By the use of asphyxia as an adequate load for LC it was thus possible to discover the different ways whereby catecholamines synthesized in the neurons of this nucleus exert their effect.

It can be postulated that LC participates in the organization of defensive responses of the body in two ways: by its specifically neural action on brain structures (directly and indirectly through the reticular formation of the brainstem) and humorally. The latter method is associated with changes in the metabolism of the neuron and glial cell.

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CHANGES IN THE ULTRASTRUCTURE OF THE RAT MYOCARDIUM FOLLOWING ADAPTATION FOR 12 MONTHS TO HIGH ALTITUDES

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The myocardium of the right and left ventricles of rats during adaptation for 12 months to high altitudes (3200 m above sea level) was studied. During the animals' long stay in the mountains hypertrophy mainly of the right and partly of the left ventricles developed. Hyperplasia and hypertrophy of individual organelles, especially mitochondria, were found in most cardiomyocytes of both ventricles. In animals adapted to high altitudes succinate dehydrogenase activity in the mitochondria was higher than in the control. The results are evidence of intensification of intracellular metabolism, reflecting compensatory and adaptive responses of the organs.

KEY WORDS: *high mountain altitude; hypertrophy of the myocardium, mitochondria; succinate dehydrogenase.*

During a prolonged stay in the mountains hypertrophy of the heart muscle develops in animals and man on account of pulmonary hypertension [6, 8]. An increase in the intensity of function of the intracellular structures is also found, which may amount to an increase in the number of mitochondria and other organelles [1, 2, 5]. During adaptation to high-altitude hypoxia the hypertrophy of the right ventricle caused by pulmonary hypertension leads to an increase in its mass by 40-80% within the course of only 7-10 days [4]. Hyperplasia of the ultrastructures arises in the cells with the need for stimulation of their working activities. Under these circumstances the dimensions of the cell and organ as a whole are increased [7]. Individual studies of changes in the ultrastructure of the myocardium of intact rats from the age aspect have been published [3, 11]. Recently investigations

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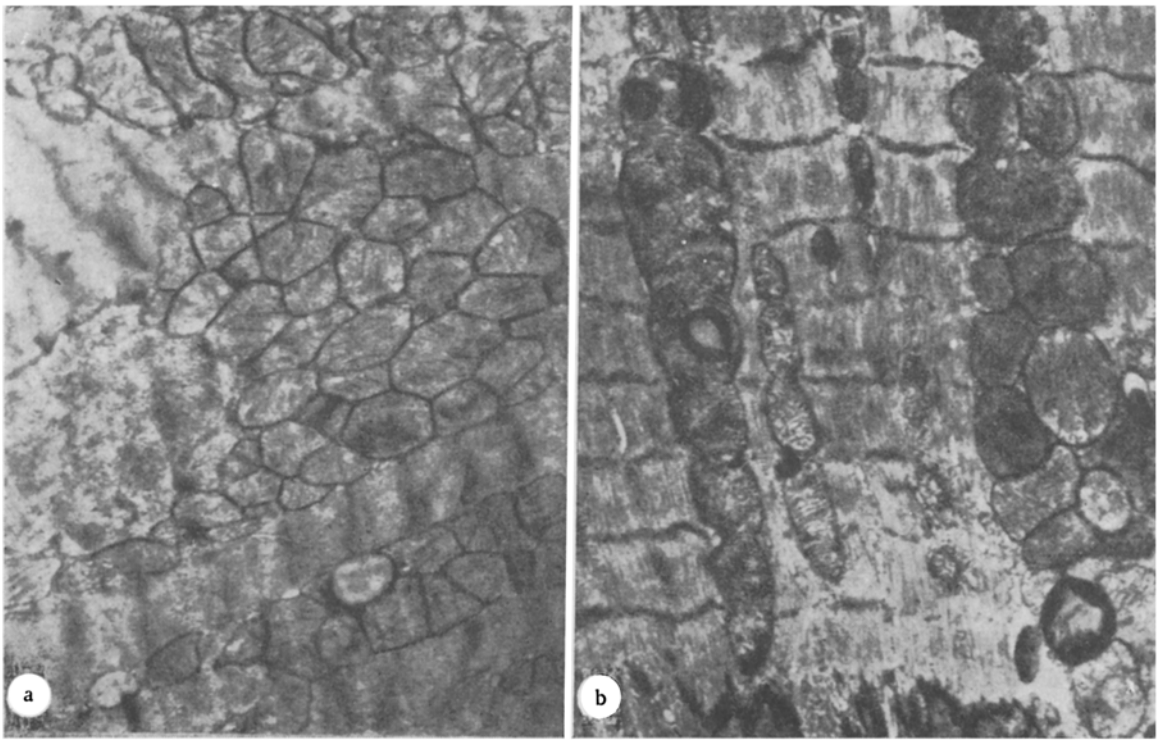

