Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 07, pp.71595-71599, July, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

CONTRADICTIONS INTHE CLINICAL IMMUNOLOGY POLYFUNCTIONALITY OF GENETIC MARKERS OF BLOOD FOR IMMUNE RESPONSE

[1,2*]Vladimir M. Zemskov, [1]Konstantin N. Pronko, [3]Andrey M. Zemskov and [3]Veronika M. Zemskova

[1]Department of Research and Development at Facecontrol, Inc., Florida, Miami, USA
[2]Clinical Immunology Group, A.V. Vishnevsky National Medical Research Center of Surgery, Moscow, Russia
[3]Department of Microbiology of Burdenko Voronezh State Medical University, Voronezh, Russia

ARTICLE INFO

Article History:
Received 09th April, 2018
Received in revised form
07th May, 2018
Accepted 21st June, 2018
Published online 31st July, 2018

Key words:
Genetic Markers of Blood,
Immune Response,
Morbidity Rate,
Immunocorrection.

ABSTRACT

The dependence of morbidity rate, state of factors of anti-infective resistance, hormonal status, severity, intimate mechanisms of formation of immune disorders, the effectiveness of their pharmacological correction, and the antigen distribution of the ABO system was established on extensive literature and own clinical material. The determination of the signaling targets of the action of modulators on the immune system makes it possible to determine laboratory markers for prescribing medications.

Citation: Vladimir M. Zemskov, Konstantin N. Pronko, Andrey M. Zemskov and Veronika M. Zemskova. 2018. "Contradictions inthe clinical immunology polyfunctionality of genetic markers of blood for immune response", *International Journal of Current Research*, 10, (07), 71595-71599.

INTRODUCTION

The current definition of the immune status as a summary of the gene activity of HLA, ABO systems, Rhesus factor, haptoglobins etc., which encode the severity of the body's reactions to various antigens, the development of diseases, changes in the endocrine status, disruption of homeostasis, their outcomes, correction capability simultaneously has a fundamental, applied, diagnostic and therapeutic-prognostic significance and implies the concreteness of the immune response (Zaretskaya *et al*., 2002). It should be recognized that along with the known genetic systems of the body, blood groups (ABO) are the simplest and most accessible criterion for evaluating the general patterns of human immune control. The genes of this system should be considered supergenes, because they encode several characteristics. For example, in the indigenous population of North America (Mexico, Argentina) there is a predominance of carriage of the phenoisogroup O(I), in Europe, especially in the northern part, A(II), in Asia B(III).

Corresponding author: **Vladimir M. Zemskov,**
Head of Department of Research and Development at Facecontrol, Inc., Florida, Miami, USA
Head of Clinical Immunology Group, A.V. Vishnevsky National Medical Research Center of Surgery, Moscow, Russia.
DOI: https://doi.org/10.24941/ijcr.31118.07.2018

Blood groups and morbidityrate

It is known that, all other things being equal, the owners of the genetic marker 0(I) have an increased risk of developing of abscesses, lymphadenopathies, syphilis, gastric and intestinal ulcers, liver cirrhosis, cholecystitis, appendicitis, as well as pancreatic and stomach cancer, breast, lung, liver, bowel, bone, head cancer and soft tissuescancer. Having the A(II) phenotype indicates an increased incidence of purulent-septic infections, primarily caused by staphylococcus, syphilis, tuberculosis, salmonella, diphtheria, dysentery, influenzaand parainfluenza viruses, adenoviruses, RC viruses, intestinal nematodes, high incidence of cancer lips, salivary glands, stomach, gall bladder, milk glands, cervix, as well as atherosclerosis, acute rheumatic fever, myocardial infarction, ischemic stroke, B12-anemia, arterial hypertension, epilepsy, cholesterinemia and β-lipoproteinemia. Theisogenogroup B(III) is associated with an increase in the incidence rate of dysentery, parainfluenza, intestinal cancer, breast cancer, genitourinary system and blood cancer, Alzheimer's disease. With the fourth blood group, purulent septic infections, acute respiratory infections, viral hepatitis, echinococcaldamage, hyperergic reactions to smallpox vaccine, intestinal cancer, cancer of soft tissues, bones, skin, neck, head, hemoblastosis and mycosis often occur. Apparently, this phenomenon is based on the phenomenon of antigens labeling of the ABO system of

differentiated immune reactivity (Zemskov*etal*., 1999). An illustration of this data is the frequency of occurrence of genetic markers of blood for various diseases (Table 1).

