THE EFFECT OF PHYSICAL STRAIN ON THE DEVELOPMENT OF EXPERIMENTALLY INDUCED ATHEROSCLEROSIS

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The effect of physical exertion on the development of atherosclerosis has not yet been studied systematically. Observations reported in the literature show that atherosclerosis is less frequent and less pronounced in persons who do physical work and lead active lives than in persons who do intellectual work and lead sedentary lives; the coronary arteries of persons in the latter group are particularly likely to be affected. Ia. L. Rappoport [2] found severe atherosclerosis to be 3 times more common in persons doing intellectual work than in persons doing physical work.

We found no reports in the literature of experimental investigation of this matter and therefore determined to study the effect of physical exertion on the rate of development, the degree, and the character of atherosclerosis of the aorta and coronary arteries, using N. N. Anichkov's cholesterol-feeding technique for inducing atherosclerosis.

EXPERIMENTAL METHODS

Our experiments were performed on 45 rabbits of the same breed which had been kept under identical conditions and fed a standard diet; each rabbit weighed from 2000 to 2500 g. We induced atherosclerosis of the aorta and coronary arteries by feeding the rabbits a 10% solution of cholesterol in vegetable oil daily for six months (this corresponded to 0.3 g of cholesterol per kg of body weight).

For physical exertion the rabbits were made to run daily on an electrically driven wheel during the whole course of the experiment. After each cholesterol feeding rabbits were made to run on the wheel until they began to become exhausted. This usually required from 5 to 7 minutes of running, with the wheel making 12 revolutions per minute; since the inner circumference of the wheel was 4 m 75 cm, the rabbits ran 57 m per minute.

The experimental animals were divided into 3 groups. The rabbits of group I, the control group (12 rabbits), were fed cholesterol but were not made to exercise. The rabbits of group II (25 rabbits) were fed cholesterol and were also made to exercise. The rabbits of group III (8 rabbits) were made to exercise but were not fed cholesterol.

Twice a month we measured the blood cholesterol of all the rabbits, using Grigaut's method. At the beginning and at the end of the experiment the activity of the thyroid gland of 25 rabbits (10 from group I, 15 from group II) was studied by means of radioactive iodine, I^{131}. At the end of the experiment all the animals were killed by the injection of air into an ear vein. The aorta and heart were removed from each animal. The aorta was stained in toto with Sudan III. The heart was studied in serial sections in the usual way. We indicated the degree of atherosclerosis of the aorta and coronary arteries which we found with plus marks: + slight, ++ moderate, +++ pronounced alterations.

EXPERIMENTAL RESULTS

Twelve animals died in the course of the experiment: 1 rabbit of group I (of pneumonia), and 11 rabbits of group II. These animals died during the 3rd, 4th, and 5th months of the experiment. Electrocardiographic examinations showed that before their death the animals were suffering from acute coronary insufficiency. Histological study of the heart disclosed extensive areas of necrosis in the muscle of the left and, less often, of the right ventricles; in one case an acute aneurysm of the heart was found in a necrotic area.

The rabbits of group II died at different times during the period of cholesterol feeding (during the 3rd, 4th, and 5th months), but in order to compare the degree of atherosclerosis which developed in the rabbits of group II with that which developed in the rabbits of group I it was necessary to study all animals which had been fed cholesterol for 6 months. In this report we will consider only the 14 rabbits (out of the original 24) of group II which did not die during the experiment but which were killed at the end of 6 months (our study of the myocardium of all the rabbits used in the experiment is described in a separate report).

In group I (rabbits which were fed cholesterol but not made to exercise) the blood cholesterol rose quickly to high values, to as much as 1730 mg % in individual cases, and to an average of 1028 mg %; afterwards it fell gradually to an average of 627 mg % at the end of the experiment.

In group II (rabbits which were fed cholesterol and also made to exercise) the blood cholesterol was considerably lower than that of the rabbits of group I; in most cases it did not exceed 600-700 mg % (Fig. 1), toward the end of the experiment it fell to an average of 310 mg %. The blood cholesterol of the rabbits in group III (rabbits which were not fed cholesterol) varied within normal limits.

