The decrease in the intensity of fluorescence of platelets of groups A and B in these experiments was evidently the result of their degranulation under the influence of the staphylococcal toxic substance.

Degranulation of platelets, i.e., enhancement of their secretory function, leads to the release of biologically active substances (serotonin, ADP, calcium ions, platelet factor 3), contained in the 5-HT-organelles, into the blood stream, activating the blood clotting system, potentiating aggregating properties and, as a result, giving rise to thrombohemorrhagic manifestations and microcirculatory disturbances.

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PREVENTION OF STRESS-INDUCED DYSLIPIDEMIA BY ADAPTATION OF ANIMALS TO PERIODIC HYPOXIA

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UDC 612.172.4-06:613.863

KEY WORDS: dyslipidemia; stress; adaptation.

Negative correlation exists [1, 12] between the blood level of high-density lipoproteins (HDL) and the degree of atherosclerosis of the coronary vessels in man, whereas correlation between low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL), on the contrary, is positive [2, 4]. These facts, confirmed in extensive epidemiologic [2] and experimental [4] investigations, lay at the basis of the view that HDL have an anti-athermogenic role, whereas LDL have an atherogenic role, and they have been used to determine the so-called "cholesterol coefficient"(ChC) of atherogenicity, or ratio between the concentration of cholesterol (Ch) in lipoproteins of different density

$$\frac{(Ch_{ldl} + Ch_{vldl})}{Ch_{hdl}}$$

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(Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 12, pp. 681-683, December, 1986. Original article submitted December 17, 1985.

0007-4888/86/0012-1666$12.50

for use in determining the probability of development of coronary atherosclerosis [10]. This indicated the value of a study of the effect of environmental atherogenic and antiatherogenic factors on the ratio between low- and high-density lipoproteins.

The aim of this investigation was to assess the dyslipidemia arising under the influence of stress [8] and to study the possibility of preventing dyslipidemia by adaptation to periodic high-altitude hypoxia, which in many cases has been shown to prevent the harmful action of stress on the circulatory system [3].

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 160-180 g. In the experiments of series I the effect of emotional-painful stress (EPS) was studied on the serum lipoprotein concentration. The animals were divided into three groups: 1) control, 2) animals used in the experiments 2 h after exposure to stress, 3) animals used in the experiments 48 h after exposure to stress.

In the experiments of series II the effect of preliminary adaptation to periodic hypoxia in a pressure chamber on the dyslipidemia which usually arose 24 h after EPS was studied. The animals of this series were divided into four groups: 1) control, 2) animals adapted to hypoxia, 3) animals used in the experiments 24 h after exposure to stress, 4) animals adapted to hypoxia and used in the experiments 24 h after exposure to stress. EPS was produced in the form of an anxiety neurosis, by the usual method [7] in the course of 6 h. Adaptation to high-altitude hypoxia was carried out in a specially constructed hypobaric pressure chamber, simulating gradual ascent to an altitude of 5000 m above sea level. The animals were adapted to low "altitude" for one week, and then kept at an "altitude" of 5000 m for 6 h daily. During the remainder of the 24-h period the animals were kept under standard animal house conditions. The adaptation cycle included 40 sessions of hypoxia and reoxygenation [3].

All the animals were decapitated, blood serum was obtained, and concentrations of total Ch, Ch_{hdl}, and of triacylglycerides were determined by the method in [5], as used and monitored by the Laboratory for Standardization of Lipid Investigations, Institute of Preventive Cardiology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR. On the basis of the results, the ChC of atherogenicity was calculated for each group of animals.

EXPERIMENTAL RESULTS

Changes in the ratio of Ch in lipoproteins of different densities and in ChC of atherogenicity after exposure of the animals to stress, and also the effect of preliminary adaptation to high-altitude hypoxia can be evaluated on the basis of the data in Table 1. At least 3 tentative conclusions can be drawn from these data.

The first is that EPS had no significant effect on the total serum Ch level of the rats, yet at the same time, it induced regular changes in the Ch distribution in the different lipoprotein fractions. In fact, 24 h after the end of exposure to stress the Ch_{hdl} concentration was reduced by more than half, whereas Ch_{ldl} concentration, on the other hand, was more than trebled. Other changes were irregular. As a result ChC of atherogenicity increased fourfold.

EPS by itself thus leads to the development of dyslipidemia which, in the modern view, is atherogenic. In principle this result is in agreement with the results of previous experiments showing the development of atherogenic changes in animals under the influence of stress [6], and also with epidemiologic data indicating that atherogenic changes arise in the blood plasma of persons receiving a constant diet under the influence of stress situations [9, 13].

The second conclusion is that gradual adaptation to periodic hypoxia itself can increase the concentration of Ch_{hdl} by 20% ($P < 0.01$) and, at the same time, can depress the concentration of Ch_{ldl} and Ch_{vldl} very substantially (by 42-44%).

As a result the ChC of atherogenicity in the animals of this group was reduced by more than half compared with the control.

Adaptation to periodic high-altitude hypoxia thus causes changes in the Ch distribution in lipoprotein fractions, which can be assessed as antiatherogenic.

This fact, not previously noted in the literature, is also in agreement with the results of passed epidemiologic investigations which showed that ischemic heart disease is rare and perfused a relatively mild course in persons adapted to life at medium altitudes in the mountains [11].

TABLE 1. Ch Content of Lipoproteins of Different Densities (in mg/dl) after Stress in Rats Unadapted and Adapted to Hypoxia

Experimental conditions	Total serum Ch	Ch_{hdl}	Triacylglycerides	Ch_{vldl}	Ch_{ldl}	ChC of atherogenicity
1. Control (n = 20)	69,49±3,62	52,64±2,86	52,84±4,18	10,6±0,84	8,54±1,36	0,4±0,04
2. 24 h after EPS (n = 20)	58,59±4,46	22,74±1,73	40,80±3,24	8,11±0,66	27,3±3,9	1,6±0,26
P_{1-2}	<0,05	<0,001	<0,05	<0,05	<0,001	<0,001
3. Adaptation to hypoxia (n= 20)	73,6±2,89	63,62±2,8	31,17±3,60	6,23±0,72	4,8±1,6	0,15±0,03
P_{1-3}		<0,01	0,001	<0,001	<0,01	<0,001
4. 24 h after EPS, in rats adapted to hypoxia (n = 20)	63,78±1,7	45,86±2,8	22,93±2,80	4,59±0,56	10,06±1,82	0,35±0,06
P_{3-4}		<0,001	<0,05	<0,05	<0,05	<0,05

Finally, the third conclusion is that preliminary adaptation to high-altitude hypoxia, while not completely preventing the decrease in the Ch_{hdl} concentration and the increase in the Ch_{ldl} concentration usually observed 24 h after exposure to stress, does significantly limit these changes. As a result the increase in ChC of atherogenicity was less marked in the rats of this group.

It will be evident that gradual and sufficiently "gentle" adaptation to periodic hypoxia has an antiatherogenic action.

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