

Regurgitation Cholecystitis and Cholelithiasis *

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THE ETIOLOGY of cholecystitis is not perfectly understood at the present time, but the origin of this disease seems related in most instances to obstruction of the cystic duct by stone, with infection of the gallbladder wall a secondary and a relatively unimportant feature, when it occurs. The present report is concerned with the demonstration that ascending infection of the bile passages may occur when the sphincter of Oddi is cut or bypassed and that this infection is likely to localize in the gallbladder and may be accompanied by the formation of gallstones.

EXPERIMENTAL

In the course of recent experiments on bile duct reconstruction, it was found convenient to perform some of the studies on dogs with intact gallbladders. Whenever, in such an animal, the previously obstructed common bile duct was anastomosed to the duodenum or to a long Roux-Y loop of jejunum below the level of the cystic duct, the gallbladder would become inflamed within a few weeks, its contents infected, and stones or concretions often would form within its lumen. These inflammatory changes occurred throughout the entire biliary tract but were found to be most marked in the gallbladder and less evident elsewhere, although at times ascending cholangitis and liver abscesses developed.^{4, 5} Inasmuch as no evidence of spread of the

infection was found within the walls of the bile ducts or in the periductal lymphatics, and the contents of the gallbladders and ducts revealed positive culture in all instances, it seemed evident that regurgitation infection was the basis for this type of experimental cholecystitis. It is interesting that Colp, Doubilet and Gerber¹ years ago reported similar inflammatory changes in the gallbladders of dogs following endocholedochal sphincterotomy.

These findings may be contrasted to those seen when the gallbladder was removed at the time of duct reconstruction. Ten such animals so treated and observed for periods up to 18 months showed only minimal histologic evidence of infection of the bile ducts and liver (Fig. 1) and remained clinically well,³ whereas those with intact gallbladders and ascending infection went gradually downhill and sometimes died as a result of the infection. Evidently the constant downward flow of bile exerts a continuous washing effect in the bile ducts to prevent any appreciable degree of regurgitant infection from taking place.

The conclusion seems inescapable that under the conditions of these experiments the gallbladder acts simply as a blind pouch communicating with the bile ducts, and that its mechanism of emptying and filling is interfered with once the sphincter of Oddi is gone, so that the gallbladder no longer serves any useful purpose but acts simply as a convenient stasis bed for the perpetuation of ascending infection. Indeed such a gallbladder sometimes appears to

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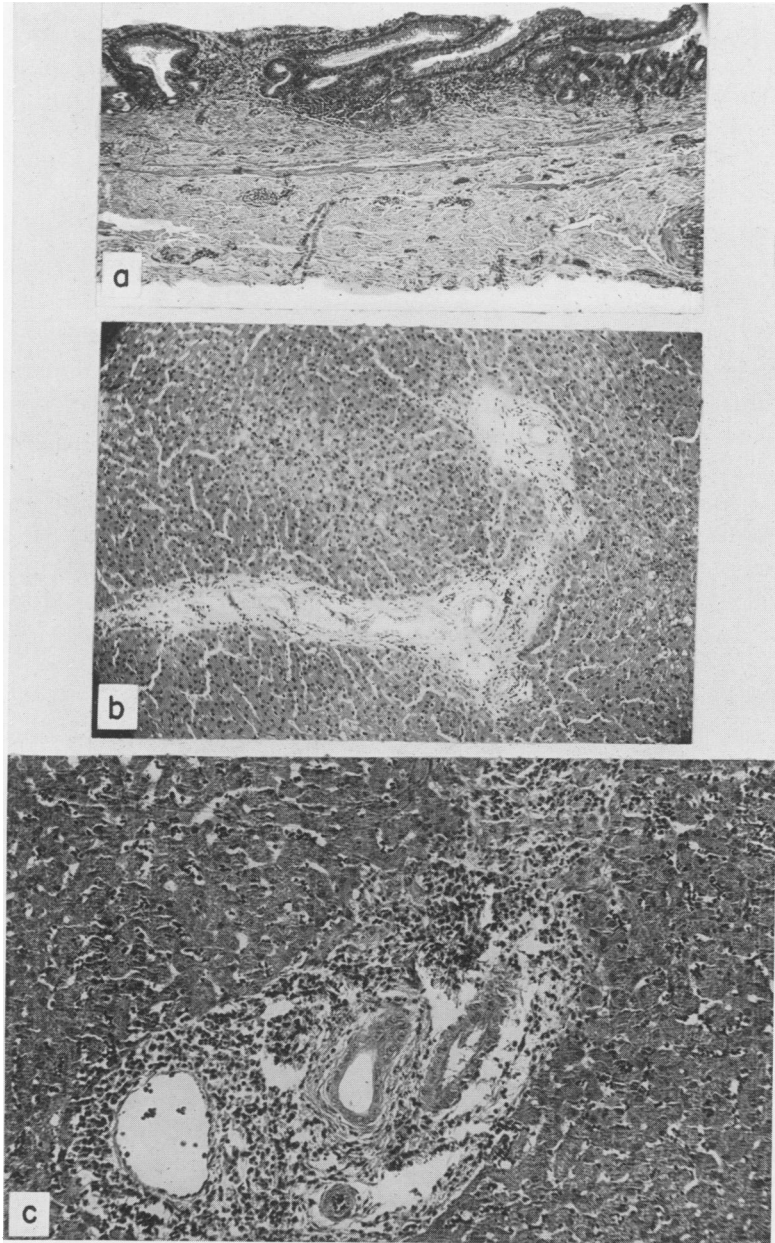


