PATHOGENETIC ASPECTS OF THE IMPACT OF THE FACTOR OF CHEMICAL ETIOLOGY IN THE FORMATION OF INDICATORS OF THE IMMUNE SYSTEM

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ABSTRACT
This paper deals with the actual problem of the impact of pathogenic environmental factors on the immune system of persons whose professional activity is associated with highly toxic production. The set of indices of the immune system in general is a finely arranged and highly sensitive indicator system, with all its links being closely related. Under the influence of harmful factors of production, the human body uses its adaptive-compensatory potential, which includes immunity. Under the pressure of adverse exogenous effects, the immune system begins to function in a new regimen aimed at restoring internal homeostasis and minimizing the possible damage to health. The paper presents the research and analysis of the effects of pathogenic production factors on the immune system of servicemen with a view to further development of a set of measures to prevent possible medical and social losses. The results of the study show the presence of pronounced leukocytosis, neutrophilia, increase in lymphocyte count, shift in immunoglobulin indices, increase in NBT-test values, as well as lower CIC values. The statistical picture of the study shows that the immune system of servicemen is an indicator of pathological changes in the body, which in turn evidences harmful effects on the health of workers. This work is a tactically important base for the development of preventive measures aimed at compensating for dysfunctional changes in the body of military personnel working in the facilities for storage and disposal of highly toxic chemicals.

Keywords: immune system, military technogenesis, carcinogenesis prevention, chemical weapons, occupational diseases.

INTRODUCTION
An important feature of the central nervous and immune systems is their lability and high sensitivity to the influence of external factors, which causes a violation of their functions and a decrease in the quality of life, and the development of certain occupational diseases with significant medical and social losses [1,2,3,4]. On this basis, the study of changes in the immune system is important in terms of detecting new indicators for reducing the stress-resistance of the body, as well as performing the protective function of the immune system of people working in the facilities for storage and disposal of highly toxic chemicals [5,6,7].

To improve the medical support of military personnel, minimize morbidity, improving thereby the level of health, regular monitoring of the health of servicemen is required [8,9,10]. In order to optimize monitoring, it is necessary initially to collect data on the health and morbidity of military personnel, to regularly conduct clinical examination, including blood chemistry [11,12,13]. This will also help to make a general forecast and develop preventive measures [14,15,16].
The research was carried out on the basis of the sample of servicemen of various experience and different kind of troops, and was aimed at studying the complex state of the immune system of servicemen associated with the storage and destruction of chemical weapons at service facilities. Servicemen undergo chemical effects of various levels.

Objective of the study is to identify changes in the normal level of the integrated immune system indicator associated with the impact of chemical factors at the service facilities.

METHODS
The research involved both servicemen working at the facilities for storage and disposal of chemical weapons, and civilians not employed in the uniformed services.

Using statistical methods that consider the service experience and type of troops, the results were processed and divided into two groups:

1) by experience: 1-2 years, 3-9 years, 10-19 years, 20-29 years, and 30-39 years;
2) by type of troops: the Land Forces, the Air Forces, the Missile Forces, Signal Corps, the Navy Forces, the Space Defense, the Airborne Forces, and the Ministry of Defense.

We conducted a study based on biomedical indicators: using a blood chemistry test. Blood, as the main information carrier, can describe the state of human health, and therefore its immune status. Thus, if a painful process occurs in the body or if there is any painful process, then the blood test methods will help us to detect it.

To determine the number of blood leukocytes, the most commonly used method is the counting of leukocytes in the Goryaev chamber and in an automatic hematological analyzer.

The nitroblue tetrazolium test (NBT-test) is used to identify the so-called activated granulocytes and monocytes. The activation of phagocytes is based on a sharp increase in oxidative reactions. Among the indicators of this phenomenon is the reaction with nitroblue tetrazolium: it is absorbed from the solution, and under the influence of oxidative processes in the cell turns into an insoluble formazan. The latter is found in the cell in the form of dark blue granules.

