increased rapidly. To begin with they formed a chain, but later they were arranged in rows (Fig. 2b). This led to the fact that many pulmonary capillaries were excluded from the microcirculation, and although the parameters of the blood flow were restored, severe hypoxemia developed. At this time, proximally to the embolus, blood plasma passed through into the lumen of the alveoli. Death of the animal took place from established hypoxemia and pulmonary edema. Thus fat and mechanical microembolism differ not only in the character, intensity, and rate of development of pulmonary edema, but also in their final result. Although in mechanical microembolism changes in the hemodynamic parameters are much more severe in character than in fat embolism, in the first case pulmonary edema develops less intensively.

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EFFECT OF ADAPTATION TO ANOXIA ON ANTIOXIDATIVE ENZYME ACTIVITY IN THE LIVER OF STRESSED ANIMALS

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KEY WORDS: adaptation; anoxia; antioxidative enzymes; stress.

Dyslipoproteinemia of atherogenic nature develops in the blood serum under the influence of emotional—painful stress (EPS), whereas preliminary adaptation of animals to periodic exposure to pressure chamber anoxia prevents disturbances of lipoprotein metabolism [7]. Despite the fact that activation of lipid peroxidation (LPO) in the liver does not change the rate of lipoprotein secretion by hepatocytes [9], an important role for intensification of LPO in the mechanism of stress-induced liver damage seems likely, for damage of this kind can be prevented by gradual adaptation to moderate degrees of anoxia [3, 4].

To test this hypothesis the effect of EPS and of preliminary adaptation to anoxia on the malonic dialdehyde (MDA) concentration and activity of antioxidative enzymes, utilizing active forms of oxygen (superoxide dismutase) and of lipoperoxidases (glutathione peroxidase, glutathione-S-transferase) was studied in the liver of animals.

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TABLE 1. MDA Concentration and Activity of Antioxidative Enzymes in Liver of Rats Not Adapted to Anoxia (M ± m)

Parameter	Animals not adapted to anoxia			Animals adapted to anoxia		
	Control	2 h after EPS	24 h after EPS	Control	2 h after EPS	24 h after EPS
MDA, nmoles/mg protein	1,9±0,14	3,7±0,25*	2,2±0,15	1,5±0,06	1,7±0,08	1,5±0,10
SOD, units of activity/mg protein	64,6±7,3	30,8±2,0	50,0±3,9	106,6±4,8*	78,2±4,0*	75,0±8,5
Glutathione peroxidase, units of activity/mg protein	0,44±0,10	0,30±0,02	0,44±0,10	0,12±0,01	0,11±0,01	0,11±0,01
Glutathione transferase, units of activity/mg protein	0,30±0,03	0,29±0,02	0,25±0,02	0,28±0,01	0,24±0,03	0,22±0,02

Legend. Results averaged for 10 animals. *$P < 0.001$ compared with control.

EXPERIMENTAL METHOD

Male Wistar rats weighing 240 ± 10 g were used. EPS was induced in the animals in the form of an anxiety neurosis by Desiderato's method [8] and the rats were killed 2 or 24 h after the end of exposure. Adaptation of the rats to periodic anoxia was brought about by taking them up to an "altitude" of 5000 m in a pressure chamber 6 times a week (for 6 h each time) over a period of 1.5 months. On the day after the last section of adaptation to anoxia the animals were subjected to EPS and were killed 2 and 24 h after the end of the procedure. Intact animals or animals adapted to the action of anoxia (without induction of EPS) served as the control. The liver of the rats was homogenized in 50 mM phosphate buffer, pH 7.4 and centrifuged at 800g for 19 min; activity of antioxidative enzymes in the supernatant was then determined.

