CHANGES IN THE MYOFIBRILLARY SYSTEM OF THE RAT HEART IN EARLY POSTNATAL ONTOGENY AT HIGH ALTITUDES AND DURING PHYSICAL EXERTION

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The adaptive reaction of the adult heart to high altitude conditions in the mountains is accompanied by hypertrophy of the myocardium, which is based on hyperplasia of muscle cell ultrastructures [2]. Since the most specific of the latter are myofibrils, it was decided to study relations between the change in weight of the heart and its myofibrillary apparatus during exposure to the high altitude hypoxia combined with physical exertion in the growing myocardium, i.e., during the period of its development when hyperplasia and differentiation of structures are particularly well marked [4-6], and the investigation described below was carried out for this purpose.

EXPERIMENTAL METHOD

Experiments were carried out on 108 young rats of two age groups: newborn (1–3 days) and 15 days; the animals were moved from the foothills (760 m above sea level) to a high altitude in the mountains (3200 m above sea level). Some of the animals at the age of 15 days were exposed to physical exertion from the first days of their stay in the mountains, by swimming for 15 min during the first week and for 30 min during the subsequent period of the experiment. The control consisted of 40 newborn rats kept in the foothills. The hearts of the control and experimental animals were tested on the 1st, 3rd, 7th, 15th, 30th, and 45th days. The body weight and weight of the heart, and cardiac index (CI) (the ratio of the weight of the heart to body weight) were studied. The heart was fixed in neutral formalin and embedded in paraffin wax. Histotopographic sections cut transversely through the heart were stained with Heidenhain's iron hematoxylin. Quantitative analysis of the myofibrillary apparatus was undertaken in 100 muscle cells followed by statistical analysis of the data by Student's method.

The degree of change of the absolute and relative indices of weight of the heart was compared with changes in the number of distribution of myofibrils in the muscle cells, taking the age norm into consideration.

EXPERIMENTAL RESULTS

Normally during postnatal ontogeny, with growth of the rats the absolute weight of the heart increased but CI decreased (Table 1). In the newborn rats aged 1–3 days the myofibrils were thin and were distributed around the periphery of the muscle cell in the form of a single-layered ring, staining palely (Fig. 1a). By the 5th day after birth of the rats the myofibrils were distributed as before in a single-layered ring in the cell, but more compactly, and more deeply stained. By the 15th day after birth of the rats single myofibrils containing a fragment of a second layer began to appear in some cells (Fig. 1b). By the age of 1–1.5 months, myofibrils were distributed in several rings and occupied the whole cross-section of the muscle cells, and were deeply stained (Fig. 1c). Under high altitude conditions there was a smaller increase in body weight of the young rats than in the control, starting from the 3rd and until the 30th day of the animals' stay in the mountains. By the 45th day the body weight of rats kept in the mountains did not differ significantly from the control. The absolute weight of the heart in the first week of stay of the newborn rats in the mountains also was reduced: on the 3rd day of the experiment by 6.7%, on the 7th day by 4.6% of the age norm. Values of CI under these circumstances were increased by 10.4 and 12.5% respectively (Table 1).

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TABLE 1. Relationship of Weight of Heart and Number of Myofibrils in Muscle Cells of Rats Aged 1–3 Days in Control (A) and under High Altitude Conditions (B)

