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ADP010946

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Immunogenetic Approach to Prognosis of Military Specialists' Health Status

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The dispensary system is the basis of the curative-preventive support of military personnel in the Armed Forces of Ukraine. The main purpose of this system is to take preventive and medical-diagnostic measures, directed to health preservation, maintenance and recovery. An additional important task is the medical selection of servicemen and military specialists for particular professional activities, and also the dynamic monitoring of the health of these groups.

Today, the Ukrainian army uses combat and technical equipment and installations which contain sources of ionizing and electromagnetic radiation, toxic components and other health hazards. Moreover, many military units are deployed in parts of Ukraine which have been polluted with radionuclides deposited as a consequence of the Chernobyl Atomic Power Station accident. Therefore, an adequate selection of military specialists who have to work in adverse professional and ecological environments is a very urgent and complicated issue for the military-medical service, and this requires new organizational and methodical approaches and essential expenses.

In the Ukraine military-medical services, there is a system in place which regulates the medical selection of military specialists who are in contact with sources of ionizing radiation or toxic substances. This system includes special medical examinations, the establishment of norms for permissible levels of ionizing radiation or toxic substances in a given working environment, individual and collective protection and decontamination measures, and other provisions.

However, as was established, servicemen and military specialists with a similar health status who work in the same occupational and environmental conditions, may show considerable individual variation in their resistance to toxic factors. Exposure to these factors has resulted an increased morbidity and incapacity among specialists with a poor health status. This has caused significant expenditures.

Therefore, it was deemed necessary to develop a radically new approach to the selection of military specialists who work in adverse environments. This approach should be aimed at the detection, before any exposure has taken place, of individual markers of the sensitivity or resistance of healthy persons to damaging environmental factors. In addition to the selection and dynamic observation of the health status of military specialists who are exposed for a long time to toxic influences, more attention should be paid to the early, pre-clinical detection of physiological disorders by implementing regular medical examinations. It is necessary to identify risk- groups and to carry out timely medical-preventive measures.

A joint scientific project, in which medical specialists of the Research Institute of Military Medicine of the Ukraine Armed Forces, the Main Military Clinical Hospital and the Research Center of the National Medical University were involved, has resulted in the development and introduction of new principles for the

medical selection and dynamic monitoring of the health status of military personnel who are exposed to ionizing radiation, toxic substances or other health damaging factors. The most important aspect of this new methodology is its unified approach to the prognosis of the health status of military personnel. This approach is based on the detection of individual genetic markers , "the genetic passport", which determine the status of the main homeostatic systems in the body (nervous, immune and hormonal). These genetic factors the manage direction and intensity of adaptive responses, and thereby determine individual predispositions to the development of certain pathological processes under the influence of hazardous factors. The great value of this approach is that it is universal, economic, and that it provides both a long-term and a short time prognosis of the health status and performance capability.

The immune-genetic approach for the medical selection of military specialists is based on the evidence that the genetic system of Human Leukocyte Antigens (HLA) - the major histocompatibility complex – plays a leading role in determining human individuality, and in the control of the biochemical and physiological body responses and of the antigenic spectrum of proteins, enzymes, nucleic acids, antioxidants. Many studies have identified genetic HLA markers as the determinants of the relative risk for pathological processes and the development of immune disorders, for the susceptibility to the pathogenic microorganisms, etc. Associations of "HLA and disease" give the possibility to use the HLA-markers ("genetic passport") in the long-term monitoring of the health status and the predisposition to given pathologies. The great number of associations of the HLA-antigens with various diseases has recently been estimated and documented. Thus, when we know a person's set of HLA-antigens we can predict the probability of the development of certain pathological processes, the susceptibility to specific harmful factors, medicines, etc.

Our research was directed to the identification of the immuno-genetic markers of the susceptibility to low doses of ionizing radiation as well as toxic substances, which may predispose military personnel working under extreme conditions to develop pathological reactions and diseases.

We first studied the distribution of particular HLA-antigens and analyzed health status indices among carriers of particular set of HLA – antigens specific exposure. As a first step, the objective physiological indices were selected which reflect disturbances of the health status in the pre-clinical stage of diseases. Once this set of physiological parameters, indices of biochemical and immune homeostasis, cell metabolism, receptors expression, and cytokine synthesis has been determined, the most sensitive indices are selected and compared with the presence of certain HLA-antigens. This type of testing is only used during the first phase of the research to identify particular HLA-antigens associated with individual susceptibility or resistance to the harmful factors or his predisposition to some diseases.

