secretion by the posterior lobe of the pituitary. Renal function is thus partially corrected, and the degree of the damaging effect of excess of aldosterone and vasopressin on the myocardium is probably reduced. Elevation of the neuropeptide concentration in the blood and cerebrospinal fluid in various types of stress is probably aimed in this same direction [5]. The inhibitory effect of enkephalins on secretion of these hormones is specific and is mediated through opiate receptors, since blocking of these receptors by naloxone abolishes their effect.

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CHANGES IN HOMEOSTATIC BALANCE OF PROSTACYCLINE-THROMBOXANE GENERATING SYSTEMS IN ZOOSOCIAL STRESS

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Blood vessel walls have the property of forming a powerful antiaggregating substance, namely prostacycline (PGI_2), which has a vasodilator action [7, 8], from arachidonic acid and its unstable metabolites, prostaglandins (PG) H_2 and G_2. The antiaggregating activity of the wall of the abdominal aorta can be judged from the degree of inhibition of ADP-induced platelet aggregation on incubation of healthy rat plasma with pieces (9 mg) of the aorta of experimental animals [5, 9]. Incubation of platelets with an aggregating agent, especially thrombin, leads to a considerable increase in the malonic dialdehyde (MDA) level, and the thromboxane concentration can be judged by the MDA level [5].

The functional state of the prostacycline-thromboxane system in stress, especially in its zoosocial version, has been inadequately studied. To shed light on this problem the writers studied the antiaggregating activity of the aortic wall (AAAW) and the thromboxane concentration in zoosocial stress (ZS), which is classed as a negative-emotional type of the general adaptation syndrome.

EXPERIMENTAL METHOD

Experiments were carried out on rats weighing 250-300 g. Chronic ZS was stimulated by prolonged social isolation. The rats were kept in single iron cages for 16 weeks, which induced negative emotion, leading to stress [3]. Under pentobarbital anesthesia (1 ml of 1% solution/200 g body weight) the abdominal aorta of the animals was excised, rinsed in 50 mM Tris-HCl buffer, pH 7.5, and the prostacycline activity of the aortic wall was determined by the method described previously [9]. To obtain platelet-rich plasma, blood was taken from the abdominal aorta of healthy animals, stabilized with 3.14% sodium citrate solution (9:1), and subjected to differential centrifugation in order to obtain platelet-deprived and platelet-enriched plasma. Platelet aggregation was induced with the disodium salt of ADP in a final

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TABLE 1. MDA Concentration (in relative units) in Healthy and Stressed Rats during Thrombin-Induced Platelet Aggregation (M ± m)

Aggregation time, min	Control	ZS
0	217±6	222±10
1/2	217±7	379±23**
1,0	236±5	503±32*
3,0	282±3	602±40*
5,0	427±2	769±49*

Legend. *P < 0.001, **P < 0.01 compared with control.

TABLE 2. AAAW during ZS (M ± m)

Experimental conditions	Index of spontaneous aggregation	AAAW	ADP-induced aggregation, after 1 min	Maximal aggregation	Degree of disaggregation
		%			
Control	0,92±0,1	73±7	46,8±5	55,8±3	32,9±7
ZS					
2 months	1,13±0,1	32±4**	44,4±2	49,5±4	39,6±8*
4 months	1,03±0,1	21±3	20,9±5	38,4±5	66,5±15

Legend. *P < 0.05, **P < 0.01 compared with control.

concentration of 5×10^{-5} M. The thromboxane concentration was judged from the change in MDA concentration, using thrombin for aggregation in a final concentration of 2.5 units/ml [5]. Spontaneous intravascular platelet aggregation was determined by the method in [10].

EXPERIMENTAL RESULTS

Platelets from rats kept entirely at a low altitude in the plains normally contain (aggregation for 0-5 min) an average MDA concentration (131-309 relative units) [5]. In rats kept in the foothills (Table 1) the MDA level was rather higher, namely 217-427 relative units. The MDA concentration rose during ZS (Table 1). Chronic ZS thus leads to increased biosynthesis of thromboxane A_2 in the platelets.

As regards the state of prostacycline activity during ZS, 2 months after its development AAAW was 41% below normal, and 2 months later it was 52% below normal (Table 2). The tendency of the platelets to undergo spontaneous aggregation showed some increase, but compensatory disaggregation under these circumstances was present on a considerable scale ($P < 0.001$).