There are spontaneous and induced (stimulated) NBT-tests. The results of the spontaneous test indicate the number of activated cells in the patient's blood, for example under the influence of infection. The results of the induced test give an insight into the ability of the neutrophils under study to activation in vitro.

Immunoglobulin quantification: Antigens (in this case - the immunoglobulins of the test serum) diffuse in the gel, forming in the gel cells strong settled immune complexes with antibodies (a monospecific serum against immunoglobulins) contained in the gel. The test serum added to the wells diffuses radially with the formation of precipitate rings. The diameter of the precipitation ring, in comparison with the control, determines the concentration of the antigen. Then, with a round die (diameter 1.5-2 mm), the wells are stenciled in the gel, or according to the rule: the distance from the edge of the slide to the wells, and between the holes must be at least 10 mm. Given this condition, 48 wells can be placed on the slide. The agar from the wells is removed with a Pasteur pipette connected to a water jet pump to prevent the sera from drying out in the wells.

A method based on Iu.A. Grinevich and A.N. Alferov’s technique was also used, which determines the level of circulating immune complexes in blood serum.

RESULTS
First group indicators (service experience):
A statistically significant increase in the number of leukocytes relative to the norm was noted in service intervals of 1-2 years - 25%, 3-9 years - 57.1%, 10-19 years - 41.2%, 20-29 years - 44.8% 30-39 years - 58.2% (p<0.05), whereas in service interval of 30-39 years a decrease was registered in 1.5% of persons (p<0.05).

There is an increase in neutrophils in service intervals of 1-2 years - 26.2%, 3-9 years - 57.1%, 10-19 years - 47.1%, 20-29 years - 55.2%, 30-39 years - 62.7%; the increase is statistically significant with a probability of less than 0.05.

With regard to lymphocytes: a statistically significant increase in T-lymphocytes is observed in service intervals of 1-2 years - 76.2%, 3-9 years - 85.7%, 10-19 years - 88.2%, 20-29 years - 69%, 30-39 years - 70.1%, and in the service interval of 1-2 years, in contrast, there was a decrease in 1.2% of persons (p<0.05); the similar situation is with B-lymphocytes: there is an increase in service intervals of 1-2 years - 73.8%, 3-9 years - 85.7%, 10-19 years - 88.2%, 20-29 years - 69%, 30-39 years - 70.1%, as well as a decrease in the service interval of 1-2 years in 1.2% of persons (p<0.05).

Immunoglobulins: A “not normal” level of IgA was found in service intervals of 1-2 years - 1.2%, 30-39 years - 4.5% (p<0.05); a noticeable, statistically significant increase in IgM in the service interval of 1-2 years is 44%, 3-9 years - 42.9%, 10-19 years - 41.2%, 20-29 years - 24.1%, 30-39 years - 26.9% (p<0.05), and a decrease in service intervals of 1-2 years is 1.2%, 10-19 years - 11.8%, 30-39 years - 6% (p<0.05); there is also an increase in IgG in service intervals of 1-2 years - 16.7%, 3-9 years - 14.3%, 10-19 years - 5.9%, 20-29 years - 10.3% with probability less than 0.05, and a decrease in service intervals of 1-2 years - 14.3%, 3-9 years - 42.9%, 10-19 years - 17.6%, 20-29 years - 10.3%, 30-39 years - 37.3% (p<0.05).

Significant deviations from the normalized index of the NBT-test are found both in the spontaneous and in induced NBT-test: the increase of the first was revealed in service intervals of 1-2 years - 70.2%, 3-9 years - 81.3%, 10-19 years - 71.4%, 10-19 years - 88, 2%, 20-29 years old - 69%, 30-39 years - 71.6%, and the second - in service intervals of 1-2 years - 38.1%, 3-9 years - 42.9%, 10-19 years - 58.8%, 20-29 years - 55.2%, 30-39 years - 73.1% (p<0.05), respectively; as for the statistically reliable decrease, it was noted by spontaneous NBT-test in 2.4% of persons with service experience of 1-2 years, and by induced NBT-test - in service intervals of 1-2 years - 2.4%, 10-19 years - 5.9% (p<0.05).

