FEATURES OF CHANGES OF THE ERYTHROBLASTIC ISLANDS ON THE STAGES OF POSTNATAL ONTOGENESIS UNDER TOXIC STRESS AND PHARMACOLOGICAL CORRECTION

O.A. Ovsyannikova[1], A.A. Zhidovinov[1], D.V. Karpeeva[1], M.D. Osipenko[1], A.V. Naumov[1], D.A. Shikunov[2], T.A. Shishkina[1]

[1] Astrakhan Medical State University, Astrakhan, Russian Federation
[2] Burnazyan Federal Biophysical Center, Moscow, Russian Federation

Correspondence address:
414000, Astrakhan, st. Bakinsky, 121, Astrakhan State Medical University, e-mail: ovolga-a@ya.ru, tel. +79086134100

ABSTRACT — The study found that the process of erythropoiesis is dependent directly on the age group of experimental animals. The toxic effects of exogenous pollutants leads to a decrease of erythroid islands regeneration processes in the bone marrow dramatically reduces appear erythroid islands in involution. Especially vulnerable are the group of young and old animals during ontogeny. Against the background of the drug "etoksidol" with a strong antioxidant effect of the number of erythroid islands remodel increases in all study groups of experimental animals.

KEYWORDS — erythropoiesis, red bone marrow, a sulfur-containing gas, the experimental animals.

Olga Ovsyannikova, *professor of department of pathological physiology*

Alexei Zhidovinov, *professor, Head of the Department of Pediatric Surgery*

Darya Karpeeva, *assistant of department of pathological physiology*

Marina Osipenko, *assistant of department of pathological physiology*

Aleksandr Naumov, *assistant of department of pathological physiology*

Dmitry Shikunov, *radiologist of department of radiation and radioisotope diagnosis*

Disturbance of the natural balance in a surrounding medium, connected with air pollution, water, soils, the emergence of emergency situations provoked by economic activity of the person by the beginning of our century essentially changed a natural xenobiotic profile of many territories that is especially shown in urbanized regions. From numerous technogenic toxic gases – the pollutants which are contained in the atmosphere and in the air of industrial production have the greatest value. Permanent release into the environment these pollutants leads to their accumulation, especially in the continuous production on oil and gas processing plants, which ultimately leads to chronic ecotoxicity of the environment [1, 2, 3, 5, 8].

The system of red blood is very sensitive to influences of production adverse factors of industrial en-

Tatyana Shishkina, *assistant of department of histology and embryology*

vironmental factors [4, 10, 12]. The modern research shows that the majority of xenobiotics has pro-oxidant properties. There is an activation of peroxide oxidation of lipids, balance upset between the formation and destruction of peroxides and excess accumulation of toxiferous free radicals in a blood plasma and erythrocytes, which is an important component of the pathogenesis of negative conditions, in particular, of violations of erythropoiesis [7, 9; 13]. In this regard, the problem of protection of system of a hematopoiesis of the population living in the zone of influence of gas-chemical enterprises from influence of gaseous sulfur-containing pollutants, remains urgent now [14, 15].

The purpose of our research was the studing of feature of changes of the erythroblastic islands (EI) of red bone marrow at stages of a post-natal ontogenesis in the conditions of influence of sulfur-containing pollutants, and also at and pharmacological correction of antioxidant of a new generation — the medicine "ethoxydale". The properties, characteristic of this medicine, are: improvement of rheological behavior of blood, strengthening of cell metabolism, a high antioxidant activity, the ability to an inhibition of processes of peroxide oxidation of lipids, membrane-protective effect, speed of approach of effect, and also lack of negative consequences from its application [1].

The experiment is made on 72 white not purebred rats, who are contained in standard vivarium conditions in accordance with the "Rules of laboratory practice in the Russian Federation" (the order of MH of the Russian Federation № 708n from 23.08.2010). Group of three types were formed: I. — control; II. — exposed to sulfur pollutants; III. — treated as a protector domestic product "etoksidol" (JSC "Synthesis") intragastrically at a dose of 2.5 mg/kg, one time a day every day of the experiment.

As a toxic agent the natural drained gas of the Astrakhan gas condensate deposit was applied. In experiments the concentration of gas in steam-and-gas mixture making 90±4 mg/m^3 of hydrogen sulfide, which is 30 times more of threshold limit value of a hydrogen sulfide for working zones at simultaneous presence of hydrocarbons was used.

