# EFFECT OF PRELIMINARY ADAPTATION TO HIGH-ALTITUDE HYPOXIA ON THE CONTRACTILE FUNCTION OF THE HEART DURING ACUTE OVERLOADING

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Preliminary adaptation to high-altitude hypoxia increases the resistance of the heart to acute overloading produced by an experimental heart defect; in animals adapted to high-altitude hypoxia, in contrast to unadapted animals, no decrease takes place in the indices of myocardial contractile function.

Previous investigations have shown that during adaptation of animals to high-altitude hypoxia, the synthesis of nucleic acids and proteins in the myocardium is activated, leading to hypertrophy of the ventricles [2]. It has also been shown that adaptation of animals to high-altitude hypoxia increases the resistance of the heart to acute overloading [1-4].

The object of this investigation was to compare changes in the contractile function of the heart during acute overloading produced by an experimental lesion in animals adapted to high-altitude hypoxia and in unadapted animals.

## EXPERIMENTAL METHOD

Male albino rats were adapted to hypoxia by keeping them for 6 h daily for 40 days in a pressure chamber. The rats gradually became accustomed to the "high altitude," for on the first day of adaptation the atmospheric pressure in the chamber corresponded to an altitude of no more than 1000 m, and every day it was increased by 1000 m up to 6000 m. This last level was maintained in the pressure chamber throughout the period of adaptation. Acute overloading of the heart was produced by creation of coarctation of the abdominal aorta. Some animals underwent a similar operation, but without constriction of the aorta. Two days after the operation on the animals, in an acute experiment under urethane anesthesia and with artificial respiration, indices of the contractile function of the myocardium were determined. By means of an electromanometer the pressure in the left and right ventricles was recorded at relative physiological rest and also during isometric contraction of the ventricles. To produce isometric contractions the aorta or pulmonary artery was completely occluded for 30 sec. By analysis of the curves of intraventricular pressure, indices of the force of myocardial contraction were calculated: the maximal pressure and the intensity of functioning of the structures ($IFS=\frac{\text{pressure inside ventricle}}{\text{weight of ventricle}}$).

## EXPERIMENTAL RESULTS AND DISCUSSION

Coarctation of the aorta in control, unadapted animals led to a significant increase in the relative weight of the left ventricle by 19%. The weight of the right ventricle remained unchanged. As a result of adaptation to high-altitude hypoxia, appreciable hypertrophy of the left and, in particular, the right ventricle took place: their weight increased by 25 and 39% respectively. Coarctation of the aorta produced in animals

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TABLE 1. Weight of Animals and Relative Weight of Ventricles During Adaptation to High-Altitude Hypoxia and Acute Overloading of the Heart

| Group of animals | No. of animals | Weight of rats (in g) | Relative weight | |
|---|---|---|---|---|
| | | | of left ventricle | of right ventricle |
| Control, mock operation (1) | 15 | 209 | 20.6 ± 0.4 | 9.05 ± 0.4 |
| Control, coarctation of aorta (2) | 16 | 206 | 24.5 ± 0.5 | 9.65 ± 0.4 |
| Adapted, mock operation (3) | 12 | 208 | 25.7 ± 0.9 | 12.60 ± 0.4 |
| Adapted, coarctation of aorta (4) | 16 | 205 | 25.9 ± 0.9 | 11.90 ± 0.4 |
| Significance of differences | | | | |
| $P_{1-2}$ | | < 0.001 | | > 0.5 |
| $P_{3-4}$ | | > 0.5 | | > 0.1 |
| $P_{1-3}$ | | < 0.001 | | < 0.001 |

TABLE 2. Indices of Contractile Function of Left and Right Ventricles During Adaptation to High-Altitude Hypoxia and Acute Overloading of the Heart