Consequently, during ZS the homeostatic balance between the prostacycline-generating and thromboxane-generating systems was disturbed. Synthesis of the prostacycline-like substance on which AAAW depends was depressed, whereas that of thromboxane, on the other hand, was increased. To determine the reactivity of the level of prostacycline activity in the vessel wall during ZS, various tests were carried out: Rats with ZS were exposed to adaptation at a high altitude (1600 m, on the shore of Lake Issyk-Kul') in the mountains, which has an antistress effect. The beginning of adaptation was characterized by a gradual increase in spontaneous aggregation and a tendency for the prostacycline activity of the aortic wall of rats with ZS to decrease compared with healthy animals (Table 3). However, the degree of ADP-induced platelet aggregation was lower in these rats than in intact animals. On the 15th day of adaptation spontaneous aggregation in rats with ZS was indistinguishable from the control, although the level of prostacycline activity of the vessel wall was lower than in adapted healthy rats ($P < 0.01$). This could account for the low value of disaggregation ($P < 0.05$) observed during this period. On the 30th day spontaneous platelet aggregation both in healthy rats and in rats with ZS diminished as a result of adaptation ($P < 0.001$). However, the difference between the indices of spontaneous aggregation in stress and healthy rats also remained significant ($P < 0.001$). Differences of this kind between the two groups of animals also were observed with respect to AAAW ($P < 0.01$). However, because of the increase in AAAW during adaptation in rats with ZS, the degree of disaggregation was the same as in healthy rats.

During adaptation (30 days) of stressed rats, together with healthy rats, to a high mountain climate a greater decrease in AAAW and a greater increase in the index of spontaneous platelet aggregation were observed in the former. The reason evidently must be differences (before adaptation) in the functional state of the prostacycline-generating and thromboxane-generating systems of stressed and normal rats. Chronic ZS leads to a decrease in the prostacycline concentration in the vessel wall and to an increase in the MDA concentration in the platelets, with a simultaneous increase in the index of spontaneous intravascular platelet aggregation. This state indicates prethrombosis and spasm of the arterioles [4], for the hyperaggregating and vasopressor action of thromboxane is stronger than the hypoaggregating and vasodepressor action of prostacycline. Mountain adaptation, starting with activation [1, 2, 6] of the sympathicoadrenal and hypothalamo-hypophyseo-adrenocortical systems, in the early

TABLE 3. Dynamics of Changes in ADP-Induced Aggregation, Disaggregation, Spontaneous Aggregation, and Changes in Prostacycline Activity of Aortic Wall in Rats Exposed to High Mountain Conditions (M ± m)

Experimental conditions	Spontaneous aggregations, relative units	Aggregation after 1 min, %	Maximal aggregation, %	Degree of disaggregation, %	AAAW, %
Second day of adaptation:					
control	1,1±0,01	53,5	57,3±3	35,2±9	46±9
ZS	1,3±0,07*	36±2**	40,4±3**	22,1±9	39,7±3
Fifteenth day of adaptation					
control	1,2±0,09	44,9±6	52,4±4	51,1±10	61,8±7
ZS	1,34±0,01	47,2±4	56,8±5	27±4*	34,8±14**
Thirtieth day of adaptation					
control	0,66±0,04	40,7±2	50,5±4	39,6±5	58,3±6
ZS	0,91±0,09***	38,1±5	45,5±4	39,7±6	42,1±2***

Legend. *P < 0.05, **P < 0.01, ***P < 0.001 compared with control.

stages causes an increase in aggregating activity of the platelets, and leads (as a result of the action of endogenous adrenalin and corticosteroids) to a decrease in prostacycline synthesis in the aortic wall, even in normal rats. Against this background, stress (catecholamine model) inhibits prostacycline synthesis by the vessel walls even more. The antistressor and antiaggregating action of mountain adaptation [2] are exhibited at later periods (30 days) in both normal and stressed rats, although the increase in prostacycline activity observed in the vessel walls of stressed rats is less than in normal rats. This is due to the initial (before adaptation to mountain conditions) stress-induced disturbance of the balance between prostacycline and thromboxane.

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