Table 1. Percentage of occurrence of genetic markers of blood in various diseases

Diseases	Geneticmarkersofblood		
	0(I)	A(II)	B(III)
Healthy (30-50 years)	34.0±0.1	35.0±1.2	21.2±0.9
PISI	29.9±7.2	45.3±6.4	19.7±13.4
Dysentery	28.8±11.3	35.6±5.4	28.8±11.3
Staphylococcal carriage	33.3±0.2	39.7±8.8	26.9±9.7
SOM	40.6±10.7	44±10.3	14.8±3.2
CSOM	28.7±3.1	42.7±4.9	21.1±7.8
BA	17.2±6.8	33.3±5.4	28.8±11.3
Ischemic stroke	35.1±9.4	44.6±8.7	19.5±10.2
CAT	34.6±11.2	32.7±11.4	25.0±12.0
ODPA	36.7±3.8	46.0±-3.4	16.5±9.0
Chronicalcoholism	34.9±7.8	47.7±7.9	22.2±9.6
Schizophrenia	21.1±9.5	43.7±7.9	22.1±9.6
Oligophrenia	22.8±7.7	46.2±8.4	23.0±7.4

Abbreviations: ODPA – occlusive diseases of peripheral arteries, other disease abbreviations refer to table 2.

From the table it follows that the incidence of antigen O(I) is from 17.2 (BA) to 36.7% (ODPA); A(II) - from 32.7 (CAT) to 47.7% (chronic alcoholism); In (III) - from 14.8 (CAT) to 28.8% (dysentery).

Blood groups and factors of non-specific anti-infective resistance, hormone level: It was found that in individuals with the first blood group minimal activity of lysozyme, complement and β-lysines is recorded. In people with the fourth group, the maximum content of lysozyme and complement is noted, and donors with genetic markers A and B are found in between. Nonspecific resistance was closely related to the hormonal level of the organism, with the largest changes in parameters registered in individuals with the first and fourth blood groups. The values of these parameters for the phenoisogroupsA(II) and B(III) have been monotonic. Additional data was found by correlation analysis, which revealed the presence of a connection between the hormonecontent and the activity of factors of nonspecific anti-infective resistance. Thus, the level of lysozyme was slightly associated with the formation of adrenocorticotropic hormone, a closer relationship was found between the content of cortisol and complement in all four blood groups. Persons with markers I(0) and III(B) show a significant inverse relationship between cortisol and β-lytic activity of blood serum. Mineralocorticoids were also in feedback with the activity of lysozyme in people with second and third blood groups. The same pattern was observed in the study of complement activity and IgA in volunteers with A(II) and AB(IV) groups. The content of androgens was found to be negatively associated with β-lytic activity of blood serum in persons with markers O(I) and A(II). The level of growth hormone positively correlated with the activity of lysozyme, especially in volunteers with the first blood group. The same relationship was established with respect to the concentration of IgG in persons with B(III). In other cases, its severity was somewhat lower, but also positive. The opposite pattern was observed for the growth hormone and IgM: an elevated level of the hormone corresponded to a decrease in IgM concentration in individuals with A(II) and B(III) phenoisogroups of blood. The more ACTH was in the blood serum, the higher was the concentration of lysozyme and β-lysine. This cannot be said about complement. The closest relationship between the level of ACTH and lysozyme was observed in donors with A(II) and AB(IV) blood groups (Drozdova, 1989).