FIG. 1. (a) Bile duct and (b) liver of dog 1 year after cholecystectomy and choledochoduodenostomy, $\times 90$. Minimal evidence of infection. (c) Liver of dog 1 year after choledochoduodenostomy with gallbladder intact, $\times 150$. Marked ascending cholangitis.

act as a nidus for spread of infection to the adjacent bile ducts and liver (Fig. 2).

The concretions which formed in these

animals' gallbladders often looked like human gallstones (Fig. 4) but they were found to be very low in cholesterol content.

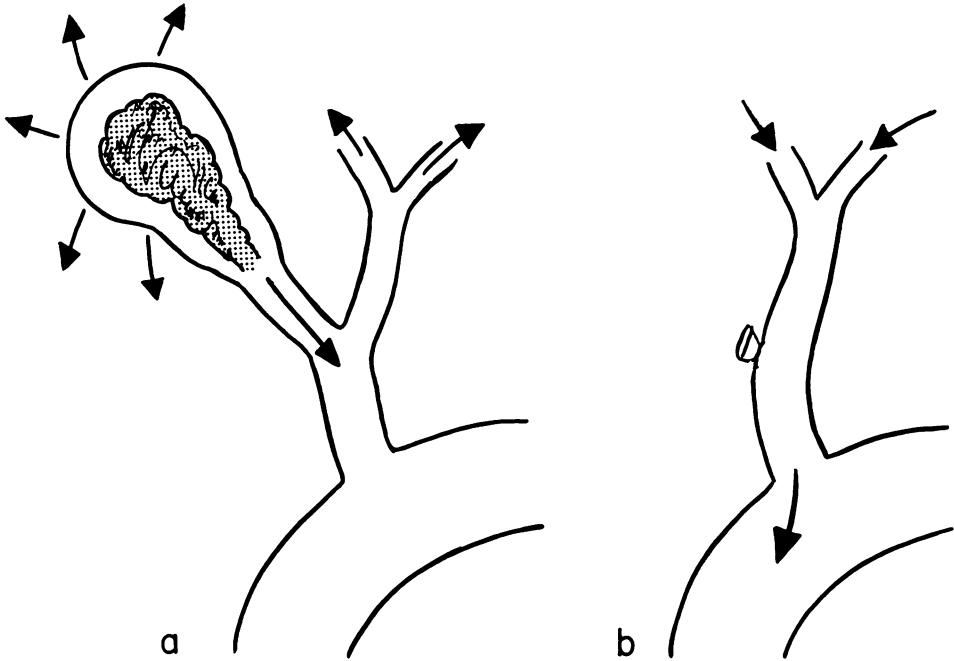


FIG. 2. (a) Drawing to show how the gallbladder may act as a nidus for the spread of infection following choledochoduodenostomy. (b) Same, after cholecystectomy; the downward flow of bile exerts a continuous washing effect to help prevent ascending infection from taking place.

Carcinoma of duodenum
obstructing
common bile duct
J.M.

