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

to flow, and thus permits the gallbladder to fill.

As Dr. Large said, this is not possible in dogs. The observations he has made would indicate that it is not possible in all humans. The sphincter of Oddi and the gallbladder are intimately associated physiologically. This relationship is well attested by the fact that in animals without gallbladders, the rat and horse for instance, there is no sphincter of Oddi.

DR. JOHNSTON: I'm glad that the Program Committee still recognizes that gallbladder disease is a surgical problem. In this very fine series of papers, it seems to be the only one on this subject.

Dr. Large presented only a small number of cases, but I'm sure he does not have to apologize for the small number of cases corroborating his experimental data.

It has long been a rule in our hospital, following the recommendations of Dr. Mulholland, that the gallbladder be removed. Furthermore, I have never felt that the gallbladder was of much use to save as a future emergency problem, because it never seemed to me to be the best available material to form a new common duct. It is not a very good type of prosthesis, and I see no reason for leaving a gallbladder in, except, possibly, temerity on the part of the surgeon.

Some years ago, Dr. Waltman Walters pointed out to us that in cases where there is no stasis in the common duct, one does not get ascending cholangitis. Originally, and before that time, the concept was that one ought to try to make a new sphincter, or a new protective mechanism to prevent regurgitation, but if the gallbladder is removed, it has been my experience that those patients with a wide-open, emptying mechanism in their common duct, with good chance for outflow, do not get cholangitis and ascending infection.

I am sure that with the gallbladder in these instances, with a wide-open common duct, some of the material which does regurgitate up into the common duct gets into the gallbladder, and it's purely a matter of stasis in—as Dr. Large has indicated—what amounts to a diverticulum, which is a good site for infection. (Applause)

DR. WANGENSTEEN: Wolfer (1931) pointed out many years ago that pancreatic juice getting access to the gallbladder could cause inflammation of the gallbladder. Bisgard and Baker (1940) and Hjorth (1947) observed that inflammation, and calculus formation occasionally, followed when pancreatic juice was allowed to enter the biliary tract.

My own interest in this matter dates primarily from the observation that in patients having gallstones, a stenosis or a narrowing at the biliary ampulla is a fairly common denominator. In fact, it has become a precept on my surgical service over the past three years to perform a short transverse duodenotomy during the course of cholecystectomy for gallstones for the purpose of examining the biliary papilla. In 29 (58 per cent) of 50 patients in whom we have done cholecystectomy over the past three years, a No. 3 Bakes dilator (3 mm. diameter) could not be passed through the biliary ampulla without using force. In each instance, the dilator was passed with the papilla in full view. In fact, in a number of instances, the terminal biliary papilla has been found to be pin-point in size.

We have come to think of a stenotic ampulla as a frequent cause of gallstones. The question then is: What causes stenosis of the ampulla? That it may be pancreatic juice activated by bile is a possibility. At least we know that bile and pancreatic juice are injurious to the gallbladder mucosa.

In perfusing the common duct of the dog with gastric juice, my colleagues, Drs. Earl G. Yonehiro and Kamil Imamoglu, have observed that the glandular epithelium of the common duct is as sensitive to injury by gastric juice as is esophageal squamous epithelium.

Ordinarily, of course, acid-peptic gastric juice does not gain entry to the common bile duct—the normal biliary ampulla precludes that happening. In the light of the circumstance that the glandular epithelium of the common bile duct is as sensitive to injury by gastric juice as is esophageal mucosa, is it possible that exposure of the tip of the biliary papilla to erosion by the digestive juices could be the responsible agency in causing stenosis of the ampulla?

I would like to show a few slides with your permission, Mr. Chairman, which demonstrate that experimental production of an incomplete obstruction of the distal portion of the common bile duct may be followed by stone formation within the gallbladder. My associates, Drs. Kamil Imamoglu and John F. Perry, observed that when a ligature of sealing tape dusted lightly with dicetyl sodium phosphate was wrapped lightly around the distal common bile duct to produce an incomplete obstruction, gallstones formed quite regularly in the gallbladder of rabbits, less frequently in the gallbladders of the dog and monkey. If a complete obstruction was established with the ligature, gallstones did not form.

In seven of eight rabbits (87 per cent), in which an incomplete occlusion of the bile duct followed application of the stenosing ligature, gallstones formed in the gallbladder. Occasionally stones formed in the common bile duct as well. You will observe on the slide that the mean period for gallstone formation was nine weeks. However, stones were observed to form as early as four weeks after application of the stenosing ligature to the distal common bile duct.

