

THE EFFECT OF FASTING ON THE CHOLESTEROL METABOLISM

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The work of G. G. Samsonidze [4], S. V. Nedzvet-skiĭ and S. S. Dubova [3], Sugano and co-workers [7], and Bragdon and co-workers [5] has demonstrated the constant development of hypercholesteremia in fasting animals. Much doubt and controversy remains, however, on the question of the mechanism of this phenomenon. Since the liver plays an important part in cholesterol metabolism, we deemed it worth while to investigate the part played by this organ in the development of hypercholesteremia in fasting animals. In the present series of investigations, the following problems were studied: 1) the cholesterol content of the liver in normal conditions and during fasting; 2) the rate of incorporation of radioactive (1-C^{14}) acetate in the liver cholesterol in normal conditions and during fasting.

EXPERIMENTAL METHOD

Experiments were carried out on 18 rabbits (6 controls and 12 fasting animals). After fasting for different periods of time (6 and 12 hours), the rabbits received intraperitoneal injections of 2 ml of a solution of sodium acetate (1-C^{14}) in a dose of $50 \mu\text{C/kg}$ body weight. The rabbits were sacrificed by exsanguination (division of the major vessels of the neck) 4 hours after the moment of injection of the acetate. The liver was extracted as quickly as possible, frozen, and then minced. The cholesterol, extracted from the liver, was precipitated in the form of cholesterol digitonide. The activity of the latter was determined by means of an end-type counter on a "B2" apparatus. The total cholesterol content of the liver was determined by a modification of Sperry's method [6].

EXPERIMENTAL RESULTS

On analysis of the results presented in the table, the following conclusions emerge. Fasting had a very considerable effect on the total cholesterol content in the rabbits' livers. On the sixth day of starvation the cholesterol concentration in the liver exceeded that in the control animals by 60%, and on the 12th day, by 83%. After fasting for 24 days, the concentration of cholesterol in the liver was increased by approximately 150%.

The results of these investigations agree with those of other authors with respect to changes in the cholesterol content of the tissues. O. N. Abbakumova-Zepalova [2], for instance, found an increase in the cholesterol content of the muscles of fasting rats, K. V. Gordeeva [1] found an increased cholesterol concentration in the liver of dogs after fasting three days, and G. G. Samsonidze [4] found an increase in this compound in all the organs which he investigated, which included the liver. Fasting also has a strong influence on the synthesis of cholesterol in the liver. After injection of radioactive acetate, the relative activity of the liver cholesterol in the fasting rabbits in every experiment, without exception, was less than that in the controls. It may be seen from the table that the rate of incorporation of 1-C^{14} acetate in the liver cholesterol did not exceed 10-20% of that taking place in the rabbits which received a normal diet.

In our experiments, as was also observed in the researches of many other authors, fasting was accompanied by a sharp rise in the blood cholesterol. After 6 days of fasting, the total serum-cholesterol concentration exceeded the initial level, on the average, by 140%, and after 12 days, by 188%.

It should be pointed out that during investigation of dogs after fasting for 10 days, the changes in the blood cholesterol concentration were less marked than in rabbits. After administration of 1-C^{14} acetate to rabbits, radioactive cholesterol was found in the blood, although, as the figures in the table show, the relative activity of the serum cholesterol was very low, approximately $1/2$ - $1/3$ that of the cholesterol extracted from the liver. The ratio between the relative activities of the liver and serum cholesterol (4 hours after injection of radioactive acetate) was roughly the same in the normal and fasting animals.

In this investigation we discovered facts outwardly contradictory in their meaning. On the one hand, during fasting a considerable increase in the cholesterol concentration in the liver and blood was found. On the other hand, the synthesis of cholesterol in the liver (in so far as this could be judged by the rate of incorporation of C^{14} acetate) was greatly retarded. The question

Content and Relative Activity (in imp/min/mg) of the Cholesterol of the Liver and Serum

Animal No.	Total cholesterol (in mg%)		Relative activity of cholesterol		Note
	liver	serum	liver	serum	
1	302	73	93	29	Normal diet
2	216	66	59	27	"
3	237	81	104	36	"
4	271	62	77	41	"
5	177	78	61	24	"
6	186	74	89	39	"
Mean	231	72	80	32	
7	400	126	21	12	6 days of fasting
8	381	181	17	7	"
9	321	174	32	14	"
10	411	153	20	14	"
11	366	214	15	9	"
12	343	201	19	12	"
Mean	370	174	20	10	
13	387	252	18	8	12 days of fasting
14	466	212	21	6	"
15	399	191	26	9	"
16	424	222	16	12	"
17	496	175	12	10	"
18	368	197	19	9	"
Mean	423	208	18	9	

arises: how is it possible to explain the fact that the cholesterol content in the liver and blood is increased during fasting? In an attempt to answer this question, certain authors [4] have suggested that the increase in the cholesterol concentration during fasting takes place as the result of new formation of the compound in the liver. As the results of our investigations show (in agreement with those of several other authors) cholesterol synthesis in the liver during fasting is not only not increased but, quite the contrary, is considerably diminished. It might have been expected that, in fasting, the synthesis of cholesterol is intensified in other organs, from which it is taken in the blood stream to the liver. In this case the relative activity of the cholesterol of the blood would have been higher than, or at least equal to, the relative activity of the cholesterol of the liver; but, as our results show, the converse was in fact true. This supposition is thus not borne out by the facts. It is possible that the increase in the cholesterol concentration in the blood and liver is the result of a decrease in its breakdown or excretion from the body during fasting, but this is a matter for further research.

SUMMARY

The author studied the effect of starvation upon the cholesterol content in the liver and blood, as well as on cholesterol synthesis in the liver. 1-C¹⁴ sodium acetate was injected intraperitoneally into rabbits (50 µC

per kg of body weight). The animals were bled to death 4 hours after C¹⁴ administration. Cholesterol - C¹⁴ was isolated in the form of the digitonide. Starvation was connected with a considerable increase of cholesterol concentration in the blood and liver and with an acute reduction of the rate of cholesterol synthesis in the liver. The correlation between specific activities of the liver and blood serum cholesterol is about the same in normal and starving animals. The reduced cholesterol excretion and breakdown possibly causes a rise of its level in starving animals.

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