Effect of Total Pancreatectomy on Cholesterol Absorption and the Serum Cholesterol Level in Man* (33070)

C. C. Bell, Jr. and Leon Swell
McGuire Veterans Administration Hospital and Departments of Surgery and Biochemistry, Medical College of Virginia, Richmond, Virginia 23219

Several studies in rats and dogs (1–5) have shown that pancreatic secretions play an important role in the absorption of cholesterol. Cholesterol absorption is either absent or greatly diminished when the pancreas is removed or pancreatic secretions are diverted from the intestine. This absence of pancreatic secretions from the intestinal tract has also been shown to affect the blood cholesterol level in dogs. Chaikoff and Kaplan (2) reported very low levels of cholesterol in the blood of pancreatectomized dogs. When raw pancreas was added to the diet of these animals there was a marked increase in the blood cholesterol level. These findings suggest that a substantial portion of the blood cholesterol of the dog is derived both from the diet and the reabsorption of endogenous cholesterol. The purpose of the present study was to obtain definitive information on the role of the pancreas in cholesterol metabolism in man. The data presented indicate that the pancreas is essential for the proper absorption of cholesterol and the maintenance of the blood cholesterol level.

Material and Methods. Six normal subjects and two subjects with total pancreatectomy were used in these studies. The total pancreatectomy was performed on subject J. G. 17 months and on G. C. 3 months prior to the experiment. The surgical procedure did not interfere with the normal flow of bile into the intestine. Both subjects had been maintained on insulin and an oral hog pancreatin preparation (cotazym 18 capsules daily). Since subject J. G. had been placed on bile salts postoperatively to insure adequate lipid absorption, this therapy was continued during the experiment. The pancreatectomized subjects had been maintaining their body weight. There was no alteration in the diet during the experiment. The dietary intake of cholesterol was 0.6–0.8 gm/day. Serum electrolytes and liver and kidney function tests were normal. At the start of the experiment the oral pancreatin was stopped on both subjects. One week later they received a single oral dose of 50 μC of cholesterol-4-^{14}C (Nuclear-Chicago Corp.) in 400 ml of milk before breakfast. The cholesterol-4-^{14}C was uniformly dispersed in milk by sonic disintegration at 4°C for 2 min. There was no evidence of altered intestinal motility as manifested by vomiting and diarrhea during the experiment. Subject J. G. was restarted on the oral pancreatin 16 days following omission of pancreatin. After 15 days on pancreatin he was given another oral dose of 50 μC of cholesterol-4-^{14}C. Subject G. C. was not available for this portion of the study. The normal subjects also received a single dose of 50 μC of cholesterol-4-^{14}C orally in 400 ml of milk before breakfast. Blood samples were obtained serially on the subjects during the course of the experiment as indicated in Figs. 1,2,3.

The serum samples were extracted with 2:1 chloroform–methanol (6). Cholesterol was determined by the method of Sperry and Webb (7). The ^{14}C-activity of the total serum cholesterol fraction was determined on the digitonide (7) by liquid scintillation counting.

Results. The appearance of ^{14}C-activity in the serum of the pancreatectomized subjects following the oral administration of cholesterol-4-^{14}C is shown in Fig. 1. During the period when the oral pancreatin was not administered there was almost a complete absence of cholesterol-^{14}C in the serum of subject J. G. Subject G. C. had detectable amounts of cholesterol-^{14}C in the serum but the amount of ^{14}C-activitiy was very low. When subject J. G. was given the oral pancreatin preparation and later given another

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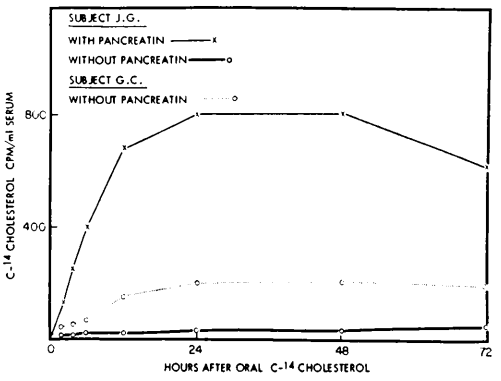

FIG. 1. The appearance of cholesterol-^{14}C in serum following the oral administration of cholesterol-4-^{14}C to pancreatectomized subjects.

cholesterol-4-^{14}C test meal, considerable amounts of ^{14}C-activity were present in the serum cholesterol fraction. However, the degree of cholesterol absorption in this subject (J. G.), while on the oral pancreatin, was approximately ⅓ that of the mean of the normal subjects (Fig. 2) as estimated from the appearance of ^{14}C-activity in the serum cholesterol.