The amount of CIC was increased in service intervals of 1-2 years - 3.6%, 30-39 years - 3% (p<0.05). A decrease in the amount of CIC is observed in service intervals of 1-2 years - 65.5%, 3-9 years - 57.1%, 10-19 years - 88.2%, 20-29 years - 69%, 30-39 years - 65, 7% with a probability of less than 0.05.

Second group indicator (type of troops):

A statistically significant increase in leukocytes was found in the Land Forces - 32.5%, the Air Forces - 55.6%, the Missile Forces - 100%, Signal Corps - 100%, the Navy Forces - 50%, the Space Defense - 18.8%, the Airborne Forces - 66.7%, and the Ministry of Defense - 87.5%. A decrease was noted only in the Land Forces - 1.3% (p<0.05).

An increase in neutrophils relative to normal was found in the Land Forces - 37.5%, the Air Forces - 62.2%, the Missile Forces - 100%, Signal Corps - 100%, the Navy Forces - 50%, the Space Defense - 18.8%, the Airborne Forces - 66.7%, and the Ministry of Defense - 100% (p<0.05).

There is a statistically significant increase in both T-lymphocytes and B-lymphocytes: the first exceed normal level in the Land Forces - 81.3%, the Air Forces - 91.1%, the Missile Forces - 100%, Signal Corps - 100%, the Navy Forces - 50%, the Space Defense - 81.3%, the Airborne Forces - 100%, and the Ministry of Defense - 100%; the second - in Land Forces - 78.8%, the Air Forces - 91.1%, the Missile Forces - 100%, Signal Corps - 100%, the Navy Forces - 50%, the Space Defense - 81.3%, the Airborne Forces - 100%.
100%, and the Ministry of Defense - 100% (p<0.05). There is also a decrease in both T-lymphocytes, and B-lymphocytes in the Land Forces - 1.3%.

A statistically significant increase in immunoglobulins was found in: IgA in the Land Forces - 1.3%, the Air Forces - 2.2%, the Missile Forces - 50%, Space Defense - 6.3%; IgM in the Land Forces - 42.5%, the Air Forces - 33.3%, Signal Corps - 33.3%, Space Defense - 37.5%; the Airborne Forces – 33.3%, the Ministry of Defense – 50%; IgG in the Land Forces – 11.3%, the Air Force – 11.1%, Space Defense – 12.5%, the Airborne Forces – 66.7%. A decrease in relation to normal was observed in IgM in the Land Forces - 2.5%, Air Forces - 4.4%, Ministry of Defense - 12.5%; and IgG - in the Land Forces - 22.5%, Air Forces - 17.8%, Signal Corps - 55.6%, Navy Forces - 50%, Space Defense - 12.5%, Ministry of Defense - 25% (p<0.05).

There is an increase in the values of spontaneous NBT-test in the Land Forces - 73.8%, Air Forces - 95.6%, Missile Forces - 100%, Signal Corps - 100%, Navy Forces - 50%, Air Forces - 75%, Airborne Forces - 100%, Ministry of Defense - 100%, and decrease only in the Land Forces - 2.5%. Increased values of induced NBT-test are in the Land Forces - 50%, Air Forces - 71.1%, Missile Forces - 100%, Signal Corps - 100%, Navy Forces - 50%, Air Forces - 31.3%, Airborne Forces - 100%, Ministry of Defense - 100%; there was also a decrease found in the Land Forces - 2.5%, and Air Force - 2.2%.

A statistically significant increase in CIC is found only in the Land Forces - 6.3% Decrease CIC values were found in the Land Forces - 68.8%, the Air Forces - 93.3%, the Missile Forces - 100%, Signal Corps - 77.8%, the Navy Forces - 50%, the Space Defense - 68.8%, the Airborne Forces - 66.7%, and the Ministry of Defense - 100% (p<0.05).

