

EFFECT OF RADIAL ACCELERATION ON MORPHOLOGICAL AND BIOCHEMICAL CHANGES IN THE CARDIOVASCULAR SYSTEM OF DOGS WITH EXPERIMENTAL HYPERCHOLESTEREMIA

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Dogs receiving cholesterol (without methylthiouracil) and subjected for long periods to the action of radial acceleration develop lesions mainly in the small intrinsic arteries of the heart, kidneys, and thyroid.

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Investigations have demonstrated an increase in the blood cholesterol, a decrease in the lecithin/cholesterol ratio, and the earlier development of atherosclerosis in persons exposed to extreme factors of flight [7, 9, etc.].

Accordingly, in the present investigation the pathological changes arising in the cardiovascular system of dogs with experimental hypercholesteremia and exposed to the prolonged action of overloading were studied.

EXPERIMENTAL METHOD

Experiments were performed on 18 adult dogs. Some of the animals (6) were exposed for long periods to repeated radial acceleration (for up to 2 years, 8 g, duration 3 min) with intervals of between 1 day and 2-3 months between exposures. Four dogs were fed with cholesterol (2 g/kg body weight) for 4-5 months against the background of acceleration.

Twelve dogs with experimental atherosclerosis (L. A. Shekun's modification of the model of Steiner and Kendall) were used as controls. The aorta and main arteries including their branches within the organs were studied morphologically; in the heart, the orifices of the coronary arteries and their branches, the wall of the left and right ventricles, and the papillary muscles were so investigated.

The following histological and histochemical methods were used: staining with Sudan III, hematoxylin-eosin, picrofuchsin by Van Gieson's method, fuchselin, toluidine blue, alcian blue, and for glycogen by Shabadash's method. For demonstration of the localization of lipid deposits in the heart and aorta, total preparations were stained with Sudan.

For the biochemical investigations the heart was extracted from the dogs under ether anesthesia with artificial respiration. The tissue was treated in a cold room ($\pm 2^\circ$). The protein fractions of the myocardium and the myosin content were determined by I. I. Ivanov's method [5], the ATPase activity of the actomyosin and myosin was investigated by P. M. Zubenko's method [4], followed by determination of phosphorus by Lowry's method [11], and the content of free sulfhydryl groups are determined by the nitroprusside method as modified by F. F. Poglazov [6]. Cholinesterase activity was estimated from the amount of acetylcholine hydrolyzed by 1 g tissue during incubation for 1 h at 60° . The residual acetylcholine after incubation was estimated by Hestrin's method [10].

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TABLE 1. Morphological Changes in Vessels of Dogs with Experimental Hypercholesteremia Exposed to Radial Acceleration

Animals' name	Exptl. conditions	Cholesterol content during whole period (in g)	Duration of experiment (in months)	Blood pressure at end of expt. (in mm)	Morphological changes					small branches of coronary artery (papillary muscle)
					aorta	small arteries of kidneys	small arteries of thyroid	large coronary arteries		
Valet	Radial acceleration and cholesterol	2880	12	170	+	+	-	-	++	
Nora		2881	12	174	+	+	-	+	++	
Yunets		1610	19	174	-	-	-	-	+	
Pirat		6240	25	-	++	+	+	+	+++	
Sivyl	Radial acceleration	-	10	154	+	-	-	-	++	
Dzhek			24	150	-	-	-	-	±	
Ugolek	Cholesterol, methylthiouracil, and vitamin D ₂	5860	6	150	+	±	±	-	+	
Druzhek		8250	12	150	++	++	++	++	-	
Reks		8700	12	150	+	+	-	-	±	
Yunets		22,920	35	110	++	+++	+++	++	+++	
Lis	Cholesterol	3170	9	150	+	-	-	+	-	

Legend: + accumulation of interstitial material in intima and punctuate infiltration with lipids; - absence of changes; ± thickening of vessel wall and accumulation of interstitial material; +++ marked changes consisting of atherosclerotic plaques.

