PHAGOCYTIC ACTIVITY OF THE BLOOD LEUKOCYTES AND CELLS OF THE RETICULOENDOTHELIAL SYSTEM AND ANTIBODY PRODUCTION IN MICE KEPT AT A LOWERED ATMOSPHERIC PRESSURE

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Facts described in the literature show that a decrease in the oxygen concentration in the inspired air has a marked effect on the state of the protective mechanisms of the body, responsible for its resistance to exogenous and endogenous infection [7, 9, 10, 12-14]. Since the resistance of the body to infection depends, besides on other factors, primarily on the state of the cellular and humoral immunity, the attention of investigators has naturally been concentrated mainly on these two protective reactions. Whereas some authors [2] have observed a decrease in the phagocytic activity of the cells of the reticuloendothelial system (RES) in animals at a lowered atmospheric pressure, others [5, 6] have not observed this phenomenon. The reports in the literature concerning the effect of hypoxia on the intensity of antibody production likewise are extremely contradictory. According to results obtained by some investigators, antibody production rises in hypoxia [8, 16, 17], while others describe the opposite [2, 5]. This contradiction has not yet been explained, and to some extent it may depend on differences in the experimental conditions and on species differences between the animals used in the experiment.

The object of the present investigation was to study the effect of hypoxic hypoxia on the state of the cellular and humoral immunity in mice.

EXPERIMENTAL METHOD

Experiments were carried out on 200 male mice of the Balb/c line weighing about 20 g. In experiment 1, 70 mice were kept continuously for two weeks in a ventilated pressure chamber at an atmospheric pressure of 569 mm Hg (corresponding to an altitude of 2000 m). During experiment 2, 70 mice were kept 6 h daily for 10 days in a pressure chamber, the pressure inside which was lowered by 25 mm Hg every consecutive 2 days, the initial pressure in the chamber being 462 mm Hg (corresponding to an altitude of 4000 m) and the final pressure 330 mm Hg (corresponding to an altitude of 6500 m). Two hours after the end of the experiment 40 animals from each experimental group, and also 40 control mice (kept at a normal atmospheric pressure), received a subcutaneous injection of 400 million cells of an alcohol-killed typhoid vaccine into the right thigh. The mice were sacrificed 3 and 24 h and 3, 4, 5, 7, 10, and 14 days after immunization (5 animals at each period). The concentration of Vi antibodies in the blood serum of the mice was determined by the passive hemagglutination reaction [15] as modified by N. A. Kraskina and N. M. Gutorova [4].*

The phagocytic activity of the blood leukocytes and of the cells of the RES was studied in unimmunized mice of experimental groups 1 and 2 at intervals of 1, 3, and 5 days after the end of the experiment (10 mice at each time). The phagocytic power of the RES cells was determined from the rate at which the blood was cleared from intravenously injected particles of ink [11]. The index K (reflecting the total phagocytic power of the RES cells) and the index α (reflecting the intensity of phagocytosis of ink by the RES cells of the liver and spleen) were calculated. To assess the phagocytic activity of the blood leukocytes the phagocytic number and phagocytic index were calculated [1]. As a control for this part of the investigation, the indices of the phagocytic power of the RES cells and phagocytic activity of the blood leukocytes of 20 mice kept at a normal atmospheric pressure were used. The numerical results were analyzed by statistical methods.

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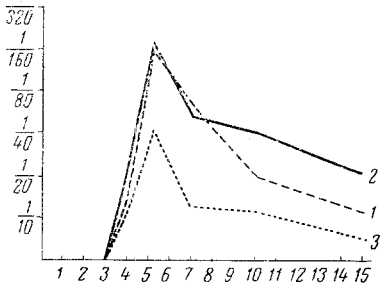
Changes in Phagocytic Activity of RES Cells and Blood Leukocytes in Mice kept at a Lowered Atmospheric Pressure of 596 mm Hg (Expt. 1) and 462-330 mm Hg (Expt. 2)

