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Action of Choline on Experimental Aortic Atherosclerosis.

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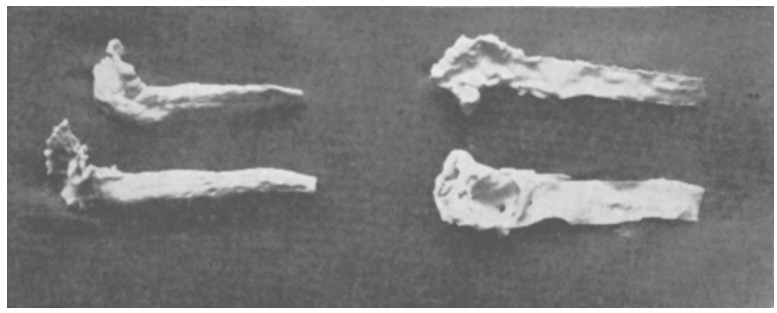
A previous communication[1] reported that the administration of choline to cholesterol-fed rabbits failed to prevent gross atherosclerosis, but did nevertheless result in a temporary delay in the appearance of aortic atheromata. The present study was designed to determine whether choline is effective in causing a reabsorption of the lesions previously produced in cholesterol-fed rabbits.

Twenty male chinchilla rabbits approximately 6 months old were used. The animals were kept indoors in individual cages. The diet consisted of oats, carrots and cabbage. One gram of cholesterol was mixed into the food of each rabbit 3 times a week for 110 days. The animals were then divided into 3 groups. Groups I-A and I-B, consisting of 5 animals each, were designated as controls. Group II contained 10 animals. Group I-A animals were sacrificed immediately after the 110-day cholesterol feeding period was completed. Group I-B animals were placed on the regular diet for 60 days after the cholesterol feeding period was discontinued. Group II animals were fed 0.5 g of choline daily for 60 days in addition to the regular diet after the 110 days of cholesterol feeding was completed. Groups



Group I-B (Control) Group II (Choline)

FIG. 1.

The 2 aortæ in group I-B are those from rabbits Nos. 310 and 406 which received cholesterol for 110 days and were fed a regular diet for an additional 60 days.

The two aortæ from group II are those from rabbits Nos. 244 and 245 which received similar feeding with cholesterol for 110 days and choline for an additional 60 days.

Note the absence of gross atheromata in aortæ of choline-fed animals.

[1] Steiner, A., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 231.

TABLE I.
The Blood Cholesterol Values and Autopsy Findings in Groups I-A, I-B and II.

	Blood cholesterol mg/100 cc, days								Degree of Lipoid Infiltration			
	0	30	60	90	110	130	150	170	Aortic Atheromata	Liver	Adrenal	Kidney
No.					Group I-A (Cholesterol for 110 days).							
248	156	500	500	454	454				+++	++	+	+
257	156	454	847	1204	1000				++++	+++	++	++
345	210	625	632	625	884				+++	++	+	+
249	147	333	561	436	456				++++	++	0	+
405	125	454	501	629	724				+++	++	+	0
					Group I-B (Cholesterol for 110 days and regular diet for 60 days).							
109	153	586	724	700	357	370	394	284	+++	+++	++	+
265	146	442	833	100	1010	625	370	384	++	+	0	0
269	138	820	1081	1408	1234	666	649	500	++++	+++	++	++
310	147	416	746	662	625	714	606	500	++++	+++	+	+++
406	66	132	238	847	800	454		303	+++	+++	+	+
					Group II (Cholesterol for 110 days, regular diet plus choline for 60 days).							
250	155	263	270	436	476	149	81	96	0	0	0	0
251	208	704	934	1041	1265	2000	1250	1250	+++	+++	+	+
255	132	276	372	490	512	357	108	125	0	0	0	+
244	131	282	282	413	500	123	208	104	0	0	0	0
335	144	285	568	892	900	746	624	544	++	+	+	+
344	118	316	355	526	592	431	275	500	+	+	++	+
379	126	303	352	350	400	263	200	240	0	0	+	0
381	127	666	655	800	1087	510	500	934	+++	+++	++	+++
382	114	314	400	434	385	361	140	125	0	0	0	+
327	130	213	417	333	454	582	666		0	0	+	0

I-B and II with one exception, were sacrificed on the 170th day of the experiment. One animal in Group II was sacrificed after 30 days of choline feeding on the 140th day of the experiment. The choline was administered by dissolving choline hydrochloride (Merck) in 5 cc of water and mixing with ground carrots. Food was withheld from the animals for 5 hours before the feeding of either cholesterol or choline to insure ingestion.

Blood was obtained from the ear vein at monthly intervals. Cholesterol determinations were made on the whole blood by the method of Bloor, Pelkan and Allen.[2] An autopsy was performed in each case. The extent of fatty change in the aorta, liver and kidney as shown macroscopically and the degree of adrenal enlargement was noted and graded from zero to 4 plus. The results are expressed in Table I.

From Table I it can be seen that 6 animals in Group II were entirely free of gross atherosclerosis, although the blood cholesterol in each was significantly elevated over a 4 to 5 month period. The question of spontaneous reabsorption of the aortic atheromata might be raised in view of the 60 day period of cholesterol-free diet previous to postmortem examination of the tissues. Anitschkow[3] and Scarff,[4] among others have shown that the characteristic arterial lesions do not disappear, but persist for periods up to 815 days following the withdrawal of cholesterol from the diet. This repeatedly corroborated finding together with the control data in the present series, would appear to deny the possibility of spontaneous reabsorption. It can also be seen in Table I that the 6 animals which failed to show aortic lesions exhibited no gross hepatic lipoid infiltration. This latter finding is consistent with the results obtained by Best and his coworkers[5, 6] in which choline was shown to relieve fatty livers in rats induced by feeding diets rich in fat or cholesterol.

The degree of lipoid infiltration in the kidney and of adrenal enlargement was similarly less in Group II.

Animal No. 327 was sacrificed after 30 days of choline feeding. It was of interest to note that lipoid involvement of the aorta, liver, and kidney was absent although the blood cholesterol level reached 666 mg/100 cc at the time of sacrifice.

From the evidence presented herewith, it is highly suggestive that choline causes reabsorption of the atheromatous lesions produced in the aortæ of rabbits by cholesterol feeding.

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2 Bloor, W. R., Pelkan, K. E., and Allen, D. H., *J. Biol. Chem.*, 1922, **52**, 191.

3 Anitschkow, N., *Verhandl. d. deutsch. path. Gesellsch.*, 1928, **23**, 473.

4 Scarff, R. W., *J. Path. and Bact.*, 1927, **30**, 647.

5 Best, C. H., Ferguson, G. C., and Hershey, J. M., *J. Physiol.*, 1933, **79**, 94.

6 Best, C. H., and Ridout, H. H., *Ibid.*, 1936, **86**, 343.