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Antigens of the HLA System and Indicators of Immunogenetic Status - As a Means for Predicting the Adaptive Capabilities of the Body of Athletes to Increased Physical Activity

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ABSTRACT

The article studies the nature of the immune response in response to typhoid vaccination in athletes of the Uzbek population. The dependence of the immune response on the characteristics of the HLA-phenotype has been established: a high level of immunoreactivity and production of specific antibodies is characteristic of individuals - carriers of the HLA-B15 antigen in the phenotype; a low level of immune response and a titer of specific antibodies were detected in the presence of HLA-B5 and HLA-B35 antigens in the phenotype. The nature of the immune response, taking into account the HLA-phenotype, reflects the adaptive capabilities of athletes and can be successfully applied in sports selection. A sharp decrease in the frequency of occurrence of antigens HLA-A11, HLA-B35 in the group of highly qualified athletes was found in comparison with dischargers ($P < 0.05$).

Key words: Genotype, athlete's phenotype, immune response, HLA antigen complex, antibody titer, T and B lymphocytes, vaccination, prognosis of physical qualities.

Introduction

Currently, the biological role of the HLA system in maintaining the body's immunological homeostasis is considered proven, since the role of antigens in the regulation of the immune response and the development of cellular cooperation is known (1; 2; 10).

Numerous studies have established both positive and negative associations of HLA antigens with various diseases. The identified associative connections can be limited when a certain antigen is associated with a narrow range of diseases or has a general character when the association is detected with a wide range of pathologies (3, 4, 5, 8). Work on the identification of associative relationships between the carriage of HLA - antigens and predisposition to diseases is possible only if there is data on the distribution of HLA - antigens among healthy individuals in the population. It should be noted that the HLA system is an effective genetic marker for anthropology, population genetics, and the undoubted importance of studying the distribution of HLA antigens in various population groups (14;15). Such studies provide information about the genetic profile of different nationalities, with the identification of the influence of geographic zones on the genetic distances between different populations.

Modern sport is associated with loads on the verge of a person's physical and psychological capabilities. Under these conditions, a scientifically grounded approach to the organization of the training process with its insufficient individualization, the combination of intense training with other types of activity provokes the manifestation of hidden defects in the state of health, prevents the achievement of high sports results and leads to a loss of sports form at the time of intensive

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training and responsible competitions. An additional factor provoking breakdowns of athletes at the time of important competitions is the depletion of their functional reserves -" overtraining syndrome". It often arises due to the lack of objectivity of the indicators of the state of the body of athletes.

The most labile structures, very sensitive to the effects of exogenous and endogenous factors, and in particular to physical stress, include the immune system. Early research indicates a stimulating effect of moderate exercise on the immune system and immunological reactivity. The analysis of the research results at the subsequent stages made it possible to state that the intense loads characteristic of modern sports, reaching a stress level, negatively affect the immunity and cause disorders of immune homeostasis. This is expressed by changes in the quantitative characteristics of the T - and B - systems of the immune system, indicators of the natural resistance of the severity of autoimmune processes. The phenomenon of complete disappearance of certain classes of immunoglobulins and antibodies from the blood and biological fluids in athletes at the time of important competitions was also established, indicating the disruption of the processes of immunological adaptation and the depletion of immunity reserves. The state of the immune system, which develops in violation of the adaptation processes, can be characterized as a very pronounced secondary immunodeficiency. (6).

For the timely detection of the discrepancy between the presented loads and the capabilities of the immune system, as well as predicting the body's tolerance to heavy physical exertion, an individual approach is required, with the obligatory consideration of the genetic determinism of the immune response (1). However, to date, the assessment of the immune status of athletes using genetic markers has not become widespread. It is considered established that among the absolute genetic markers, antigens of the HLA complex dominate in the determination of immune processes since they include genes that determine specific cellular immune responses (2;4;16).

Taking into account the association of the genes of the HLA complex with the development of a number of immunopathological conditions, we carried out studies to study the dependence of the dynamics of the parameters of the immune system of athletes with the HLA phenotype under antigenic exposure. Routine typhoid vaccination was used as an antigenic effect.

