of other authors using different methods. Hamilton and associates(8), measuring pressures with a needle directly inserted into the vessels of normal unanesthetized dogs breathing quietly, recorded in the pulmonary veins average pressures of 3 to 12 mm of mercury. In this study, average pressures recorded in the pulmonary veins were 3.9 to 12.2 mm.

A lesser distensibility of the left atrium cannot account for the high pressures observed in the pulmonary veins draining into vena cava and right atrium.

Summary. 1. During cardiac catheterization, a pressure gradient was found between a distal point in a pulmonary vein and either or both atrial chambers during the major portion of the cardiac cycle in 2 cases of atrial septal defect, in a third case wherein an anomalous pulmonary vein drained into the right atrium, and in a fourth in which an anomalous pulmonary vein emptied into the superior vena cava.

2. The magnitude of the gradient between pulmonary vein and *right* atrium varied from 3.0 to 5.8 mm of mercury with an average value of 4.2 mm in the 4 cases studied.

3. Evidence that this gradient could not be entirely due to an end pressure or Pitot effect was obtained from study of a model in which the end pressure effect was shown to be 0.5 to 0.8 mm of mercury at the same calculated flow velocities.

4. It is suggested that this pressure gradient is a result of the pressure transmitted by the right ventricle through the pulmonary circulation, and is an important factor in the left-to-right shunt observed at rest during quiet breathing in uncomplicated cases of atrial septal defect.

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Effect of Choline Chloride on Development of Atherosclerosis in the Rabbit.* (18033)

J. B. FIRSTBROOK. (Introduced by C. H. Best)

From the Banting and Best Department of Medical Research, University of Toronto, Canada.

The demonstration of the lipotropic activity of choline has led to the testing in experimental animals of its ability to prevent the arterial lipid deposition characteristic of atherosclerosis. Although some observers(1,2) have failed to find any protective action, others(3-6) have claimed that choline administration retards the development of lesions.

In investigating this subject we have administered choline chloride to rabbits by force-feeding gelatin capsules rather than by mixing choline with the food, not only to ensure a known and uniform dosage, but also in order to avoid a possible depression in the food intake of choline-treated animals due to the brackish taste of the chloride. It has previously been shown(7) that caloric restriction with consequent weight loss or decreased rate of weight gain inhibits the development of atherosclerotic lesions.

Methods. Fourteen adult male rabbits of various breeds, kept in individual cages and allowed Purina Rabbit Chow Checkers and water *ad libitum*, were used as experimental

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TABLE I.
Summary of Experimental Data.

Animal	Avg blood total cholesterol (mg %)	Initial wt (kg)	Ratio of final to initial wt	Avg food consumption per kg body wt (g per day)	Degree of atherosclerosis
1	101	3.79	1.12	41	0
2*	109	3.28	1.15	37	0
3	117	3.29	1.25	46	0
4	124	3.03	.96	35	1
5*	140	3.40	.93	32	1
6*	149	3.25	.96	30	2
7	154	3.32	1.08	40	2
8	166	3.39	.96	32	3
9*	202	3.35	.87	27	3
10	235	2.78	1.03	38	2
11	238	3.56	.92	35	3
12	271	3.26	.91	25	4
13	320	3.72	.81	25	4
14*	329	2.99	.93	31	3
		Means and Standard Errors.			
Choline	185.8 ± 38.8	3.254 ± .071	0.968 ± .048	31.4 ± 1.6	1.80 ± .58
Control	191.8 ± 25.6	3.349 ± .106	1.004 ± .044	35.2 ± 2.4	2.11 ± .51

* Animals given choline.