The priming sour sulfur-containing gas was carried out 4 hours in autumn and winter seasons by a static method with simultaneous stay in the camera of 6 individuals daily within 30 days, except Sundays, strictly from 10 to 14 o'clock, temperature in the camera was +22±2° C. The relative humidity during the experiment increased from 53±4% to 66±6%, fogging of the walls was not noted. Concentration of gas and experimental conditions completely conform to the requirements stated in the edition of WHO [11] and the MH of the Russian Federation №267 from 19.06.2003. Control rats were of similar age experimental groups which 6 individuals in each group were also 4 hours in the air-locked inoculation camera in the same condations, as experieced, but in lack of sour gas were controled.

Bone marrow from the femurs was taken by means of the method developed by Yu.M. Zaharov, I.Yu.Melnikov and A.G.Rassohin [6]. Calculation of quantitative indicators characterizing a condition of an erythropoiesis in the EO was made by the method L.V. Vorgova Yu.M. Zaharov on the basis of the obtained data of the number of EO in the bone marrow of animals and their distribution by maturity classes. [6]

The quantitative data obtained in the course of the study, analyzed by methods of variation statistics and determine the significance of differences on Ulkokson-Mann-Whitney test. When carrying out statistical processing used OpenOffice Calc utility of free software OpenOffice (Ver. 3.0), running under Windows XP Home Edition (OEM X12-53766 certificate) operating system.

RESULTS OF A RESEARCH

When analyzing the results of an experimental research with a protective action "etoksidol" desire of age dynamics of content of all types of EO approach the level of the age norm is noteworthy that can be viewed as a relative normalization of erythropoiesis as a result of the process of improving its conditions. However, the severity of this process for various types of EO varies. In particular, EO maturity class can show a very significant and statistically highly significant increase in their number in response to the combined effects of pollutants and the tread in an immature age. In the following, an adult, a sharp drop in the number of islets of this species occurs under the tread that their number becomes scarce distinguishable from the age norm, ie, It is on the verge of statistical significance of differences.

In senile period of ontogenesis action tread leads to practical normalization of the structure and the amount of EO1, as the difference in their number and age control becomes statistically insignificant. As seen in Figure 1, the dynamics of the number of EO1 is almost completely determined by the involutive processes in the background of a slight effect of sulfur pollutants from the mature to old age in the conditions of the tread impact.

Age dynamics of the number of EO2 is similar in general terms to the same parameter EO1 under the combined effects of pollutants and the tread. However, the effectiveness of the protective action is not

as strongly dependent on the age, as in the previous case. It revealed that the protector reduces the amount of EO2 almost the exact same amount as a result of increased toxic effects, regardless of age. At the same time difference to the control remains reliable for all ages in the number using EO2 tread.

Deformed picnotic central macrophage determined statistically significantly less in comparison with the impact of sulfur-containing pollutants, namely 21±8% of the cases (P <0,05), while they themselves erythroblastic islands have a symmetrical structure. Age dynamics of content EO3 under the action of tread is very interesting. The desire to increase sharply reduced under the influence of this type of pollutant the number of the erythroblastic islands in the bone marrow is clearly expressed in an immature age. Content EO3 is virtually identical age control on the mature stage of ontogenesis.

