REVERSIBILITY OF CARDIAC HYPERTROPHY DUE TO ALTITUDE HYPOXIA

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Whatever its cause, prolonged hyperfunction of the heart is consistently accompanied by the development of hypertrophy of the organ. The compensatory strengthening of the cardiac activity and the development of hypertrophy of the myocardium as a result of a prolonged stay in an atmosphere with a low partial pressure of oxygen are particularly well known [4,6,8,12,13]. However, further study is required to elucidate the time and course of development of this hypertrophy, and also to determine whether or not it is reversible when the action of the hypoxic factor ceases. There is no mention in the literature of investigations of the reversibility of the cardiac hypertrophy associated with a stay in an atmosphere deficient in oxygen. So far as the reversibility of hypertrophic changes in the myocardium from other causes (diseases of the heart valves, hypertension, etc.) is concerned, only a limited amount of evidence on this subject is to be found in the literature [3,5,7,9,10].

The object of the present experimental investigation was to study the times and dynamics of development of hypertrophy of the heart during prolonged altitude hypoxia and its reversibility after cessation of the action of the hypoxic factor.

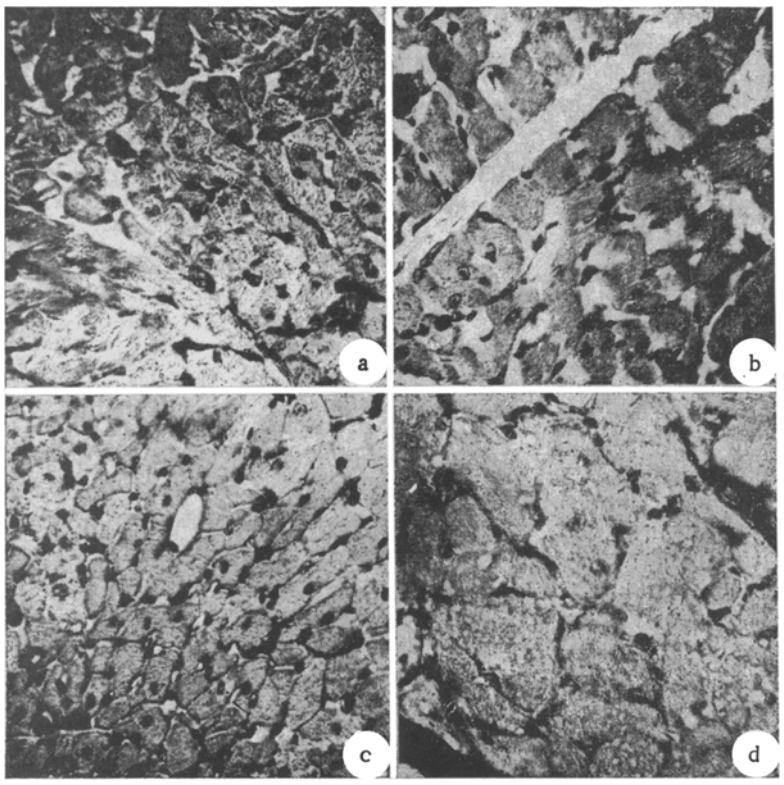
EXPERIMENTAL METHOD

Forty young, sexually mature male albino rats, weighing 200-220 g, were kept in a pressure chamber at a low atmospheric pressure, equivalent to an altitude of 7500-8000 m above sea level, for 5 h daily. The size of the pressure chamber and the volume of its ventilation precluded any risk of the accumulation of excess of carbon dioxide therein as a result of expiration by the animals. Twenty control rats of the same age and weight were kept in similar conditions as regards diet, temperature, and illumination. Five animals were sacrificed after a stay of 30 h at a "high altitude," 5 after 50 h, 10 after 160 h, and the remaining 20 animals 30 days after exposure to the action of hypoxia had ceased. After each animal had been removed from the pressure chamber, the ratio between the weight of the heart and the body weight was determined and the myocardium was examined histologically.

EXPERIMENTAL RESULTS

The results given in the table show that the increase in the relative weight of the heart did not take place uniformly: it reached its maximum after 30 h, when it attained an average value of 162% of the initial weight, and during its further stay in the pressure chamber it decreased slightly, to an average weight of 148% of the mean control value after 50 h and to 145% after 160 h. Thirty days after cessation of the action of altitude hypoxia, the mean relative weight of the heart of the animals kept in the pressure chamber for 160 h had fallen almost to its original value.