animals. Each animal received 1 g of cholesterol 6 days a week enclosed in 2 size 00 gelatin capsules. Five animals received, in addition, 1 g of choline chloride 6 days a week in capsules. The 9 controls received 2 empty capsules 6 days a week. In using this method of administration, suggested by Pollak(8) for cholesterol feeding, some difficulty was encountered in getting the animals to swallow the capsules and several rabbits were lost from respiratory obstruction before a satisfactory technic was developed. Good results were obtained when the capsule being administered was gently introduced into the pharynx while the animal's head was displaced (not rotated) backwards. Each animal was weighed weekly, its food consumption recorded daily, and its blood total cholesterol level determined weekly on heparinized ear vein blood by the Schoenheimer-Sperry method(9). After 9 weeks of cholesterol and choline administration the animals were killed and the whole aortas removed and fixed in 10% formalin. The aortas were stained with Sudan IV and graded as unknowns into 5 arbitrary groups according to the area of intima involved by lesions.

Results and discussion. The data are summarized in Table I in order of increasing average blood cholesterol level. Animals given choline are indicated by asterisks. The blood cholesterol averages do not include determinations made before the beginning of cholesterol administration. Food consumption values are averages of the 9 weekly averages computed for each animal on the basis of its average daily food intake and average body weight each week.

There is an obvious increase in the degree of atherosclerosis with increasing average blood cholesterol level. The two rabbits (10 and 14) whose degrees of atherosclerosis are less than would be expected from consideration of blood cholesterol levels alone had the lowest initial weights of the group. This is consistent with our previous finding(7) that animals of low initial weight tend to develop less atherosclerosis than animals of high initial weight, other factors being equal. However, with the foregoing exceptions, the variations in initial weight, weight change, and food consumption in the present experiment are relatively small and are insufficient to affect appreciably the correlation between degree of disease and blood cholesterol level.

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The means of the average blood cholesterol levels, initial weights, ratios of final to initial weight, food consumptions, and degrees of atherosclerosis in the choline-treated and control groups do not differ significantly.

The statistical significance of the difference between the mean degrees of atherosclerosis in the two groups adjusted to the common mean blood cholesterol level can be tested by the analysis of covariance. The adjusted means do not differ significantly, since the variance ratio F (0.23) is well short of the 5% point (4.84). Moreover, it is unlikely that any feasible increase in the number of experimental animals would lead to the demonstration of a significant difference under these experimental conditions; for it can be estimated that control and test groups of approximately 110 animals *each* would be required to demonstrate significance at the 5% level assuming that the relative standard deviation will be the same for the larger sample(10).

In a recent investigation(6), the results of which indicated that choline retarded the development of lesions, Steiner offered 1 g of cholesterol mixed with the food 3 times weekly to 54 rabbits. Ten were offered 1 g and 19 were offered 0.5 g of choline chloride daily mixed with the food. The remaining 25 served as controls. Assuming that choline was offered 6 days a week, and, assuming that equal proportions of the cholesterol and choline offered were actually ingested, the ratio of the cholesterol and choline weekly dosages in the 19 animals offered 0.5 g of choline daily was $3/3 = 1$. In our experiment, the ratio of cholesterol and choline weekly dosages was $6/6 = 1$, so that we believe our choline dosage relative to cholesterol dosage was comparable to that used by Steiner in his animals on the lower choline dosage.

A larger dosage of choline than we have used may inhibit the atherosclerotic process. However, in view of earlier findings(7), we believe that, in order to demonstrate that any agent specifically inhibits the development of lesions independently of any effect on blood cholesterol level or body weight, it should be shown that the treated and control groups do not differ significantly in duration or level of cholesterol administration, in average blood cholesterol level, in initial weight, or in relative weight change during the experiment.

Summary. The degree of aortic atherosclerosis found in 14 male rabbits given 1 g of cholesterol in gelatin capsules 6 days a week for 9 weeks showed a highly significant positive linear correlation with the average blood total cholesterol level.

Five of these animals which received 1 g of choline chloride in gelatin capsules 6 days a week for the 9 weeks did not differ significantly from the 9 control animals in average blood cholesterol level, in body weight, or in the degree of atherosclerosis which developed.

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