DISCUSSION
We considered the relevant problem affecting the immune status of servicemen undergoing highly toxic effects.

Under the influence of chemical factors, the human immune system changes its standard regime in order to normalize the set of indicators.

We conducted research and, analyzing the data, obtained quantitative indicators of the effect of pathogenic factors on the immune status of servicemen, which would help to further develop and conduct preventive measures.

Thanks to statistical methods, we see that servicemen have biochemical deviations from the norm associated with their service at facilities for the storage and disposal of chemical weapons.

The statistical picture shows the following pathological changes in the immune system:

- Leukocytosis;
- Neutrophilia;
- Lymphocytosis;
- Non-normalized immunoglobulin indices;
- Increased NBT-test values;
- Decreased CIC values.

Statistically reliable research data show that both troops of various types, as well as society may soon suffer social losses. Thus, this study should be the starting point for creating a set of measures aimed at preventing pathological conditions of the body.

SUMMARY
The following major conclusions can be drawn from the results:
1. The servicemen have a pronounced leukocytosis. A statistically significant increase in the number of leukocytes, 58.2%, was found in a group of military personnel with 30-39 years of experience. The groups by types of troops had the highest frequency of leukocytosis detected in the Missile Forces - 100%, Signal Corps - 100%, Airborne Forces - 66.7% and Ministry of Defense - 87.5% (p<0.05).

2. The presence of neutrophilia. A group of service interval of 30-39 years showed an increased amount of neutrophils - 62.7%, as well as in the Missile Forces - 100%, Signal Corps - 100%, Airborne Forces - 66.7%, and the Ministry of Defense - 100%.

3. Increase in lymphocytes. The groups of service interval of 3-9 years have increased levels of B-lymphocytes - 85.7%, 10-19 - 88.2%, 30-39 - 70.1%, in the Missile Forces - 100%, the Navy Forces - 91.1%, Signal Corps - 100%, the Airborne Forces - 100%, and the Ministry of Defense - 100%. The groups of service interval of 3-9 years have increased levels of T-lymphocytes - 85.7%, 10-19 years - 88.2%, in the Missile Forces - 100%, Air Forces - 91.1%, Signal Corps - 100%, Airborne Forces - 100%, and the Ministry of Defense - 100%.

4. Non-normalized immunoglobulin value. The group of service interval of 30-39 years had increase in IgA – 4.5%, in the Missile Forces - 50%. The group of military personnel with 1-2 years of experience showed the excess of normal IgM level in blood - 44%, in the Land Forces - 42.5% and Ministry of Defense - 50%. Reduction in the normal level was observed among servicemen with experience of 10-19 years (11.8%). The groups of service interval of 3-9 and 30-39 years had a decrease in the normal level of IgG found in 42.9% and 37.3%, respectively, as well as in Signal Corps - 55.6%, and Navy Forces -50%. Elevated values were also observed in the group with 1-2 years of experience - 16.7%, and in the Airborne Forces - 66.7%.

5. Exceeded NBT-test values. The group of service interval of 30-39 years had a high level of the NBT-test - 73.1% (iNBT), 71.6% (sNBT), similarly in the Missile Forces, Signal Corps, Airborne Forces and Ministry of Defense - 100% for iNBT and sNBT.

6. Decreased CIC values. The group of service interval of 10-19 years had a decreased CIC level (88.2%), as well as in the Missile Forces and the Ministry of Defense - 100%.

CONCLUSIONS

The statistical picture of the study shows that the immunity of servicemen has undergone significant changes, which evidences the effect of the service on the health of a serviceman. The drop in the concentration of IgM and IgA in the blood testifies to the weakening of the immune barrier of the organism, and accordingly - its low resistance to various kinds of antigens. In such cases, the lack of immunocompetent agents is compensated by increasing the amount of IgG and enhancing the secondary immune response. Another significant indicator of immunodeficiency is the increased activity of sNBT and iNBT.

Thanks to the monitoring of the complex state of the immune system, we can develop preventive measures that will help to normalize the level of health indicators of military personnel.

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