

the acute ischemic cerebrovascular disturbances in the vertebrobasilar system is high among the population of Petrozavodsk; working-age people prevail among the patients, and more and more younger people suffer from the disease.

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THE IMMUNITY STATE & PURINE NUCLEOTIDES ENZYMES ACTIVITY AT THE RATS, HAVING EXPOSED TO THE DUST AND RADIATION FACTOR & THEIR CORRECTION

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Actuality

The structural and functional disorders of the tissue homeostasis, having accompanied by this or that pathology beginning and development, are always connected with the tissue integrity disorder, the various cell populations' death and reproduction just in the lesion focus. In its turn, this means, that some universal characteristics of the destructively and reparative processes, having proceeded in the organism's organs and tissues, have to be existed, besides the specific metabolic shifts, having caused by the ethiopathogenetic diseases factors. The enzyme systems of the free predecessors exchange of the nucleic acids and their derivatives are belonged to a number of such pathological processes characteristics. So, the immunodeficient states are connected with the enzymes activity disorder, having controlled the adenosine level in the lymphocytes: the adenosine deaminase (ADA) insufficiency results in the serious immunodeficiency, at which the number is being lowered and the T – and B – lymphocytes function is being disturbed; the 5 – nucleotidase insufficiency results in the easier immunodeficiency form, at which the B – lymphocytes functions are being left normal, but the T – lymphocytes functions are being violated [4, 5]. The catabolic processes of the purine nucleotides exchange in the organism have the large significance for the immunological organism reactivity regulation.

And the adenylate cyclase system is also involved in the adenosine immunosuppressive system and cytotoxic action. But the cyclical adenosine monophosphate (cAMPH) can be served not only the negative, but and the positive lymphocytes function's regulator. The cAMPH effects different orientation

can be conditioned by the its content change in the various immune system cells compartments, by these compartments functions, having provided the lymphocytes biological qualities or the other cells [2].

The Aim

The aim in the experiment on the animals at the combined influence of the asbestos dust and the ionizing radiation the has been defined by us, to study the immune status change, and the enzymes activity of the purine nucleotides metabolism: the adenosine deaminase (ADA), the adenosine monophosphate deaminase (AMPH – DA) and 5' – nucleotidase (5' – HT) in the more sensitive tissues of the liver, the thymus gland organs, and in the blood lymphocytes. Our aim is, moreover, to find it out the immunity changes interconnection presence with these enzymes activity, and also to study the Be phytopreparation action (e.g. triterpenoid from the *Betula Pendula* Roth).

The Research Methods

Three tests series on 40 albino rats have already been carried out for the assigned task realization. The I – st group – the intact ones (n=10), the II – nd group – the irradiated ones in 6 gr. dose, having primed by the asbestos dust, at the same time (n=15), and the III – rd group – the irradiated and primed ones by the dust and having received the Be phytopreparation (n=15). The II – nd and the III – rd groups' animals have been one time irradiated during 30 days and nights before the examination on the «Teragam ⁶⁰Co» radio therapeutic installation (Czech Republic) in the 6 gr. dose. We have carried out the animals' topometric and dosimetric preparation on the «Terasix» X – ray photography simulator, which is provided the correct bringing to the planned dose, before to conduct the irradiations. The asbestos dust was brought into the rats' lungs (e.g. intratracheally) for the pneumoconiosis reproduction by the method, which had been developed by us [1]. The animals have been killed by means of the incomplete decapitation, having, preliminarily, put to sleep by the chloroform. This kind of work with the experimental animals has been conducted, in accordance with the principles of the Helsinki Declaration of the World Medical Association on the humane treatment with the animals. The immune status has been estimated on the basis of the content study in the lymphocytes' peripheral blood and their subpopulation with the phenotypes: CD3⁺, CD4⁺, CD8⁺, CD19⁺ by the method of the immunofluorescent staining of the cells with the antibodies use, having conjugated with the ФИТИ phenylizothiocyanate (PHETC) (the «CALTAG Laboratories» Company, the USA), having adapted, exactly, for the rats' analyses. The neutrophils' phagocytal activity (PHA) definition, the serum immunoglobulins level of the A, M, G classes, the CIC (the circulating immune complexes), ITML (the inhibition test of the migration of leukocytes) number have been conducted.

The 5'-HT activity in the lymphocytes has been defined by the AMPH hydrolysis speed up to the adenosine and the phosphoric acid, and they have been expressed in the H_3PO_4 mmole number per 1 mg of the protein. The AMPH – DA and ADA activity have been defined by the methods, which have been developed by Mr. Tambergenov C.O., by the deamination rate, and they are expressed in the ammonia mmole per the protein mg (1984). Especially, for this investigation, the lymphocytes have been isolated from the peripheral blood, and the homogenates have been prepared from the liver and the thymus gland. The triterpenoid from the (Be) *Betula Pendula* Roth has been used, as the phytopreparation, and it has been prescribed by the 2,5 mg./100 gr. of the mass per os during 14 days. The immunological and biochemical indicators have been defined in the all above – mentioned groups with the statistical processing and with the Student's criteria calculation carrying out.