Blood groups and vaccinal immunity: An increased production of typhoid antibodies in patients with a genetic marker A (II) was noted in comparison with persons of the first blood group after immunization with an appropriate preventive drug. In this case, the former synthesizes 3.5 times more than 7S (IgG) and 3.5 times less than 19S (IgM) immune globulins than the latter. A more pronounced immune response to typhoid, A- and B-paratyphoid vaccines, tetanus toxoid was observed in individuals with markers A(II) and B(III) than with O(I). According to the literature, healthy people with a second blood group gave a more pronounced immune response to the typhoid vaccine than people with other genetic markers. In this case, patients with chronic alcoholism, having a second and third blood group, were equally highly responsible for immunization. Patients with schizophrenia accounted for an approximately equal immune response for all blood groups (Zemskov*et al*., 2003).

Blood groups and immune reactivity: As evaluation criteria of immune status, a rank method was chosen that determines the general differences in the grouped laboratory parameters of patients from the normative level, with a scale <33% of the indices (minor changes), 34-66% (significant changes),> 66% (the most significant changes) and immune parameters selected using the diagnostic significance factor, formalized as aFormulaof Immune System Disorder [FISD](Zemskov*et al*., 2013,2016).The subject of the examination were healthy individuals aged 20-30 and 30-50 years old, as well as suffering from three variants of infectious processes (purulent infections of soft tissues (PIST), dysentery, carriers of pathogenic staphylococcus), persons with secretory, viral and purulent otitis, pulmonary diseases - bronchial asthma, obstructive bronchitis and pathology of various genesis - ischemic stroke, glaucoma, autoimmune thyroiditis.According to the data of the rank evaluation of the general expression of immune reactivity in 12 groups of healthy and sick persons (Table 2), its differentiated association with the carriage of antigens of the ABO system and the type of diseases is shown. Thus, in healthy individuals of 20-30 years old, the highest level of immune responses was shown in the presence of marker A(II), then O(I) and B(III), while in volunteers aged 30-50 years the distribution of blood groups became different, respectively – B(III) and O(I) → A(II). In patients with PIST, the occurrence of phenotypic blood markers B(III) → A(II) and O(I) was different from that in dysentery – A(II) → O(I) → B(III), etc. (Zemskov*et al*., 2016). A point mathematical analysis of the results of an immune examination of patients made it possible to reveal signal tests of immune disorders in patients with various diseases, presented in the form of standard formulas (Table 1). Thus, for example, in patients with MTR with the first group of blood group, there was a decrease in the number of B-cells, total lymphocytes, T-cells - 3-2 degrees, with phenotype A (II) - deficiency of T- and B-lymphocytes and T-helpers - 1-2 degrees; with the phenotype B(III) - a decrease in the level of T-regulators, T-cytotoxic and total lymphocytes is significant (2) severity. Comparison of typical FISD in patients from different groups, taking into account the set, the order of location, the vector and the degree of changes in the signal indices, showed their personalization by 2-3 terms of three (Zemskov*et al*., 2013).