Time of experiment, days	Group of animals	Body weight		Weight of heart		CI		Number of myofibrils in cell	
		g	percent of control	mg	percent of control	absolute	percent of control	absolute	percent of control
1	A	6,3±0,12		40,8±0,77		0,0064		5,2±0,16	
	B	6,1±0,11	96,8	40,7±0,71	99,7	0,0066	103,1	5,3±0,18	100
3	A	6,8±0,13		43,8±0,79		0,0064		5,3±0,13	
	B	6,1±0,12	89,7	40,9±0,60*	93,3	0,0067	110,4	5,1±0,17	96,2
7	A	12,6±0,33		63,6±0,58		0,0048		8,1±0,21	
	B	11,2±0,11	88,8	607±0,53*	95,4	0,0054*	112,5	7,2±0,23*	88,8
15	A	23,4±0,63		119,3±1,63		0,0051		13,6±0,32	
	B	20,1±0,54	85,2	130,5±3,30*	109,4	0,0064*	125,5	13,1±0,31	96,3
30	A	41,0±0,80		199,8±6,18		0,0047		24,6±0,67	
	B	37,2±0,90	90,7	247,2±10.45*	123,7	0,0064*	136,1	30,4±0,83*	123,6
45	A	90,0±0,81		390,5±7,9		0,0043		31,4±0,91	
	B	88,1±0,79	97,8	475,6±14,4*	121,8	0,0054*	125,6	37,3±1,11	118,8

*Here and in Table 2, $P < 0.05$.

TABLE 2. Relations Between Weight of the Heart and Number of Myofibrils in Muscle Cells of Rats Aged 15 Days in Control (A) and under High Mountain Conditions (B) and Exposed Additionally to Physical Exertion (C)

Time of experiment days	Group of animals	Body weight		Weight of heart		CI		Number of myofibrils in muscle cell	
		g	percent of control	mg	percent of control	absolute	percent of control	absolute	percent of control
1	A	20,1±0,41		104,5±1,21		0,0052		13,4±0,30	
	B	20,6±0,65	102,5	105,5±1,16	100,9	0,0051	98,1	13,8±0,33	102,9
	C	19,8±0,22	98,5	107,6±1,31	102,9	0,0054	103,8	14,0±0,27	104,5
3	A	23,4±0,63		121,6±1,63		0,0052		13,6±0,32	
	B	23,8±0,61	101,7	120,6±1,89	99,1	0,0051	98,1	14,1±0,28	103,7
	C	22,5±0,41	96,1	127,3±2,34*	104,7	0,0056*	107,9	16,1±0,59*	118,4
7	A	25,8±0,71		126,4±2,46		0,0049		19,6±0,45	
	B	24,3±0,63	94,2	131,8±2,12	104,3	0,0054	110,2	20,6±0,51	105,1
	C	21,9±0,57*	84,8	143,2±2,67*	113,3	0,0065*	132,6	24,4±0,67*	124,5
15	A	41,0±0,80		194,8±3,18		0,0047		24,6±0,56	
	B	37,7±0,71*	91,9	216,9±7,11*	111,3	0,0057*	121,3	27,7±0,60*	112,6
	C	33,8±0,70*	82,4	246,2±7,80*	126,4	0,0072*	153,2	34,2±0,76*	139,0
30	A	90,0±0,87		390,5±7,90		0,0043		31,4±0,62	
	B	86,4±0,73*	96,0	466,7±8,13*	119,5	0,0054*	125,6	36,7±0,73*	116,9
	C	76,7±0,53	85,2	572,4±15,3*	146,6	0,0074*	172,1	43,3±0,96*	137,9
45	A	110,7±2,15		442,6±11,7		0,0040		33,6±0,83	
	B	106,2±1,71	95,9	540,2±12,8*	124,1	0,0051*	127,5	41,1±0,91*	122,3
	C	94,8±0,86*	85,6	603,6±13,4*	136,4	0,0063*	157,5	49,6±1,23*	147,6

The distribution of myofibrils in the muscle cells in the first week of the experiment remained basically the same as in the control: The myofibrils were arranged in a single row and stained palely. Their mean number on the 3rd day of stay of the rats in the mountains did not differ significantly from the age norm, but on the 7th day it was reduced by 11.2% below the norm. On the 15th day of the experiment, against the background of a maximal reduction in the increase in body weight (difference from the control 14.2%) the absolute weight of the heart increased by 9.4%, and the value of CI by 25.5%. Myofibrils in most cells, just as in the control, were arranged in a single-layered ring. Their mean number in the muscle cell did not differ significantly from normal (Fig. 1d). With an increase in the duration of stay of the newborn rats in the mountains, different relationships were established between the weight parameters of the heart and the myofibrillary apparatus. On the 30th and 45th days of the experiment the increase in value of the absolute weight of the heart and CI by 23.7 and 36.1% and by 14.4 and 25.6% respectively, was accompanied by an increase in the number of myofibrils in the muscle cell by 23.6 and 18.8% compared with normal. The myofibrils were arranged compactly and haphazardly in the cross-section of the muscle cell.

