THE EFFECT OF CORN OIL ON THE DEVELOPMENT OF FATTY INFILTRATION OF THE LIVER AND ON THE BIOSYNTHESIS OF CHOLESTEROL IN EXPERIMENTAL ATHEROSCLEROSIS

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Fatty infiltration of the liver is the most constant feature of experimental lipoidosis in animals [4, 5, 7, 14]. As a rule the changes in the liver precede atherosclerosis of the aorta [1]. A. L. Myasnikov [3] found lipid inclusions in the liver cells of persons with a high blood cholesterol and cutaneous xanthomatosis. Consequently, the degree of fatty infiltration of the liver may be used as an index of the efficacy of agents used to produce experimental atherosclerosis. It is usual, however, in such cases to examine the morphological changes in the aorta and the coronary arteries only, and the study of the state of the liver has been neglected.

The object of our investigations was to compare the effect of corn oil and sunflower oil on the development of lipoidosis of the aorta and coronary arteries, and fatty infiltration of the liver, and the synthesis of endogenous cholesterol.

Vegetable oils, especially corn oil, are known to be beneficial in atherosclerosis [8, 10, 11].

EXPERIMENTAL METHOD

Experiments were carried out on 32 male chinchillas weighing 2.1-3.8 kg, kept in identical conditions and receiving a normal diet.

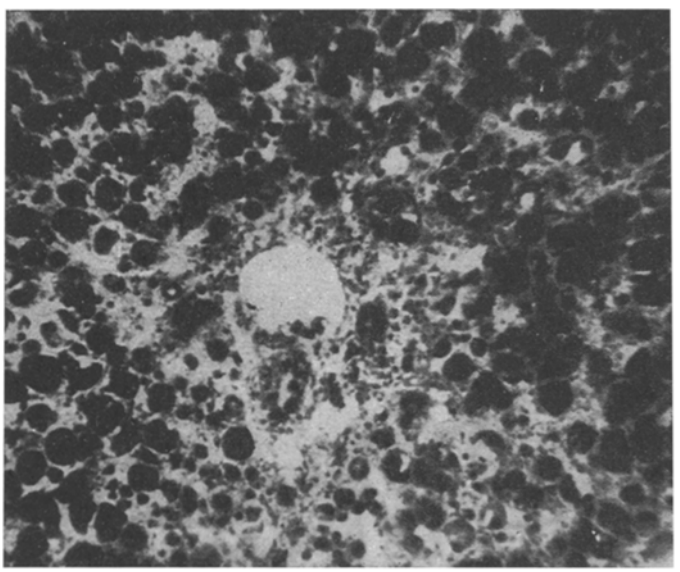

Fig. 1. Infiltration of liver cells of a rabbit with large droplets of fat on the 120th day of feeding with cholesterol in sunflower oil. Stained with Scharlach R and hematoxylin. Photomicrograph. Magnification 160×.

In the first series of investigations, with the object of producing atherosclerosis, 11 rabbits of the control group received 5% cholesterol solution daily in a dose of 0.2 g cholesterol in 4 ml sunflower oil per 1 kg body weight. The experimental animals (11) received the same dose of cholesterol, but in the form of a 5% solution in corn oil.

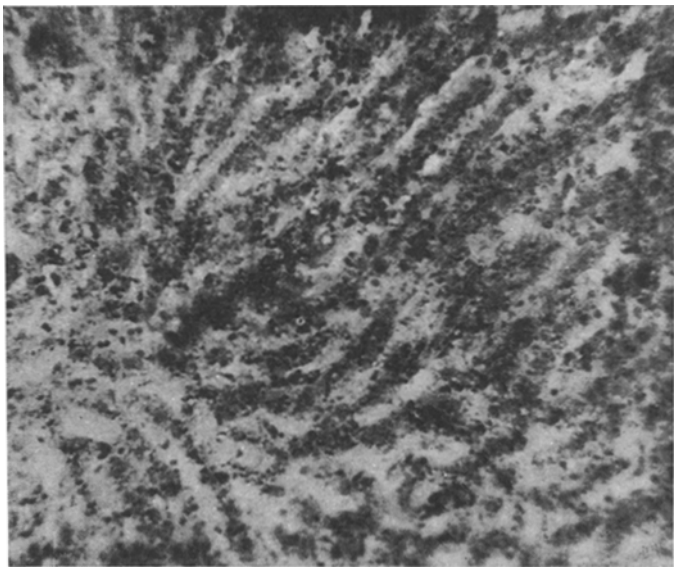

Fig. 2. Infiltration of liver cells of a rabbit with dust-like droplets of fat on the 120th day of feeding with cholesterol in corn oil. Stained with Scharlach R and hematoxylin. Photomicrograph. Magnification 160×.

At the end of the experimental period (4 months) the rabbits were sacrificed by air embolism, and the aorta, heart, and liver were extracted and fixed in 20% formalin solution. The aorta was stained in toto with Sudan III, and the changes observed in it were reproduced diagrammatically. Serial sections of the heart were stained with Sudan III and hematoxylin, and the degree of the atherosclerotic changes was studied under the microscope. Serial sections of the liver, stained with Scharlach R and hematoxylin were examined under the microscope and the degree of fatty infiltration assessed: First degree) slight, second degree) moderate, third degree) marked, and fourth degree) very marked fatty infiltration.

In the second series of investigations (10 rabbits) the rate of biosynthesis of cholesterol was studied by the method of labeled atoms. Three hours before they were sacrificed, all the animals received intraperitoneal injections of carbon-labeled acetate in a dose of 200 μC/kg body weight. The rabbits were sacrificed by air embolism, and the liver was extracted immediately from the peritoneal cavity and a sample weighing 1 g was taken. Cholesterol was extracted by the method of Sperry and Webb [12]. The cholesterol extracted from the liver was precipitated by a 1% solution of digitonin.

