ide concentration in all soft tissues studied while changes in the phosphorus content were less pronounced.

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Effects of Pancreatectomy on Development of Atherosclerosis in the Rabbit.* (28473)

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Because of the known association of diabetes and a higher incidence of severe atherosclerosis in man, experiments were undertaken to observe the effect of pancreatectomy on atherogenesis in the rabbit. It was postulated that pancreatectomized animals would be unable to metabolize lipids normally and that the feeding of small amounts of cholesterol to these animals would enhance the formation of atheromata. However, contrary to expectation, pancreatectomy resulted in a limitation in hypercholesteremia and atherosclerosis.

Materials and methods. Adult, male, Belgian hares were used. The normal diet consisted of Rockland Rabbit Ration Pellets (17.41% protein, 1.61% fat, 65.8% carbohydrate, choline 110 mg/100 g, fiber, ash, vitamins, and minerals). Two groups of rabbits, B. and E, received a cholesterol-enriched diet prepared by coating pellets with a solution of cholesterol in ether, calculated to give a final pellet cholesterol concentration of ¼%. The average daily intake of pellet per animal was 250 g, resulting in a daily intake of 625 mg of cholesterol. Each day the pancreatectomized animals received an additional 500 mg of orally administered choline to prevent deficiency changes (1); this resulted in a total average daily choline intake of 725 mg. Pancreatectomy with splenectomy was performed under ether-oxygen anesthesia in 2 stages, according to the method described by Greeley(2). Because of the diffuse distribution of the pancreas in a rabbit, total pancreatectomy is an extremely difficult procedure. The post-operative mortality rate was very high and explains the small number of animals that survived to the end of the experiment. Only animals that survived for a postoperative period of at least 6 months are included in this report. Total serum cholesterol(3) and blood sugar(4) were analyzed weekly in control and pancreatectomized rabbits for the first month after pancreatectomy and monthly thereafter until they were sacrificed. Twenty-four hour collections of urine were examined for glucose in pancreatectomized animals and the amount of insulin for replacement was calculated from the degree of glycosuria. The animals were weighed at regular intervals. Terminally, the animals were sacrificed, and heart, aorta, great vessels, brain, lungs, liver and kidneys were examined grossly and microscopically. A thorough search was made for residual pancreatic tissue but none was found. Bile is known to be essential for absorption of fat from the

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TABLE I. Effects of Pancreatectomy on the Dev lopment of Atherosclerosis in the Belgian Rabbit.

Group	No. of rabbits	Months followed post operatively	Insulin replacement	Glycosuria	Weight: No. of animals	Weight: Mean gain (+) or loss (—) (g)	Blood glucose (mg%): Initial	Blood glucose (mg%): Experimental	Blood cholesterol (mg%): Initial	Blood cholesterol (mg%): Experimental	Atherosclerosis of aorta (Grade)
A Non-operated controls; normal diet	4	6	None given	0	2 1 1	+230 —900 No change	Range: 51–137 Avg: 89		Range: 2–56 Avg: 23		0
B Non-operated; ¼% cholesterol-enriched diet	4	6	"	0	4	+1000	76	Range: 67–118 Avg: 98	28	Range: 203–496 Avg: 349	4
C 1st stage pancreatectomy; normal diet	5	6	"	0	4 1	+333 —980	74	Range: 70–154 Avg: 88	18	Range: 4–80 Avg: 40	1
D 1st & 2nd stage pancreatectomy; normal diet	3	6	Administered (see text)	3	3	+210	90	Range: 49–175 Avg: 104	42	Range: 16–62 Avg: 21	0
E 1st & 2nd stage pancreatectomy; ¼% cholesterol-enriched diet	2	10	"	2	2	+330	67	Range: 70–124 Avg: 125	6	Range: 5–93 Avg: 45	1

gastrointestinal tract(5). There was no evidence of interruption of bile flow as a result of the surgical procedure; *i.e.*, the presence of bile-stained food in the intestine and the absence of any lesions in the liver associated with biliary obstruction. The aorta and great vessels were stained in the gross with Sudan III(6) to aid in evaluation of the amount of atherosclerosis. The severity of the atherosclerosis was graded from one to four: Grade 1 = mild streaking; 2 = isolated, elevated atheromata; 3 = confluent patches of atheromata and 4 = severe and extensive atherosclerosis of entire circumference of the aorta.

Results. Initially, 48 rabbits were used but only 18 survived until the end of the experiment; most of the deaths occurred after the first-stage pancreatectomy. The laboratory and anatomic data are summarized in Table I. All of the non-operated rabbits on a cholesterol-enriched diet (Group B) developed grade 4 lesions. In those animals subjected to first-stage pancreatectomy (Group C) one rabbit showed slight atherosclerosis; in animals totally pancreatectomized and on a cholesterol-enriched diet (Group E) only one of the 2 that survived showed minimal atherosclerosis. Microscopic examination of sections from all animals confirmed the gross findings of atherosclerosis in the aorta but failed to reveal atherosclerosis of the coronary or basilar arteries or of the small and medium sized arteries in lungs, kidneys, liver and meninges.

Discussion. These findings, despite the small number of animals that survived the operative procedure, suggest that pancreatectomy in the rabbit limits the degree of hypercholesterolemia and atherosclerosis in animals fed cholesterol-enriched diets. Possible explanations for the findings are: that either 1) the rabbits did not ingest the cholesterol; 2) they failed selectively to absorb the cholesterol; and/or 3) they did not metabolize the cholesterol in the same manner as did the non-operated rabbits on a cholesterol-enriched diet. Eight of the 10 animals that were operated upon gained weight (Table I) effectively eliminating the first explanation. Endogenous cholesterol synthesis appears to be minimally altered, if at all, by pancreatectomy, as evidenced by the serum cholesterol levels in pancreatectomized rabbits given a normal diet (Group D). It is hypothesized that pancreatectomy affected absorption of the cholesterol so that there was little elevation in serum cholesterol levels and minimal subsequent atherosclerosis. Duff and McMillan(7) and McGill and Holman(8) showed that atherosclerosis was retarded in both time and degree in rabbits fed cholesterol and made diabetic by alloxan administration. Hypercholesteremia was a constant(7) or common finding(8) in their rabbits.

Summary. 1. Pancreatectomy in the rabbit causes a limitation of hypercholesterolemia and atherosclerosis in cholesterol-fed rabbits. 2. It is postulated that this effect is due to diminished absorption and that pancreatic secretions are necessary for absorption of cholesterol from the gastrointestinal tract.

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