

THE INFLUENCE OF THYROIDIN ON TISSUE CHOLESTEROL IN EXPERIMENTAL ATHEROSCLEROSIS

A. L. Myasnikov and V. F. Zaitsev

Institute of Therapy (Director, Active Member AMN SSSR A. L. Myasnikov),
AMN SSSR, Moscow

(Presented by Active Member AMN SSSR A. L. Myasnikov)

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It has long been thought that in humans hyperthyroidism prevents the development of an increased blood cholesterol and atherosclerosis. It has been shown experimentally [3, 4] that thyroidin prevents the development of alimentary atherosclerosis in rabbits and accelerates recovery from it. The effect of powdered thyroid gland on rabbits is to reduce the amount of cholesterol in the blood and in the aorta [5]. The mechanism of the influence of thyroid hormones on cholesterol metabolism has been interpreted in various ways. Evidently under the influence of the hormone there is a change either of cholesterol metabolism as a whole [2] or a change in the function of some organ or other related to this metabolism. It is on this account that we have undertaken a study of the influence of thyroidin on the amount of cholesterol in the tissues of various organs.

We have studied the influence of this hormone on total blood cholesterol and in the cholesterol of the organs of rabbits maintained either on a normal diet or on a diet inducing atherosclerosis.

EXPERIMENTAL METHOD

The experiments were carried on 30 chinchilla rabbits weighing from 2.5 to 3 kg. In the first set of experiments 12 animals were maintained on a normal diet, and of these 6 received 0.06 g/kg weight for 45 days. In the second set of experiments 18 rabbits received 0.2 g/kg weight for 45 days, and of this group 8 animals in addition received 0.06 g/kg of thyroidin at the same time. The total blood cholesterol was determined at the start and at the end of the experiment. On the 46th day the animals were killed by the injection of air. After death we determined the amount of cholesterol in the aorta, liver, adrenals, and brain. The organs were washed free from blood by perfusion, carefully separated from the surrounding tissues, and the adventitia was removed from the aorta. The organs were then dried by warming in a vacuum to a constant weight, and then were dissolved in alkali. Total cholesterol was determined and referred to 100 mg of dried tissue. The cholesterol was extracted with a 2 : 1 mixture of chloroform and methanol. The amount was determined calorimetrically by the Lieberman-Burchard method.

EXPERIMENTAL RESULTS

In rabbits kept on a normal diet there was no change in the amount of blood cholesterol during the period of observation. In the healthy animals the mean level at the start was 70 ± 4.6 mg%, and at the end 69 ± 5.7 mg%; in the animals treated with thyroidin, the corresponding values were 67 ± 5 and 71 ± 5.9 mg% (see Table). The amount of cholesterol in the aorta, kidney, and brain of rabbits kept on a normal diet was also approximately the same both in healthy animals and in those receiving thyroidin. Only in the adrenals of the latter group was the cholesterol content somewhat increased.

In rabbits which received cholesterol for 45 days, i.e., in animals treated so as to produce atherosclerosis through the diet, the amount of blood cholesterol at the end was greatly enhanced (mean value ranged from 80 ± 5.1 to 1120 ± 137 mg%). In animals which received thyroidin together with the cholesterol blood cholesterol on the 45th day showed a small increase (on average from 70 ± 5.2 to 485 ± 96 mg%).

At postmortem in all the animals which received only cholesterol, scattered lipid plaques visible to the naked eye were present in the aorta (chiefly in the aortic arch), and at the origins in the aorta of the large arteries. In animals which received cholesterol and thyroidin simultaneously there were no directly visible changes. In the aorta of rabbits in which atherosclerosis had been induced there was a considerably greater amount of cholesterol than in