Fig. 1. Myocardium of rat after adaptation to high mountain conditions for 12 months. a) Right ventricle: marked hyperplasia of mitochondria in many areas of cardiomyocytes (11,000×); b) left ventricle: Besides hyperplasia, grossly hypertrophied mitochondria can also be seen, measuring 7 or more sarcomeres in length (11,000×).

into the effect of short- and long-term adaptation to high mountain conditions have been reported [1, 2, 9]. However, no data can be found on morphological and functional changes in the myocardium during longer adaptation (12 months) to high-mountain hypoxia. It was accordingly decided to carry out the investigation described below.

EXPERIMENTAL METHOD

Experiments were carried out on 20 noninbred male albino rats. At the age of 4-6 months they were transported to the Tuya-Ashu Pass (3200 m above sea level). The rats were decapitated 12 months later. Twenty male rats of the same age, killed by decapitation but in the city of Frunze (760 m above sea level), acted as the control. Morphometric, light-optical, electron-microscopic, and electron-cytochemical methods of investigation together with quantitative electron microscopy were used. As a first step each rat, its heart, and the right and left ventricles separately were weighed. Pieces of myocardium for light microscopy were fixed in a 10-12% solution of neutral formalin and embedded in paraffin wax. The sections were stained with hematoxylin–eosin. Semithin sections 1 μ thick, cut on the type III LKB ultramicrotome, were stained with hematoxylin–eosin and toluidine blue.

Material for electron microscopy was fixed for 2 h in 3-6% glutaraldehyde solution in phosphate buffer, pH 7.4. Postfixation was carried out in a refrigerator at 4°C for 2 h in a 1% solution of osmium tetroxide in veronal–acetate buffer, pH 7.4. The fragments were dehydrated in alcohols of increasing strength. The material was embedded in a mixture of Epon 812 and Araldite. Ultrathin sections were stained with lead citrate by Reynolds' method and examined in the JEM-100B electron microscope.* Quantitative analysis of the intracellular organelles (mitochondria) was carried out on negative film under a magnification of 5000-7000×. The product of the reaction for succinate dehydrogenase (SD) in the cristae of the mitochondria were detected electron histochemically by Kerpel-Fronius' method [10].

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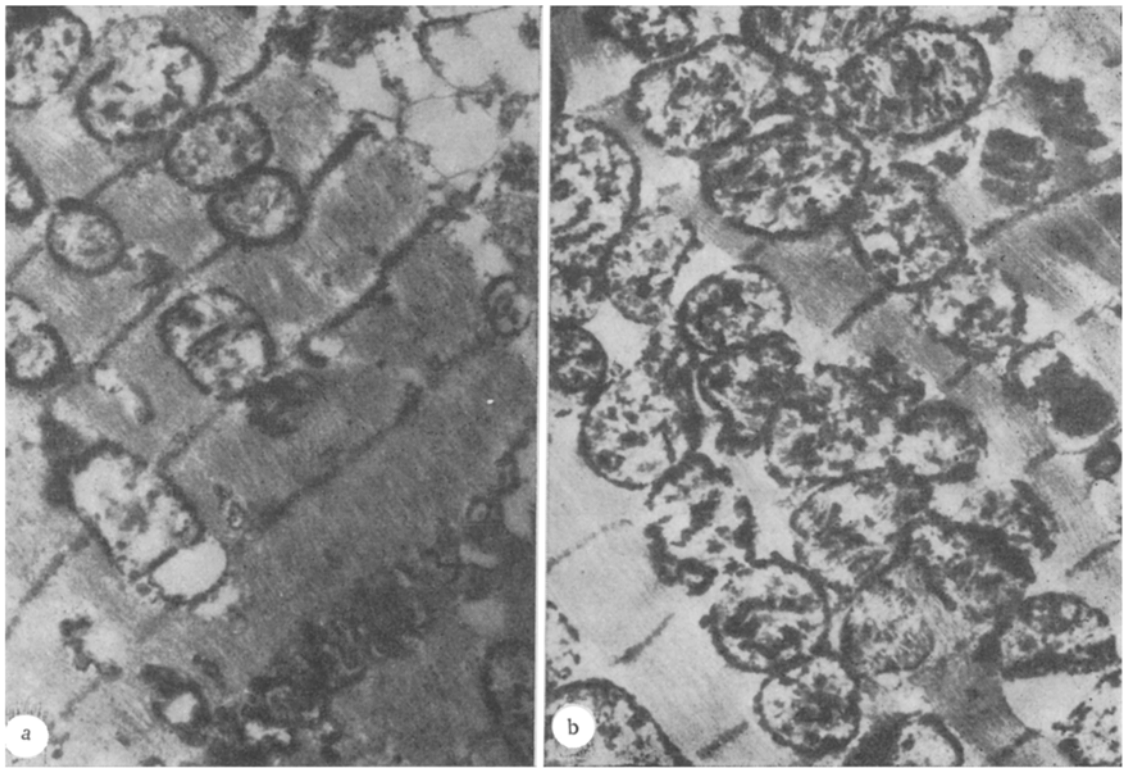

