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Relationship of Prolonged Drainage of Bile through Pancreatic Duct System to Pancreatitis.* (21984)

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The role of reflux of bile into the pancreatic duct system in the etiology of acute hemorrhagic pancreatic necrosis has been a subject of intensive investigation for many years. It is well known that when sterile bile is injected into the pancreatic duct of experimental animals, under certain conditions, a fulminating hemorrhagic pancreatic necrosis results quite regularly. However, there is a great deal of evidence that under other more physiologic conditions the presence of bile in the pancreatic duct is harmless to the pancreas. Mann and Giordano(1) found that, if the pressure exerted during retrograde injection of bile into the pancreatic duct were maintained within physiologic limits, no pancreatitis developed. It was shown in this laboratory(2) in cats that when the common bile duct was occluded distal to the entrance of the pancreatic duct so that bile could flow into the pancreatic duct under secretory pressure of the liver or pressure of the contracting gall bladder, pancreatitis developed in only a small proportion of animals, unless the cats were fed fatty meals supplemented with bile salts. Leven(3) and Colp and Doubilet(4) showed that reflux of iodized oil into the pancreatic duct could be demonstrated in cholangiograms in about 20% of patients with common bile duct drainage. This reflux was attributed in most cases to spasm of the sphincter of Oddi. Hicken and McAllister(5) using a water soluble contrast agent and very low injection pressures found that even in patients with no intraductal pathology, reflux of contrast material into the pancreatic duct could be demonstrated on routine cholangiograms in a high percentage of cases. Fisher *et al.*(6) drained the bile through the pancreatic duct by connecting a catheter in the common bile duct with a catheter in the pancreatic duct. In their 4 experiments the longest follow-up was 7 days. None of these animals developed any pancreatitis.

The experiments reported here, from August 1950 to July 1951, were designed to show the effect upon the pancreas of draining all of the bile secreted by the dog's liver through the pancreatic duct system over long periods of time.

Methods. The entire biliary flow in a series of dogs was caused to pass through the pancreatic duct into the duodenum by one of 3 operations. Type I: the duct of Santorini

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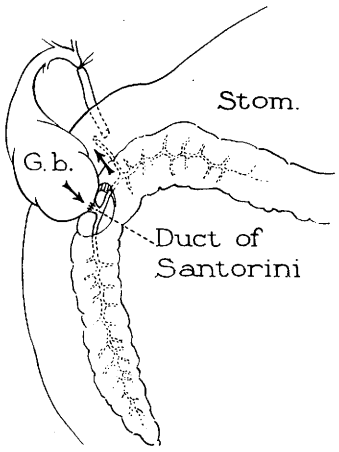

Fig. 1

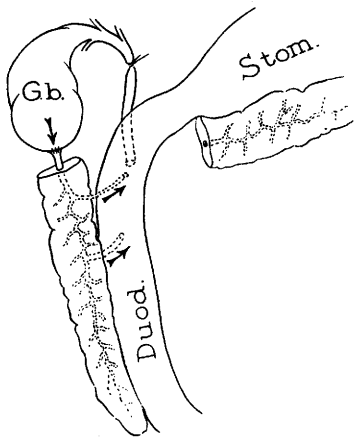

Fig. 2

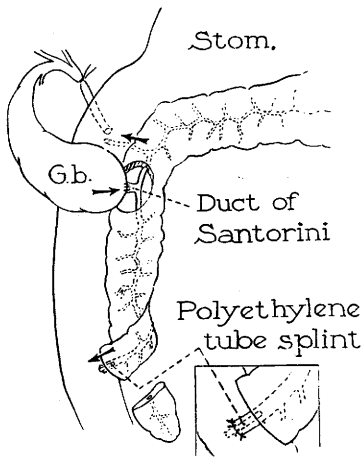

Fig. 3

FIG. 1, 2 and 3 show Type I, II and III operations, respectively. Bile drains through pancreatic duct system as indicated by arrows.