Effect of Thyroidin on the Cholesterol Content of the Blood and Organs

Rabbits	Number of rabbits	Mean blood cholesterol level at end of experiment (in mg%)	Mean amount of cholesterol per 100 mg of dried tissue (in mg)			
			Aorta	Liver	Adrenals	Brain
Healthy	6	69 ± 5.7	0.08 ± 0.007	0.26 ± 0.03	1.8 ± 0.4	1.7 ± 0.3
Receiving thyroidin	6	70 ± 5.8	0.10 ± 0.02	0.28 ± 0.03	5.1 ± 1.6	1.6 ± 0.3
Receiving cholesterol	10	1120 ± 137	0.24 ± 0.04	1.43 ± 0.3	10.6 ± 1.2	1.2 ± 0.2
Receiving cholesterol and thyroidin	8	480 ± 95	0.24 ± 0.04	3.48 ± 0.5	13.7 ± 1.0	2.0 ± 0.4

the aorta of healthy animals. In rabbits which received thyroidin in addition to the cholesterol, the amount of cholesterol in the aorta was the same as in those treated with cholesterol without thyroidin. Therefore, despite the fact that in the animals treated with cholesterol macroscopically visible lipid spots were present, and in rabbits which, in addition, received thyroidin there were no such visible changes, the amount of cholesterol per unit dry weight of the aorta were identical.

This method of referring to total cholesterol in terms of dry tissue revealed no appreciable difference in the amount of cholesterol in the aorta of rabbits treated with cholesterol alone or with cholesterol + thyroidin. Possibly the explanation is that the aorta normally contains cholesterol, and that in atherosclerosis induced by diet it is considerably enhanced (in our experiments it was increased three times). The effect of thyroidin on the cholesterol level in the aorta evidently conceals this great increase in total cholesterol when large amounts are given by mouth. Clearly the extent of development of atherosclerosis induced is determined not only by the total amount in the aorta. An estimate of the different influences in rabbits on the development of atherosclerosis according to the amount of cholesterol in the aorta (per unit weight of aorta) can be made only in the case of gross effects which alter the amount in the aorta by not less than 1½ times. The inaccuracy of the weighing method may explain the results obtained by K. G. Volkova [1] who failed to find any influence of ascorbic acid on the development of atherosclerosis in rabbits when she determined the "total lipid content" of the aorta.

The amount of cholesterol in the liver and adrenals of rabbits in which atherosclerosis had been induced dietetically was considerably greater than in healthy animals. It was greater still in those organs in animals which had received thyroidin, in addition to the cholesterol. Therefore the treatment with thyroidin under conditions in which atherosclerosis was induced by feeding cholesterol, besides preventing the development of hypercholesterolemia led to a considerable increase in the liver cholesterol content and a less marked increase in the adrenals and brain. The increased deposition of cholesterol in these organs under the influence of thyroidin may be one of the reasons for the reduced blood cholesterol. Under these conditions the greatest difference in the cholesterol content related to treatment with thyroidin was found in the liver. Probably under the influence of thyroidin the chief change in cholesterol metabolism occurs in the liver. The effect is to cause an increased accumulation of cholesterol in this organ, which leads subsequently to an increased secretion of cholesterol with the bile [7]. Our results confirm that the change of cholesterol metabolism induced by the thyroid hormone depends not only on an increased basal metabolic rate [6, 8], but also to a considerable extent on the influence of thyroidin on the liver.

SUMMARY

A study was made of the effect produced by thyroidin on blood cholesterol and on the cholesterol content of various organs of rabbits kept on the usual diet, and developing atherosclerosis induced dietetically. In rabbits kept on a normal diet administration of 0.06 g/kg thyroidin for 45 days did not influence the cholesterol content of the blood, aorta, liver, or brain, but did cause an increase in the adrenal glands.

When cholesterol was fed to animals for 45 days, the same doses of thyroidin caused a greater accumulation of cholesterol in the liver, adrenal glands, and brain than was found in animals given cholesterol alone. In the animals treated with thyroidin the increased blood cholesterol was prevented. When thyroidin and cholesterol were given no lipid plaques developed in the aorta, though they did when the rabbits received cholesterol alone. Nevertheless, the amount of cholesterol per unit dry weight of aorta was the same in both groups of animals.

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