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An Experimental Study of Fat Necrosis in Bile Peritonitis.*

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During a recent study of the reaction of the peritoneum to sterile bile, fat necrosis was frequently observed in the mesentery near the pancreas. The term fat necrosis has come to mean a special form of necrosis characterized by the hydrolysis of neutral fat into fatty acids and glycerol, the former combining with calcium to form insoluble soaps.

In a series of 20 dogs after ligating the common bile duct and making a stoma in the gall bladder, bile was allowed to drain into the peritoneal cavity. Eighteen hours later the peritoneal cavity presented the picture of an acute severe general peritonitis and contained several hundred cubic centimeters of a serosanguinous exudate in which were observed polymorphonuclear leukocytes and *B. welchii*. Areas of fat necrosis 1 cm. in diameter were present in the fat of the mesentery adjacent to the pancreas in 15 out of 20 dogs in this series. The pancreas of these animals when examined both grossly and microscopically was normal.

The effect of an intraperitoneal injection of 2.5 cc. of a 10% solution of bile salts was then studied in a series of 20 dogs, and extensive areas of fat necrosis were observed in all instances. A peritonitis identical with bile peritonitis was produced and fat necrosis was observed in the fat near the pancreas, in the omentum, mesentery and the retroperitoneal fat. Gross and microscopic examination of the pancreas failed to find any evidence of necrosis, distension of the ducts or an inflammatory exudate.

Inasmuch as *B. welchii* was cultured from the peritoneal exudates of the peritonitis produced by both bile and bile salts, the effect of an intraperitoneal injection of cultures of this organism was studied. When 20 cc. of an 18-hour broth culture of *B. welchii* was administered, a peritonitis identical with bile peritonitis was produced; however no fat necrosis was observed.

The question then arose as to whether the bile salts *per se* were able to produce fat necrosis or whether the necrosis was produced by pancreatic enzymes liberated by the local action of the bile salts on the pancreas. In a series of 6 dogs the pancreas was completely

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excised before administering intraperitoneally 2.5 cc. of a 10% bile salt solution per kilo. Even though a peritonitis identical with bile peritonitis was produced no fat necrosis was observed.

The data in this investigation tend to show that bile free in the peritoneal cavity will produce fat necrosis. Experiments with bile salt solutions show that the bile salts are the active agents in the bile. Although there is no evidence to show that bile salts *per se* will produce fat necrosis there is evidence to show that bile salts free in the peritoneal cavity and the presence of the pancreas are essential for its production. Inasmuch as there is no gross nor microscopic evidence of pancreatic necrosis, it is necessary to postulate that the pancreatic enzymes were liberated by permeability changes produced by the local action of the bile salts on the pancreas.

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Effect of Stasis on the Calcium Content of the Bile.

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When bile is stored in the gall bladder its solid constituents undergo a 6 to 8 fold concentration due to the absorption of water. This should produce very high calcium levels theoretically, unless some of the calcium was also absorbed. The solution of this problem is of interest on account of the calcium content of gall stones.

Dogs were anesthetized with ether, the abdomen opened and the cystic duct clamped immediately to prevent emptying of the gall bladder. Then the common duct was opened, cannulae inserted and sufficient liver bile collected for analysis. In 5 experiments the average content of the liver bile on fasting animals was 14.6 mg. per 100 cc. while the simultaneous gall bladder bile contained 52.2 mg. per 100 cc. This is a concentration of about three and a half times, considerably less than the total concentration of the bile, indicating that some calcium as well as water had been absorbed.

The average concentration of normal cystic duct bile in 10 control electrocuted fasting animals was 47.7 mg. In 11 animals in whom the cystic duct had been ligated for varying periods the average calcium content was 39.2 mg. per 100 cc. indicating that a progressive absorption of calcium was taking place. These figures do not truly represent the amount of absorption as the total volume of the gall