The Results and the Discussion: The investigation results have shown that the leucopenia is registered at the combined gamma – irradiation and the asbestos dust exposure. The lymphocytes quantity has been increased, for certain, in the experimental groups: in the II – nd group for 41,44%, in the III – rd group – 28,63%. The $CD3^+$ lymphocytes absolute and the relative quantity lowering has been registered, reliably, in the II – nd group: in 2,33 times (e.g. $p<0,001$) and 1,34 time (e.g. $p<0,05$), correspondingly. After the treatment, the $CD3^+$ lymphocytes absolute quantity rise takes its place for 65,82 % and OK – for 27,45% (e.g. $p<0,05$), in comparison with the group, which has been exposed to the dust and the radiation factor.

The $CD4^+$ lymphocytes absolute and the percentage quantity at the animals, which have been exposed to the dust and the radiation factor, statistically, are being lowered, for certain: the absolute quantity – in 1,78 time (e.g. $p<0,001$), the relative quantity – in 1,43 time (e.g. $p<0,05$), but at the animals, having received the phytopreparation, the $CD4^+$ lymphocytes absolute quantity is being increased in 1,88 time (e.g. $p<0,01$), the relative quantity – in 1,55 time (e.g. $p<0,01$). It has been determined, that the dust and the radiation factor is resulted in the main indices lowering of the cellular immunity system. All these given changes have resulted in the ($CD4^+/CD8^+$) immunoregulatory index increasing, that is made up, in average, $1,83\pm0,07$ (e.g. $p<0,01$), in comparison with the II – nd group $1,31\pm0,08$, that is for 21,83%. The ITML (the inhibition test of the migration of leukocytes) results have shown, that it has been mentioned the migration index lowering down to $0,60\pm0,04$ (e.g. $p<0,05$) in the III – rd group, in comparison with the II – nd group. It is connected, possibly, with the Be preparation influence – the $CD3^+$ cells lymphokine producing capacity has been increased. The B – lymphocytes absolute and relative quantity were rushing to the normalization under the influence of the phyto-

preparation, in comparison with the II – nd group. At the same time, the statistically significant immune complexes are increased up to $(1,56\pm0,10)$ standard units (e.g. $p<0,01$) in the group, having received the phytopreparation, has been registered. The phagocytal activity (PHA) of the blood cells at the animals of the II – nd group has been made up $31,24\pm2,76\%$, the increase, for certain, up to $39,61\pm2,55\%$ (e.g. $p<0,05$) has been registered in the III – rd group. The IgA common level in the blood serum, at the animals of the II – nd group has been reliably lowered ($2,01\pm0,17$ gr./l. (e.g. $p<0,05$)). It has, moreover, been revealed the IgA level increase in the III – rd group. It has been registered the reliable increase in the II – nd group ($6,49\pm0,57$ gr./l. (e.g. $p<0,05$)) at the IgM common level research. The statistically IgM level lowering, for certain, takes its place in the III – rd group (e.g. $p<0,05$) just after the herbal therapy. The IgG level has been increased in the II – nd and the III – rd groups, in comparison with the intact group.

Having generalized the received results, it is quite possible to state, that have been revealed the significant changes, which have been characterized by the leucopenia, the $CD3^+$, $CD4^+$, $CD8^+$ quantity lowering, the CIC (the circulating immune complex), PHA (the phagocytal activity), and IgA levels, and also by the $CD19^+$ quantity, and the IgM and IgG levels increase at the experimental animals, having exposed to the dust and the radiation factor. The almost all indications normalization takes its place, having increased the organism's protective reaction just in the adaptation mechanisms, having possessed the immunomodulating property at the Be phytopreparation introduction.

The enzymes activity state of the purine nucleotides cycle, as at the dust and radiation exposure, well as at the phytopreparation introduction has also been studied. In the first place, the ADA activity is being defined by the T – cells content, whereas the 5' – HT activity is being depended from the B – lymphocytes. The ADA activity sharp lowering, the purine nucleoside phosphorylase (PNPH), and the 5' – HT in the lymphocytes of the chronic leucoses patients, is testified to on the processes slowing down of the purine nucleotides decomposition, and it also promoted to the toxic for the lymphoid cells of the metabolites accumulation – e.g. the adenosine and the deoxyadenosine. Their concentration increase in the lymphocytes short – term culture of the chronic leucoses patients under the ADA inhibition conditions is caused these cells lysis. As the research results have shown, it has been observed the ADA enzyme activity increase at the animals in 1,79 time (e.g. $p<0,001$), and the 5' – HT and AMPH – DA enzymes activity, for certain, has not been distinguished just from the benchmark, from the side of the purine exchange in the thymus gland at the dust and radiation exposure. It has been registered the reliable all investigated enzymes activity increase in the thymus gland cells just

after the medical treatment. Thus, the enzymes stimulation and activation of the purine exchange take its place against the background of the medical treatment for the balanced action of the immune system components.