A histotopographical investigation of total sections of the heart from animals sacrificed after a stay of 30 h at a "high altitude" (see the figure) revealed a considerable, but variable thickening of the fibers, together with a very marked thickening of the fibers of the conducting system, more especially in the right than in the left ventricle. After staining with hematoxylin-eosin, some of the fibers with the most marked thickening showed basophilia. The nuclei of the fibers were of different sizes and shapes and contained a clearly defined nucleolus. Individual nuclei showed degenerative changes, here and there with signs of pyknosis. The vessels were engorged and venous stasis was present. The perivascular spaces were enlarged, and proliferation of the cells of the stroma was observed. These changes were seen in the subendocardial and subpericardial layers of the myocardium, but were absent or ill defined in its central portion. Local thickenings of the endocardium with proliferation of the endothelium were also noted.



Subendocardial layer of the myocardium of the left ventricle of a control rat (a), and of experimental rats after a stay of 30 h (b) and 160 h (c) in the pressure chamber, and 30 days after cessation of the action of hypoxia (d), showing the course of the changes in the volume of the muscle fibers. Van Gieson. 400 ×.

The changes in the myocardium of the animals exposed to "altitude" hypoxia for 50 h differed from the pattern described above by the presence of atrophic changes in individual muscle fibers, accompanied by signs of proliferation of the nuclei of the stroma, and also by the appearance of sclerotic changes in the subendocardial layers with marked proliferation of histiocytes and of the endocardial endothelium.

After a stay of 160 h at a "high altitude" the changes in the myocardium consisted of a more marked thickening of the muscle fibers, extending also to the deep layers of the myocardium (see the figure). Homogenization of the fibers was seen in some places. The nuclei of the fibers were enlarged, varied in their configuration, with a clearly outlined nucleolus, but without signs of degeneration. Numerous foci of sclerotic changes were scattered throughout the myocardium, more marked along the course of the vessels near and endo- and pericardium. The vessels had thickened, sclerotic walls, here and there with signs of proliferation of their endothelium.

The investigation of the hearts of the animals exposed to the action of "altitude" hypoxia for 160 h and sacrificed 30 days after cessation of the action of the hypoxic factor (see the figure) revealed the almost complete disappearance of hypertrophy of the muscle fibers and the restoration of their normal volume. The staining properties of the fibers remained unchanged. Their nuclei were of the usual size and shape. Marked signs of focal cardiosclerosis persisted, with hypertrophy of the connective tissue along the course of the vessels and in the intermuscular spaces, but with no increase in the number of its cells. The vascular walls remained sclerotic.

The dynamics and rates of the hypertrophic changes in the myocardium during prolonged exposure to a rarefied atmosphere corresponding to an altitude of 7500-8000 m above sea level as revealed by these experiments showed a great resemblance to the changes found in the heart by F. Z. Meerson [1] in experimental valvular disease. The changes which we found, with a sharp increase in the mass of the myocardium in the initial, short-lasting stage of compensation of hypoxic hypoxia, corresponded in character and duration to the "emergency" stage distinguished by

Relative Weight of the Heart of Rats after Different Lengths of Stay of an "Altitude of 7500-8000 m" and 30 Days after Cessation of the Action of Hypoxia

Rabbit No.	Control	Length of stay at a "high altitude"			30 days after cessation of the action of hypoxia
		30 hours	50 hours	160 hours	
1	0,0027	0,0045	0,0041	0,0037	0,0028
2	0,0027	0,0045	0,0041	0,0038	0,0029
3	0,0027	0,0047	0,0044	0,0041	0,0029
4	0,0027	0,0047	0,0044	0,0042	0,0029
5	0,0028	0,0049	0,0044	0,0043	0,0029
6	0,0028			0,0043	0,0030
7	0,0028			0,0045	0,0030
8	0,0029			0,0046	0,0030
9	0,0029			0,0046	0,0030
10	0,0029			0,0047	0,0031
11	0,0029				0,0032
12	0,0029				0,0032
13	0,0029				0,0032
14	0,0029				0,0032
15	0,0029				0,0034
16	0,0030				0,0035
17	0,0032				0,0036
18	0,0032				0,0036
19	0,0032				0,0036
20	0,0034				0,0036
Mean ...	0,0029 (100%)	0,0047 (162%)	0,0043 (148%)	0,0042 (145%)	0,0032 (110%)

Meerson, and the subsequent changes, with stabilization of the mass of the heart, corresponded to the stage of "relatively stable hyperfunction" of the compensatory process in valvular disease of the heart.

Investigations by several workers [1,2,3,12,13] have shown that the increase in the mass of the heart during hyperfunction and hypertrophy is the result of stimulation of protein synthesis in the myocardium. According to F. Z. Meerson [1,2], the immediate cause of the stimulation of the synthesis of nucleic acids and proteins is hyperfunction of the heart muscle. Removal of compensatory hyperfunction of the heart, and consequently, of the stimulus activating synthesis in the myocardium, was evidently responsible for the reduction observed in our experiments in the mass of the hypertrophied heart almost to its initial value within a comparatively short time after cessation of the action of the hypoxic factor.

The processes of protein synthesis in the hypertrophied myocardium after cessation of its hyperfunction will be the subject of future investigations.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.