Material and research methods.

During routine vaccination with sorbed typhoid vaccine, 110 athletes aged 17 to 21 years were examined. At the time of vaccination, 10-12 and 28-30 days after vaccination, the quantitative content of the populations of T-lymphocytes and B-lymphocytes, subpopulations of Tlymphocytes, as well as antigen-binding lymphocytes (ASL), specifically sensitized to the vaccine antigen, was studied. At the time of vaccination and on days 28-30, the titer of specific antibodies was studied. In all studies, blood was drawn from the cubital vein.

The HLA phenotype was determined in a standard lymphocytotoxic test using a panel of antisera obtained from the Center for Immunological Tissue Typing at the St. Petersburg Research Institute of Blood Transfusion. Peripheral blood lymphocytes were isolated in a ficoll-verografin density gradient.

ASL was determined by the method of Gurarii N.I. (6). The titer of specific antibodies was determined in the passive hemagglutination reaction (RPHA) with erythrocyte salmonella Odiagnosticum according to the principle of paired sera. The reaction was carried out on normal rabbit serum with the corresponding control in an isotonic solution. The effectiveness of vaccination was assessed by the degree of increase in the antibody titer.

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Numerical data were subjected to statistical processing. The mean values, the significance of their differences, and mutual correlations were calculated. Differences satisfying $p < 0.05$ were considered significant.

Results and its discussion.

The dynamics of antibody production in athletes with different HLA phenotype varied within wide limits. Both the increase and decrease in the antibody titer in most of the subjects had values that were relatively close to the average group indicators. However, in the phenotypes HLA-B5, HLA-B15 and HLA-B35, the differences in antibody titer are significant: if the phenotypes of HLA-B5 and, especially, B-35 were associated with a low content of the antibody titer up to a decrease, then the HLA-B15 phenotype was associated with a pronounced increase in the titer of specific antibodies (Table 1).

The dynamics of ASL in the surveyed contingent of athletes on the 10-12th day after vaccination is characterized by an increase in the average group indicators. However, the most pronounced differences in the dynamics of ASL were also noted in individuals with the HLA-B5, HLA-B35, and HLA-B15 phenotypes. The dynamics of ASL in individuals with the HLA-B5 and HLA-B35 phenotype is characterized by an insignificant increase or decrease in the amount of ASL both relative to the initial and relative to the average group indicator. At the same time, a pronounced increase in ASL both relative to the initial and relative to the average group indicator was noted in carriers of the HLA-B15 phenotype, in which the most significant increase in the frequency of antibody titer was revealed.

Table 1.Dynamics of changes in the content of antigen-binding lymphocytes depending on the HLA phenotype of athletes

HLA phenotype	Dynamicsofantibodyproduction		ASL dynamics
	NormalRabbitSerum	Isotonicsolution	
HLA-A9	-2,7	-2,2	8,25
HLA-A10	+1,5	+2,0	+9,36
HLA-B5	-4,0	-1,5	**-0,5**
HLA-B13	-1,7	-2,2	+7,0
HLA-B15	+0,5	+4,0	**+20,0**
HLA-B16	-1,4	-1,7	+3,24
HLA-B35	-1,5	-3,0	**+2,0**

The analysis of indicators of the T- and B-cell link showed that in the dynamics of postvaccination immunity there is an increase in the pool of T-lymphocytes, which is associated with the prevalence of the T-helper subpopulation over the T-suppressor subpopulation. The dynamics of B-lymphocytes are characterized by a persistent decrease in their content as the intensity of antitelogenesis increases. Fluctuations in T- and B-lymphocyte counts after vaccination were the least pronounced in individuals with the HLA-B5 and HLA-B35 phenotype, while the highest degree of fluctuations in indices was observed in the HLA-B15 phenotype. This suggests that immunogenesis with the formation of a high titer of antibodies is accompanied by a high degree

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of fluctuations in the dynamics of indicators of cellular immunity, while at a low level of antitelogenesis, the degree of severity of fluctuations in the T- and B-links of immunity is insignificant.

