Differences in the level and velocity of outflow of K^+ in Cat^{Fr} mice may perhaps be due to morphological differences: preservation of the layer of epitheliocytes not only in the surface layers of the lens, but also in its thickness, and the formation of lacunae.

The development of senile cataract in man [13] and of hereditary cataract in mice of the Nakano strain [12] is known to be accompanied by a disturbance of the distribution of K^+ and Na^+ ions. In particular, human lenses, as they become opaque, lose K^+ and Na^+ is drawn inside. As a result, a relative increase in the content of water, transported passively with Na^+, is observed [13]. Previously the writers reported [2] an increase in the weight of the lens in mammals with diabetic cataract, and during the development of an opacity of the lens in vitro. The development of cataract in Cat^{Fr} mice probably proceeds along a totally different path. As the results in Fig. 3 show, with age or (which amounts to one and the same thing) with an increase in weight of animals the weight of the lens is reduced, and this may reflect an increase in the K^+ concentration or a decrease in synthesis of crystallins.

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ROLE OF MONOAMINE OXIDASE IN THE INTENSIFICATION OF MITOCHONDRIAL LIPID PEROXIDATION IN EXPERIMENTAL MYOCARDIAL NECROSIS

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In recent years the participation of lipid peroxidation (LPO) reactions in the pathogenetic mechanism of ischemic and anoxic heart damage has been demonstrated [6]. Analysis of the results of experimental studies of myocardial damage has shown that an excess of catecholamines and of their incomplete oxidation products during stress is one way whereby LPO is intensified [5, 7].

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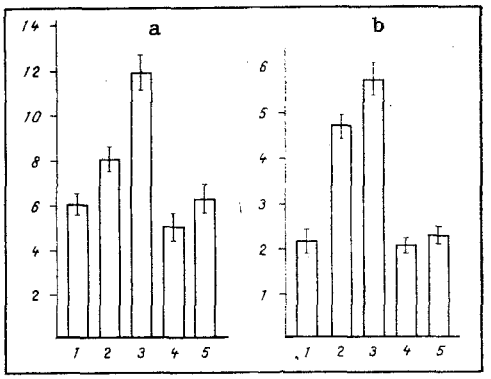

Fig. 1

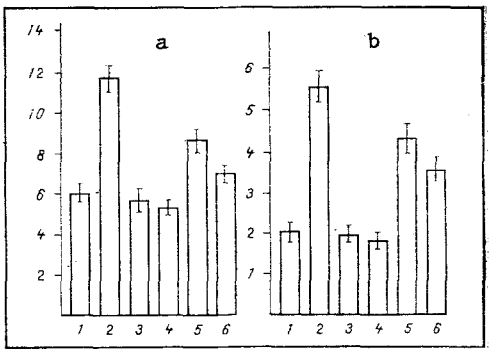

Fig. 2

Fig. 1. Changes in MDA concentration (a) and MAO activity (b) in myocardial mitochondria in experimental necrosis. 1) Control, 2-5) 2 and 24 h and 7 and 12 days respectively after injection of adrenalin. Here and in Fig. 2: vertical axis: a) MDA level (in nmoles/mg protein), b) MAO activity (in nmoles NH_3/min/mg protein). Average results of five experiments shown.

Fig. 2. Effect of antioxidants on changes in MDA concentration (a) and MAO activity (b) in myocardial mitochondria in experimental necrosis. 1) Control, 2) 24 h after injection of adrenalin, 3) 16 h after injection of ionol, 4) 16 h after injection of vitamin E, 5) 24 h after injection of adrenalin preceded by ionol, 6) 24 h after injection of adrenalin prededed by vitamin E.

The study of intensification of LPO in various biological membranes in anoxia has now yielded much factual evidence. On the basis of these results it is suggested that the increase in the intensity of LPO is due to an increase in the concentration of active forms of oxygen (O_2^-, $HO^\cdot$, H_2O_2), which react with unsaturated fatty-acid residues of membrane phospholipids [6]. An urgent problem in the study of the damaging action of LPO products during ischemia at the present time is thus to discover the mechanism of formation of active forms of oxygen. The solution of this problem is dependent primarily on the identification of the site of this process in the cell. Our previous experiments showed that a leading role in the triggering mechanism of peroxide-induced cell damage during anoxia both inside and outside the tissues is played by the outer mitochondrial membrane [4].