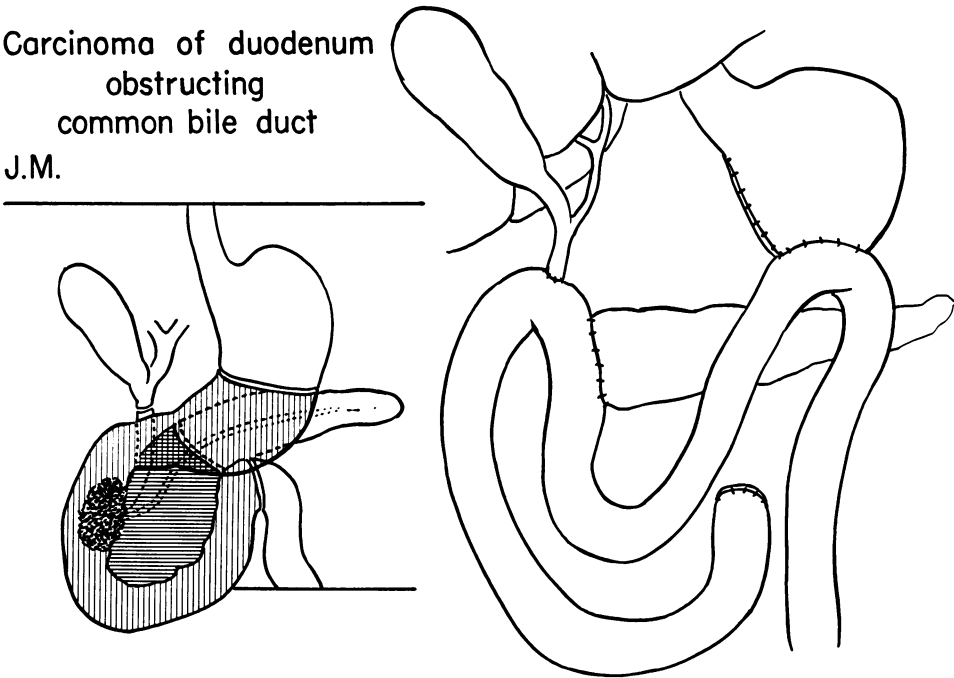


FIG. 3. Drawing of operation and reconstructive procedure in Case 1.



FIG. 4. Concretions removed from dog's gallbladder 3 months after choledochoduodenostomy.

This is not surprising since dog bile contains much less cholesterol than does human bile.

CLINICAL

The experiments just described constitute good evidence that when a wide opening has been made between the dog's bile duct and intestine, regurgitation infection of the bile passages occurs, is maximal in the gallbladder, and sometimes spreads from the gallbladder to other parts of the biliary tract. The biliary-intestinal apparatus is anatomically similar in the dog and man. Therefore it is reasonable to expect that a similar type of ascending infection might occur in patients whose sphincter of Oddi is cut or bypassed. The following illustrative case reports indicate that such a process does take place.

CASE REPORTS

Case 1. (Courtesy Dr. D. N. Sweeny, Jr.) J. M., a 49-year-old white man, was operated upon January 12, 1954 for carcinoma of the duodenal loop. He had never been jaundiced, but at operation the gallbladder and common duct were found to be markedly dilated. The gallbladder did not contain any stones and except for dilatation of its lumen seemed perfectly normal. A one-stage pancreatoduodenal resection was performed, and the common duct, pancreatic duct, and stomach were anastomosed in that order to the jejunum (Fig. 3). The gallbladder was not removed. A T-tube was temporarily placed through the anastomosis between the bile duct and intestine and was removed 28 days later. The patient's course after operation was uneventful.

Almost 2 years later x-rays of the abdomen showed the presence of gallstones. Reoperation was performed January 11, 1956, at which time no recurrence of the tumor of the duodenum was found, but the gallbladder was small, thick-walled and contained several stones (Fig. 5). The common