The obtained research results indicate the existence of HLA-associated genetic control of cellular and humoral immunity, and the strength of the immune response and the nature of the immune response to typhoid antigenic exposure depend directly on the HLA phenotype. There are similar data in the literature on the existence of a dependence of the manifestation of functional specificity and the activity of the immune system on immunogenetic characteristics (9). It was found that the action of the HLA-B35 associated gene manifests itself through the multidirectional level of two different subpopulations of immune component cells: increased activity of natural killer cells (NK) and decreased mitogenic response of T-lymphocytes. The athletes of the Uzbek population examined by us with certain HLA-B15 expressed an increase in the antibody titer, a significant increase in the amount of ASL in the blood, pronounced fluctuations in the indicators of the total pool of T- and B-lymphocytes, which indicates an adequate immune response in response to antigenic exposure and characterizes a high level of immunoreactivity with intensive production of specific antibodies. This allows us to predict that athletes of the Uzbek population, carriers of the HLA-B15 antigen in the phenotype, also have the ability to adapt to a high degree of physical activity of various volumes and power. The opposite nature of the immune response was revealed for athletes with phenotypes HLA-B5 and HLA-B35: an inadequately low level of immune response allows one to judge the limited adaptive capacity of the immune system in them, one of the main systems for controlling and maintaining homeostasis. Individuals with this type of immune response are often prone to prolongation and chronicity of a number of infectious diseases (4,7). Consequently, athletes who are carriers of the HLA-B5 and HLA-B35 phenotypes can be attributed to the risk group, which can cause breakdowns during the period of important competitions. The results obtained indicate the possibility of predicting the adaptive abilities of the body of athletes to increased functional loads based on the signs of the immune status and taking into account their HLA-B5 and HLAphenotype features.

Since we examined athletes of the Uzbek population, the tasks of our study also included determining the characteristics of HLA antigens in the population of the indigenous population of Uzbekistan, studying the genetic status of athletes and their haplotypes. It was found that the Uzbek population has, in terms of the composition of HLA antigens, loci A and B, in common with Caucasoids (to a greater extent) and orienta, but at the same time is characterized by a certain specificity. HLA-B13 antigens can be regarded as a population marker of the Uzbek population. There is evidence in the literature that a number of physical qualities have a hereditary nature, and with the help of genetic markers, it is possible to predict the tendency to manifest certain sports inclinations (11,12,13). We have also established the peculiarities of the set of histocompatibility antigens of the HLA system among highly qualified athletes and sportsmen-dischargers of the Uzbek population. It was found that the antigenic composition in both survey groups is basically identical. However, there are differences between the two antigens. Thus, the noted sharp decrease in the frequency of occurrence of antigens HLA-A11, HLA-B35 in the group of highly qualified athletes compared with dischargers ($P < 0.05$).

Conclusions

1. In athletes of the Uzbek population, the nature of the immune response in response to typhoid vaccination depends on the characteristics of the HLA phenotype: a high level of immunoreactivity and production of specific antibodies was observed in carriers in the HLA-

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B15 antigen phenotype; a low level of immune response and a titer of specific antibodies was detected in the presence of HLA-B5 and HLA-B35 antigens in the phenotype.

2. The immune response to typhoid vaccination with the production of a high titer of specific antibodies is associated with an increase in the number of T-lymphocytes and T-helper subpopulation in the blood, the content of antigen-binding lymphocytes specifically sensitized to the vaccine antigen, as well as a decrease in the level of B-lymphocytes.
3. High immune reactivity in athletes of the Uzbek population with the HLA-B15 phenotype indicates broad adaptive capabilities and a low immune response with the HLA-B5 and HLA-B35 phenotypes.
4. In the group of highly qualified Uzbek athletes. population marked a sharp decrease in the frequency of occurrence of antigens HLA-A11, HLA-B35. Considering the role of the HLAB35 antigen associated with the locus that determines the activity of T-suppressors and determines the relationship with HLA-A11, it can be assumed that certain features of the immune system directly or indirectly affect the indicators of sportsmanship and the limited adaptive capabilities of the organism, in particular to increased physical activity.

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