The functional characteristics and physicochemical properties of structural components of the outer mitochondrial membrane suggest that the enzyme monoamine oxidase (MAO), which is currently being intensively studied, plays a direct or indiect part in the intensification of LPO in the heart during anoxic damage. This suggestion is also based on the fact that oxidative deamination of the terminal amino group with the participation of MAO is accompanied by H_2O_2 formation [11].

With the above considerations in mind, it was decided to investigate the relations between changes in the intensity of LPO and MAO activity in mitochondria isolated from the myocardium in adrenalin-induced necrosis.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 200-300 g. Myocardial necrosis was induced by intramuscular injection of 0.1% adrenalin hydrochloride [2]. Mitochondria were isolated from the heart by the method in [1]. The intensity of LPO was judged from the concentration of the secondary LPO product — malonyl dialdehyde (MDA), determined by the reaction with 2-thiobarbituric acid [9]. Mitochondrial MAO activity was determined by the method in [3], in which tyramine was used as the substrate. The protein concentration was determined by Lowry's method [10]. In experiments with antioxidants, the animals were given a preliminary injection of vitamin E and ionol in doses of 120 and 80 mg/kg respectively.

EXPERIMENTAL RESULTS

The experimental results showed that 2 h after injection of adrenalin the MDA content in the myocardial mitochondria had a tendency to increase (Fig. 1a). During the 24 h after the injection the MDA concentration increased significantly and amounted to twice the control level. However, 1 week after the injection of adrenalin, judging by changes in MDA, the

intensity of LPO was restored almost to the control level, evidently in connection with the protective capacity of the animal.

Experiments showed that 2 h after injection of adrenalin into the animal MAO activity was significantly increased (Fig. 1b). In the course of 24 h, MAO activity continued to increase, but later it returned to the control level.

As was pointed out above, the mechanism of the increase in intensity of LPO in adrenalin-induced myocardial damage has not been fully elucidated. On theoretical grounds it can be suggested that one possible mechanism of the intensification of LPO during myocardial ischemia is a disturbance of metabolism of MAO, present in the structure of the outer mitochondrial membrane, in which it plays a more active role in anoxic cell damage [4]. Consequently, a series of experiments was carried out to study changes in MAO activity in experimental myocardial necrosis, induced by injection of adrenalin.

MAO belongs to the group of amine oxidases which catalyze oxidative deamination of the terminal amine group in the following manner [11]:

$$RCH_2NH_2 + O_2 \xrightarrow{MAO} RCH = NH + H_2O_2$$
$$RCH = NH + H_2O \longrightarrow RCH = O + NH_3$$

Administration of adrenalin to the animal evidently induces its intensive deamination, which is achieved through increased MAO activity, leading to an increase in the H_2O_2 concentration in the myocardium. Intensification of H_2O_2 formation, in turn, leads to generation of other active forms of oxygen: the superoxide anion-radical and hydroxyl radical [8, 12], which interacts with lipids to yield the primary molecular product of LPO, namely lipid hydroperoxides [6].

Among the various membrane protectors, preventing ischemic and anoxic heart damage, a special place is ascribed to antioxidants. With this in mind, it was decided to study the action of vitamin E and ionol on the intensity of LPO and on mitochondrial MAO activity in the myocardium in adrenalin-induced necrosis.

The investigations showed that preliminary injection of vitamin E and ionol before the injection of adrenalin significantly lowered the MDA level (Fig. 2a). In this case vitamin E was a more active antioxidant. Similar data were obtained when MAO activity was determined. Preliminary administration of antioxidants to the animals led to a fall in MAO activity (Fig. 2b).

Injection of vitamin E and ionol into control animals caused no significant changes in the MDA level of MAO activity.

It can be concluded from these data that intensification of mitochondrial LPO in the myocardium during adrenalin-induced cardiac necrosis is connected with an increase in MAO activity. Intensification of LPO and activation of MAO under these circumstances are under the regulatory influence of antioxidants.

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