Time of investigation of mice (in days)	Index α (in days) (M±m)	P	Phagocytic no. (M±m)	P	Phagocytic index (M±m)	P
			Experiment 1			
1	0,028±0,001	<0,05	59±5,0	<0,05	5,2±0,5	>0,05
3	0,018±0,001	>0,05	43±6,0	>0,05	4,5±0,3	>0,05
5	0,021±0,003	>0,05	43±7,0	>0,05	3,7±0,3	>0,05
			Experiment 2			
1	0,024±0,001	>0,05	73±2,4	<0,05	10,0±0,6	<0,05
3	0,026±0,003	>0,05	39±2,6	>0,05	2,6±0,3	<0,05
5	0,024±0,002	>0,05	49±4,0	>0,05	2,8±0,4	<0,05
			Control			
	0,024±0,001		42±3,0		4,5±0,6	

EXPERIMENTAL RESULTS

Twenty four hours after a two-week stay of the mice in the pressure chamber at an atmospheric pressure of 596 mm Hg (Expt. 1) the phagocytic power of the RES cells of the liver and spleen was slightly raised and the number of blood neutrophils showing phagocytic activity was increased, whereas the phagocytic index of the neutrophils were unchanged (see table). These changes continued for a short time, and three days after the end of the experiment the phagocytic power of the RES cells (index α) and the phagocytic number returned to normal. The increase in the phagocytic power of the RES cells was possibly associated with stimulation of the physiological system of the connective tissue (PSCT) arising under the influence of the moderate hypoxia.



Changes in titers of Vi antibodies in blood serum of mice kept at a lowered atmospheric pressure of 596 mm Hg (Expt. 1) and 462-330 mm Hg (Expt. 2) and immunized with typhoid vaccine. 1) Control; 2) Expt. 1; 3) Expt. 2. Along the axis of ordinates—titer of antibodies; along the axis of abscissas—days after immunization.

Similar stimulation of the elements of the PSCT was observed in rabbits raised to an altitude of 2000 m [6], and also in patients with oxygen insufficiency due to a circulatory disturbance of the first degree [3].

The intensity of production of Vi antibodies in mice immunized with typhoid vaccine and kept at a lowered atmospheric pressure was unchanged by comparison with the level in control animals (see figure).

Twenty-four hours after the end of Expt. 2, during which the mice were kept in a more rarefied atmosphere (462-330 mm Hg), the number of neutrophils showing phagocytic activity was clearly increased and the phagocytic index was elevated (see table). However, as in Expt. 1, these changes were of short duration, and by the 3rd day the number of neutrophils showing phagocytic activity had fallen to normal and the phagocytic index was actually below normal. These changes could be the results of stimulation of the PSCT, as mentioned above, or of the "stress" reaction arising during ascent and descent of the animals. The phagocytic power of the RES cells in the experimental mice remained within normal limits in contrast to that of the animals used in Expt. 1. Evidently the stimulating effect of moderate hypoxia on the elements of the PSCT was absent at the lower atmospheric pressure.

The results of determination of the Vi antibodies in the blood serum of the immunized mice showed that the general character of the curve reflecting the changes in antibody titers at different times after immunization remained the same as in the control animals; the level of the antibodies in the blood of the experimental animals, however, fell especially at the height of immunogenesis (see figure). The results obtained are in good agreement with the results of investigations by Soviet authors [2, 5] who reported a fall in the intensity of antibody formation at approximately the same degree of rarefaction of the atmosphere, but they do not agree with reports by Western investigators [8, 16, 17], who found the opposite.

When summarizing the results described above it must, however, be remembered that the 2 week stay of the mice at a lowered atmospheric pressure of 596 mm Hg (corresponding to an altitude of 2000 m) had no significant effect on the state of the cellular and humoral immunity. After repeated ascents of the mice to altitudes of 4000-6500 m (an atmospheric pressure of 462-330 mm Hg), antibody production fell slightly, but definitely, and this may be connected with disturbance of the synthesis of immune proteins in the cells producing antibodies or with a decrease in the number of these cells. In these circumstances the phagocytic activity of the RES cells was undisturbed.

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