Stress-Induced Rearrangement of the Myocardium: Time Course of Structural Changes in Various Types of Stress

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Common morphological changes in the myocardium were revealed in rats exposed to three different types of stress. At the initial stages of stress, the structural changes were stereotypical (contractures) irrespective of the type of stress factor and differed only by their severity. At later stages contractures were gradually replaced by cytolytic injuries, which did not depend on the type of stress either. Early predominance of myocytolysis in combination with excessive contracture injuries led to rapid death, which is probably a manifestation of genetically determined low capacity to adapt to stress in some individuals.

Key Words: *stress; myocardium; focal injuries*

The problem of myocardial resistance to stress has been studied mainly from the pharmacological viewpoint [2,3,9]. There are no publications about morphological aspects of stressed heart from the viewpoint of individual genetically determined resistance of the myocardium to damage. Structural characteristics of myocardial injury caused by different types and terms of stress are unknown, while such data will promote progress in technologies of experimental stress simulation and formation of principles of controlled adaptation protection of the myocardium in patients. Stress is now regarded as the main pathogenetic factor for the most prevalent cardiac diseases [6,10,11]. Some characteristics of stressed heart are now investigated, but its functional and biochemical parameters are studied much better [1,5,12,14] than structural [4,13].

We studied the relationship between structural disorders in the myocardium and type of stress, time course of these disorders, and morphology of the myocardium in animals which died during the experiment.

MATERIALS AND METHODS

Experiments were carried out on male Wistar rats (220-250 g). The animals were divided into 4 groups: control; 1) immobilization stress (fixation in the supine position for 8 h); 2) stress from exhausting swimming (32°C water for 20 min with a load of 3% body weight); and 3) enclosure stress (24 h in a small cage with water and food). The animals were sacrificed 24 and 96 h after exposure. Structural changes in left-ventricular myocardium were studied on intact and hematoxylin-eosin stained (after Selye and Heidenhain) sections under common and polarized light. Focal myocardial injuries were morphometrically assessed using Leitz histological structure analyzer. Rats which died 18-36 h after stress exposure (4 after immobilization stress and 3 after swimming) were united in a special group.

The significance of differences was evaluated using Student's t test.

RESULTS

Interstitial edema and lymphostasis were observed 24 h after stress in all experimental rats; later these symptoms was notably reduced. All three types of stress induced diffuse focal lesions in the left-ventricular myocardium; at the initial stages contractures of different severity predominated among these lesions.

Under common light these changes were characterized by increased tinctorial properties (hypereosinophilia of the cytoplasm); the contractures looked or-

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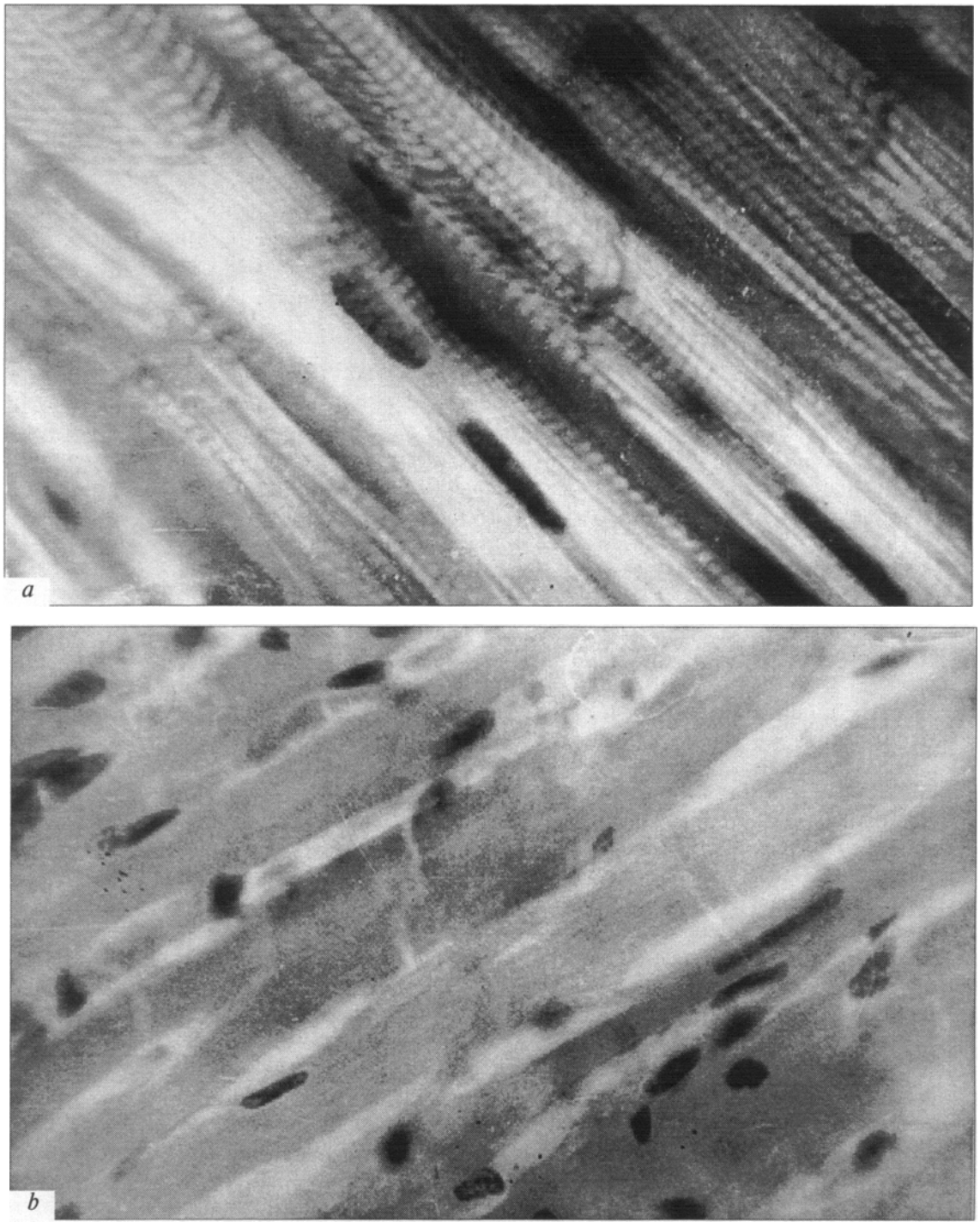

