CONTRACTILE FUNCTION OF THE HEART AND ITS REACTIVITY TO NORADRENALIN DURING ADAPTATION TO MEDIUM ALTITUDES

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Acute experiments on rats adapted for 1 month to an altitude of 2100 m showed that in the early period of exposure at this altitude the systolic pressure in the left ventricle and the rate of its development and fall were considerably greater than the corresponding indices in control experiments in Moscow. The indices of contractile function subsequently stabilized gradually. Four weeks later the hearts of the adapted animals showed a much greater rise in the indices of contractile function in response to injection of adrenalin and greater stability of this function at very high heart rates.

KEY WORDS: *adaptation to hypoxia; noradrenalin; heart; contractile function.*

It was shown previously that adaptation to interrupted exposure to hypoxia in a pressure chamber can lead to an increase in the maximal indices of contractile function of the heart muscle [5, 6, 9]. Similar changes were observed in animals adapted to an altitude of 3000 m in the mountains [7]. The question accordingly arises whether similar changes are observed during adaptation to lower altitudes, of the order of 2000 m above sea level, altitudes to which people climb more frequently and at which more people live than at 3000 m.

EXPERIMENTAL METHOD

Experiments on male Wistar rats were carried out at the Medical Biological Station, Academy of Sciences of the Ukrainian SSR, in the village of Terskol, in the vicinity of Mt. El'brus, at an altitude of 2100 m at which the animals had been kept for 2-4, 14-16, and 28-30 days. Control experiments were carried out in Moscow. Under urethane anesthesia (160 mg/100 g body weight) and during artificial respiration at a frequency of 68/min, a cannula was introduced through the apex of the heart into the left ventricle of the rats and the pressure measured electromanometrically and recorded on the Mingograph-34 instrument. The first derivative of pressure was recorded by the DÉ-1 differentiator and the ECG in lead II

TABLE 1. Effect of Adaptation to Altitude on Contractile Function of Heart

Index	Control	Duration of adaptation, days		
		2—4	14—16	28—30
Heart rate, beats/min	335±14	365±12	300±7	320±11
Pressure in left ventricle, mm Hg	102±9	170±8*	145±9*	105±10
Rate of development of pressure, mm/sec	6970±670	13 000±120*	10 000±520*	7240±370
Rate of fall of pressure, mm/sec	2750±260	4100±300*	3300±210	2900±250
IFS, mm Hg·min/mg	98±15	179±8	108±8	77±8
Increase in pressure in response to injection of noradrenalin, mm Hg	29±7	34±5	61±8*	56±7*

*P < 0.05 compared with control.

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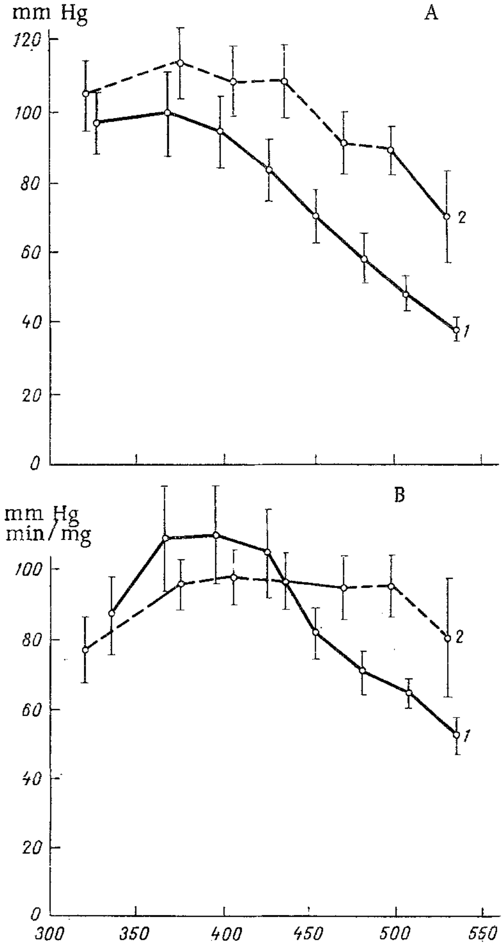

Fig. 1. Dynamics of pressure developed (A) and IFS index (B) of left ventricle during gradual increase in heart rate in control experiments (1) and after a stay of 4 weeks at 2100 m (2).

at the same time. Cardiac function was assessed under conditions of relative physiological rest and during three types of loading: an increase in heart rate, injection of a standard dose of noradrenalin (0.5 μg/kg), and transient compression of the ascending aorta. The pressure developed by the ventricle, the maximal rates of rise and fall of pressure in the ventricle, and the intensity of function of structures (IFS), i.e., the product of the pressure developed and the heart rate divided by the weight of the ventricle [7], were determined. Altogether 40 experiments were carried out (10 controls and 10 at each period of adaptation).