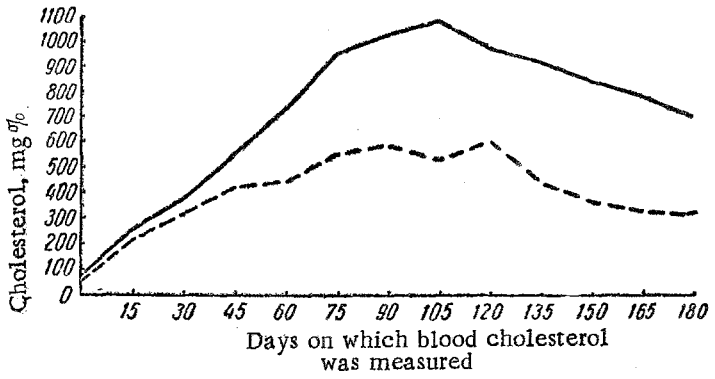

Fig. 1. The effect of physical exertion on the development of hypercholesterolemia.
---Cholesterol and exercise; ——cholesterol only.

TABLE 1

Changes in Blood Cholesterol Following Physical Exertion

Nos. of the rabbits of Group II	Cholesterol in mg %			Nos. of Group III rabbits	Cholesterol in mg %			Nos. of healthy rabbits	Cholesterol in mg %	
	before exercise	immediately after exercise	3 hr. after exercise		before exercise	immediately after exercise	3 hr. after exercise		before being placed on wheel	after being placed on wheel
165	218	280	210	150	96	90	86	218	48	72
168	324	412	286	166	100	62	74	219	60	86
171	376	424	318	167	68	54	62	220	82	108
172	390	438	362	181	108	98	94			
191	640	712	574	182	88	88	80			
193	764	820	640	183	72	64	68			

A review of the literature on this subject shows that different authors have reached conflicting conclusions about the effect of physical activity on blood cholesterol and phospholipids. Chailley-Bert, P. Labignette, and Fabre-Chevalier [6] observed a fall in blood cholesterol in persons who changed from a sedentary to an active life and who took up sport. E. S. Mnukhina [1], in careful experiments on rats, found that muscular exertion of short duration was associated with an increase in phospholipids and cholesterol in the muscles, but that muscular exertion over a long period of time resulted in a fall in blood phospholipids and cholesterol. She concluded that muscular activity involves consumption by the active muscles of lipids and of cholesterol. However, G. Amelotti [3] found in experiments on rats that rapid exhaustion leads to a fall in the blood lipids, and slow exhaustion to a rise.

Inasmuch as all of the authors just mentioned conducted careful research, we decided to study the blood cholesterol of our rabbits immediately after they had been exercised. We measured the blood cholesterol of 6 rabbits of group II and 6 rabbits of group III before exercise, immediately afterwards, and 3 hours afterwards (Table 1). We found that the blood cholesterol of the rabbits of group III (which had not been fed cholesterol) fell immediately after exercise.

The blood cholesterol of the rabbits of group II (which had been fed cholesterol) rose immediately after exercise, but three hours later fell to below its original level. We made these investigations during the fourth and fifth months of the experiment, when the rabbits had become used to running on the wheel; we can therefore exclude the operation of emotional factors which, as several investigators have shown [7-9], cause a temporary rise in blood cholesterol. That emotional factors did not play a role is further shown by the fact that the