In the dog stones formed in the gallbladder in only 25 per cent of the animals (two out of eight dogs). Only two monkeys were operated on; one animal was killed at 19 weeks, the other at 22 weeks; one of them had gallstones.

It would appear that we should reverse the long standing idea that a fibrosed ampulla is the result of gallstones; on the contrary, it is more likely the cause of gallstones.

What makes for a stenotic biliary ampulla in the first place? It is a good question and an inquiry that must be pursued. Six years ago it occurred to me that hypertrophy of the sphincter muscle of the ampulla might represent a type of achalasia, such as is seen in the esophagus (Ann. Surg., **134**: 301, 1951). There seems to be little or no information on this and my colleague, Dr. Theodore B. Grage, who has examined some of our biopsy specimens, removed for histologic study when sphincterotomy was done for stenosed biliary papilla, tells me that he finds no suggestion of absence of the parasympathetic ganglion cells in the muscle of the terminal portion of the bile duct, based on a comparison of known normals obtained at autopsy from patients dying of causes other than disease of the biliary tract. Obviously, there is need for more information on this aspect of the minute anatomy of the bile tract.

In dripping saline solution into the common duct at the time of operation in man, in the presence of an observed stenotic ampulla, the sphincter resistance seems to fall within the normal range—an observation which suggests that a stenotic ampulla will not be recognized by the making of a cholangiogram. This observation that a stenosed biliary papilla permits a ready flow of saline solution into the duodenum within the resistance range of the normal ampulla—these observations have persuaded me that it is better and safer to look at the ampulla than to make a cholangiogram which may fail to detect a stenotic papilla. Bile obviously is considerably more viscous than saline solution. The premise, upon which the thesis developed herein rests, is that an ampulla which will not allow a 3 mm. probe to pass is abnormal and can cause biliary stasis which in turn will lead to gallstone formation.

It is, I feel, a circumstance of great importance that a stenotic biliary papilla is found so frequently when gallstones are present in the gallbladder. It is, I believe, a significant relationship concerning which we need to know a great deal more. It is my opinion that when one finds gallstones in the gallbladder, it is best to have a look at the ampulla. Serious study needs to be devoted to the mechanism which underlies the origin of a stenosed biliary papilla.

If additional studies corroborate the observations made herein concerning the sensitivity of the glandular mucosa of the gallbladder and bile ducts to injury by the digestive juices, it may be necessary to revise somewhat our practice of relieving such obstructions by the performance of sphincterotomy. This procedure which permits free entry of the digestive secretions, including acid-peptic juice into the terminal reaches of the biliary tract, in the long run, therefore might not be as physiologic an operation to overcome obstruction at the biliary papilla as attachment of the gallbladder or the dilated common duct to an isolated 30 cm. loop of jejunum. This loop in turn, of course, would need to be drained back into the duodenum near the normal biliary ampulla in order to thwart the formation of a duodenal ulcer.

In the assessment of the origin of gallstones, it is important to consider any and all factors which lead to biliary stasis. Possibly the frequency with which gallstones attend pregnancy is owing to the biliary stasis accompanying the latter months of pregnancy. Gerdes and Boyden (Surg., Gyn. & Obst., **66**: 145–155, 1938) observed retarded emptying of the gallbladders of pregnant women which disappeared after the termination of the pregnancy. My purpose in entering this discussion is to indicate that an atretic ampulla, by causing biliary stasis, may be an important cause of gallstones. (Applause)

DR. LARGE: I would like to thank Dr. Mulholland, Dr. Johnston and Dr. Wangensteen for their comments.

Perhaps the term "regurgitation" is not a very good one. It seems likely that bacteria pass up the duct and into the gallbladder in these instances we have reported, but we don't think that, very often—in humans, anyway—the actual intestinal content gets up into the bile ducts.

We have not felt that this ascending type of infection (which we think is intraluminal, because all the cases in animals, at least, have had positive cultures in the lumen) is a factor in the ordinarily developing cases of cholecystitis and cholelithiasis; and we have not encountered a patulous sphincter in these latter cases, nor indeed, have we been impressed in ordinarily seen cases with the occurrence of an ampulla, but perhaps that is because we haven't looked carefully enough for it. (Applause)