EXPERIMENTAL RESULTS

The results in Table 1 show changes in the indices of contractile function of the left ventricle of the rats. In the early period of the stay at a high altitude there was a sharp increase in pressure in the left ventricle and in the rate of its rise and fall. The IFS index was almost doubled. After 14-16 days this increase had almost disappeared and by the 28th-30th day the indices of the contractile function were indistinguishable from the control. The same dynamics of contractile function also was observed during adaptation to high altitudes [7] or during interrupted adaptation in a pressure chamber [9]. It also agrees with observations of an increase in the heart rate, blood pressure, and minute volume in man in the early stage of exposure to high altitudes [1, 2, 4, 8].

With an increase in the heart rate in the control experiments the pressure gradually started to fall after a short plateau. This decrease became statistically significant ($P < 0.02$) when the heart rate was 480/min (by 40%). The IFS index at first rose a little and then fell to half its maximal value (Fig. 1).

The dynamics of these indices was similar in the early stages of adaptation to medium altitudes. However, 4 weeks after the beginning of adaptation the dynamics of these indices differed in character. The pressure developed by the ventricle fell but not significantly ($P > 0.05$) even at the highest heart rate. Within the range from 470 to 530 beats/min a much higher pressure was recorded in the heart of the adapted animals than of the controls ($P < 0.02$). As a result, the IFS index remained stable throughout almost the whole range of heart rates. Under the influence of adaptation for 4 weeks the stability of the cardiac function was thus increased at a high heart rate.

The action of noradrenalin on the indices of contractile function was maximal 20 sec after its injection and was shown as an increase in the pressure developed by the ventricle and in the rates of its rise and fall, whereas the heart rate remained unchanged. The effect of noradrenalin increased with adaptation: After 1 month it was almost twice as high ($P < 0.05$) as in the control rats.

By contrast with these clear changes the value of the IFS index during transient compression of the aorta remained approximately the same at all stages of adaptation and was indistinguishable from its value in the control animals (153 ± 12 mm Hg·min/mg).

During a stay at medium altitude the initially increased contractile function of the left ventricle thus gradually returned to normal, but its increase in response to loading caused by an increase in the heart rate or injection of noradrenalin also was considerably greater than in the control. These results are similar in principle to those obtained by studying cardiac function of animals adapted to an altitude of 3000 m [7] and they are evidence that the increase in the maximal performance of the heart also takes place during adaptation to medium altitudes.

Adaptation to altitude hypoxia has recently been used for the prevention of certain heart lesions produced by excessive overloading by pressure or sympathomimetics [1, 6]. The choice of the optimal adaptation regime thus assumes special importance. An increase in the intensity of hypoxia in the pressure chamber abolished the beneficial effect of adaptation on the contractile function of heart muscle and on the sympathetic control apparatus of the heart [5, 6, 9, 10]. Another interesting observation is that people adapted for a long time to an altitude of 2100 m possessed higher working capacity at a high altitude than mountaineers [3]. All these facts must be taken into account when the optimal adaptation regime is fixed.

LITERATURE CITED

1. N. A. Agadzhanyan and M. M. Mirrakhimov, Mountains and Resistance of the Body [in Russian], Moscow (1970).
2. M. A. Aliev, S. I. Arestova, R. B. Sultakeev, et al., in: Outlines of the Physiology and Pathology of Man and Animals under High-Altitude Conditions [in Russian], Leningrad (1967), p. 75.
3. P. V. Beloshitskii and V. I. Danileiko, in: Mountains and Health [in Russian], Kiev (1974), p. 17.
4. E. J. Van Liere and C. J. Stickney, Hypoxia, Univ. Chicago Press, Chicago (1963) [Russian translation: Moscow (1967)].
5. V. I. Kapel'ko, Fiziol. Zh. SSSR, No. 12, 1787 (1970).
6. F. Z. Meerson, The General Mechanism of Adaptation and Prophylaxis [in Russian], Moscow (1973).
7. F. Z. Meerson, M. G. Pshennikova, V. I. Kapel'ko, et al., Kardiologiya, No. 12, 50 (1975).
8. M. M. Mirrakhimov, The Cardiovascular System at High Altitudes in the Mountains [in Russian], Leningrad (1968).
9. N. A. Novikova and V. I. Kapel'ko, Byull. Éksp. Biol. Med., No. 11, 30 (1970).
10. M. G. Pshennikova, Fiziol. Zh. SSSR, No. 3, 421 (1973).