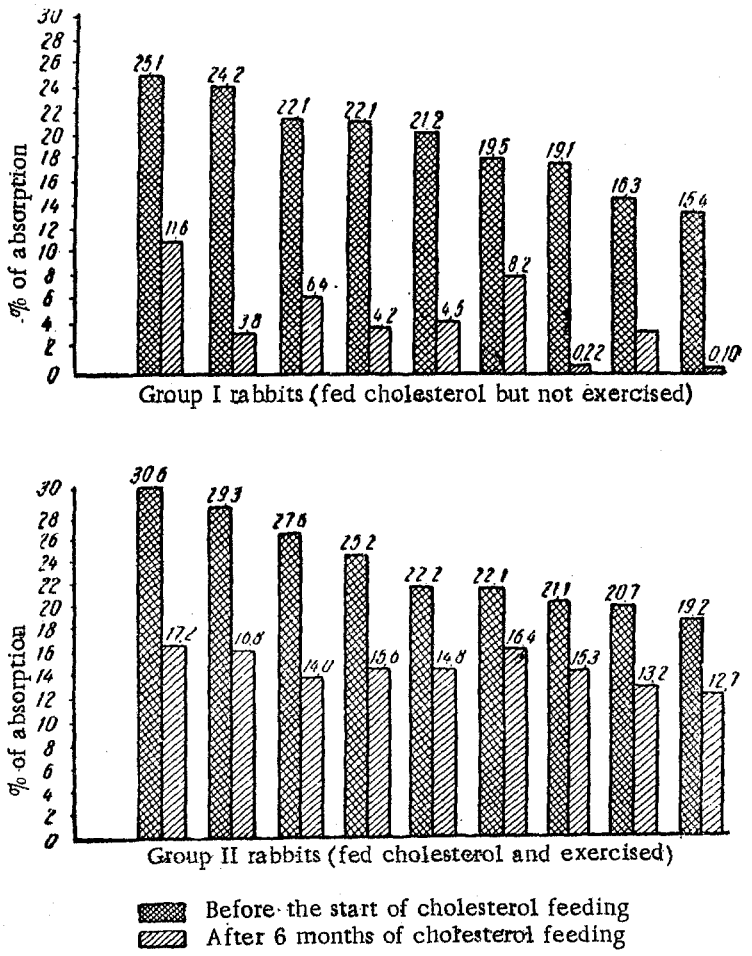

Fig. 2. Absorption of radioactive iodine (I^{131}) by the thyroid gland of rabbits of groups I and II.

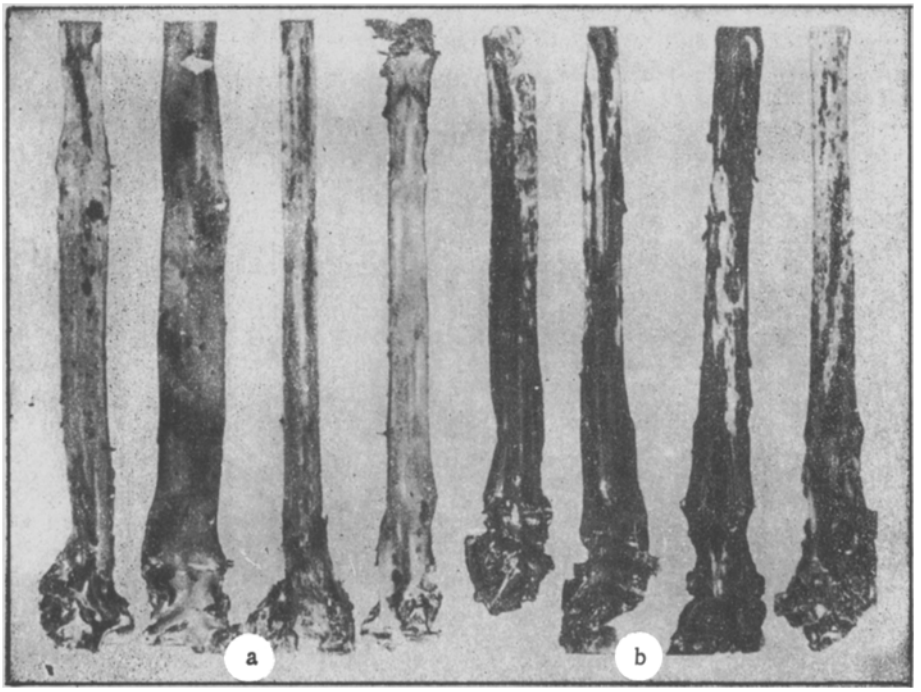

Fig. 3. Aortas of rabbits which had been fed cholesterol and made to exercise (a), and aortas of rabbits which had been fed cholesterol but not made to exercise (b).

blood cholesterol of the rabbits of group III fell immediately after exercise.

In addition we placed 3 healthy rabbits on the wheel and found a temporary rise in their blood cholesterol, which can only be explained by the operation of emotional factors (reaction to the noise of the motor, the motion of the wheel). In exact experiments in which animals are made to do exercise of a type to which they are unaccustomed, the emotional element must be taken into account.