These results suggest that acceleration of relative growth of the heart in the first week and the increase in absolute weight by the end of the 2nd week of stay of newborn rats at high altitudes take place mainly on account of hyperplasia of the muscle cell. This is in agreement with observations of other workers [1, 7, 8] who

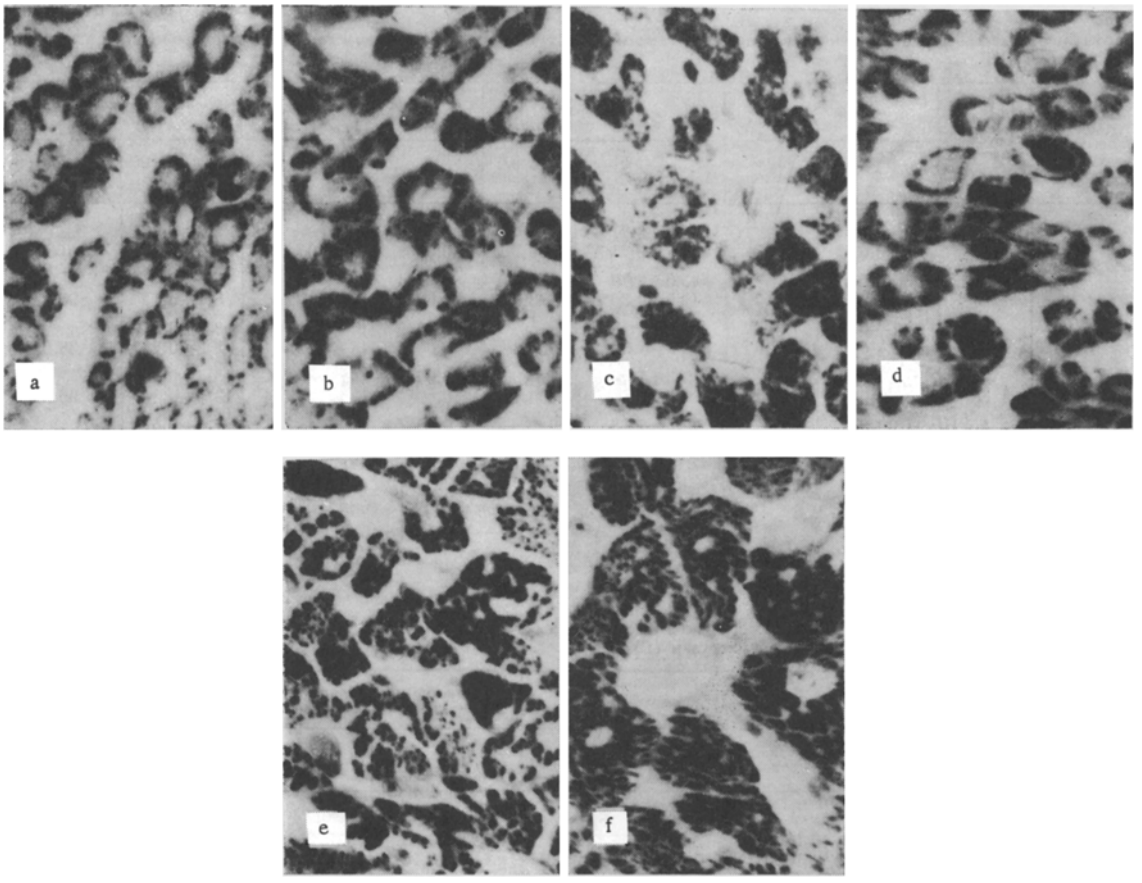

Fig. 1. Myofibrils in cross-section through myocardial cells of rats aged 3 days (a), 15 days (b), and 30 days (c) in the high mountains (d) and with additional exposure to physical exertion in the mountains (e, f). Stained by Heidenhain's iron hematoxylin. 450 ×.

consider that growth of the heart during early postnatal ontogeny can take place as the result of an increase in the number of muscle cells, and not only as a result of their hypertrophy.