| Index | Group of animals | Right ventricle | | Left ventricle | |
|---|---|---|---|---|---|
| | | relative rest | isometric contraction | relative rest | isometric contraction |
| Systolic pressure (in mm Hg) | Control, mock operation (1) | 29.2 ± 3.2 | 45.1 ± 3.3 | 105 ± 8.8 | 214 ± 11.1 |
| | Control, coarctation of aorta (2) | 32.7 ± 3.0 | 42.5 ± 11.3 | 86 ± 11.9 | 179 ± 22.2 |
| | Adaptation, mock operation (3) | 52.5 ± 7.4 | 82.2 ± 6.9 | 165 ± 18.6 | 251 ± 15.8 |
| | Adaptation, coarctation of aorta (4) | 48.8 ± 4.7 | 72.4 ± 9.7 | 137 ± 15.1 | 195 ± 22.2 |
| | Significance of differences | | | | |
| | $P_{1-2}$ | > 0.5 | > 0.5 | > 0.2 | > 0.1 |
| | $P_{3-4}$ | > 0.5 | > 0.5 | > 0.5 | > 0.05 |
| | $P_{1-3}$ | < 0.02 | < 0.001 | < 0.02 | < 0.05 |
| | $P_{2-4}$ | < 0.02 | < 0.05 | < 0.02 | > 0.5 |
| IFS (in mm Hg/100 mg) | Control, mock operation (1) | 14.7 ± 1.0 | 22.6 ± 2.0 | 25.0 ± 2.9 | 49.9 ± 3.1 |
| | Control, coarctation of aorta (2) | 16.3 ± 2.1 | 21.8 ± 5.5 | 17.1 ± 2.6 | 22.8 ± 4.8 |
| | Adaptation, mock operation (3) | 20.7 ± 2.5 | 30.7 ± 2.5 | 32.1 ± 4.1 | 46.2 ± 4.7 |
| | Adaptation, coarctation of aorta (4) | 19.5 ± 2.3 | 31.2 ± 3.3 | 23.0 ± 5.6 | 36.6 ± 5.2 |
| | Significance of differences | | | | |
| | $P_{1-2}$ | > 0.5 | > 0.5 | < 0.05 | < 0.001 |
| | $P_{3-4}$ | > 0.5 | > 0.5 | > 0.01 | > 0.1 |
| | $P_{1-3}$ | < 0.05 | < 0.05 | > 0.5 | > 0.5 |
| | $P_{2-4}$ | > 0.5 | > 0.1 | > 0.5 | > 0.05 |

adapted to high-altitude hypoxia did not lead to an increase in weight of the already hypertrophied left ventricle (Table 1).

These results agree well with those obtained by Meerson et al. [2], who found that activation of protein synthesis does not take place in animals adapted to high-altitude hypoxia after the production of an experimental lesion.

Under conditions of relative physiological rest, the systolic pressure both in the left and right ventricle was much higher in animals adapted to high-altitude hypoxia than in unadapted animals (by 57 and 80% respectively; Table 2). During isometric contraction the systolic pressure in both ventricles of the adapted animals likewise was higher than in the controls (by 82% in the right ventricle and by 17% in the left). Two days after the creation of coarctation of the aorta, the pressure in the left ventricle, both at relative physiological rest and during isometric contraction, was slightly reduced in all animals, but the decrease was not statistically significant.

The disturbance of the contractile function of the myocardium of the left ventricle as a result of acute overloading of the heart under these conditions was reflected much more clearly by the other index of the force of contraction (IFS). As Table 2 shows, this index in the control animals two days after creation of coarctation of the aorata was significantly reduced at relative physiological rest by 32%, while during isometric contraction it was reduced by 54%. In animals adapted to high-altitude hypoxia this decrease was much less marked – by 28 and 21% respectively – and was not statistically significant. The pressure at the end of diastole in all groups of animals under these conditions was not very different and, consequently, the decrease in the force of contraction of the left ventricle was actually due to a change in the state of the contractile function of the myocardium and was independent of the degree of diastolic filling of the ventricle.

Coarctation of the aorta did not disturb the contractile function of the right ventricle, as the absence of changes in IFS showed. All that was noted was that in animals adapted to high-altitude hypoxia this index was higher than in unadapted animals at relative rest by 41% and during isometric contraction by 36%.

Disturbance of the contractile function of the left ventricle in acute overloading of the heart produced by an experimental lesion is thus manifested by a marked decrease in the indices of force of myocardial contraction. In animals adapted to high-altitude hypoxia, this disturbance is less severe. This means that the myocardium of animals adapted to high-altitude hypoxia has become more resistant, as a result of this adaptation, to acute overloading of the heart produced by increased resistance to the explusion of blood.

## LITERATURE CITED


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