Fig. 1. Myocardium of rats surviving immobilization stress (*a*) and exhausting swimming (*b*). *a*) contractures of the second and third degrees. Selye staining. Polarized light, ×800; *b*) uneven staining with background stains; hypoeosinophilic muscle fibers with loose myofibrils alternating with hypereosinophilic fibers. Hematoxylin and eosin staining, ×400.

ange after Selye staining and brick-brown after Heidenhain staining. Under polarized light this type of injuries was characterized by increased anisotropy of A disks (first degree), thinning of isotropic disks (second degree) and their complete disappearance with fusion of anisotropic disks and formation of anisotropic agglomerations (third degree, Fig. 1, *a*). These structural disorders are regarded as the result of Ca overload of cardiomyocytes due to membrane pump dysfunction [6,7].

Contractures of all degrees were seen in experimental material, but second- and third-degree contractures predominated in the myocardium of groups 1 and 2 rats, while in group 3 rats contractures of the first

TABLE 1. Morphometrical Characteristics of Myocardial Lesions in Rats Exposed to Stress of Different Types ($M \pm m$)

Parameter		Control (n=7)	Stress			Dead (n=7)
			immobilization (n=6)	exhausting swimming (n=7)	enclosure (n=10)	
Density of contractures	24 h	1.60±0.07	34.20±0.91	30.10±0.78	22.10±0.52	45.80±1.22*
	96 h	1.40±0.05	15.50±0.42	11.10±0.27	8.60±0.29	—
Density of cytolytic lesions	24 h	0.50±0.01	5.70±0.22	3.8±0.2	1.20±0.11	15.10±0.84*
	96 h	0.60±0.02	14.20±0.31	6.00±0.24	2.60±0.19	—

Note. *p<0.001 *vs.* respective values in the immobilization stress group.

and second degree were more incident. This type of structural disorders predominated at the early stages of experiment in all cases. The density of myocardial contractures was maximum in group 1 animals (Table 1).

The time course of reduction of these structural changes was similar in all groups (2-3-fold from day 1 to day 4 after stress).

Myocytolysis, in contrast to contractures, was characterized by attenuation of tinctorial properties of cardiomyocytes (Fig. 1, *b*); examination under polarized light showed weakened myofibril anisotropy, defibrillation, and complete disappearance of fibrils. According to modern views, these structural changes are manifestations of regeneratory plastic insufficiency due to activation of catabolic processes in the cell [4,7,8]. L. Nepomnyashchikh [8] considers stress as a model of plastic insufficiency of the organism. Our experiments showed that the time course of cytolytic disorders is opposite to the time course of contracture injuries: the number of such focal lesions increases 1.5-2 times with time and by the end of day 4 myocytolysis becomes the predominant type of structural changes in stressed myocardium in all experimental groups. The highest density of such foci is characteristic of immobilization stress.

The time course of structural changes in the myocardium of rats dying during the experiment differed from that in survivors. The intensity of contractures and especially myocytolytic focal lesions was higher in the myocardium of rats which died. Catabolic processes in these animals were very intensive and by the moment of the lethal outcome (after 24 h on average) the density of myocytolysis foci was the same as on day 4 in survivors. These data indicate disordered pattern of post-stress rearrangement of the myocardium in animals with low resistance to stress. Presumably, myocardial resistance to stress is determined, among other things, by the initial level of its plastic reserve, which, in turn, seems to be genetically determined. These data provide the basis for studies of hereditary capacity of the organism with consideration for its stress resistance, development of life-time parameters of plastic reserve of the myocardium, and search for agents increasing plastic potential of the heart.

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