Our findings, that rabbits fed cholesterol and made to exercise developed hypercholesterolemia more slowly and had lower levels of blood cholesterol, may be explained by an increased consumption of cholesterol by active muscles, with a consequent lowering of its level in the blood. Several authors are of this opinion [1, 4, 5].

In our study of thyroid functioning by means of I^{131} we found in the rabbits of group I (which had been fed cholesterol but not made to exercise) a great decrease in radioactive iodine absorption toward the end of the experiment, whereas the decrease in the case of the rabbits of group II (which were fed cholesterol and made to exercise) was unimportant (Fig. 2).

As is known, muscular activity increases the activity of the endocrine glands, particularly the thyroid gland, and causes an acceleration of the metabolic processes of the organism.

Atherosclerosis of the aorta was very marked in the rabbits of group I (which had been fed cholesterol but not made to exercise). Large confluent atheromatous plaques were prominent on the surface of the aorta all along its length and were particularly extensive in the arch and ascending branch. We evaluated the atherosclerosis of this group at +++ (Fig. 3).

We also found marked atherosclerosis of the coronary arteries, mainly in the intramyocardial branches. The atheromatous plaques greatly narrowed the lumen of the vessels. In the large subepicardial branches we more often found lipid infiltration of the intima, although very large atheromatous plaques did occur in some of the animals. We evaluated the atherosclerosis of the coronary arteries at ++.

In examining the aortas of the rabbits of group II (which had been fed cholesterol and made to exercise) we found remarkably little atherosclerosis in most cases. The occasional atheromatous plaques were situated

TABLE 2

Atherosclerosis of the Aorta and Coronary Arteries (Group I: control group, rabbits fed cholesterol; Group II: rabbits fed cholesterol and made to exercise)

Nos. of rabbits group I	Atherosclerosis		Nos. of rabbits group II	Atherosclerosis	
	aorta	coronary arteries		aorta	coronary arteries
120	+++	++	165	+	+
121	+++	++	168	+	+
122	+++	++	171	+	+
123	+++	++	172	+	+
125	+++	++	175	+	++
126	+++	++	177	++	++
127	+++	++	179	+	++
128	+++	++	186	+	+
129	++	+	188	+	+
130	+++	+	190	++	++
131	+++	++	191	++	++
132	++	+	102	+	+
			193	++	++
			194	++	++

mainly in the ascending branch of the aorta, in the arch, and at the orifices of the intercostal arteries. We evaluated most cases of atherosclerosis of the aorta in group II at +, the remainder at ++ (Table 2).

Atherosclerosis of the coronary arteries in group II affected mainly the intramyocardial branches of the left and, less often, the right coronary arteries. There were no atheromatous plaques in the large subepicardial branches.

We thus found the same range of atherosclerotic changes (+ and ++) in the coronary arteries of the rabbits of group I and group II.

However, the proportion of animals with only slight alterations of the coronary arteries (+) was much higher (7 out of 14) in the group which had been made to exercise (group II) than in the control group (group I), which had not been made to exercise (3 out of 12).

The relatively small difference in the atherosclerotic changes in the coronary arteries of the two groups of rabbits can be explained be the heavy functional load on the coronary circulation of the rabbits which were made to exercise. This explanation is in agreement with the findings of M. Schmidtmann [11] and E. Pfleiderer [10].

Our findings support the view that daily physical exercise hinders the development of hypercholesterolemia. This effect appears to be associated with increased activity of the thyroid gland, which occurs in connection with physical exertion. The physical exercise done by one group of cholesterol-fed rabbits resulted in these rabbits developing less atherosclerosis of the aorta than did a control group of cholesterol-fed rabbits which did not do exercise and which developed pronounced atherosclerosis of the aorta. The difference between the two groups in the development of atherosclerosis of the coronary arteries was less significant, probably because of the heavy functional load on the coronary circulation of the rabbits which were made to exercise.

SUMMARY

The effect of physical strain on the development of atherosclerosis of the aorta and of the coronary arteries was studied in rabbits.

It was established that physical exercises (daily running of rabbits) combined with cholesterol feeding

inhibits the development of hypercholesterolemia and, therefore, the development of aortic atherosclerosis is not very intense. The activity of the thyroid gland is increased under the effect of physical strain. This possibly has an effect on the condition of lipid metabolism.

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