As the researches have shown, the AMPH – DA activity factor is not being undergone the special changes in the blood lymphocytes at the dust and radiation exposure. The 5-HT activity is being increased in 6,33 times, and the ADA is, on the contrary, being lowered almost in 1,7 time. These changes are being promoted to the adenosine and deoxyadenosine quantity accumulation, which in the increased concentrations are able to exert the cytostatic and cytological effect upon the lymphoid cells [5]. It has been registered the positive changes of the enzymes activity against the background of the medical treatment, that is in the increase direction: the ADA activity has been increased for 59,09% and AMPH – DA – for 56,25%. The research results have shown, that the ADA, 5 – HT, and AMPH – DA enzymes activity in the liver at the animals just after the dust and radiation exposure has been increased up to $0,452 \pm 0,035$ (e.g. $p < 0,001$), up to $0,044 \pm 0,004$ (e.g. $p < 0,05$), and up to $0,229 \pm 0,022$ (e.g. $p < 0,001$), correspondingly. It has been registered the subsequent enzymes activity increase, which is being resulted in the metabolism activation of the purine nucleotides at the medical treatment.

It is quite known, that the cytoplasmic enzymes of the adenosine deaminase ADA and $\text{PIH}\Phi$ are being catalized the consequent stages of the adenosine and deoxyadenosine degradative transformations, which are the intermediate metabolic exchange products of the purine nucleotides. The superficially – membrane 5' – nucleotidase is dephosphorylized the extractocellular AMPH with the adenosine formation, which is easily able to be transported inside the cell.

Thus, all these enzymes are being taken their part in the maintenance of the metabolites intracellular balance of the purine exchange – that is, the adenosine and deoxyadenosine, which in the increased concentrations are able to exert the cytostatic and cytological effect upon the lymphoid cells [5]. The pathogenetic mechanism has been defined at the molecular level with the indication of the specific deficient enzyme at the IDS (immunodeficiency states) series: the ADA one at one from the IDS and $\text{PIH}\Phi$ or the transcobalamin II forms at the IDS one, having accompanied by the megaloblastic or hypoplastic anaemia. The defects at the ADA and $\text{PIH}\Phi$ enzymes level are being broken the adenosine metabolism. These enzymes defects are being blocked the hypoxanthine production, so the adenosine, ADPH, and ATPH excessive accumulation is being taken its place just in the tissues, that is being blocked the T – cells maturation, by the unknown reasons. It is quite possible to use the metabolism enzymes of the purine nucleotides in the functional condition analysis of the immune status and also in the

immune reaction adequacy [3]. Thus, it has been registered in our experiment that the dust and radiation factor is being brought to the functions disorder of the immune system cells, having changed their activity that is being accompanied by the activity lowering of the exchange enzymes of the purine nucleotides. The dysfunction state of the immune protection system is being appeared, that it is quite able to intensify the adaptative mechanisms disorders. The immunomodulatory quality of the Be phytopreparation has also been revealed.

References

1. Zhetpisbaev B.A., Iljderbaev O.Z., Bazarbaev N.A. et. al. "The Facility for the Intratracheal Introduction of the Pathogenic Sprays in the Experiment" // The Preliminary Patent for the Invention №190023, The Bulletin №1, 15.01.2008. PK.
2. Tapbergenov S.O., Tapbergenov T.C., "The Adreno-Thyroidal System. The Cell's Bioenergetics and the Adaptation Mechanisms for the Stress." The Monograph. Semipalatinsk. 1998, p. 158;
3. Tapbergenov S.O., Tapbergenov T.C., "The Metabolism Enzymes of the Purine Nucleotides in the Analysis of the Immunity Functional Adequacy" // The Biomedical Chemistry. Moscow, 2005, vol. 51, №2, -C., p.p.199 – 205;
4. Barankiewicz J., Ronlov G., Jimenez R., Gruber H.E., "The Selective Adenosine Release from Human B, but not T Lymphoid Cell Line.", J.Biol.Chem. 1990, Sep. 15; 265(26): p.p. 15738 – 43;
5. Stolk J.N., de Koning D.G., Pennings A.H., De Abreu R.A., van de Putte L.B., Boerbooms A.M., "The Reduced Purine 5-Nukleotidase Activity in Lymphocytes of Patients with Systemic Lupus Erythematosus: the Results of a Pilot Study". Ann.Rheum.Dis. 1999, Feb; 58(2): p.p. 22 – 5.

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PHARMACOLOGICAL AND SURGICAL SYMPATHECTOMY OF VERTEBRAL ARTERIES

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With degenerative damages of cervical spine (CS), by force of closely linked with the second segment of vertebral arteries (VA), the symptoms of vertebral-basilar insufficiency (VBI) are often developed. Hypoperfusion in the bath of VA with spondylogenic damage is sometimes caused by their irritative or reflector spasm, even for lack of considerable