FORMATION OF TRANSVERSELY ORIENTED MYOFIBRILS IN MYOCARDIOCYTES OF THE HYPERTROPHIED HEART

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Hypertrophy of the myocardium was induced in rats and mice by training in a pressure chamber or ligation of the apex of the heart. Two weeks later the formation of transversely oriented myofibrils was observed beneath the sarcolemma in some of the ventricular myocardiocytes. It is suggested that this phenomenon depends on the development of transverse mechanical forces beneath the sarcolemma as a result of an increase in volume of the cells.
KEY WORDS: hypertrophy of the myocardium; transversely oriented myofibrils.

The problem of the causes of the regular arrangement of structures in cells has received little study. When investigating the myocardium of mice and rats during the development of experimental hypertrophy of the heart the writers found that transversely oriented myofibrils are formed beneath the sarcolemma of many of the muscle cells of both the right and the left ventricle.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200 ± 20 g were exposed for 6 h daily in a pressure chamber for 5 days each week in accordance with the following program: During the first days the "altitude" was increased by 1000 m daily up to 7000 m, after which further exposures were at the same "altitude." Five rats were killed 2 weeks after the beginning of training and 17 rats after 4 weeks. A group of five rats was subjected to a more intensive training program, namely exposure for 8 h daily to an "altitude" of 8000 m, and they were killed 2 weeks later. The hearts of five adult mice in which the apex of the heart had been ligated by Selye's method [2], and which were killed 2 weeks (two mice) and 4 weeks (three mice) after the operation, also were investigated. Five animals undergoing a mock operation served as the control. The hearts were examined in the electron microscope.

EXPERIMENTAL RESULTS

In rats exposed for 2 weeks in a pressure chamber the mass of the heart was increased compared with the control: 126 ± 7% for the right ventricle and 114 ± 4% for the left. After exposure for 4 weeks the increase in mass of the heart was virtually the same (127 ± 6 and 115 ± 3%, respectively). A greater increase in the mass of the heart was observed after 2 weeks in rats subjected to more intensive training (188 ± 8 and 157 ± 4%). The ligated apex of the heart developed necrosis, as a result of which up to one third of the mass of the ventricles was lost, but the remainder restored the original mass by hypertrophy in the course of 1 month.

Signs of intensification of both lytic and plastic processes were observed electron microscopically in the myocardiocytes of the experimental animals [1]. Particularly intensive formation of new myofibrils was observed in the region below the sarcolemma; in some muscle cells the newly formed myofibrils were oriented, not parallel to the long axis of the myocardiocytes as usual, but transversely, perpendicularly to the remaining myofibrils, forming an annular layer girdling the cell. Pictures of this sort were more frequently

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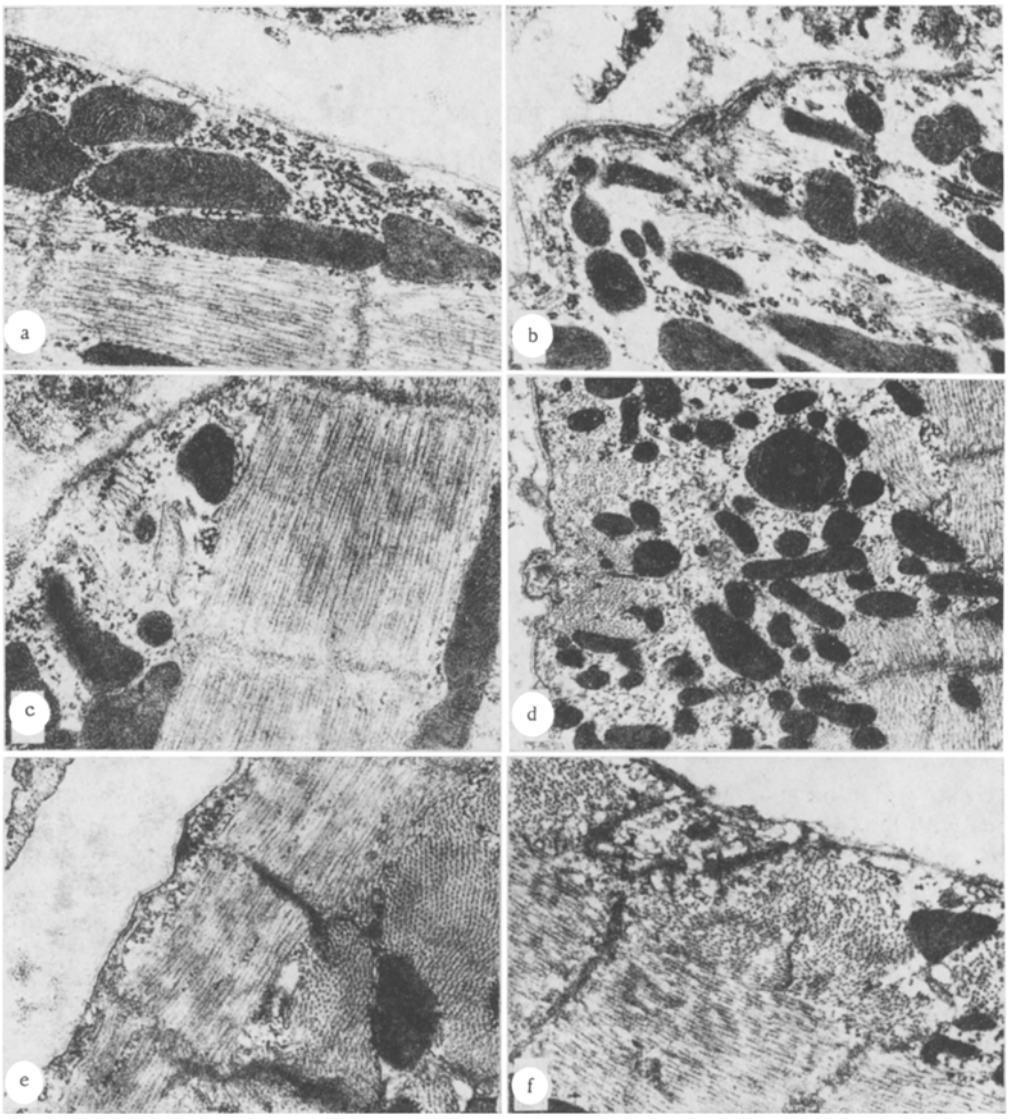