The activity of the extracted cholesterol was estimated by means of an end-type counter and a B-2 apparatus. The precipitate of cholesterol digitoninide was also used for determination of the total cholesterol in the liver by a cholorimetric method.

Before the labeled acetate experiments began, for 15-17 days all the animals received cholesterol daily through a gastric tube in a dose of 0.2 g/kg, dissolved in sunflower oil (control group) and in corn oil (experimental group).

EXPERIMENTAL RESULTS

We thought it would be interesting to compare the changes in the liver with the extent of the lipoidosis of the aorta and coronary arteries in the animals of each group, and then to compare one group with another (Tables 1 and 2).

TABLE 1. Degree of Development of Lipoidosis of the Aorta and Coronary Arteries and of Fatty Infiltration of the Liver in Rabbits Receiving Cholesterol in Sunflower Oil (Control Group)

Organ	Degree of lipoidosis and fatty infiltration				
	very marked (++++)	marked (+++)	moderate (++)	slight (+)	no changes
	No. of rabbits				
Aorta	4	3	2	2	–
Coronary arteries	3	4	2	2	–
Liver	2	5	3	1	–

TABLE 2. Degree of Development of Lipoidosis of the Aorta and Coronary Arteries and of Fatty Infiltration of the Liver in Rabbits Receiving Cholesterol in Corn Oil (Group of Experimental Animals)

Organ	Degree of lipoidosis and fatty infiltration				
	very marked (++++)	marked (+++)	moderate (++)	slight (+)	no changes
	No. of rabbits				
Aorta	1	1	1	2	6
Coronary arteries	1	1	1	2	6
Liver	1	3	5	–	2

It will be clear from Tables 1 and 2 that in all 11 rabbits of the control group atherosclerotic changes were found in the aorta and coronary arteries and fatty infiltration was present in the liver. In 7 of the 11 rabbits the atherosclerosis of the aorta and the coronary arteries was marked, and in the remainder the lipoidosis was slight. The same 7 rabbits showed a well marked diffuse infiltration of the liver cells and reticulo-endothelial cells with large droplets of fat as shown in Fig. 1.

A more moderate degree of involvement of the aorta, coronary arteries and liver would be observed in the rabbits receiving cholesterol in corn oil (Table 2).

TABLE 3. Content and Relative Activity of Cholesterol in the Liver of Rabbits on the 15th-17th Day of Feeding on Cholesterol in Sunflower Oil (Controls) and in Corn Oil (Experimental Animals)

Group	Rabbit No.	Total cholesterol (in mg %)	Relative activity of cholesterol (in impulses per minute per mg)
Controls	11	367	33
	12	860	62
	15	687	103
	16	900	233
	19	630	214
Experimental animals	13	370	62
	14	602	202
	17	233	62
	18	315	736
	21	312	47

The figures in Table 2 show that marked lipoidosis of the aorta and coronary arteries was present in only two rabbits, and marked fatty infiltration of the liver was observed in 4 of the 11 rabbits. Moderate atherosclerotic changes were observed in the aorta coronary arteries of one rabbit, and a moderate degree of fatty infiltration of the liver cells in 5 rabbits. In 6 of the 11 rabbits no lipoidosis was found, whether in the aorta or the coronary arteries. In 2 rabbits the liver was completely free from lipid inclusions. The remaining experimental rabbits showed a dust-like infiltration of individual groups of liver cells with fat (Fig. 2). No fatty infiltration of the reticulo-endothelial cells was observed.

Thus the fatty infiltration of the liver in the rabbits receiving cholesterol in corn oil was far less severe than in the animals receiving cholesterol in sunflower oil. Nevertheless, it must be emphasized that the liver lesions in the rabbits were more marked than the changes in the aorta and coronary arteries.

In addition to the changes in the aorta and coronary arteries, the degree of involvement of the liver may be used as a test of the severity of the pathological condition and of the effect of the various agents used in experimental atherosclerosis.

The effect of corn and sunflower oils on the biological synthesis of cholesterol was studied in 10 rabbits. The results of the determination of the total cholesterol in the liver and its relative activity are given in Table 3.

The figures in Table 3 show that the daily feeding of rabbits with cholesterol greatly influenced the total cholesterol content of the liver. Whereas in the normal rabbits this figure is 231 mg % [6], in our experiments the

cholesterol content of the liver in the rabbits receiving cholesterol in sunflower oil rose to 367-900 mg %. This increase was also observed in the rabbits receiving cholesterol in corn oil, but it was much less than in the control animals (312-602 mg %).

The relative activity of the cholesterol in the liver was low in both groups of animals. It must be mentioned that in the earliest stages of cholesterol feeding (after 3 days) a marked depression of the process of cholesterol synthesis in the liver was observed [2]. According to M. G. Kritsman and M. V. Babina [2], even the administration of substances preventing the development of atherosclerosis (methionine, choline, ascorbic acid) does not appreciable counteract this depression of cholesterol synthesis.

SUMMARY

As a result of investigations conducted on 32 rabbits (which received a daily dose of 0.2 gm/kg of cholesterol for four months) it was shown that prophylactic use of corn had a retarding effect on the development of fatty degeneration of the liver and a marked preventive effect on the rise of cholesterol content in the liver, also inhibiting the development of atherosclerosis of the aorta and coronary blood vessels. Corn oil produced no significant positive effect on the processes of cholesterol biosynthesis in the liver at the early stages of experimental atherosclerosis in rabbits. To assess the efficacy of the agent used in experimental atherosclerosis, one should take into consideration not only the character of changes occurring in the aorta and coronary arteries, but also the degree of hepatic affection.

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