultraviolet irradiation			+
Kipferon	+	+	+	Ultraviolet blood irradiation	+	+	
Quercetin	+	+		Phenazepam	+		+
Bloodletting	+	+	+	Cycloferon	+	+	+
Leakadin	+	+	+	Cinnarizine	+		
Levamisole	+	+	+	Cimetidine	+		+
Leukinferon	+		+	Cygapan	+	+	+
Low-intensity laser radiation	+	+	+	Erythrocytes	+	+	+

Legend: (C) cellular, T-dependent, (H) humoral, B-dependent, (N) nonspecific links of immunity, + target of positive action of the drug

Table 3: Distribution of the action of modulators on the parameters of the immune system

Preparation	CD3+	CD4+	CD8+	CD16+	CD19+	Ig	CIC	MWM	CD11в	AF	MF	Tc-Lph
Autohemotherapy	+				+	+				+		
Vitamins	+	+	+	+		+						
Viferon	+		+			+				+		+
Hemodez	+	+	+		+	+						
Hypoxene	+	+			+	+				+	+	+
Gepon	+	+	+			+	+			+	+	+
Glutoxim	+					+					+	+
Dalargin		+			+	+						+
Decaris/levamisole	+		+		+	+	+					
Derinat	+	+	+			+			+		+	+
Diuciphon		+			+	+	+			+	+	
Donor γ-globulin	+	+				+	+			+	+	
Isoprinosine	+					+		+		+	+	+
Imudon						+				+	+	+
Immunomax	+	+							+	+	+	+
Imunofan	+	+	+	+		+				+	+	+
Combined immune preparation (CIP)					+	+		+		+		+
CIPferon	+		+	+		+	+			+	+	+
Leakadin	+	+	+	+	+	+		+				
Leukinferon	+	+	+		+	+				+	+	
Likopid	+				+	+			+	+	+	
Limontar	+	+	+			+	+	+		+		
Therapeutic plasmapheresis	+	+		+		+	+	+				
Myelopid	+	+	+		+	+				+		+
Neovir	+	+			+	+						
Low-intensity laser radiation	+	+	+		+	+				+		+
Sodium nucleinate	+	+	+	+	+	+	+	+		+	+	
Ozone	+	+			+	+	+			+	+	
Polystim	+	+			+	+						
Polyoxidonium	+	+	+	+	+	+		+		+	+	
Polysaccharides	+	+	+	+	+	+				+	+	+
Ridostin		+	+		+	+	+			+	+	
Sorbents	+	+	+		+	+				+		
Splenin	+	+	+	+		+	+					+
Superlimph	+						+			+	+	+
Tamerid	+	+	+	+								+
Thymomimetic	+	+	+	+	+	+	+			+	+	+
Tikveol					+	+		+			+	
Ultraviolet blood irradiation		+		+	+					+	+	
Cygapan						+	+			+		
Esberitox	+	+	+		+	+					+	

Legend: AF - absorption function (phagocytic index and number), MF - metabolic function (NBT-test spontaneous or activated), CIC- circulatory, immune complexes, MWM - medium-weight molecules, Tc-Lph - cytotoxic T-lymphocytes, + the effect of the drug is established

