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Some Effects of Iodine Given to Rabbits After a Period of Cholesterol Feeding.*

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In rabbits with hypercholesterolemia resulting from long-continued cholesterol feeding, the administration of potassium iodide caused a marked rise in the blood cholesterol.[1] A possible explanation for this rise was that the iodide caused a mobilization of cholesterol in the blood with a corresponding decrease of cholesterol in the tissues, roughly comparable to the effect of the parathyroid hormone on calcium.

To test this hypothesis, the liver cholesterol of cholesterol-fed rabbits with and without the administration of potassium iodide was determined.

The liver was selected for analysis because of the following observation: When rabbits are killed immediately after a prolonged period of cholesterol feeding widespread lipoid infiltration is usually evident including atheromatous patches in the aorta and gross changes in the liver, spleen, adrenals and kidneys. If, however, the cholesterol feeding is discontinued for several months before the animals are sacrificed, the aortic lesions persist but changes in the other organs are less frequent and less marked when present. This is particularly noticeable in the liver and suggests that the lesions in that organ, contrary to those in the aorta, are reversible. Furthermore, Meeker, Kesten and Jobling[2] have recently shown that iodine did not decrease the cholesterol content of atheromatous aortas in rabbits.

Dutch belted rabbits approximately 6 months old and averaging 2 kg. in weight were used. They were kept in individual cages indoors and given a diet of oats and fresh vegetables. Cholesterol determinations[3] were made on whole blood weekly.

A total of 72 rabbits was used. The sex ratio was approximately equal. Sixty-two of the animals were fed one gm. of crystalline cholesterol mixed with the grain 3 times a week. Seventeen of these failed to develop a hypercholesterolemia and were discarded.

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1 Turner, K. B., and Bidwell, E. H., *J. Exp. Med.*, 1935, **62**, 721.

2 Meeker, D. R., Kesten, H. D., and Jobling, J. W., *Arch. Path.*, 1935, **20**, 337.

3 Bloor, W. R., Pelkan, K. F., and Allen, D. M., *J. Biol. Chem.*, 1922, **52**, 191.

The rabbits were divided into 4 groups as follows:

Group I. Controls. Killed after 2 months (Table I).

Group II. Cholesterol fed for 2 months and killed (Table II).

Group III. Cholesterol fed for 2 months, kept on a normal diet for a third month and killed (Table III).

Group IV. As in Group III except that during the third month one gm. of potassium iodide was given 3 times a week (Table IV).

At autopsy the aorta was examined for atheromata. The adrenals were removed and weighed at once. The liver was dissected out, cut into small pieces and dried to a constant weight in an oven at 70 to 80°C. A portion of the dried material was pulverized and stored

TABLE I.
Normal Rabbits Used as Controls.

Rabbit No.	Blood Cholesterol mg. per 100 cc. Range	Aver.	Total Liver, Cholesterol, mg.	Cholesterol per 100 gm. Dried Liver, gm.	Weight of Adrenals mg.
341	103-126	113	281	1.56	400
342	96-114	104	229	1.19	400
343	135-156	145	260	1.67	380
344	105-129	118	217	1.43	150
345	110-134	125	222	1.41	390
346	109-124	116	226	1.28	350
355	93-106	100	231	1.35	230
358	119-145	132	159	1.40	190
359	96-128	108	205	1.52	240
360	99-124	112	154	1.39	240
	Aver.	117	218	1.42	297

TABLE II.
Rabbits Fed Cholesterol for Two Months.

Rabbit No.	Blood Cholesterol mg. per 100 cc. Range	Aver.	Total Liver, Cholesterol, mg.	Cholesterol per 100 gm. Dried Liver, gm.	Weight of Adrenals mg.
264	138-887	527	942	4.81	1420
262	130-725	482	1475	5.57	1420
312	115-403	347	645	6.33	360
287	111-443	303	1182	6.25	470
314	158-305	265	1930	12.37	320
273	132-325	246	445	2.64	420
331	126-333	204	344	2.16	220
261	110-305	203	948	5.61	910
320	125-245	199	1280	5.52	590
278	108-227	183	391	1.96	830
296	113-217	169	446	2.79	380
329	114-206	167	397	2.66	200
266	93-238	158	750	3.79	510
289	107-205	154	728	2.62	320
304	111-198	150	417	2.36	260
	Aver.	250	821	4.50	575

in a desiccator. For analysis, about 2 gm. of the powdered liver were weighed out, placed in a volumetric flask, and the total chol-

TABLE III.
Rabbits Fed Cholesterol for Two Months and Kept on a Normal Diet for a Third Month Before Killing.

Rabbit No.	Blood Cholesterol mg. per 100 cc. Range	Aver. Feeding Period	Aver. 3rd Month	Total Liver Cholesterol, mg.	Cholesterol per 100 gm. Dried Liver, gm.	Weight of Adrenals, mg.
285	167-834	557	423	772	3.86	1030
279	152-770	512	495	1080	4.87	800
274	111-431	359	316	1188	4.77	630
330	123-450	318	198	276	1.19	340
272	114-431	282	274	1478	4.94	780
300	157-250	251	193	258	1.24	260
327	130-368	250	252	425	1.92	310
318	127-352	243	271	571	2.53	660
277	106-329	234	124	230	1.13	320
270	108-352	233	143	126	1.25	360
286	112-294	217	161	191	1.27	490
328	95-243	197	144	250	1.39	340
322	118-223	174	125	231	1.26	180
297	114-200	174	153	179	1.09	260
284	81-238	170	142	143	1.43	200
315	108-197	163	124	251	1.29	300
	Aver.	271	221	478	2.21	454

TABLE IV.
Rabbits Fed Cholesterol for Two Months and Given KI for a Third Month Before Killing.

