9801 P

Effect of Choline on Production of Experimental Atherosclerosis in Rabbits.

ALFRED STEINER. (Introduced by Kenneth B. Turner.)

From the Research Division of Chronic Diseases, Department of Hospitals, City of New York, and the Department of Medicine, College of Physicians and Surgeons, Columbia University.

Best and his coworkers[1, 2, 3] have shown that the administration of choline prevents the fatty infiltration of the liver in rats fed fat or cholesterol. The present study was designed to determine whether choline had any effect on the deposition of cholesterol esters in the arteries of rabbits fed cholesterol.

Methods. Thirty-eight male, chinchilla rabbits approximately 6 months old were used. The animals were kept indoors in individual cages. The diet consisted of oats and fresh vegetables. One gram of cholesterol was mixed into the food of each rabbit 3 times a week.

The animals were divided equally into 2 groups, 19 in each. Group I consisted of control rabbits fed only cholesterol. Group II rabbits were given choline in addition to cholesterol. Seventeen of the second group were fed 500 mg. of choline daily and the remaining two 750 mg. daily. The choline was administered by dissolving it in 5 cc. of water and then mixing it with a combination of oats and ground carrots. Food was withheld from the animals for 5 hours before the feeding of cholesterol and choline in order to insure ingestion.

Blood was obtained from the ear vein at weekly or bi-weekly intervals. Cholesterol determinations were made on the whole blood by the method of Bloor, Pelkan and Allen.[4]

The rabbits died or were killed over a period of from 40 to 100 days after the beginning of the experiment. An autopsy was done in each case and the extent of fatty change in the aorta, liver, and kidneys as shown macroscopically, and the degree of enlargement of the adrenals, was noted and graded from zero to 4 plus.

Level of blood cholesterol. All except 3 of the animals in both groups exhibited an immediate, progressive and sustained rise in the level of the blood cholesterol. In rabbits Nos. 126, 140, and 145, the amount of cholesterol in the blood was so great that it crystal-

[1] Best, C. H., and Huntsman, M. E., *J. Physiol.*, 1932, **75**, 405.

[2] Best, C. H., Ferguson, G. C., and Hershey, J. M., *Ibid.*, 1933, **79**, 94.

[3] Best, C. H., and Ridout, H. H., *Ibid.*, 1936, **86**, 343.

[4] Bloor, W. R., Pelkan, K. F., and Allen, D. H., *J. Biol. Chem.*, 1922, **52**, 191.

lized out of the alcohol-ether solution after standing for a short time in the ice box. The animals that did not show a significant increase in the level of blood cholesterol were Nos. 150, 159, and 162 of Group I. It is known that some rabbits, usually males, are "resistant" to cholesterol feeding and do not develop either hypercholesterolemia or lipoid infiltration into the tissues.

There was no appreciable difference in the levels of blood cholesterol between Group I, the control, and Group II, the choline-fed animals.

Gross appearance of the tissues. Autopsies were done on the rabbits at varying intervals from 40 to 100 days after the beginning of the feeding. In Group I, 15 showed definite gross atheromatous plaques, 16 lipoid deposits in the liver, 10 enlargement of the adrenals, and 13 deposition of lipoid in the kidneys. In Group II, 9 showed definite gross atheromatous plaques, 16 gross lipoid infiltration of the liver, 5 adrenal and 8 renal lipoid infiltration. The autopsy results show a greater amount of lipoid involvement in the control rabbits. On a statistical basis the results are not striking.

TABLE I.
The Occurrence of Gross Aortic Atheromata in Groups I and II.

Days	40	45	50	60	65	70	80	90	100
Group I									0
Rabbits fed	—	+	0	++	++	+++		+	++
cholesterol		+		+		+		++	0
				++		++++	+++		++
									+
									0
									+++
Group II		0				0		+	+
Rabbits fed	0	0	0	0	0	0	0	+	+
cholesterol									+
and choline									+++
									+
									++
									++

However, Table I reveals a definite and significant difference between the autopsy findings of the 2 groups in those animals killed from the 40th through the 80th day of the experiment. In Group II, the rabbits fed choline, 10 were killed between the 40th and 80th day, and none showed macroscopic lipoid infiltration of the aorta. In Group I, 11 animals were killed during this same period on corresponding days and 10 of these exhibited characteristic gross atherosclerosis.

The extent of lipoid infiltration in the liver, adrenal and kidney was likewise less in Group II, but the difference was not as great as in the aorta.

All of the animals killed after the 80th day showed gross lipoid involvement of the aorta except numbers 150, 159, and 162 of Group I. These 3 rabbits whose blood cholesterol did not rise significantly, were considered to be "resistant".

The results reported by Best and his coworkers quoted above were not obtained in the choline-fed rabbits. Gross lipoid deposition in the liver occurred in 16 out of 19 animals.

Summary and Conclusions. 1. The oral administration of 0.5 gm. of choline daily to 19 rabbits fed 1 gm. of cholesterol 3 times weekly did not prevent the development of a hypercholesterolemia comparable to that produced in 19 control animals fed cholesterol alone. 2. Ten of the choline-fed rabbits killed at intervals between the 40th and 80th days failed to show macroscopic atheromata in the aorta. Ten of the 11 control rabbits fed the same amounts of cholesterol and sacrificed at similar periods showed gross atherosclerosis. 3. After 80 days the macroscopic lesions of the aorta were similar in both groups. 4. It is concluded that choline delays but does not prevent atherosclerosis in cholesterol-fed rabbits.

9802 P

Magnesium as a Bronchodilator Agent in Perfused Guinea Pig Lungs.

VICTOR G. HAURY. (Introduced by Charles M. Gruber.)

From the Department of Pharmacology, Jefferson Medical College, Philadelphia.

A series of perfusion experiments were performed on isolated guinea pig lungs to test the efficacy of magnesium as an antagonist against the bronchial constriction produced by histamine, pilocarpine and barium chloride.

Isolated guinea pig lungs were used. Except for slight modifications, the procedure was essentially the same as that described by Sollmann and Von Oettingen[1] and Tainter, Pedden and James.[2] Histamine 1:10,000, pilocarpine 1:1000 and barium chloride 2.5% were used as the constrictor drugs. Magnesium sulfate ($MgSO_4.7H_2O$) was used in a 10.13% solution (1 cc. = 10 mg.

[1] Sollmann, T., and Von Oettingen, W. F., PROC. SOC. EXP. BIOL. AND MED., 1928, **25**, 692.

[2] Tainter, M. L., Pedden, J. R., and James, M., *J. Pharm. and Exp. Therap.*, 1934, **51**, 371.