Superoxide dismutase (SOD) activity in the supernatant was determined as inhibition of reaction of nitro-BT in a xanthine–xanthine oxidase system [2], glutathione peroxidase activity was determined by measuring oxidation of NADPH in a coupled glutathione reductase system, using tert-butyl hydroperoxide as the substrate [2], and glutathione-S-transferase activity was determined by measuring the formation of conjugates of glutathione with 1-chloro-2,4-dinitrobenzene [9]. Activity of the enzymes was measured on a "Hitachi 220A" spectrophotometer and an "FP-901" chemical analyzer; the unit of SOD activity was taken to be the quantity of enzyme required to produce 50% inhibition of reduction of nitro-BT under the conditions of determination; the unit of glutathione peroxidase activity was taken to be the quantity of enzyme required to oxidize 1 μ mole of reduced glutathione; the unit of glutathione-S-transferase activity was the quantity of enzyme required to conjugate 1 μ mole of glutathione.

The MDA concentration in liver homogenates was determined by the reaction with 2-thiobarbituric acid [10] on an SF-26 spectrophotometer; the protein concentration in the samples was determined by the microbiuret method on the "FP-901" chemical analyzer, using test kits from "Medics" (Finland).

EXPERIMENTAL RESULTS

The results are evidence of a sharp increase in the MDA concentration in the liver of intact rats 2 h after EPS; characteristically the MDA concentration in the animals' liver reached its initial level as early as 24 h after EPS (Table 1). Although the increase in the concentration of MDA, a secondary product of LPO, does not contradict the conclusion that LPO processes in the tissues are intensified, it must be recalled that these data alone are insufficient to allow this conclusion to be drawn [1]. Previously, in analogous experiments, accumulation of primary LPO products (lipoperoxides) also was observed [5] along with accumulation of MDA.

Further evidence of the possible intensification of LPO in the animals' liver 2 h after EPS was given by a sharp fall (by 2.1 times; Table 1) in SOD activity. However, activity of enzymes utilizing lipoperoxides, namely glutathione peroxidase and glutathione-S-transferase, was virtually unchanged both 2 h and 24 h after EPS.

Long-term exposure to periodic measured degrees of anoxia did not lead to any change in the MDA concentration in the liver either of the control animals or of animals exposed to EPS.

This fact was matched by a considerable (by almost 65%) increase in SOD activity in the liver of animals adapted to anoxia, and a smaller decrease (by not more than 27%) in SOD activity after exposure to EPS. Adaptation to anoxia did not lead to any change in the level of glutathione-S-transferase activity; the level of activity of this enzyme, moreover, remained constant after EPS also. Nevertheless, glutathione peroxidase activity in rats adapted to anoxia was depressed (by 3.7 times), although it was unchanged after exposure to EPS.

The results of this investigation do not contradict ideas on the important role of LPO in the mechanism of liver damage associated with EPS and the possibility of protecting the liver by adaptation to anoxia.

Thus although the mechanism of prevention of the dyslipoproteinemia developing under the influence of EPS by adapting the animals to anoxia probably involves inhibition of LPO in the liver, the disturbance of lipid metabolism in the liver associated with EPS may be due to the action of other factors.

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EFFECT OF PROSTAGLANDIN E_2 ON DEVELOPMENT OF ADRENALIN-INDUCED MYOCARDIAL DYSTROPHY

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KEY WORDS: adrenalin-induced myocardial dystrophy; prostaglandin E_2; lipid peroxidation.

One of the most important steps in the pathogenesis of heart damage following injection of large doses of catecholamines (CA) [1, 5, 9] or their synthetic analogs [8], and also during emotional–painful stress, is over-activation of lipid peroxidation (LPO) [3]. Lipid hydroperoxides damage membranes of the sarcoplasmic reticulum and mitochondria, as a result of which the Ca^{++} concentration in the sarcoplasm of the cardiomyocytes increases; an excess of Ca^{++} gives rise to a combination of changes known as the calcium triad, which leads ultimately to irreversible contracture of the myofibrils and to the development of foci of necrosis [4]. There are indications that potentiation of adrenergic influences on various organs and increased noradrenalin secretion in them lead to activation of synthesis and secretion of prostaglandins (PG) of the E group, which may limit the action of CA by a feedback mechanism [11, 12].

The aim of this investigation was to study the effect of PGE_2 on LPO activity during the development of adrenalin-induced myocardial dystrophy.

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