Rabbit No.	Blood Cholesterol mg. per 100 cc. Range	Aver. Feeding Period	Aver. 3rd Month	Total Liver Cholesterol, mg.	Cholesterol per 100 gm. Dried Liver, gm.	Weight of Adrenals, mg.
271	131-781	525	527	364	1.78	690
263	129-758	522	521	590	2.77	1020
319	131-704	303	395	536	3.57	700
321	130-476	248	174	238	1.54	290
269	108-275	224	208	382	1.84	710
276	92-385	218	311	384	1.99	840
326	121-284	214	153	262	1.69	230
280	120-250	187	162	239	1.41	320
323	118-258	184	135	216	1.71	220
290	108-333	181	211	234	1.16	300
317	115-208	174	164	263	2.09	670
316	112-302	172	254	742	4.10	600
311	96-191	154	114	237	1.34	500
291	118-203	152	135	216	.80	240
	Aver.	247	259	350	1.99	524

esterol determined by the method used for the blood.[3] The weighing was done as quickly as possible to prevent the dried liver from taking up atmospheric moisture.

Liver Cholesterol. The figures for the liver cholesterol in the 4 groups may be summarized as follows:

Group	Total Aver. mg.	Per 100 gm. dried liver gm.
I	218	1.42
II	821	4.50
III	478	2.21
IV	350	1.99

When no cholesterol was fed (Group I) the total cholesterol in the liver varied widely but was uniformly less than 300 mg. Contrasted to this was the finding that each animal in Group II had more than 300 mg. in the liver after 2 months of cholesterol feeding. The tendency of the liver cholesterol to return rapidly to normal levels when cholesterol feeding is discontinued was strikingly shown in Groups III and IV, indicating an apparent reversibility of the liver lesions at this stage. The difference in averages between the rabbits that did and those that did not receive KI was due to the presence of a few very high figures in Group III, while the number with normal amounts of cholesterol in the liver was the same for the 2 groups.

The independence of the level of the cholesterol in the blood and the total amount in the liver is clearly shown in the tables. A further point of interest is that the liver cholesterol was markedly increased in 3 rabbits with a normal blood cholesterol after feeding, hence not included in the tables. This is in sharp contrast to the occurrence of atheromata which, in our experience at least, never appear without a preceding rise in blood cholesterol.

Adrenal Weights. These varied widely. The average weight of a pair from a control rabbit was 297 mg. After cholesterol feeding for 2 months the average weight was 575 mg., presumably due to an increase in lipoids. A month after cholesterol feeding had been stopped the average weight had fallen to 454 mg., but if KI had been given it was 524 mg. If anything, the iodide inhibits the reduction in adrenal weight that occurs normally when cholesterol feeding is stopped.

Blood Cholesterol. The results may be summarized as follows:

Group		Range of individual averages mg.	Group average mg.
I		100-145	117
II		150-527	250
III	feeding period	163-557	271
	3rd mo. (no KI)	124-495	221
IV	feeding period	152-525	247
	3rd mo. (KI)	114-527	259

The rise in blood cholesterol with cholesterol feeding showed the usual individual variation, but was roughly comparable in the 3 groups fed. During the third month when cholesterol had been stopped, the blood cholesterol began to fall promptly in the rabbits that did not receive KI, while, in contrast, there was an actual rise in the average blood cholesterol for the group given KI.

It is a common experience to find that certain rabbits in a group fed cholesterol fail to develop a hypercholesterolemia. There has been no explanation for this resistance. The high incidence of this in the present series was unusual. Thus, of 62 rabbits fed cholesterol, 17 failed to develop a hypercholesterolemia A point of possible significance was that 13 of the 17 animals were males, a ratio of 3:1, whereas in the total group of 62 rabbits only 30, or approximately one-half, were males.

Atheromata. Gross aortic lesions were present in 8 of the 15 animals killed after 2 months of cholesterol feeding, in 6 of the 14 that received KI during the third month, and in 11 of the 16 that received no KI. The period of feeding by this method was too short to attach much significance to these results.

Conclusions. (1) The cholesterol content of rabbit liver, increased by cholesterol feeding, tends to return spontaneously to a normal value when the feeding is stopped. KI apparently does not accelerate this fall. (2) The normal decrease in adrenal weights and the prompt fall in the blood cholesterol occurring when cholesterol feeding is stopped are both inhibited by the administration of KI at the conclusion of the feeding period. (3) The high incidence of males among rabbits failing to develop a hypercholesterolemia with cholesterol feeding warrants further study.

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The Deterioration of Vitamin D in Aqueous Solutions.

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The vitamins may be generally grouped into two classes, namely: (1) those soluble in fats and (2) those soluble in aqueous solutions. Vitamins A, D, and E are found nearly exclusively in association with fats, and vitamins B and C with substances soluble in water.