Table 2. Blood groups and immune reactivity in rank evaluation

Disease	Geneticmarkersofblood		
	0(I)[FISD]	A(II) [FISD]	B(III) [FISD]
Healthy (20-30 years)	$2/Tr^{+}{}_{1}Tc^{+}{}_{1}B^{+}{}_{1}$	$1/Tac^{+}{}_{1}Th^{+}{}_{1}B^{+}{}_{2}$	$3/B^{+}{}_{1}Tr^{+}{}_{1}T^{-}{}_{1}$
Healthy (30-50 years)	$2/Tc^{+}{}_{1}Th^{-}{}_{1}Lym^{-}{}_{1}$	$2/Th^{-}{}_{1}T^{+}{}_{1}IgM^{-}{}_{1}$	$1/Lym^{-}{}_{1}Th^{-}{}_{1}T^{-}{}_{1}$
PIST	$2/B^{-}{}_{2}IgM^{+}{}_{1}T^{-}{}_{2}$	$2/IgM^{-}{}_{1}T^{-}{}_{3}B^{-}{}_{1}$	$1/IgM^{-}{}_{1}B^{+}{}_{1}IgA^{+}{}_{2}$
Dysentery	$2/Th^{-}{}_{2}T^{-}{}_{2}Tac^{-}{}_{2}$	$1/BC^{+}{}_{3}Tac^{-}{}_{1}Th^{-}{}_{2}$	$3/T^{-}{}_{2}Th^{-}{}_{3}Tac^{-}{}_{2}$
Staphylococcal carriage	$1/IgG^{-}{}_{3}T^{-}{}_{1}Lym^{-}{}_{1}$	$2/IgG^{-}{}_{3}WBC^{-}{}_{3}T^{-}{}_{3}$	$1/T^{-}{}_{1}IgM^{+}{}_{1}Lym^{-}{}_{2}$
SOM	$2/B^{-}{}_{3}Lym^{-}{}_{2}T^{-}{}_{3}$	$3/T^{-}{}_{1}B^{-}{}_{2}Th^{-}{}_{2}$	$1/Tr^{-}{}_{2}Tc^{-}{}_{2}Lym^{-}{}_{2}$
CSOM	$1/Lym^{-}{}_{2}B^{-}{}_{2}Tc^{+}{}_{1}$	$3/B^{-}{}_{2}Th^{-}{}_{2}Lym\text{-}^{-}{}_{2}$	$2/Tr^{-}{}_{2}T^{-}{}_{2}B^{-}{}_{1}$
BA	$1/B^{-}{}_{3}Tc^{-}{}_{3}T^{-}{}_{3}$	$2/Tc^{-}{}_{3}B^{-}{}_{3}ClC^{+}{}_{3}$	$2/Th^{-}{}_{3}ClC^{+}{}_{3}B^{-}{}_{3}$
COB	$1/NBTsp^{-}{}_{3}ClC^{+}{}_{2}PI^{-}{}_{1}$	$3/NBTac^{+}{}_{3}PI^{-}{}_{1}Tc^{-}{}_{2}$	$2/Lym^{-}{}_{1}NBTsp^{+}{}_{3}T^{-}{}_{2}$
Ischemic stroke	$3/IgM^{+}{}_{2}Tc^{+}{}_{1}IgG^{-}{}_{1}$	$1/IgA^{+}{}_{2}IgM^{+}Lym^{-}{}_{1}$	$2/IgG^{-}{}_{1}IgA^{+}{}_{1}IgM^{+}{}_{2}$
Glaucoma	$3/B^{-}{}_{2}IgG^{+}{}_{3}Th^{-}{}_{2}$	$1/Tac^{+}{}_{3}IgM^{+}{}_{3}IgG^{+}{}_{3}$	$2Tr^{+}{}_{3}IgA^{+}{}_{3}Tc^{-}{}_{2}$
CAT	$2/B^{-}{}_{1}IgG^{+}{}_{1}Tc^{-}{}_{1}$	$1/Th^{-}{}_{1}IgM^{+}{}_{1}T^{+}{}_{1}$	$2/IgA^{+}{}_{1}B^{-}{}_{1}IgM^{+}{}_{1}$

Designations: 1,2,3 - maximum, average and minimum levels of immune reactionin the ranks, PIST - purulent infection of soft tissues, SOM- secretory-chronic otitis media,CSOMchronic suppurative otitis media, BA – bronchial asthma, COB - chronic obstructive bronchitis, chronicobstructive bronchitis, staphylococcal carriage, CAT - chronic autoimmune thyroiditis, numerator - the magnitude of common differences in ranks, the denominator -value of the FISD (sign "+" or "-" above - a significant increase or decrease in theindicator; the number "1", "2" or "3" from the bottom - the value of the degree of change from the reference group: 1 - minor, 2 significant, 3 - the most significant