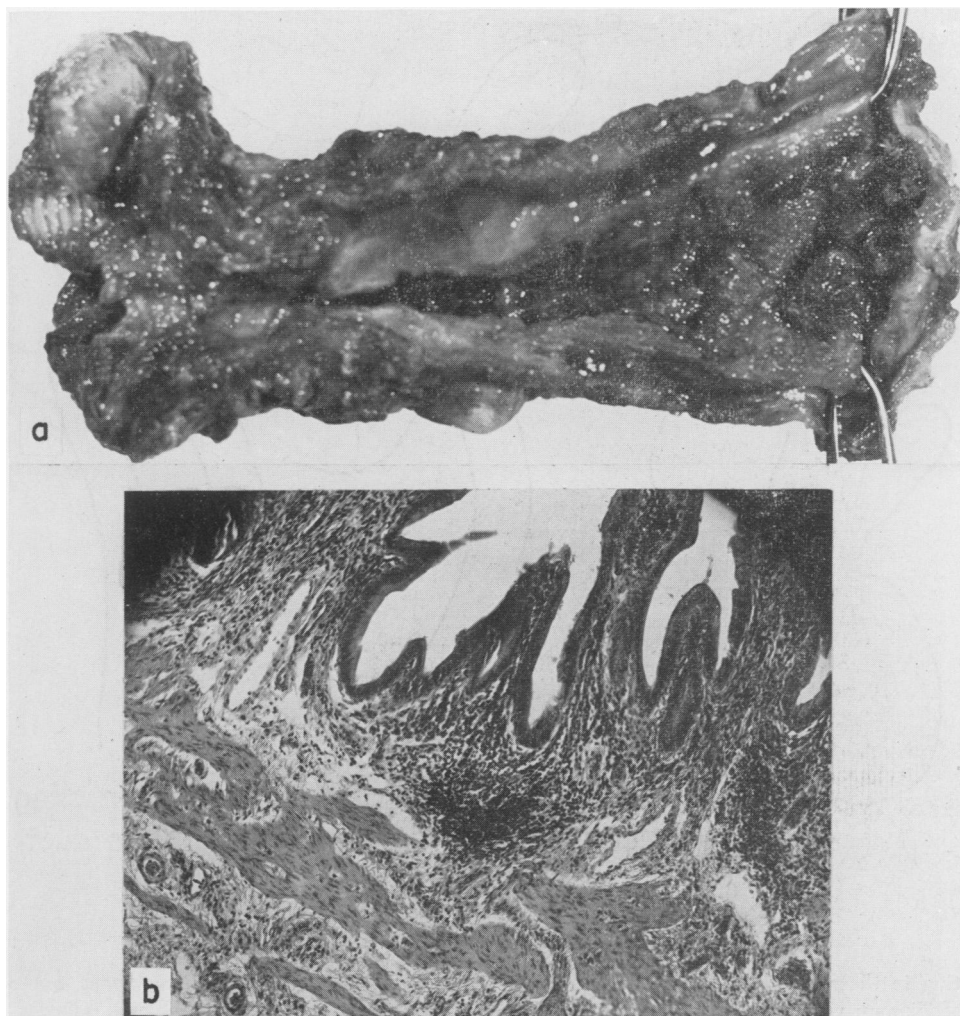


FIG. 5. (a) Gallbladder, Case 1, opened longitudinally. Stones can be seen, on the right, in the fundus. (b) Histologic appearance of gallbladder wall, Case 1, $\times 90$.

duct was thickened but otherwise normal. The gallbladder was removed, and the patient has remained well since his most recent operation.

Case 2. G. S., a 60-year-old white male, was operated upon December 29, 1954, for carcinoma of the head of the pancreas with obstructive jaundice. Resection of the head of the pancreas and duodenum was performed, in one stage, and the pancreatic duct, common duct and stomach anastomosed in that order to the jejunum, with a long loop intervening between the common duct and the stomach anastomoses (Fig. 6). A T-tube was placed in the biliary-intestinal anastomosis as a

temporary splint. The gallbladder, which was dilated but otherwise normal, was not disturbed.

The patient did nicely for a time but in about 18 months developed signs of recurrence of his tumor and died October 14, 1956, 22 months after resection.

Autopsy showed abdominal carcinomatosis, but also revealed that the lumen of the gallbladder was filled with small stones and its wall thickened and infiltrated with many inflammatory cells.

Comment: These first 2 cases are examples of regurgitation cholecystitis and cholelithiasis occurring following pancreatoduodenal resection. The bile passages were markedly dilated at the time of