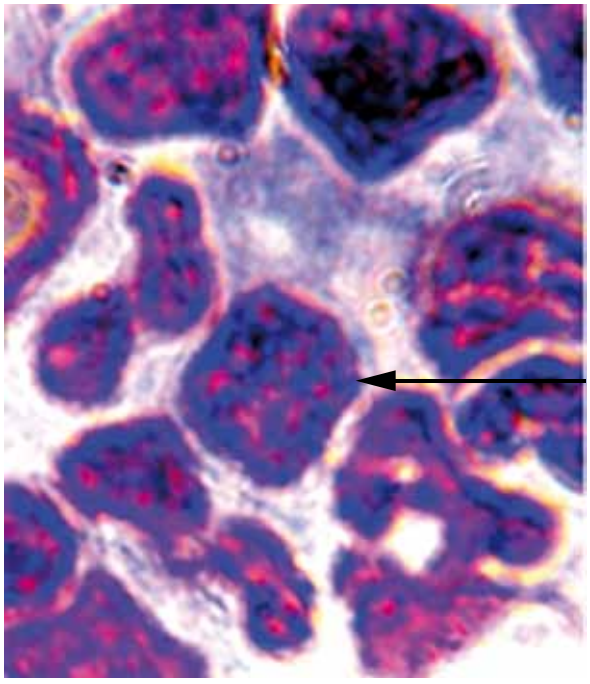

Fig. 1. *EO 3rd class maturity rat elderly. Central macrophage is one large vacuole (arrow). Painting neutral red. × 90*

Further, in old age, there is a slight, but statistically significant excess of the amount EO3 over the age control, indicating, perhaps, the activation of the transformation in EO2 EO3 use as tread compounds and stimulation of erythropoiesis. Erythroblastic islands of this type under the tread actions look more organized compared to the experience without it. In the central macrophages pycnosis less pronounced. Vacuolation retained, however, in most cases, instead of multiple small observed 1–2 big vacuole. The protective effect on the content of erythroblastic islands in involution in terms of exogenous intoxication immature age is quite small.

This is confirmed by the lack of a statistically significant difference in the magnitude of this parameter in the case of the tread and without it. But in the mature period of ontogenesis the use of the tread gives a very noticeable effect, manifested in a high fidelity increasing number of EO in involution by 15% compared to only effect gas.

In old age the protective effect decreases, and does not ensure compliance with the age norm amounts erythroblastic islands in involution, although still statistically significant, because the number of EO of this type is significantly superior to the same amount without tread. Structurally EO in involution in the application of the tread differ slightly from similar, but only exposed to pollutants, as, indeed, and the last of the intact. In a small number of cases (9±3%) present picnotic central macrophages. At the same time, the number of central vacuolated macrophages, particularly those with large vacuoles statistically significant (P <0.05) reduced to 42 ± 8% as compared with the experiment without the protector.

Using the tread under the impact of pollutants it is accompanied by the desire to remodel the dynamics EO content closer to the age norm. It turns out quite confident in immature and mature age of the experimental animals, as evidenced by highly significant difference (P <0.01) between the respective values.

In old age the tread less effective, since the difference between the amount of EO is reconstructed with the use of the tread and dramatically reduced without him, but still remained statistically significant (P <0.05). This fact indicates a significant slowing of the formation of this type of EO at this age, despite the use of the tread. Morphological studies show one of the mechanisms of this phenomenon. Since the total number of EO reconstructed in this case about 37% are composed of more than one of the macrophage and, frequently, 3–5 (fig. 2), the latter apparently insufficient to produce the required amounts of EO type. Vacuolization central macrophages retained similar to that observed in the experiment, only the influence of the sulfur-containing pollutants. More fully characterize the process of erythropoiesis by using the tread and its difference from a similar process in the conditions of exposure to sulfur pollutants only allow functional parameters are calculated based on the number of different types of EO.

The general tendency of the age dynamics of functional parameters using erythropoiesis tread, with rare exception, is the desire to return to the age norm.

Fig. 2. *Remodel EO rats adulthood with several central vacuolated macrophages (arrow). Neutral red*

Especially clear desire to return to normal with the help of the tread, despite the effect of the sulfur-containing gaseous pollutants, expressed in immature and mature stages of ontogeny of experimental animals. However, in old age is not so clear. These facts show a slight positive effect on the inhibited protective effects of intoxication intensity of involvement of dividing cells in the erythroid differentiation of macrophages and re participation in erythropoiesis. Despite the use of the tread, erythropoiesis continues to experience the negative impact of sulfur-containing gaseous pollutants, which is reflected in the decrease in the number of dividing cells of erythroid family, entered into differentiation. So, in response to the toxic effects of increasing the number of proliferating EO (EO1, EO2, EOrek) and drops EO, in which there is the maturation of red blood cells (EO3, EOinv). These processes are most intense in the immature age, their severity diminishes in adulthood and in old dies. The greatest environmental sensitivity erythrone system has in immature age, it is relatively stable in the mature and exhibits imbalance of self-regulation processes in the senile. This, in particular, is confirmed by the lack of effectiveness of protective effects.

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