Adaptation to Physical Load Increases the Activity of Prostaglandins E and I_2 and Reduces Stress Reaction

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Adaptation to physical load protects against stress and other damage. It is suggested that this protection is associated with activation of prostaglandins E (PGE) and I_2 (PGI_2). Plasma contents of PGE_2, PGI_2, and thromboxane A_2 (TxA_2) and the severity of stress reaction are measured in male Wistar rats adapted to swimming. Training increases the concentrations of these prostaglandins and the prostaglandin/TxA_2 ratio, reduces almost 2-fold the severity of stress reaction as assessed by the plasma corticosterone concentration and corticosterone/insulin ratio. After stress, the PGI_2 and PGI_2/TxA_2 in adapted rats were, respectively, 33 and 31% higher than in unadapted. These findings suggest that prostaglandins are involved in the reduction of stress reaction.

Key Words: *adaptation to physical load; stress; prostaglandins; corticosterone; insulin*

It has been generally accepted that the activation of stress-limiting systems is an important component of the protective effects of adaptation to physical load and environmental factors. Prostaglandins (PG) E and I_2 play a substantial role in the protection against stress. They limit the activation of the adrenergic system via which the stress reaction is realized, thus reducing the damage caused by catecholamines [9, 15], elicit direct cytoprotective effect [7,8,13], and inhibit vasoconstriction and thrombosis of coronary arteries [11,12]. It was demonstrated that the PG system is activated upon adaptation to high-altitude hypoxia [4] and stress [5]. It can be expected that adaptation to physical loads also stimulates the PG system. As far as we are aware, no investigation has been carried out in this field. Therefore, we examined the effect of physical load on plasma contents of PGE_2, prostacyclin (PGI_2) and thromboxane (TxA_2) and the severity of stress reaction as assessed by blood levels of corticosterone and insulin in rats.

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MATERIALS AND METHODS

Experiments were performed on male Wistar rats weighing 300±20 g. The animals were divided into four groups: intact rats (control, group 1), rats exposed to stress (stress, group 2), rats adapted to physical load (adaptation, group 3), and rats exposed to acute stress after adaptation (adaptation+stress, group 4). Adaptation to physical load was attained by forcing the rats to swim in warm (32°C) water for 45 days, 5 days per week, according to the following scheme: 15 min of swimming on day 1, the swimming period was then prolonged to 60 min by adding 5 min every day. Acute stress was created by immobilization in the supine position for 1 h. The rats were decapitated immediately after stress (group 2), 24 h after the last swimming (group 3), and immediately after exposure to stress 24 h after the last swimming (group 4). Blood was collected on ice using heparin (0.2 ml) as anticoagulant, divided into two portions which were transferred to vials containing EDTA and indomethacin for determination of PG and TxA_2 and in a vial with EDTA for de-

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TABLE 1. Plasma Contents of PG, Corticosterone, and Insulin During Stress and Adaptation to Physical Load

Parameter	Control	Stress	Adaptation	Adaptation+stress
Corticosterone, μg/dl	45.5±3.3 (7)	119.0±1.0 (9)***	37.8±4.1 (8)	75.5±1.7 (7)**
Insulin, μU/ml	20.7±2.7 (7)	19.5±2.2 (9)	16.5±1.7 (9)	17.5±1.3 (8)
C/I	1.0 (7)	2.8 (9)	1.0 (8)	1.9 (7)
PGE_2, ng/liter	337.5±41.2 (8)	219.5±32.0 (6)*	520.0±54.4 (8)*	312.5±32.5 (6)
PGI_2, ng/liter	138.2±4.0 (10)	237.5±11.2 (6)**	229.4±22.0 (8)***	314.8±17.5 (6)***
TxA_2, ng/liter	273.0±20.0 (9)	403.3±6.6 (6)***	331.8±22.3 (8)	381.7±4.6 (6)*
PGI_2/TxA_2	0.52±0.03 (9)	0.57±0.03 (6)	0.70±0.08 (8)*	0.75±0.06 (6)*

Note. *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with the control; *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with values obtained during stress. The number of animals is given in parentheses.

termination of corticosterone and insulin, and then centrifuged at 4°C for 15 min at 3000 rpm. The supernatant was frozen at -24°C. The contents of PGE_2, PGI_2 (by the stable metabolite 6-keto-$PGF_{1\alpha}$) and TxA_2 (by the stable metabolite TxB_2) were determined by radioimmune assay using standard DRG Instruments kits. The insulin content was determined by the same method with RIO-INS-PG-^{125}I kits. Radioactivity was measured in a Mark-3 counter or Tracor-Analytic γ-counter. The corticosterone content was determined fluorimetrically [6]. Stress reaction after immobilization and swimming was assessed according to the ratio between the percent of plasma contents of corticosterone and insulin (C/I). The contents of corticosterone and insulin in control rats were accepted as 100%. An increase in C/I reflects enhanced catabolism and reduced energy production [2,14]. Results were analyzed by Student's *t* test.