In the second phase, HLA-markers are used as independent criteria for illness prognosis and for the determination of the individual response to the damaging factors without any other additional examination. This selection procedure is cheap, takes just a few hours and it consists only of determining the genetic passport and the assessment of the health risk degree.

This approach we have used for the professional selection of military specialists.

In phase 1, we selected a number of physiological, biochemical, biophysical and immuno-genetic indices which allow to detect early changes in the person's health status under certain ecological and occupational conditions. More than 400 military and civil subjects living in Central–Ukrainian were examined. Among them were healthy subjects, subjects who had previously been exposed to low doses of ionizing radiation (LDIR) or to toxic substances, and patients with various somatic pathologies. The control group included healthy subjects and patients with similar pathologies, who lived in non-polluted regions of Ukraine and who had not been exposed to harmful occupational factors.

The findings indicated that military personnel living in territories polluted with radionuclides or which had been exposed to LDIR had the following patterns of early changes in health status:

1. A tendency to the development of immunodeficiency was typical for participants who took part in the cleanup operations following the Chernobyl accident. This immunodeficiency can transfer into an autoimmune reaction in the case of the development of any somatic pathology. Moreover, anti-prooxidant disorders, leading to the development of many pathological processes have been observed.

2. The autoimmune type of immunogramme with tendencies to develop allergies and high autoimmune responses was observed among military personnel living or working in polluted territories of Ukraine, and those exposed to LDIR. As manifested by the lipid metabolism in the blood and cell membranes, the development of atherosclerosis was demonstrated in these persons.

A large-scale immuno-genetic analysis was carried out and it was found that under the influence of LDIR, there are specific associations of certain HLA-antigens with increased risks for health disorder. It was established that the following HLA-antigens should be considered as risk factors for military specialists working under LDIR exposure: A2, A9, A10, B8, B12, B14. Resistance to radiation exposure is indexed by A3, A19, B7-antigenes. The associations of A3-B5, A3-B8, A2-B7, A19-B12 indicate low resistance of the individual to LDIR. Individuals who are carriers of A10, A12 and B8- antigens in the phenotype have an increased risk for the development of inflammatory and free radical injuring processes.

We also determined immuno-genetic criteria for the prognosis of the health of military personnel which participated in dismantling ballistic missiles (FOM). Is was established that the susceptibility to components of liquid rocket fuel increased when there were low initial levels of antioxidants and high concentrations of poliunsaturated fatty acids in the cell membranes and the blood. All military personnel that was investigated, had an immune dysbalance and the functional activity of their lymphocytes was suppressed. This creates the conditions for the development of immunopathological syndromes and somatic diseases.

After finishing their work, military personnel which had been exposed to components of rocket fuel showed a marked increase of autoantibody production and cell hyperreactivity to lung and liver autoantigens. These are unfavorable prognostic markers, which indicate that there may be damage of the cells of the given organs due to components of fuel, as well as deep changes in the immune response to "self" antigens.

Disorders of lymphocyte function are early markers of immune dysbalance in military specialists. This can cause various pathological process in personnel exposed to LDIR. Probably, both factors have an unspecific stress-dependent impact to the immune system, thereby causing similar patterns of pathogenic changes. Rocket fuel components, however, also exhibit a toxic effect which is characterized by damage of the liver cells and the development of autoimmune disorders. Repression of the antioxidant protection is another early pathogenic element in the chain of many pathologic processes. Carriers of A10, A12 and B8-HLA-antigens who were exposed had a higher risk to develop the "oxidant stress" and inflammation processes. Finally, we also established that the resistance of healthy military personnel to stress is determined genetically and is associated with A2, A9, A10, B8 and B14 HLA-antigens. Other factors are A3 and the B7-antigens association.

In summary, the immuno-genetic approach to the prognosis of changes in the health status of military specialists has enabled us (a) to develop new methodological and organizational medical principles for the dispensary system and for the rehabilitation of military personnel working under extreme conditions, (b) to set new criteria for a scientific evaluation of working conditions, (c) to unify the medical screening of military personnel which has repeatedly been exposed to adverse and harmful occupational and environmental conditions, and (d) to obtain information on which medical-prophylactic and preventive rehabilitation measures can be based.