

Absorption of Aortic Atherosclerosis by Choline Feeding.*

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A previous report by the authors described the preventive action of choline against the development of atherosclerosis of the aorta in a series of rabbits fed cholesterol and choline simultaneously.¹ Steiner² found highly suggestive evidence that 0.5 g of choline daily caused some reabsorption of atheromatous lesions produced in the aortas of 6 rabbits by cholesterol feeding for 170 days. In 4 other rabbits similarly treated by Steiner, choline failed to cause significant aortic atheromatous reabsorption. The present study was undertaken to determine whether choline could effect reabsorption of aortic atheromatosis in a larger series of rabbits fed double the dose of choline heretofore employed and studied over twice as long a period of time.

Anitschkow,³ Scarff,⁴ and other have demonstrated that the characteristic atheromatosis of the aorta does not disappear after withdrawing cholesterol from the diet of rabbits. This atherosclerosis persists up to 815 days after cholesterol withdrawal from the diet, indicating that spontaneous reabsorption of the aorta does not occur.

Forty-four white male rabbits approximately 3 months old, who were litter mates were used in this study. These animals were divided into Groups A and B each containing

21 and 23 animals respectively. All the animals were individually fed 0.5 g of cholesterol daily with a basic diet of Purina Chow for 184 days. The cholesterol was mixed with the chow as prepared especially for this study by the Golden State Milling Co. of Downey, Calif. The rabbits took their feedings without difficulty and showed a gain in weight in each instance.

At the end of the 184-day cholesterol feeding period and the cholesterol feedings were stopped in all animals. The regular chow diet was then given to the 21 Group A animals for 185 days; the animals were then sacrificed. After the discontinuation of the cholesterol feedings 23 Group B animals were fed 1.0 g choline daily for 185 days mixed with the chow as above. The animals took these feedings without difficulty, gaining weight and showing normal activity in all cases. At the end of the 185-day period the animals were sacrificed.

At postmortem examination the grade of aortic atherosclerosis was described as 0 whenever no involvement of the aorta by atherosclerosis was grossly visualized or palpated by the examining fingers. Grade 1 was employed to describe a slight degree of atherosclerotic involvement of the intima of the aorta. Grade 2 described moderate atherosclerosis of the aorta. Grade 3 indicated marked atherosclerosis. Grade 4 described complete atherosclerotic involvement of the surface area of the aorta.

Table I, Group A—the 21 control rabbits fed cholesterol alone for 182 days then the regular diet for 185 days showed at autopsy aortic atherosclerosis of varying degree in each animal.

Table I, Group B—the 23 rabbits fed cholesterol alone for 182 days, then the regular diet with 1.0 g choline daily for 185 days showed aortic atherosclerosis at autopsy

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¹ Morrison, L. M., and Rossi, A., to be published.

² Steiner, A., *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 411.

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

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

TABLE I.
Atherosclerotic Involvement of the Aorta in Rabbits Fed 0.5 g Cholesterol Daily for 184 Days.

Grade of involvement	0	1	2	3	4	Total affected
No. of rabbits	0	2	3	5	11	21
% of rabbits affected	0	9%	14%	24%	53%	100%

TABLE II.
Atherosclerotic Involvement of the Aorta in Rabbits Fed 0.5 g Cholesterol Daily for 184 Days,
Then 1.0 g Choline Daily for 185 Days.

Grade of involvement	0	1	2	3	4	Total affected
No. of rabbits	17	4	2	0	0	23
% of rabbits affected	74%	17%	9%	0	0	26%

in 26% of animals. Seventy-four percent of animals were free of demonstrable aortic atherosclerosis.

Conclusion. Choline caused reabsorption

of aortic atherosclerosis in the majority of rabbits whose lesions had been produced by cholesterol feeding.

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The Relationship of Heparin Activity to Platelet Concentration.

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(Introduced by G. S. Mirick.)

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An increased susceptibility of thrombocytopenic blood to heparin has recently been reported by Allen and his associates.¹ These authors found that following the addition of a standard concentration of heparin to blood, more protamine sulfate was necessary to restore the normal clotting time in thrombocytopenic blood than was required by normal controls. They interpreted this observation as suggesting that in thrombocytopenia an increased amount of a heparin-like substance may be present in the blood. Studies in our laboratory² on 12 patients with hemorrhagic diathesis associated with thrombocytopenia in no instance revealed evidence of a circulating anticoagulant. It therefore seemed quite plausible that the increased susceptibility of thrombocytopenic blood to heparin may be

a direct result of the decreased number of platelets present.

Experiments. Using silicone-treated apparatus and high speed centrifugation (12,000 to 14,000 RPM, 17,500 to 22,000 g's) at low temperature (4°C), platelet-free plasma was obtained from normal individuals without the use of anticoagulants. This plasma could be kept fluid in iced silicone-treated tubes for at least several hours. Platelet-rich plasmas were obtained by a similar technic except that the blood was centrifuged only at 3000 RPM (about 1300 g) for 5 minutes. Platelet counts were performed on these plasmas. These two plasmas were mixed in different proportions and varying amounts of heparin* added. Clotting times of these plasmas in glass tubes were then determined using a 3 tube method at 37°C. Results are shown in the table.

These results clearly indicate that the

¹ Allen, J. G., Bogardus, G., Jacobson, L. O., and Spurr, C. L., *Ann. Int. Med.*, 1947, **27**, 382.

² Conley, C. L., Hartmann, R. C., and Morse, W. I., II, *Bull. Johns Hopkins Hosp.*, in press.

* Solution of heparin (sodium salt), Lederle Laboratories, Inc.