(the larger duct in the dog) was anastomosed to the gall bladder and the common bile duct was tied off. Under these circumstances, bile flows from the duct of Santorini into the duct of Wirsung through anastomoses between the two duct systems which are regularly present in the dog and thence into the intestine through the duct of Wirsung. Type II: the body of the pancreas was transected and the cut end of the pancreatic duct in this part of the pancreas was anastomosed to the gall bladder and the common bile duct was ligated. In this preparation bile flows from the gall bladder into the pancreatic duct through the anastomosis and reaches the intestine by way of the normal pancreatic duct orifices. Type III: the duct of Santorini was divided just proximal to its orifice in the duodenum, and this duct was anastomosed to the gall bladder. The distal end of the duodenal portion of the pancreas was transected and the cut end of the duct was located and anastomosed into the duodenum using a small polyethylene tube as a splint. The common bile duct was either ligated or anastomosed to the gall bladder. Bile flows into pancreas through the major duct and out into the intestine through the point where the duct is implanted into the duodenum. Serum amylase and serum bilirubin determinations were made on all dogs at weekly intervals.

Results. Of the 47 dogs used in these experiments, 18 had patent functional anastomoses between the gall bladder and the pancreatic duct system and between the pancreatic duct and intestine at the time that they died or were sacrificed, and these are the animals included in this study. Eleven of the remaining animals are not included because at the time of death it was found that the anastomosis between gall bladder and pancreatic duct or between pancreatic duct and intestine was not patent, and 18 were not included either because they did not survive for a significant period after their operation or because there was insufficient data on them.

Of the 18 dogs with intact anastomoses, only 3 had clinically significant degrees of pancreatitis, and only one of these had a typical full-blown pancreatic necrosis. The case of severe pancreatic necrosis occurred 22 days postoperatively in a dog in which a normal serum bilirubin and only a moderately elevated serum amylase had been noted only 4 days earlier. The other 2 dogs had only local areas of necrosis in the pancreas.

Fifteen of the 18 dogs with intact anastomoses did not develop significant degrees of pancreatitis. Eight were not jaundiced at the time of death, indicating that the bile was passing relatively unimpeded through the pancreatic duct system into the intestine. Four of these 8 dogs lived from 58 to 138 days, and

the average survival time for the group was 60 days. Gross inspection at autopsy showed the pancreas to be firm and atrophic; the gall bladder and bile ducts were dilated and the liver was firm and rough. Microscopic examination of the pancreas usually showed only mild degrees of interstitial pancreatitis and fibrosis.

The remaining 7 dogs with intact anastomoses had a significant degree of clinical jaundice at the time of death even though a patent channel was demonstrated from the gall bladder through the pancreatic duct system into the duodenum at autopsy. This circumstance suggests that although some bile was probably passing through the pancreatic duct system, the flow was not free enough to maintain the serum bilirubin at normal levels.

Summary and conclusions. 1. The entire flow of bile was successfully diverted through the pancreatic duct system into the intestine in a total of 11 dogs. Eight of these dogs did not develop any significant degree of pancreatitis even though the average observation period for this group was more than 60 days, and only one dog in the series developed a full-blown acute pancreatic necrosis. 2. The results of these experiments indicate that the presence of bile in the pancreatic duct system under physiologic pressures is tolerated for long periods of time without any serious damage to the pancreas in most cases.

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Lactic Dehydrogenase Activity in Blood.* (21985)

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The observation that during experimental and clinical myocardial infarction glutamic oxaloacetic transaminase is released from cardiac muscle resulting in increased enzyme activity in the serum(1-5), suggested that other cardiac tissue enzymes behave similarly during myocardial infarction. Although present in other tissues in greater activity, lactic dehydrogenase, the enzyme concerned primarily with the reduction of pyruvic acid to lactic acid, is present in appreciable activity in cardiac musculature. In order to ascertain whether lactic dehydrogenase (hereafter referred to as LD) activity is increased in the serum during myocardial infarction, it was necessary to first demonstrate its presence in human and animal blood, and to delineate variations in LD activity in the blood of normal and diseased man.

Methods and materials. Lactic dehydrogenase is concerned with the reduction, in the presence of reduced diphosphonucleotide (DPNH), of alpha-keto and of alpha, gamma-diketo acids; maximum reduction by LD has been shown to occur with pyruvic acid. Inasmuch as LD catalyzes the reduction of various alpha-keto and alpha, gamma-diketo acids, the reduction of a substrate in the presence of LD cannot be used to specifically identify an alpha-keto or an alpha, gamma-diketo acid. However, the catalytic reduction of a known amount of a specific keto acid may be used to quantitatively estimate LD activity(6). The *LD activity* of human serum was measured

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