Fig. 1. Regions beneath sarcolemma of myocardiocytes of ventricles of rats exposed for 2 weeks in pressure chamber (high-altitude hypoxia). Electron micrographs stained with uranyl and lead. a) Accumulation of mitochondria and polysomes beneath sarcolemma (28,000 ×); b) appearance of first fibrils connected with polysomes (28,000 ×); c) further formation of transversely oriented myofilaments (28,000 ×); d) transversely oriented myofibrils formed beneath sarcolemma (15,000 ×); e) transverse section through myocardiocytes with mature myofibrils situated beneath sarcolemma; connection between Z bands of transversely and longitudinally oriented myofibrils can be seen below (28,000 ×); f) same picture in longitudinal section through myocardiocyte (28,000 ×).

found in the myocardium of the rat after exposure for 2 weeks in the pressure chamber, especially after intensive training. After training for 4 weeks, transverse myofibrils were much less frequently observed.

The process takes takes place asynchronously in different cells and by comparing the pictures observed within the same section and also in different animals, it can be represented as follows. In cells exposed to rapidly developing hypertrophy accumulation of mitochondria is observed in the region below the sarcolemma, and between the mitochondria numerous ribosomes appear, some of them lying freely and aggregated into polysomes, others lining the tubules of the endoplasmic reticulum (Fig. 1a). Thin fibrils, evidently newly formed myofilaments (Fig. 1b, c) are in close contact with the ribosomes. In the next stages myofibrils are already formed; initially they are thin and loosely arranged (Fig. 1d), but later they attain the thickness of normal mature myofibrils and are in no way distinguishable from them in structure, but they are oriented

transversely (Fig. 1e, f). A striking feature is that the formation of Z bands in the transverse myofibrils is connected with the same T systems as the analogous bands in the deep, longitudinally oriented myofibrils, as a result of which the substance of the Z bands of the perpendicularly arranged myofibrils is interconnected (Fig. 1e, f).

In the mice in which hypertrophy of the myocardium was produced by ligation of the apex of the heart the formation of numerous transversely oriented myofibrils was observed 2 weeks after the operation, but 4 weeks after the operation there were substantially fewer of them. This indicates that during the process of renewal of structures constantly taking place in the cells, the oriented myofibrils are subsequently replaced by myofibrils oriented normally, in the longitudinal direction.

The formation of transversely oriented myofibrils in these experiments thus took place in the relatively early stage of hypertrophy, when the volume of the cells was rising rapidly. The cause of the transverse orientation of the newly formed myofibrils, in the writer's opinion, is that under these conditions transverse forces arise in the region below the sarcolemma as a result of stretching, whereas in normal fibrils the longitudinal orientation is due to longitudinally directed forces. This hypothesis is supported by observations on embryonic cardiogenesis [4] and on myocardiocytes in organ culture [6], where the absence of strict orientation of the myofibrils throughout the mass of cells has been described. Some workers [3, 5, 7] described longitudinally and obliquely oriented myofibrils in hypertrophied myocardiocytes in man, a finding interpreted as the development of mechanical forces in unusual directions under pathological conditions [5]. The present experiment also confirmed the view that mechanical forces are a factor determining the orientation of myofibrils in muscle cells.

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