Table 4: Typical immune disorders in certain diseases

Diseases	FDIS
I. Bronchopulmonary diseases	
Acute pneumonia	$CD3_2^- IgM_2^- IgA_2^-$
Chronic pneumonia in adults	$CD3_3^- IgA_2^- IgM_2^-$
Chronic pneumonia in children	$CD3_2^- CD19_2^- IgM_2^-$
The mixed form of bronchial asthma in adults	$CD3_2^- CD19_2^- IgA_2^-$
Exogenous bronchial asthma	$Lph_2^+ CD4_2^- CD3_2^-$
Endogenous bronchial asthma	$RN_2^+ CD3_2^- NBTsp_2^+$
The mixed form of bronchial asthma in children	$CD3_2^- CD4_2^- CD8_2^-$
Corticosteroid bronchial asthma in adults	$CD3_2^- CD19_2^- IgA_3^-$
The mixed form of bronchial asthma, stage of exacerbation	$L_2^+ CD4_2^- CD3_2^-$
The mixed form of bronchial asthma, stage of remission	$RN_3^+ CD19_2^- MWM_2^+$
Chronic bronchitis	$CD3_2^- CD19_2^- IgA_3^-$
Chronic obstructive pulmonary disease	$CD4_3^- CD8_3^+ CIC_3^+$
Infectious destruction of the lungs	$CD3_2^- CD19_2^- IgA_3^-$
Chronic obstructive bronchitis	$CD3_2^- CD19_2^- IgA_2^-$
II. Purulent-inflammatory diseases	
Deep pyoderma	$IL8_3^+ CIC_3^+ NBTac_3^-$
Purulent soft tissue infection	$CD8_3^+ E_3^+ CD19_2^-$
Acute salpingo-oophoritis	$L_3^+ CIC_3^+ CD4_2^-$
Exacerbation of chronic salpingo-oophoritis	$Tc_3^+ IL8_3^+ T_3^+$
Acute pyelonephritis	$IgG^+_3 MWM^+_3 L^+_2$
Exacerbation of chronic pyelonephritis	$ESR_3^+ IgG_3^+ CD8_3^+$
Exacerbation of chronic calculous pyelonephritis	$CD4_2^- CD3_2^- FI_2^-$
Exacerbation of chronic non-calculous pyelonephritis	$CD8_2^- CD19_2^- CD3_2^-$
Exacerbation of chronic salpingo-oophoritis + cervicitis	$E_3^+ CD3_2^- CD3_2^+$
Cervicitis	$HLA\text{-}DR\text{-}Lph_2^+ CD3_2^- CD19_2^- IgA_2^-$
Exacerbation of chronic cystitis	$IgG_3^+ NBTac_3^- TNF_3^+$

Legend: FDIS is a formula for disorders of the immune system, built on three key parameters that are most different from the level of the norm, with an indication of the direction of the dynamics vector (+ hyperactivation, - deficiency) and the degree of these changes (1-3, where 1- I degree of changes is transient up to 33% of the norm, 2- II degree is reliable from 34 to 66%, 3- III degree highly significant> 66%), L - leukocytes, RN - rod-nuclear neutrophils, IL - interleukins. ESR- erythrocyte sedimentation rate, NBTac- NBT-test activated, NBTsp- NBT-test spontaneous, TNF- tumor necrosis factor, Tc- T-cytotoxic lymphocytes, T- T-lymphocytes, E- eosinophil, Lph- lymphocytes, FI- phagocytic index

The algorithm for prescribing differentiated immunotherapy is that the recommended drugs are selected for patients with certain diseases based on the key parameters of FDIS by the tables given. For example, in acute pneumonia with FDIS constituting $CD3_2^- IgM_2^- IgA_2^-$ (deficiency of T-lymphocytes, IgA, and IgM of the second degree), the recommended drugs for correcting $CD3_2$ deficiency are autohemotherapy, vitamins, Viferon, etc. Regarding IgM_2^-, IgA_2^- shows the same drugs, etc.

b) Generalized immunotherapy

It is used without considering the nature of the disease.[6] It is used in the severe clinical condition of patients. It is based on a generalized definition of altered links of immunity (by the presence of indicators with second-third degrees of immunodeficiency) and the choice of modulators based on grouped passport targets of action on individual links of the immune system without taking into account the nature of the diseases (Tables 2, 5).

c) Interpretation of the results of the immune examination of patients

If one or more indicators coincide in a particular patient, grouped by immunity links with tabulated ones, a conclusion is made about the deficit of the second - third degree of the link as a whole (Table 5).

Table 5: Reference values of laboratory parameters, grouped by immunity links

Immune indicator	Second - third degree of immune deficiency	Immune indicator	Second - third degree of immune deficiency
General T-Lph(CD3+)	<0,5-1,0 • 10^9/l		<1,9-3,7 CU
T-helpers (CD4+)	<0,38-0,74 • 10^9/l	CD11b+	<0,06-0,11 • 10^9/l
T-cytotoxic Lph(CD8+)	<0,14-0,28 • 10^9/l	PhI	<24,3-48,4 % neutrophils
T-activated Lph(HLA-DR+)	<0,04-0,08 • 10^9/l	PhN	<2,4-4,7microbial bodies/neutrophil
T-regulatory Lph(CD4+CD25+)	<0,03-0,07 • 10^9/l	NBTsp	<2,9-5,7 %
Natural killer cells (CD56+)	<0,18-0,36 • 10^9/l	NBTac	<7,5-15,0 %
B-Lph (CD19+)	<0,2-0,4 • 10^9/l	IL4	<6,6-13,1 pkg/ml
IgM	<0,6-1,3 g/l	IL6	5,5-10,9 pkg/ml
IgA	<0,5-1,1g/l	IL8	4,7-9,4 pkg/ml
IgG	<10,8-14,4g/l	TNF	0,06-0,13 pkg/ml
CIC	<9,1-18,3 CU		