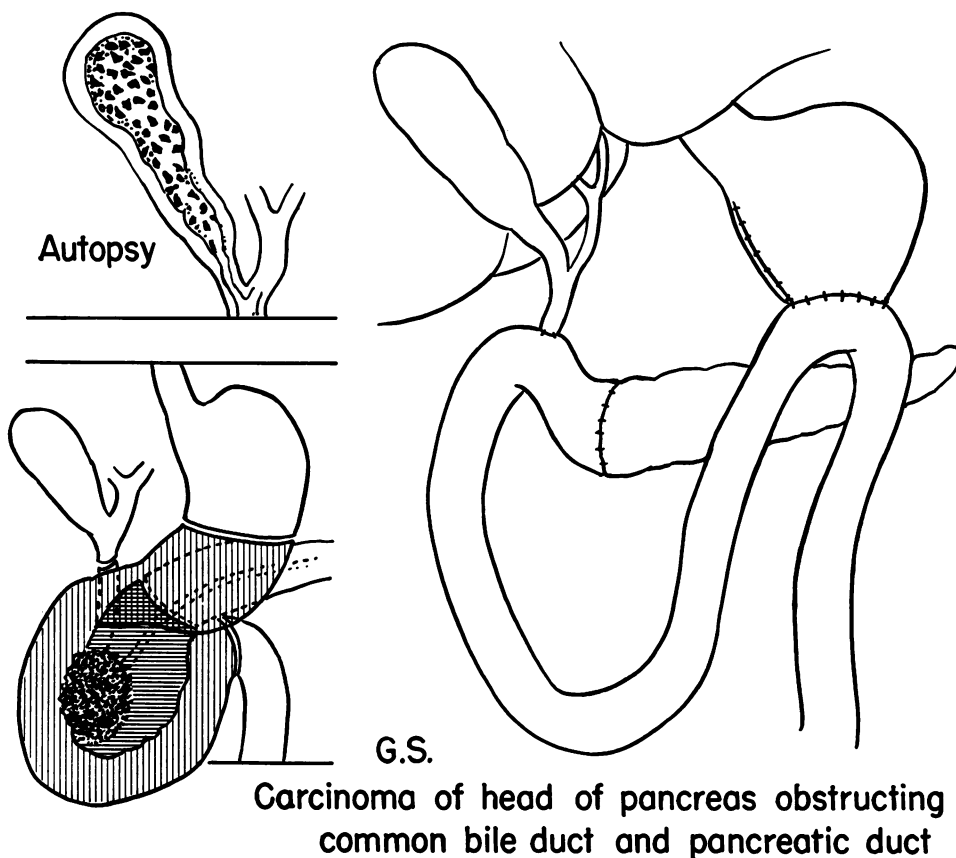


FIG. 6. Drawing of operation and autopsy findings, Case 2.

operation in these cases and even though a long loop of jejunum was placed between the bile duct and stomach anastomoses, severe infection with stone formation in the gallbladder occurred in both instances.

Case 3. J. L., a 47-year-old white man, was operated upon January 15, 1954. He had a transduodenal sphincterotomy performed for chronic pancreatitis at that time (Fig. 7). A T-tube was used to temporarily drain the common bile duct which was not dilated. The gallbladder looked normal and was not disturbed. The patient's attacks of severe pancreatic pain were relieved by this operation and he remained well for almost 2 years when attacks of upper abdominal pain began to reappear but were more localized to the right side than formerly. He was again in the hospital from February 4, 1956, to February 26, 1956, during a particularly severe attack, and at that time presented typical clinical and laboratory evidence of acute

cholecystitis. The acute attack was treated conservatively and the patient was allowed to go home. However, right upper abdominal pain continued; therefore, the patient was readmitted to the hospital March 11, 1957, and operated upon March 15, 1957, at which time a chronically inflamed gallbladder without stones was removed (Fig. 8). Convalescence was uneventful and the patient has remained well during his short follow up period.

Case 4. T. C., a 34-year-old white man, had a transduodenal sphincterotomy performed for chronic pancreatitis December 17, 1955. T-tube drainage of the common duct, which was not dilated, was performed. The gallbladder, which looked perfectly normal, was not disturbed. Attacks of upper abdominal pain, especially on the right side soon returned, and gradually became more severe and frequent accompanied by nausea and vomiting. Operation was again performed October 11, 1956, at which time a chronically in-

