

THE EFFECT OF THYROIDIN ON THE DEVELOPMENT OF HYPERCHOLESTEREMIA IN FASTING RABBITS

T. A. Mikhailova

Department of Biochemistry (Head — Professor S. V. Nedzvetskii),

Leningrad Sanitary-Hygiene Medical Institute

(Presented by Active Member AMN SSSR S. V. Anichkov)

Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*,

Vol. 54, No. 8, pp. 47-49, August, 1962

Original article submitted August 2, 1961

An interesting aspect of the study of cholesterol metabolism is the detailed elucidation of the role of thyroxin in this metabolism, for this hormone inhibits the development of alimentary hypercholesteremia and the development of atheromatous plaques [5].

We have studied the effect of the thyroid hormone on the hypercholesteremia arising in rabbits during fasting. This hypercholesteremia is a convenient model, for it appears readily and it disappears equally quickly when the rabbit resumes its normal diet.

EXPERIMENTAL METHOD AND RESULTS

Experiments were conducted on rabbits weighing 1800-3000 g. Before the experiment, 7-8 ml of blood was taken from the heart of the fasting rabbit, and, thereafter, the animal received no food, but only water, for 5 days.

TABLE 1. Effect of Thyroidin on the Blood Cholesterol Concentration (mg%) in Fasting Rabbits

Expt. No.	Time of taking blood	Conditions of experiment	
		fast-ing	fasting + thyroidin
1	Before fasting	24.7	15.2
	On the 3rd day of fasting	88.2	28
	On the 5th day of fasting	88.2	24.2
2	Before fasting	44	34.1
	On the 3rd day of fasting	63	18.6
	On the 5th day of fasting	92.3	17.5
3	Before fasting	13	16.7
	On the 3rd day of fasting	57	28
	On the 5th day of fasting	105.2	24.3

On the third and fifth days of fasting, blood was again taken. The rabbit then resumed its normal diet. Two weeks later, a similar experiment was carried out on the same rabbit, the only difference being that during the 5 days of fasting the rabbit received thyroidin by mouth in a daily dose of 0.25 g/kg body weight. In all the blood samples, the concentration of cholesterol in the plasma was determined by Bloor's method. With some animals, the experiments were performed in the opposite order: First, with fasting plus administration of thyroidin and, 2 weeks later, fasting without administration of thyroidin. Experiments were carried out on 20 rabbits and the results were in good agreement. The results of the most characteristic experiments are shown in Table 1.

It will be seen from Table 1 that the administration of thyroidin to fasting rabbits inhibited the development of hypercholesteremia in these animals.

In order to elucidate the mechanism by which thyroidin inhibits the development of hypercholesteremia, we studied the changes in the cholesterol concentration in the organs of the experimental animals: in the liver, muscles, kidneys, and lungs.

The experiments were conducted as follows. On the 5th day of fasting, the rabbit was killed by air embolism. The organ was extracted and minced in the cold. From 3-5 ml of the resulting mince was hydrolyzed with 15 ml of a 15% solution of NaOH on a water bath for 6 h. The solution was neutralized with 20 ml of 25% H_2SO_4 [1]. Cholesterol was extracted from the solution with ether, and the cholesterol concentration in the ether extract was determined by Bloor's method.

The cholesterol concentration in the liver was studied in 16 rabbits, in the muscles in 8 rabbits, in the kidneys in 12 rabbits, and in the lungs in 10 rabbits. Corresponding control determinations were made in 11, 11, 11, and 8 rabbits. The results of three of the experiments are given in Table 2.

TABLE 2. Effect of Thyroidin on the Cholesterol Concentration (mg%) in the Liver, Muscles, Kidneys, and Lungs of the Fasting Rabbits

Experiment No.	Conditions of experiment							
	Fasting				Fasting + thyroidin			
	liver	muscles	kidneys	lungs	liver	muscles	kidneys	lungs
1	403	56.2	354	561	570	60.0	462	571
2	261	57.2	430	488	470	68.9	445	565
3	321	61.5	380	500	422	59.3	409	581
Mean	344 ± 22	55.9 ± 1.7	395 ± 13	515 ± 22	449 ± 40	65.8 ± 4.4	422 ± 13	549 ± 19

It may be seen from Table 2 that the cholesterol concentration in the liver of the fasting rabbits was increased after administration of thyroidin. The cholesterol concentration in the lungs, muscles, and kidneys, however, underwent only insignificant change. It is evident that the inhibition of the development of hypercholesteremia in fasting rabbits after administration of thyroidin takes place as a result of an increase in the cholesterol content in the liver, and also, possibly, on account of the consequent inhibition of cholesterol synthesis in the liver [6].

The cholesterol metabolism of fasting rabbits is severely disturbed: hypercholesteremia develops in the blood and the hydroxycholesterol concentration rises considerably [4]. We therefore were interested in determining whether hydroxycholesterol was present in the liver of the fasting rabbits receiving thyroidin.

Experiments were conducted as indicated above. The extraction of the lipids from the liver, and the chromatography on Al_2O_3 were carried out in accordance with the method described by S. V. Nedzvetskii and T. B. Lielup [2]. The hydroxycholesterol was estimated by means of Lifshits's reagent. Experiments were carried out on 3 rabbits and 2 rabbits were used as controls.

Irrespective of whether thyroidin was given or not, hydroxycholesterol was found in the ether-methanol extract of the liver of the fasting rabbits. It should be pointed out that in our earlier research [3] we did not find hydroxycholesterol in the liver of fasting rabbits; the explanation of this fact must be that the fasting of the animals was insufficient.

SUMMARY

A study was made of the effect produced by thyroidin on the development of hypercholesteremia in starving rabbits. Daily administration of thyroidin to starving rabbits (0.25 gm per kg of body weight) for 5 days inhibited the development of hypercholesteremia in them and increased cholesterol content in the liver. Oxycholesterol was revealed in the liver of both the starving rabbits to which thyroidin was given, and the starving rabbits without thyroidin administration.

LITERATURE CITED

1. V. N. Kolmakov, Vopr. Med. Khimii, No. 6, 414 (1957).
2. S. V. Nedzvetskii and T. B. Lielup, Biokhimiya, No. 2, 349 (1959).
3. S. V. Nedzvetskii and T. A. Mikhailova, Vopr. Med. Khimii, No. 4, 276 (1959).
4. M. N. Plyutach, 7-Hydroxycholesterol in the Blood of Animals. Authors' abstract of candidate's dissertation [in Russian] (Leningrad, 1955).
5. V. V. Tatarskii and V. D. Tsinzerling, Arkh. Pat., 1, 44 (1950).
6. I. D. Frantz, Jr., H. S. Schneider, and B. T. Hinkelman, J. Biol. Chem., 206, 465 (1954).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.