Legend: CU- conventional units; PhI, PN - phagocytic index and number, other designations - see above

d) Detailed immunotherapy

It is carried out without taking into account the nature of the disease.[13] Specific critically reduced laboratory parameters of the second or third degree are determined in patients according to the table's values. Based on their coincidence with the passport targets of modulators, variants of detailed immunotherapy are selected.

e) Algorithm for prescribing detailed immunotherapy

The changed indicator/indicators in a particular patient are determined if its value coincides with the tabular value of the modulator target. According to these data, specialized drugs are selected for a prescription that can act on these indicators.

f) Personalized immunotherapy

It is carried out, taking into account the nature of the disease.[14,15,16,17] The algorithm for choosing personalized immunotherapy is implemented according to certain formulas for the targets of immunoprotection (ITF, determined by the three most altered immune parameters from the initial level after performing immunocorrection)[1] in certain diseases (Table 6). The essence of the program is that based on ITF, including the second-third degree of changes in laboratory signal parameters towards a decrease or increase, the key values of diagnostically significant immune parameters are selected, summarized in the tables. By comparing the data of laboratory examination of certain patients with tabular values, marker parameters changed from the normal level are revealed according to the vector and the degree of their changes. When the selected indicators coincide with the three key components of ITF for certain diseases, the optimal options for immunotherapy are selected, which are prescribed against the background of traditional basic treatment of diseases.

Table 6: Purulent inflammation of the skin and soft tissues

Modulators	ITF	Modulators	ITF
	PIST	Deep pyoderma	
Traditional therapy	$T_3^-IgG_2^+E_2^+$	Traditional therapy	$IgM_3^-NBTac_2^+MWM_2^+$
+Derinat	$Th_2^-B_2^-IL4_2^-$	+Hypoxene	$PhN_2^-B_2^-T_3^-$
+Gammaglobulin	$PhN_3^-NBTac_3^-NK_2^+$	+Ozone	$E_2^+B_2^-CIC_2^+$
+Derinat+ Gammaglobulin	$IL8_3^+T_3^-IgM_3^+$	+Hypoxene+ Ozone	$T_3^-CIC_2^+PhI_2^-$
+Lycopid	$CD11b_2^-PhI_2^-IgG_2^-$	+Polyoxidonium	$IgG_3^-IgM_3^-B_3^-$
+Ridostin	$Lph_3^-T_3^-NBTsp_3^+$	+Polyoxidonium+ Ozone	$PhI_3^-IgA_3^+PhN_2^-$
+Lycopid+ Derinat	$Lph_3^-MWM_2^+PhI_3^-$	+Diuciphone	$Tx_3^-Lph_2^-E_3^-$
+Cygapan	$PhN_2^-IgM_2^-E_3^+$	+Dalargin	$B_3^-IgA_2^-IL4_2^-$
+Ridostin+ Gammaglobulin + Cygapan+ Polyoxidonium	$Th_2^-T_3^-IgG_2^-$	+Diuciphone+ Dalargin+ Polyoxidonium	$IL4_3^-Tx_3^-IgM_2^-$
+Sodium nucleinate + Hypoxene	$T_3^-NRr_3^-CIC_3^+$	+enterosorbents	$NBTsp_3^-PhN_2^-Tc_3^-$

+Hypoxene	$T_3^-Tch_3^-PhI_3^-$	+autohemotherapy	$NBTsp_3^-PhN_2^-T_2^-$
+Ridostin+ Gammaglobulin	$IL8_3^+T_3^-IgM_3^+$	+thymus preparations	$T_3^-Tx_3^-NBTac_3^-$
+Limontar	$IgM_3^-TNF_3^+ClC_3^+$	+Ridostin	$NBTac_3^-T_3^-Lph_2^-$
+Limontar+ Immunomax	$IgA_3^+Tc_3^-PhN_3^-$	+Imunofan	$Th_2^-T_2^-IgG_2^-$
+Limontar+ Isoprinosine	$T_3^-PhN_3^-IL6_3^+$	+Staphyloanatoxin+ Gammaglobulin	$Tc_3^-NKt_3^-IL4_3^-$
+Limontar+ Immunomax+ Isoprinosine	$T_3^-ClC_3^+IgG_3^-$	+Tamerid	$NBTac_3^-NKT_3^-Tc_3^-$

