THE INVOLUTION OF EXPERIMENTAL CHOLESTEROL ATHEROSCLEROSIS IN DOGS

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In investigations carried out on ten male dogs, three to four years of age, we established the dynamics of change in certain hemodynamic indices during the development of experimental cholesterol atherosclerosis and compared them with biochemical, pathologicoanatomic and histological data [3, 4].

This article presents the results obtained from investigations carried out on dogs after the animals had been fed cholesterol and 6-methylthiouracil for a 120-day period. The purpose of these experiments was to demonstrate the dynamics of the involution of functional and morphological changes caused by experimental athero sclerosis.

To this end, we continued to examine the dogs by every method at our disposal after the termination of the cholesterol and 6-methylthiouracil feeding period.

A month after we discontinued feeding the above substances to the animals, the general condition of the dogs began to improve gradually. The animals became more alert to their surroundings and considerably more active, and the hypothyroid symptoms decreased quite sharply. Dyspnea developed less frequently.

Cholesteremia decreased considerably, but continued to exceed the original levels, being on the average, double the latter. The maximal arterial pressure continued, as in the primary experiment, to vary from measurement to measurement. Some improvement was observed in the indices of the ballistocardiograms and electrocardiograms. An increase was observed on the ballistocardiograms in the amplitude of the waves, which was decreased during the feeding period, while the electrocardiograms showed an increase in voltage of the waves in all leads. The expansion rate of the pulse wave in the dogs did not change after we stepped feeding them cholesterol and 6-methylthiouracil.

From the works of N. N. Anichkov's school [1] and those of other researchers [5], it is known that the vascular changes which develop in experimental cholesterol atherosclerosis of rabbits and dogs undergo involution and, therefore, that atherosclerosis is a reversible process. On the basis of this very important concept, complex investigation of two dogs of the same series was continued for six months; the administration to them of cholesterol and 6-methylthiouracil was then discontinued.

We continued for six months to record the electrocardiogram (in three standard leads) and the ballistocardiogram, to determine the spread velocity of the pulse wave and to measure the maximal arterial pressure before and after the infliction of a physical load on these dogs (No. 9 and No. 10). The physical load inflicted consisted of a five minute run on a treadmill, the belt of which moved at a rate of 6.5 km/hr. We continued regular determinations of the cholesterol content of the animals' blood (using Grigo's method).

Definite signs of the involution of atherosclerosis were observed during our six-month observation of dogs No. 9 and No. 10. The dogs became lively and cheerful; they reacted to changes in their environment and showed signs of playfulness. The weight of the dogs (Table 1), which had decreased during the feeding period, began to increase slowly, but six months after the end of the feeding period was still 1.5-2 kg less than it had been before cholesterol feeding.

The cholesterol content of the blood returned to the original levels two months after the end of the feeding period and then remained stable from this time on (Table 2). The maintenance of an increased level of cholesteremia for a considerable period following the end of the cholesterol and 6-methylthiouracil feeding period is interesting.

The persistence of hypercholesteremia for two months after the administration of cholesterol to the experimental animals was discontinued indicated, in our opinion, that this condition was not caused simply by the organ-

TABLE 1. Weight of Dogs (in kilograms) during Involution of Atherosclerosis

Animal No.	Weight at end of feeding period	Change in weight after feeding period					
		after 1 month	after 2 mos	after 3 mos	after 4 mos	after 5 mos	after 6 mos
9	17.0	17.4	18.0	18.2	19.1	19.4	19.5
10	17.5	17.0	17.7	18.0	19.7	19.2	19.4

TABLE 2. Cholesterol Content (in mg%) in the Blood of Dogs during Involution of Atherosclerosis

Animal No.	End of feeding period	Months following					
		1	2	3	4	5	6
9	504	216	180	132	144	144	144
10	240	180	168	144	132	156	144

ism's increased intake of cholesterol. The organism's reaction to the cholesterol overload was evidently associated with a more profound disturbance of the animal's metabolic processes, primarily, the processes of lipoid-cholesterol metabolism. During the initial period following the end of 6-methylthiouracil administration, however, the hormonogenic function of the thyriod gland remained depressed, so that the cholesterol content of the blood could have continued to be increased.

The maximal arterial pressure continued to fluctuate within the physiologic range from experiment to experiment as it did during the preliminary investigation and during the period the animals were fed cholesterol and 6-methylthiouracil [3]. No stable increase in the blood pressure was observed, although it usually increased somewhat after the treadmill run.

After the cholesterol and 6-methylthiouracil feeding of the animals was stopped, the dogs' ballistocardiograms, which had shown considerable changes during the feeding period [4], approximated the original indices more rapidly and more completely than did the electrocardiograms.

Six months after the animals were last fed the experimental substances, their ballistocardiograms were still somewhat flattened (Fig. 1). The electrocardiograms of these dogs continued, as during the feeding period , to differ considerably from the initial recordings (Fig. 2).