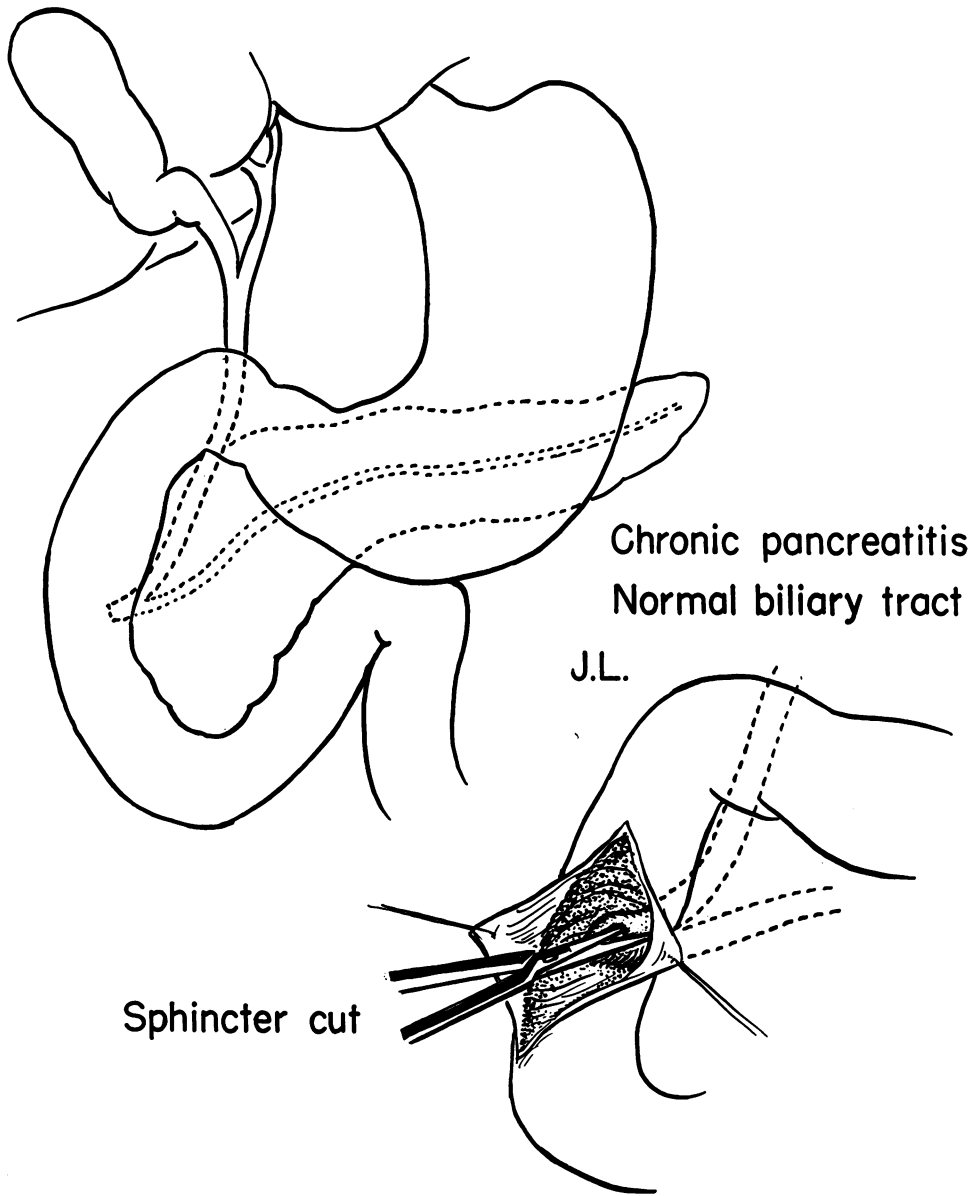


FIG. 7. Drawing of operation performed in Cases 3 and 4; transduodenal sphincterotomy for chronic pancreatitis.

flamed gallbladder was removed; pyloric obstruction from a pseudocyst of the head of the pancreas was present and gastroenterostomy and vagotomy also were performed. Sections of the gallbladder showed several inflammatory diverticula of the mucosa, marked thickening of the wall, and infiltration by chronic inflammatory cells. The patient has

remained well since his second operation although he is an alcoholic and continues to drink heavily.

Comment: Cases 3 and 4 are examples of regurgitation cholecystitis following sphincterotomy. These patients revealed milder degrees of inflammation of the gallbladder than that seen in Cases 1 and 2 and stones did not form. We believe it is

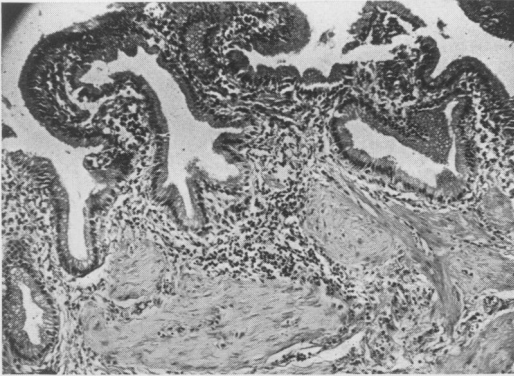


FIG. 8. Gallbladder wall, Case 3, $\times 90$. Thickening and infiltration by chronic inflammatory cells.

important that the bile ducts were not dilated prior to section of the sphincter in these latter 2 patients and feel that the milder inflammatory process and the absence of stone formation in these cases is possibly related to this factor.