Legend: ITF - the formula for the targets of immunocorrection, see the text for an explanation, PIST - purulent infection of soft tissues, NKt - natural T-killers, B- B-lymphocytes, NKr- natural killer-regulators, for other designations see above

Table 7: Reference values of immune parameters

Immune phenotypic and functional characteristics	Immune System Disorders Formulas (FDIS)			
	2 DID(-2)	3 DID(-3)	2 DIH(+2)	3 DIH(+3)
T-Lph (CD45+CD3+), 10^9/l	0,5-1,0	<0,5	2,0-2,5	>2,5
T-helpers (CD45+CD3+CD4+), 10^9/l	0,38-0,74	<0,38	1,46-1,82	>1,82
T-cytotoxic Lph(CD45+CD3+CD8+), 10^9/l	0,14-0,28	<0,14	0,56-0,7	>0,7
T-activated Lph(CD3+HLA-DR), 10^9/l	0,04-0,08	<0,04	0,16-0,2	>0,2
T-regulatory Lph(CD3+CD4+CD25+), 10^9/l	0,03-0,07	<0,03	0,15-0,19	>0,19
NK-cytolytic(CD3-CD16+CD56+), 10^9/l	0,04-0,08	<0,04	0,16-0,2	>0,2
B-Lph (CD19+), 10^9/l	0,2-0,4	<0,2	0,4-0,6	>0,6
IgM, g/l	0,6-1,3	<0,6	3,3-4,6	>4,6
IgA, g/l	0,5-1,1	<0,5	2,1-2,6	>2,6
IgG, g/l	10,8-14,4	<10,8	14,4-18,0	>18,0
CIC, CU	9,1-18,3	<9,1	36,7-45,9	>45,9
MWM, CU	1,9-3,7	<1,9	7,3-9,1	>9,1
PhI, %	24,3-48,4	<24,3	96,6-120,7	>120,7
PhN, number of bacteria\Nph	2,4-4,7	<2,4	9,3-11,6	>11,6
NBTsp, %	2,9-5,7	<2,9	11,3-14,1	>14,1
NBTac, %	7,5-15,0	<7,5	30,0-37,5	>37,5
IL4, pkg/ml	6,6-13,1	<6,6	26,1-32,6	>32,6
IL6, pkg/ml	5,5-10,9	<5,5	21,7-27,1	>27,1
IL8, pkg/ml	4,7-9,4	<4,7	18,8-23,5	>23,5
TNF, pkg/ml	0,06-0,13	<0,06	0,26-0,32	>0,32
Lymphocytes (CD95+), 10^9/l	0,02-0,05	<0,02	0,11-0,14	>0,14
L (leucocytes), 10^9/l	1,3-2,7	<1,3	5,5-6,9	>6,9
Lph (lymphocytes), %	13,8-27,5	<13,8	54,9-68,6	>68,6
Nph (neutrophils), %	20,4-40,5	<20,4	80,7-100,8	>100,8
E (eosinophils), %	0,64-1,27	<0,64	2,53-3,2	>3,2
M (monocytes), %	4,2-8,5	<4,2	13,0-17,2	>17,2
ESR, mm/hour	4,3-8,4	<4,3	16,6-20,7	>20,7

Legend: DID, DIH- the degree of immune deficiency, the degree of immune hyperfunction, Nph - neutrophil, ESR- erythrocyte sedimentation rate, for other designations, see above.

V. Conclusion

A certain problem of the current state of clinical immunology is the insufficient introduction of innovative diagnostic and therapeutic technologies into practice, which is often accompanied by not always full use of the latest immunotherapeutic effects in the treatment of patients and, as a consequence, their often insufficient effectiveness. This also includes the lack of simple and, at the same time, informative methods of immune diagnostics.

One solution to the stated problem is the development at the first level of a simplified technology for the clinical detection of marker immunopathological

syndromes with the appointment of profile "small" immunocorrectors to patients. At the second level, based on laboratory assessment of the reactivity of patients, created laboratory support and preliminary study of the effectiveness and targets of differentiated immunotherapy of certain diseases in work, mathematically justified unified, generalized, detailed, and personalized methods for choosing options for optimal immunotherapy are presented. ... They are a good help in the daily work of a practical clinical immunologist.

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