Fig. 2. SD activity in myocardium of control and experimental rats. a) Moderate activity of SD in right ventricle of control rats (15,000×); b) marked SD activity in right ventricle of experimental rats (14,000×).

EXPERIMENTAL RESULTS

The mean weight of the control rat was 302.3 ± 5.3 g and of the experimental rat 297.5 ± 5.9 g ($P > 0.2$), i.e., virtually the same. However, the weight of the heart was greater in the experimental animals: 1.335 ± 8.1 g compared with 1.016 ± 26.9 g in the controls ($P < 0.001$).

When weighed separately, the right ventricle of the control rats weighed 159.0 ± 3.86 mg and the left ventricle 314.7 ± 3.72 mg, whereas the right ventricle of the experimental rats weighed 205.1 ± 1.02 mg ($P < 0.001$) and the left ventricle 337.2 ± 1.20 mg ($P < 0.001$). This shows that, in animals staying for a long time in the mountains, hypertrophy of the heart develops as a result of hyperfunction of the organ. The right ventricle enlarges more than the left.

On electron-microscopic investigation many lipid granules and lysosomes were found among the mitochondria, although usually they are absent in the myocardium of young rats. Many glycogen granules were seen in the cytoplasm of the cardiomyocytes. The other intracellular organelles were otherwise indistinguishable from those of young rats.

On histological investigation of the myocardium of the experimental rats areas were seen where the cardiomyocytes had no cross striation, the nuclei showed polymorphism, and many of them had become large and hyperchromic. In addition, in some areas of the myocardium hemodynamic changes were observed, in the form of infiltration of leukocytes around the small vessels.

In most cardiomyocytes of both ventricles numerous mitochondria were seen. They were found not only in the perinuclear zone, beneath the sarcolemma, but they were also many between the myofibrils in the depth of the cell. There they were arranged along the myofibrils in 5 or 6 rows or more. In the right ventricle circular or oval mitochondria were found, some of them being larger, two or three sarcomeres in length. Their numerous cristae were parallel to each other and were densely packed. A characteristic feature was that the cristae had unequal electron density in the same and in different mitochondria (Fig. 1a). This evidently indicates unequal functional activity of the cristae in the same as well as in different mitochondria. In the left ventricle, besides hyperplasia, sharply hypertrophied mitochondria 7

or more sarcomeres in length were found in the cardiomyocytes. Their cristae were numerous and most of them crossed from one inner mitochondrial membrane without interruption to the opposite membrane. Lysosomes and lipid granules were found in the cytoplasm of the cardiomyocytes. These gradually became closer packed together at the edges to form a ring, they became electron dense, and some of them appeared to be directly in the matrix of the mitochondria (Fig. 1b).

Quantitative counting of the mitochondria showed considerable hyperplasia of the mitochondria of both ventricles, to more than twice or three times the normal value.

The results of electron-microscopic determination of SD demonstrated a difference in its content in the control and experimental rats. Products of the reaction for SD were located in the membranes of the mitochondria and in their cristae. Many mitochondria in the control rats gave no reaction or only a weak reaction for SD (Fig. 2a). In animals adapted to high altitude the reaction for SD in the mitochondria was stronger (Fig. 2b).

During a prolonged stay in the mountains hypertrophy of the right and, to some extent, of the left ventricle developed in animals in association with hyperplasia and hypertrophy of the intracellular structures. The results are evidence of stimulation of intracellular metabolism, reflecting compensatory and adaptive reaction of the organs to high-altitude hypoxia.

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