Moving the rats at the age of 15 days to a high altitude in the mountains was not accompanied in the first week of the experiment by any considerable changes in body weight or weight of the heart or in the arrangement and number of myofibrils in the muscle cell. After a stay of 15 days by the animals in the mountains the increase in absolute and relative parameters of the weight of the heart was accompanied by an increase in the number of myofibrils in each cell compared with parameters in the control (Table 2). The myofibrils were arranged in several layers in the muscle cell and stained deeply. Similar but less clearly defined relationships between the weight of the heart and the number of myofibrils in the muscle cell were found in rats aged 15 days, exposed to physical exertion in the mountains (Table 2). On the 3rd day of the experiment the absolute weight of the heart was increased by 4.7% and CI by 7.9%. The mean number of myofibrils in the muscle cell was increased by 18.4% compared with the control. Myofibrils were arranged compactly in the muscle cells in two or more layers. In some cells myofibrils occupied the whole cross section (Fig. 1e). An increase in the number and duration of physical exercises in the high mountains led to more marked hypertrophy of the heart and to a considerable increase in the number of myofibrils in the muscle cells. By the 45th day of the experiment the increase in absolute weight of the heart was 36.4%, the increase in CI 57.5%, and the increase in the mean number of myofibrils in the cell 47.6% of the age norm. Myofibrils were arranged compactly and haphazardly in the muscle cells and they occupied the whole of the cross-section (Fig. 1f).

The results of these investigations suggest two mechanisms of development of hypertrophy of the heart in growing rats under high mountain conditions. In newborn rats aged 1–3 days, a stay in the mountains stimulates the natural process of their age, of an increase in weight of the myocardium on account of hyperplasia of the muscle cells, and under these circumstances it accelerates the switching of the cellular form of regeneration to the intracellular form during postnatal growth of the heart muscle. In rats aged 15 days a stay high in the mountains, especially if combined with additional exposure to physical exertion, placing a considerable func-

tional load on the myocardium, the increase in weight of the contractile substance takes place mainly on account of an increase in the number of myofibrils in each muscle cell, i.e., as a result of intracellular hyperplasia [3].

When these differences in the mechanisms of myocardial hypertrophy in early postnatal ontogeny of rats under high altitude conditions are assessed, guidance must be taken not so much from the anatomical manifestations of this process, as from the nature of the regenerative-hyperplastic processes which lie at its basis.

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TISSUE STEREOLOGIC ANALYSIS OF MYOCARDIAL ATROPHY DURING HYPOKINESIA

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Prolonged limitation of movement (hypokinesia) disturbs activity of the cardiovascular system and considerably reduces the functional reserves of the heart [3, 10]. An excessive reduction of energy expenditure on active surmounting of body weight can be used as a model with which to study structural manifestations of adaptation and disadaptation processes [1]. For a more complete understanding of these processes, quantitative studies of intracellular and tissue changes in the myocardium during hypokinesia are necessary. However, there have been few investigations into this problem, and these have been conducted mainly at the ultrastructural level [5, 7, 13].

The aim of this investigation was a quantitative stereologic study of the tissue organization of the rat myocardium in hypokinesia due to immobilization of the animals.

EXPERIMENTAL METHOD

Experiments were carried out on 48 male Wistar rats weighing 250–300 g. The motor activity of the rats was restricted by confining them in special restraining cages, the size of which corresponded to that of the animal. For morphometric and stereologic investigation 18 rats aged 6 months were used (four rats in each experimental group and six in the control). The animals were decapitated after 5, 15, and 30 days of hypokinesia. The heart was removed from the thorax and cooled in a cold chamber until it stopped beating, when the

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