Table 3. Blood groups and correction of immune reactivity in rank evaluation

Diseases	Geneticmarkersofblood		
	0(I)/TFI	A(II)/TFI	B(III)/TFI
PISI	$1/B^{+}{}_{2}T^{+}{}_{2}IgM^{-}{}_{2}$	$3/LBR^{+}{}_{2}Th^{+}{}_{2}T^{+}{}_{2}$	$2/B^{-}{}_{2}IgA^{+}{}_{3}IgM^{+}{}_{2}$
Dysentery	$2/T^{+}{}_{2}SN^{-}{}_{2}WBC^{-}{}_{2}$	$2/PN^{-}{}_{2}Lym^{+}{}_{2}Tr^{+}{}_{3}$	$1/T^{+}{}_{3}WBC^{+}{}_{3}Tr^{+}{}_{3}$
Staphylococcal carriage	$1/IgG^{+}{}_{2}IgA^{-}{}_{2}PI^{+}{}_{2}$	$2/IgA^{-}{}_{2}IgG^{-}{}_{2}B^{+}{}_{2}$	$3/IgM^{+}{}_{2}B^{+}{}_{2}IgA^{+}{}_{2}$
SOM	$1/B^{+}{}_{3}Th^{+}{}_{3}Tc^{-}{}_{2}$	$3/Lym^{+}{}_{2}B^{+}{}_{2}IgG^{-}{}_{2}$	$2/T^{+}{}_{2}Tc^{+}{}_{2}IgM^{-}{}_{2}$
CSOM	$1/B^{+}{}_{2}Tc^{-}{}_{2}Lym^{+}{}_{2}$	$2/B^{+}{}_{2}Tc^{+}{}_{2}Lym^{+}{}_{2}$	$3/B^{+}{}_{2}Tc^{+}{}_{2}T^{+}{}_{2}$
Ischemic stroke	$2/IgG^{+}{}_{2}PI^{+}{}_{2}Tr^{+}{}_{2}$	$1/T^{+}{}_{2}Th^{+}{}_{2}Lym^{+}{}_{2}$	$3/Th^{+}{}_{2}IgM^{+}{}_{2}IgA^{-}{}_{2}$
Glaucoma	$3/B^{-}{}_{2}NK^{+}{}_{2}T^{+}{}_{2}$	$2/WBC^{+}{}_{2}Th^{+}{}_{2}Tc^{-}{}_{2}$	$1/T^{+}{}_{2}Lym^{+}{}_{2}PI^{+}{}_{2}$

Designations: numerator - efficiency of complex treatment in ranks, denominator - TFI, other designations, see above.

The data presented indicate a rather heterogeneous nature of the general and key changes in immune reactivity associated with the carriage of antigens of the ABO system and the type of diseases in patients. In principle, this reflects a differentiated level of compensatory possibilities of the organism for different blood groups under conditions of some kind of "genocardia" development of pathological processes.

Blood groups and correction of immunological reactivity: Patients suffering from seven nosological entities of diseases of different genesis - PIST, dysentery, SOM, CSOM, ischemic stroke, glaucoma and carriers of Staphylococcus aureus, underwent traditional treatment and additionally received a pluripotent modulator - sodium nucleinate in a standard dose. Before and after treatment, the patients were subjected to an immune examination and, according to the results, the overall effectiveness of immunocorrection in ranks and its "basic" indices in the lymphoid system by the target formula of immunocorrectors [TFI] (Zemskov*et al*., 1999, 2016), (Table 3).

As follows from the data of Table 2, a differentiated "responsiveness" of patients with different blood groups to standard immunocorrection by sodium nucleinate was found, depending on the nature of the disease. Thus, in patients with pyoinflammatory processes in soft tissues, the limiting correction of immunopathology was achieved with the carrier of marker 0(I), then B(III) and A (II). We recall that in the initial period, the distribution of phenogroups, depending on the severity of the initial changes in laboratory parameters, was different - B (III) and A(II) → 0(I). In other diseases, this regularity of the dependence of the immunotoropic effect of the RNA preparation on blood groups also took place, but was completely different in nature (Zemskov*et al*., 2016). Detailing of the corrector action mechanism on the immune system in the presence of different phenotypic markers also showed its variability. For example, in glaucoma, sodium nucleinate depending on blood groups, respectively, determined: at 0 (I) - a predominant decrease in the number of B-lymphocytes against the background of accumulation of natural killers and T-cells (grade 2); at A(II) - leukocytosis and imbalance of regulatory T-dependentsubclones (grade 2); at B(III) - stimulation of the T-cell content, lymphocytosis, activation of the absorption capacity of phagocytes [1-2 degree] (Zemskov*et al*., 2013). These data are of fundamental importance, the personalized mechanism of action of the immunocorrector in the carriage of various antigens of the ABO system and types of diseases, as well as the application aspect in terms of identifying key laboratory markers for modulator selection.For example, since TFI sodium nucleinate in patients with ischemic stroke with the first blood group ($IgG^{+}{}_{2}PI^{+}{}_{2}Tr^{+}{}_{2}$) indicates excessof IgG, activation of phagocytosis and accumulation of T-regulators, indications for immunotropic administration are a decrease in the level of immunoglobulin of this class, phagocytic index and the number of T-regulators. Recalculation of the degree of changes in the parameters relative to the reference values of health individuals makes it possible to calculate the critical values of key indicators: IgG - 10.8-14.4 g/l; PI - 24,3-48,4%; Tr - 0,03-0,07 • 10^{9} liters.