RESULTS

As Table 1 shows, plasma contents of PGE_2 and PGI_2 were 54 and 65% higher, respectively, in adapted rats than in the control. Since there were no statistically significant changes in TxA_2 content, the PGI_2/TxA_2 ratio increased by 34%. This indicates that in adapted animals the system of protective PG is activated, while the risk of ischemia- or stress-induced constriction and thrombosis of coronary arteries is substantially reduced.

In unadapted rats, stress induced a 2.6-fold increase in plasma corticosterone content: 119±1 *vs.* 45.5±3.3 μg/ml in the control, which is typical of stress reaction (Table 1). Since the insulin content remained practically unchanged, the C/I ratio increased 2.8-fold compared with the control. This indicated that catabolism predominates over anabolism, which again is typical of stress reaction. In unadapted rats stress reaction was accompanied by a 36% decrease in plasma PGE_2: 219.5±32 *vs.* 337.5±41 ng/liter in the control and an almost equal increase in PGI_2 and TxA_2 contents. As a result, the PGI_2/TxA_2 ratio was the same as in the control. Thus, the relative decrease in the amount of protective PG occurring in unadapted rats may potentiate the damaging effect of excessive catecholamines during the stress reaction [4,5].

In adapted rats, judging by the C/I ratio, plasma levels of corticosterone and insulin did not differ significantly from those in the control. Consequently, stress reaction, which generally develops after first swimming sessions and manifests itself as an increased blood level of corticosterone, is suppressed by adaptation. After acute stress, the blood corticosterone content doubled in adapted rats and increased 2.6-fold in unadapted rats in comparison with the control (Table 1). This was reflected by the C/I ratio which increased 1.9- and 2.8-fold in adapted and unadapted rats, respectively. It is noteworthy that in adapted rats the PGI_2/TxA_2 ratio was 31% higher than in unadapted rats: 0.75±0.06 *vs.* 0.57±0.03 due to a higher blood content of PG. This indicates a lower risk of stress-induced constriction and thrombosis of coronary arteries in adapted rats. Thus, adaptation not only activates the system of protective PG but also increases PG level during stress, i.e., increases the efficiency of the stress-limiting system.

Our results show that adaptation to physical load activates the system of protective PG and suppresses stress reaction. It should be remembered that during stress reaction induced by immobilization, ischemia, hypoxia, and other factors the synthesis and secretion of protective PG in the heart, blood vessels, and other organs is regulated by the "release" of nitric oxide [10], catecholamines, vasopressin, and other hormones [3]. Presumably, prostaglandins limit the activity of the adrenergic system and reduce the damaging effects of stress reaction due to in-

hibition of norepinephrine release from adrenergic terminals [9,15], direct cytoprotective effect [7,8,13], and prevention of vasoconstriction and thrombosis [11,12]. Our results suggest that the activation of protective PG may represent a mechanism responsible for the protective effect of adaptation to physical load during stress, ischemia, and other types of damage [1].

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Lipid Peroxidation After Acute Intoxication of Cats with Anthio and the Effect of Ionol on Their Survival

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Acute intoxication with the organophosphorus pesticide Anthio considerably increases the intensity of lipid peroxidation in Nembutal-anesthetized cats. Pretreatment with the synthetic antioxidant ionol prolongs the survival of the cats. Ionol has no appreciable effect on respiratory and hemodynamic parameters. Lipid peroxidation may contribute to the disturbances caused by Anthio.

Key Words: *organophosphorus pesticide; acute poisoning; lipid peroxidation; ionol; cats*

Organophosphorus compounds induce severe changes in tissue metabolism. Previously, we have shown that acute intoxication with the organophosphorus pesticide Anthio provokes pronounced metabolic acidosis, although pulmonary ventilation and blood Po_2 remained maintained within normal range [5]. This may be indicative of impaired tissue respiration. It was reported that the intensity of lipid peroxidation (LPO) is increased in people living in the areas where pesticides are widely used [1].

Our objectives were to determine LPO levels and examine the effects of the synthetic antioxidant ionol on respiratory and cardiovascular functions and on the survival of cats after acute intoxication with Anthio.

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