Case 5. (Courtesy of Dr. M. D. Cantor.) A. G., a 70-year-old white man, was operated upon March 3, 1953, for independent carcinomas of the head of the pancreas and right colon. A right hemicolectomy was done and a Roux-Y cholecystenterostomy was performed to decompress the biliary tract (Fig. 9). The bile ducts and gallbladder were dilated but otherwise were normal. The patient gradually went downhill and died June 4, 1954. Jaundice was present at the time of death. At autopsy the anastomosis between the gallbladder and jejunum was found to be open, but the gall bladder was thick-walled and contracted and both the gallbladder and common duct were filled with stones varying in size but ranging up to 1 cm. in diameter. Sections of the liver showed definite evidence of ascending cholangitis.

Comment: This case illustrates the fact that regurgitation infection and stone formation may occur even following cholecystenterostomy en Roux-Y. One would think that the wide opening at the fundus of the gallbladder might give adequate drainage of the gallbladder but it is evident that infection and stone formation still may occur.

DISCUSSION

On the basis of this experimental and clinical work it seems clear that retrograde infection of the bile passages can and does occur when the proper set of circumstances exists. Such infection may develop when-

ever the sphincter of Oddi is severed or the common bile duct anastomosed to or transplanted to the intestine if the gallbladder is not removed. The infection would appear to be particularly severe when the bile ducts have been dilated prior to operation. The observation that this type of infection occurs both in dogs and in man even following the transplantation of the common duct to a long blind Roux-Y loop of intestine or its equivalent tends to cast doubt on the idea that the active forcing of bowel content up the bile passages by intestinal peristalsis is the important factor in initiation of and perpetuation of this infection. Rather it would appear that the presence of any mechanism which might interfere with the continuous flow of bile or promote stasis along the bile ducts would allow bacterial contaminants, always present in such an open anastomosis, to gain a foothold and spread. The gallbladder itself constitutes just such a reservoir where infection may easily start and actively flourish.

The belief that one need not fear ascending infection of the bile ducts even with a wide open anastomosis of the common duct to the duodenum, unless stasis or obstruction is present, is a concept shared by many surgeons interested in common bile duct reconstruction, and there is a wealth of clinical evidence to support this view. In the light of the present work, however, this concept must be modified to the extent that such infection need not be feared only if the gallbladder has been removed.

The histologic similarity of the gallbladder wall in these ascending infections to the ordinarily seen types of cholecystitis, as well as the development of gallstones, makes one wonder whether or not ascending intraluminal infection may play a part in the usual development of acute or chronic cholecystitis. The infrequency of a patulous sphincter of Oddi in most cases of gallstones and cholecystitis and the failure of marked cholecystitis to develop in cases

Carcinoma of head of pancreas
obstructing common bile duct

A.G.