Serum blood systems: are inherited, not related, do not depend on the age and sex, have a genetically determined polymorphism. It was found that, in patients with prolonged and chronic pneumonia, the frequency of the phenotype of haptoglobin Hp1-1 (18-20%) was significantly increased in comparison with healthy people.Chronic inflammation of the lungs in children most often occurred with the carriage of the Hp1-1 and Hp2-1phenotypes, and chronic bronchitis with the Hp2-2phenotype. Changes in immune parameters in Hp1-1 owners were significantly lower than in persons with the Hp2-2phenotype.Patients with pneumonia with Hp2-1 phenotype were characterized by a more severe course of the disease

compared with Hp1-1 carriers with complications in the form of abscess formation, exudative pleurisy, lung carnification.
On the other hand, an increase in the number of patients with chronic bronchitis with a carrier of the phenotype of phosphoglucomutase (PGM11-1) is shown. The tendency to a more severe course was noted in patients with the PGM12-1 phenotype with long-term preservation of clinical laboratory signs.A study of the distribution of phenotypes of acid phosphatase showed that among patients with chronic bronchitis, the owners of the phenotypes APbb and APab were significantly more likely to occur and the carriers of the phenotypes APaa and APbc were significantly less likely.

Owners of APaa and APbbacid phosphatase phenotypes among patients with acute pneumonia were significantly more frequent, phenotypes APab and APbc were approximately equally distributed both in patients and in the control group. Among patients with prolonged pneumonia, persons with phenotypes of APab and APbbreliably predominated.In patients with acute pneumonia with the phenotype APaa, the shortest duration of the disease was noted in comparison with patients carrying carriers of other phenotypes of acid phosphatase. In these patients, the disease progressed more easily, the temperature and other clinical and laboratory parameters were normalized earlier.Long and severe was the course of the disease in the owners of the phenotype APab. In patients with chronic pneumonia, the disease progressed more easily with the phenotype APbc. The greatest number of complications in patients with both acute and prolonged pneumonia was in the carriers of APbc and APab markers. Thus, the data obtained indicate a definite dependence of the development of immune-associated processes, primarily infections, on the presence of certain blood groups.

Moreover, it is essential that the following mechanisms may be possible mechanisms of this phenomenon. First, some bacteria contain antigen glycoproteins of the ABO system, that is, cross-reacting antigens that directly affect the severity of the immune response. Secondly, there is a phenomenon of antigenic mimicry due to the preferential adsorption of certain blood group antigens on the bacteria. Thirdly, the presence of tropism of microorganisms, their toxins for cells and tissues with different isoantigenic specificity, the ability of enzymes to destroy certain structures of specific bacteria. Fourth, the relationship between blood groups and the production of endogenous hormones actively regulating immune and non-immune mechanisms has been found. Fifthly, there is a common inheritance of antigens of the ABO system and the HLA system. Sixth, tit is likely that differentiated regulation of immune responses is realized depending on the phenotype of the ABO system (Zaretskaya*et al*., 2002; Zemskov*et al*., 2016). This regularity should be expanded by the phenomenon of the relationship between the carriage of other genetic markers of blood (genes and their protein products of HLA, Rh factor, serum blood systems such ashaptoglobins, phosphoglucomutase, acid phosphatase, etc.) and the body's ability to develop protective immunopathological responses to various foreign Ag with a high or low risk of pathological procedures, their outcomes, treatment effectiveness, etc. (Vasilieva, 1992; Zemskov*et al*., 2013). As a result, on the one hand, a certain complicated situation develops, in which the genes located in different chromosomes (in the 6th - the HLA system, the 9th - the ABO system, and the 1st - the Rh factor), were able to regulate the severity of the immune responses with "unpromising" biological probability. On the other hand, there is a certain theoretical possibility of such interaction, since Boyarova *et al.* (1992), and also by other authors a certain unity of the distribution of the Ag of the HLA and ABO systems is found. The authors present data on the high and low occurrence of individual histocompatibility Ag for specific blood groups, which may indicate a certain coherence of inheritance of these factors. Associative links between the level of immune reactivity and the presence of genetic markers of blood have a wide range of severity from strong, moderate, weakly positive to weakly negative and very negative.