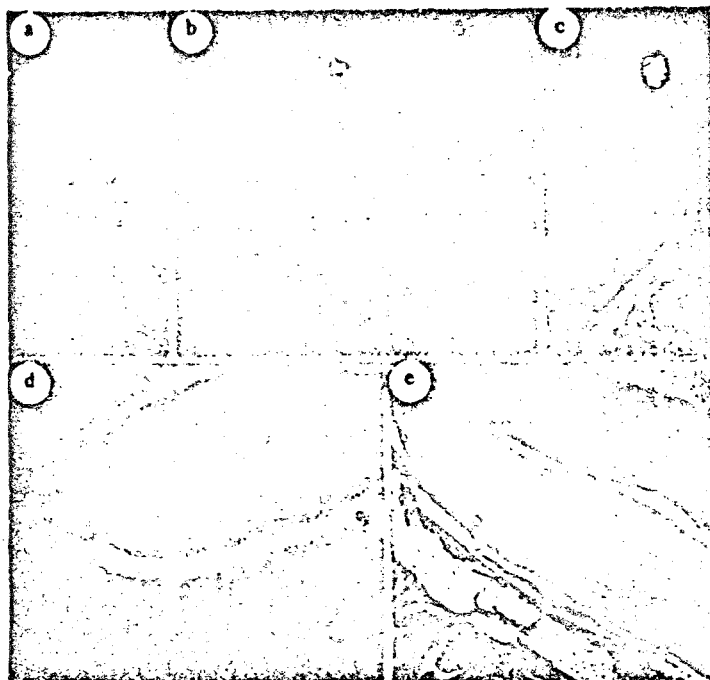


Fig. 1. Left ventricle. a) Thickening of walls of coronary arteries with marked constriction of lumen. Van Gieson, objective 10, ocular 10; b, c) plaque-like thickenings of intima with signs of xanthomatosis. The same preparation. Objective 40, ocular 10; d) infiltration of intima and media of vessel with lipids. Sudan III, objective 40, ocular 10; e) disturbance of structure of inner elastic membrane in thickenings of intima. Fuchselin, objective 20, ocular 10.

EXPERIMENTAL RESULTS

Thickening of the intima and focal lipoidosis of the walls of the aorta and of the small arteries of the kidneys and thyroid were found in the dogs receiving cholesterol and simultaneously exposed to radial acceleration (Table 1). Lipid infiltration was preceded by the accumulation of interstitial material in the intima of the vessels with an increased content of acid mucopolysaccharides, in agreement with results obtained by other workers [2, 3, 8]. The changes found in the small and medium-sized intramuscular branches (diameter 54-270 μ) of the coronary arteries were particularly noteworthy. The lumen of these vessels was greatly narrowed by plaque-like thickenings of intima containing lipids and collections of lipid macrophages (Fig. 1). The glycogen content in the myocardium and liver of the animals was reduced.

In the dogs Sivy1 and Dzhek (acceleration control) an increase in the content of interstitial material and punctuate infiltration of the thickened intima with lipids also were observed in some blood vessels.

In one of these cases a connective-tissue scar was found in the left posterior papillary muscle in the region of the modified arteries.

In the dogs receiving cholesterol combined with methylthiouracil and vitamin D₂, the aorta and the small arteries within the organs were affected to a greater degree. In the heart the changes were localized mainly in the orifices of the coronary arteries and of their subepicardial branches. No changes were seen in the dog Lis, which received cholesterol alone.

Biochemical investigation of the myocardium after exposure of the dogs to radial acceleration revealed an increase in the content of sarcoplasmic proteins in the left ventricle (from 8.5-8.7 mg nitrogen/g moist weight of tissue under normal conditions to 10.7-11 mg after exposure). The total nitrogen level of the tissue (26.9 mg/g tissue), of myofibrillary proteins (8.5-9 mg/g tissue), and of actomyosin (6-6.3 mg/g tissue) in the left and right ventricles remained unchanged. The myosin content rose slightly

in the left ventricle (1.9-2.1 mg/g tissue). However, the character of the contractile protein was considerably modified. The ATPase activity of the myosin was increased — by 74% in the left ventricle and by 42% in the right. The total content of free SH-groups of myosin was increased — by 57% (from 0.03 to 0.047 μ mole/mg protein) in the left ventricle and by 22% in the right. The content of SH-groups of myosin capable of fixing ATP increased in the ventricles by 30-35%. The cholinesterase activity of the myocardial tissue rose to twice the normal level.

Hence, animals exposed to the repeated action of radial acceleration and receiving cholesterol with the diet developed changes characteristic of atherosclerosis mainly in the intramuscular branches of the coronary arteries. The dose of cholesterol received by the dogs exposed to radial acceleration was much smaller than that received by the animals treated with cholesterol together with 6-methylthiouracil. It is particularly important to note that the animals of group 1 did not receive 6-methylthiouracil.

The increase in the level of sarcoplasmic proteins in the left ventricle could to some extent be attributed to an increase in the content of oxido-reductases, which are concentrated mainly in the sarcoplasmic proteins. The increase in ATPase activity of myosin and the increase in its content of SH-groups demonstrate increased ability of the myocardium to utilize the energy of high-energy phosphorus compounds. The increase in cholinesterase activity which we observed often accompanies increased excitability of the myocardium.

Atherosclerosis in dogs develops only when a high-cholesterol diet is combined with various additional procedures inhibiting thyroid function. In our experiments, severe atherosclerotic changes were found in the aorta and the small intrinsic arteries of the kidneys, thyroid, heart, etc. of dogs receiving cholesterol together with 6-methylthiouracil. The severity of the process varied with the duration of the experiment.

When the animals were exposed repeatedly to radial acceleration, administration of cholesterol alone with the diet in a smaller dose and without 6-methylthiouracil led to the development of atherosclerotic changes in the intramural branches of the coronary arteries, mainly in the posterior papillary muscle of the left ventricle.

Changes in the ground substance of the blood vessel walls took the form of an accumulation of acid mucopolysaccharides, mostly esterified with sulfuric acid, and they preceded deposition of lipids in them.

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