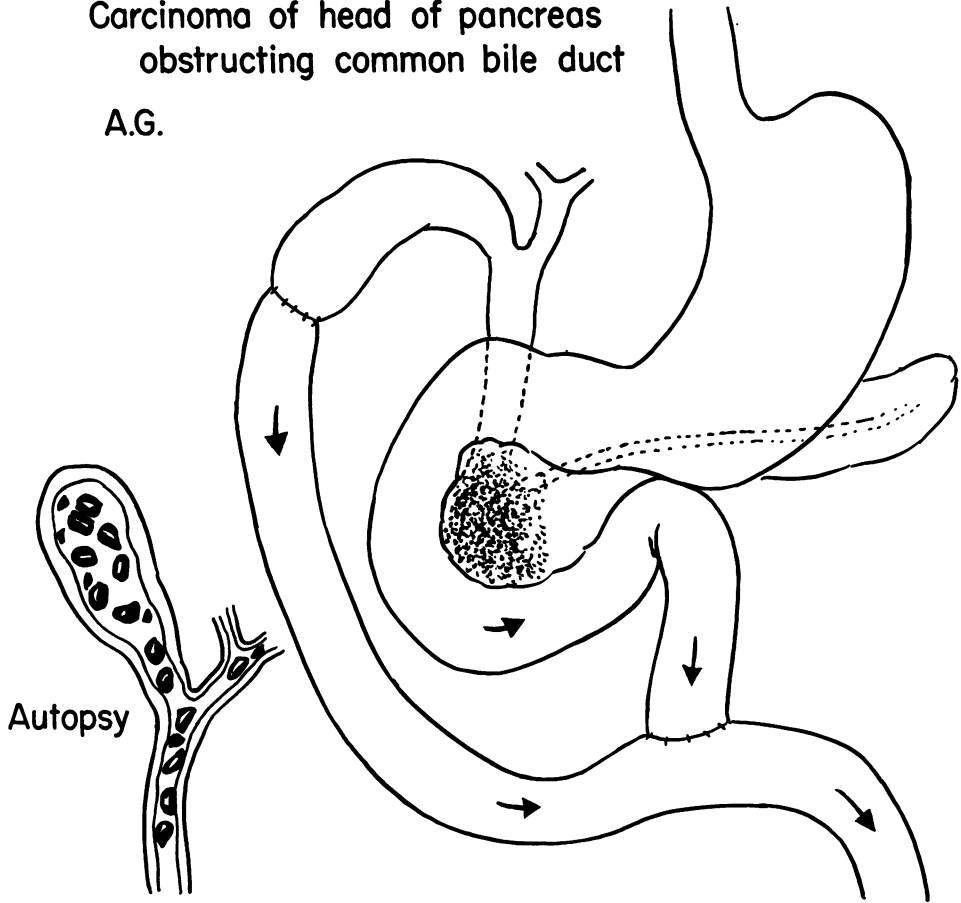


FIG. 9. Drawing of operation and autopsy findings, Case 5.

of choledochoduodenal fistula resulting from peptic ulcer⁷ would tend to negate such a hypothesis. It would appear that ascending infection of the type described in this paper with inflammation of the gallbladder and stone formation, is most likely to develop in those patients whose common ducts have previously been obstructed and who are treated by choledochenterostomy without cholecystectomy.

The method of prevention of this type of cholecystitis is, of course, quite obvious and has already been mentioned. Whenever a wide opening is made between the common bile duct and the intestine, the gallbladder ought to be removed even

though it be perfectly normal. This rule would apply particularly to all types of common duct transplantation to the intestine where the ducts are dilated, such as is usually seen at the time of the Whipple operation, and also would apply to operations such as sphincterotomy where the sphincter of Oddi can no longer function normally. Thus the old and classic rule in biliary tract surgery that the gallbladder should be preserved if it is normal so that it might possibly be used for some subsequent anastomosis, is wrong; this rule should be abandoned. Such a view is, of course, not new. Doubilet and Mulholland² have recommended cholecystectomy at the

time of sphincterotomy as long ago as 1948 and have repeatedly advocated it since that time. Others have reported the occurrence of gall stones following pancreatoduodenal resection,⁶ but as far as we are aware have not called attention to the ascending type of infection which develops.

The fifth case shows that a process of regurgitation infection may occur even when the gallbladder itself is anastomosed directly to the intestine. Such a gallbladder is able to drain and empty itself fairly well but even under these circumstances cholecystitis with stones may develop. Some degree of ascending infection doubtless occurs in these cases with the result that the gallbladder is unable to empty itself properly. It would, therefore, seem wise to perform cholecystenterostomy only as short term palliation for rapidly advancing malignancy. When biliary tract anastomoses are performed for such conditions as chronic pancreatitis it would be better to remove the gallbladder and to anastomose the common bile duct directly to the intestine.

CONCLUSIONS

Inflammation of the gallbladder and stone formation have been shown to occur in the dog and in man following the creation of a wide opening between the common bile duct and the intestine. These findings are thought to develop as a result of ascending intraluminal infection, and

represent, therefore, true iatrogenic cholecystitis and cholelithiasis. A similar process may occur even when the intestine is anastomosed to the fundus of the gallbladder.

On the basis of this evidence it is our opinion that whenever a wide opening is made between the common bile duct and the intestine, the gallbladder should be removed, even though it may be perfectly normal. If it is left in place it will become inflamed and useless for any subsequent anastomosis, stones are likely to form within its lumen, and symptoms are very likely to develop of sufficient severity to require later re-operation and removal of the gallbladder.

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DISCUSSION

DR. MULHOLLAND: Mr. Chairman, ladies and gentlemen, we are indebted to Dr. Large for calling attention to an important physiologic consideration in operative surgery.

I am not certain that the cause of the disease in the gallbladder is regurgitation or ascending infection, even though that assumption seems very attractive. Under normal conditions, the gallbladder fills passively, and to some degree at least, empties passively. Resistance to flow of bile through the common duct creates lateral pressure

which is exerted on a side arm, the cystic duct. Rapid flow through the common duct decreases lateral pressure, and in the presence of a distended gallbladder tends to empty the gallbladder. If there is no resistance to flow in the duct, the gallbladder cannot fill. If it does not distend, its contractility cannot be invoked.

I am told that in at least one instance, in a patient one year after sphincterotomy, the gallbladder could concentrate dye. In this case it is probable that duodenal musculature through which the common duct tunnels offers resistance