The mechanisms that make up the dualism of the above facts can be conditionally divided into two groups - related to the structure of the tissue Ag itself, and to the peculiarities of the genes controlling their formation and, at the same time, other functions, for example, the strength of the immune response.
Accordingly, several hypotheses are formulated: (1) The receptor hypothesis is based on the fact that microorganisms (viruses, bacteria, etc.) are fixed on special receptors, whose function can be performed by histocompatibility Ag, etc., hence the selectivity of infection of carriers of different blood markers arises.(2) The hypothesis of modification of the body's cellular receptors, for example, antigens of the ABO system or HLA, by chemical, microbial and other agents. (3) The hypothesis of molecular mimicry, in which infectious factors carry antigenic determinants that are close to or identical to certain antigens of HLA, ABO, and other systems.(4) Hypothesis of deficiency of individual components of complement, depending on the presence of certain Ag histocompatibility. (5) There are opportunities to include tissue Ag in the pathological process and their ability to bind cellular and humoral regulators of physiological processes.(6) In fact, there are specific genes responsible for the sensitivity of this organism to various pathogenic factors, the ability to deploy immune defense responses, the response to vaccines, etc. (7) New facts of genetic determinancy of biochemical processes marked with tissue Ag are revealed.For example, the connection of carrier Ag HLA-B8 and B35 with the level of bilirubin of blood, "sulfate titre", "thymol test", "activity" of ALT, sorbitol dehydrogenase, prothrombin index with the risk of development of viral hepatitis is found. In other words, a certain failure of the liver function, dependent on the possession of certain histocompatibility Ag, is a provoking factor for the development of pathology. (8) The strict dependence of the endocrine status and factors of nonspecific resistance on phenotypic blood markers should be added to the listed factors. Most likely, all these mechanisms determine the different therapeutic effect of therapeutic interventions. For example, there was an increase in the incidence of Ag HLA-DP4 in patients with immune thrombocytopenic purpura with a good therapeutic effect of corticosteroid drugs.

REFERENCES

Boyarova, LV. *et al*. 1992. Antigens of the systemof NLA, ABO and Rhesus factor in healthy individuals and patients with hemorrhagic diseases. Hemorrhagic diseases. Collected works. Kuibyshev: 74.

Drozdova, LA. 1989. Seasonal changes in the content of hormones and humoral factors of nonspecific resistance in the blood of donors of different isogenogroups: Publishedsummary of C and. Med. Sci. Thesis: Kiev.

Vasilyeva, LV.1992. Clinical and genetic associations in patients with nonspecific lung diseases.Published summary of Cand.Med. Sci. Thesis: VSMU.

Zaretskaya, YM. *et al*. 2002. Immunology and humanimmunogenetics. Moscow: Triad Publishing House, 278.

Zemskov, AM. *et al.* 2016. Immunology. Electronic textbook. Recommended by FIRO, 127 copyright sheets.

Zemskov, AM. *et al.* 1999.Immunological reactivity and genetic markers of blood. Moscow: Polydiz Publishing House, 307.

Zemskov, AM. *Et al*. 2003. 1000 Formulas of Clinical Immunology. Moscow, Medicine for all Publishing House, 332.

Zemskov, AM. *Et al*.2013. Unorthodox immunology. Moscow: Publisher Triada-X, 223.

****