The electrocardiogram continued to show the inversion of the T wave in the second and third leads, flattening of the P wave and biphasic state of these waves, and these were particularly marked after the physical load. According to the ballistocardiographic data, therefore, normalization of the contractile function of the myocardium occurred more fully and rapidly than was evident from the electrocardiograms, in which the changes remained considerable. These facts are very important to the prognosis of the clinical course of atherosclerosis. During the six-month period of involution of the atherosclerotic changes, the spread velocity of the pulse wave continued to be, as before, 7.05-10.8 m/sec [4].

Dogs No. 9 and No. 10 were killed at the conclusion of the experiment.

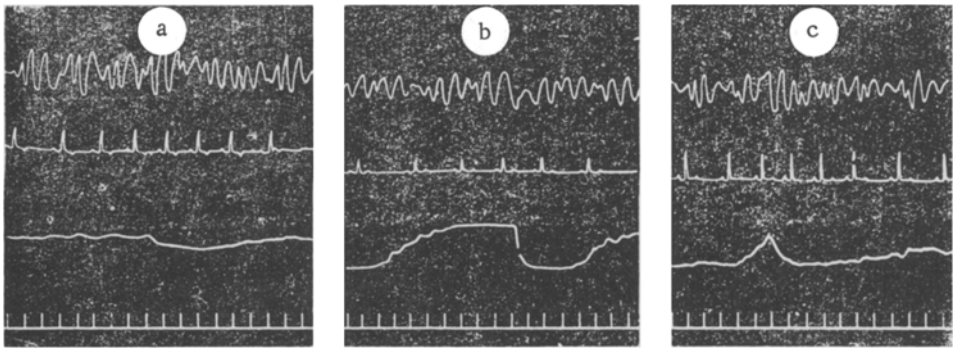

Fig. 1. Change in direct ballistocardiogram of heart rate of dog No. 9 under the different experimental conditions. a) Before feeding; b) during feeding; c) six months after the administration of cholesterol and 6-methylthiouracil was stopped. Curves (from top to bottom) represent: ballistocardiogram; lead II of ECG; respiration; time in $^1/_4$ - second marks.

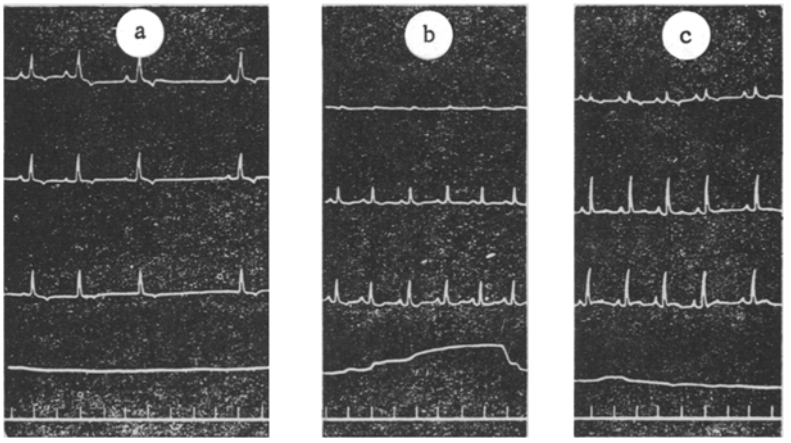

Fig. 2. Electrocardiogram of dog No. 9 under different experimental conditions. a) Before feeding; b) during feeding; c) six months after the administration of cholestrol and 6-methylthiouracil was stopped. Curves (from top to bottom) represent: ballistocardiogram; lead II of ECG; respiration; time in $^1/_4$-second marks.

Pathologico-anatomic and histological investigations of the cardiovascular system and internal organs of these dogs, performed six months after the end of the cholesterol and 6-methylthiouracil feeding period, disclosed that all the changes found earlier in the other animals of this series were considerably less pronounced in these two dogs [3]. The small quantity of atherosclerotic plaques found on the internal surface of the aorta, carotid and other arteries contained very little fat and were observed to be in a state of cicatrization. The fat deposits had disappeared almost completely from the internal organs. The microscopic picture of the thyroid gland, which (in the other dogs of the series and the dogs of the control group which had received 1.5 g of 6-methylthiouracil apiece) had a characteristic structure during the administration of 6-methylthiouracil [3], was fully normalized. Slight sclerotic changes were observed in the liver; still less expressed sclerotic changes were found in the heart muscle. The latter explain the presence of stable changes on the electrocardiograms of these dogs six months after the last feeding of cholesterol and 6-methylthiouracil to the animals.

Macroscopic and microscopic morphological investigations, performed a month after the last cholesterol and 6-methylthiouracil feeding, showed a picture of extensive atherosclerosis in all the animals of this series [3].

SUMMARY

Over a six-month period following the end of the cholesterol and 6-methylthiouracil feeding period, the ballistocardiographic changes in dogs went back more rapidly and more completely to the initial level than the electrocardiographic changes.

Pathological and histological investigations of the cardiovascular system and internal organs of these animals showed involution of atherosclerotic lesions.

High blood cholesterol 2 months after the administration of cholesterol was stopped points to important metabolic damage.

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