The serum cholesterol levels are shown in Fig. 3. Subject J. G., before stopping the oral pancreatin, had a serum cholesterol level of 205 mg/100 ml. After the oral pancreatin was stopped, serum cholesterol level fell precipitously and at the end of 16 days was 69 mg/100 ml. When the oral pancreatin was restarted, the serum cholesterol level returned to 200 mg/100 ml at 22 days. Subject G. C. initially had a low serum cholesterol level

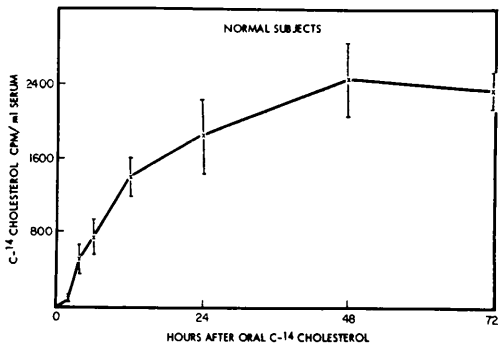

FIG. 2. The appearance of cholesterol-^{14}C in serum following the oral administration of cholesterol-4-^{14}C to normal subjects. Values represent the mean of 6 subjects ± SD.

(114 mg/100 ml). His serum cholesterol level dropped to 80 mg/100 ml 7 days after the oral pancreatin was discontinued.

Discussion. The results of the present study indicate that pancreatic secretions contain one or more factors which are essential for the proper absorption of cholesterol in man. It has been suggested (3–5) that the poor absorption of cholesterol in rats with pancreatic juice diverted from the intestine may be due to a lack of the digestive enzymes, cholesterol esterase and lipase. Pancreatic cholesterol esterase is important in promoting the hydrolysis of cholesterol esters in the intestinal lumen and it may also be involved in the esterification of cholesterol in the intestinal wall (8). Pancreatic lipase is involved in the formation of monoglycerides which together with free cholesterol, fatty

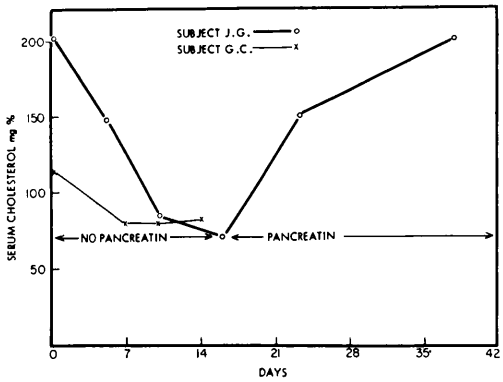

FIG. 3. Serum cholesterol levels in pancreatectomized subjects with and without oral pancreatin.

acids, and bile acids form micelles, Cholesterol absorption probably takes place after its micellar solubilization (9). It has also been reported (5) that cholesterol absorption in the absence of pancreatic secretions is dependent on the supply of bile to the intestine. Subject J. G. received suppelmentary bile salts orally during the entire experiment. This would tend to rule out the lack of an adequate bile salt supply as a factor in the very poor absorption of cholesterol when pancreatin was omitted.

The present data also indicate that the cholesterol entering the circulation via the intestine contributes substantially to the blood cholesterol pool in man. Because of the

almost complete lack of cholesterol absorption in the pancreatectomized subjects, an evaluation can be made of the significance of the intestinal phase of cholesterol metabolism on the blood cholesterol level. It can be estimated that perhaps as much as 50% or more of the serum cholesterol in man is derived from cholesterol entering the circulation via the intestine. It is also of interest that the liver and other tissues did not have the capacity to maintain the serum cholesterol level. Other lines of evidence (10–12) also indicate that the intestine makes an important contribution to the blood cholesterol pool in man. The ileal and jejunocolic bypass procedures give a pronounced drop in blood cholesterol levels. In one study (12) normal intestinal continuity was restored and serum cholesterol rose from 81 to 275 mg/100 ml.

Summary. Two human subjects with total pancreatectomy showed very little absorption of orally administered cholesterol-4-^{14}C following discontinuance of oral pancreatin. During this period their serum cholesterol dropped to under 100 mg/100 ml. When oral pancreatin was restored to one of the subjects, cholesterol was absorbed and the serum cholesterol level returned to 200 mg/100 ml. The results of the present study indicate that pancreatic secretions are necessary for the proper absorption of cholesterol and the maintenance of the blood cholesterol level in man.

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The Nonspecific Inhibitors of Rubella-Virus Hemagglutination* (33071)

H. J. DOLD[1] AND R. L. NORTHROP (Introduced by Friedrich Deinhardt)
Departments of Microbiology, Presbyterian-St. Luke's Hospital and University of Illinois Medical and Graduate Schools, Chicago, Illinois

Human serum contains nonspecific inhibitors of rubella-virus hemagglutination (1–3) which must be removed before hemagglutination-inhibiting (HI) serum antibodies can be measured. Currently kaolin is used to absorb serum prior to performing the rubella HI test. It is known, however, that kaolin is a nonselective adsorbent of serum proteins (4,5) often reducing the antibody titers of serum.

This communication reports that the nonspecific inhibitors of rubella-virus hemagglutination are removed from human serum by the addition of manganous chloride and heparin, a process which specifically precipitates β-lipoprotein (5–7).

Materials and Methods. Sera. The sera were separated sterily from the blood of infants, children, and young adults and were

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