

OBSERVATIONS ON THE BACTERIOLOGY OF CHOLEDOCHAL BILE*

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SOME YEARS AGO, considerable emphasis was placed on infection as a possible cause of gallstones, duodenal ulcer and certain other allied visceral lesions. Today few if any of these conditions are regarded as primarily of infectious origin. This is true of cholelithiasis and likewise choledocholithiasis, and it probably accounts for the paucity of articles in the literature in recent years on bacteriologic studies of choledochal bile. All surgeons recognize the importance of infection in the presence of cholangitis, secondary, for example, to the reflux of intestinal contents into the biliary tree after biliary intestinal anastomosis. Even in reported cases of this type, however, there are few details as to the types of organisms encountered. Perhaps too little attention is given currently to the bacterial content of choledochal bile in the ordinary instance of choledocholithiasis or suspected choledocholithiasis. Hence, it seemed to us that a study of the bacterial content of choledochal bile obtained at operation on a series of patients might be of value.

Numerous studies have been made in past years on bile from the gallbladder, the bile being obtained either at the time of operation or by duodenal drainage.^{1, 2, 5-7} In 1942, Elkeles and Mirizzi⁴ reported a detailed study of the bacteriology of the various parts of the biliary tree, including the common bile duct. Cole³ reviewed the subject of cholangitis in 1947 and made some reference to the bacteriologic aspects of the problem.

NATURE OF STUDY

In the present study a culture was made of choledochal bile removed at the time of

operation on the biliary tracts of 100 patients. In approximately half of these patients the gallbladder was removed because of cholecystitis with stones; simultaneous exploration of the common bile duct had been performed. In most of the remaining cases, the gallbladder had been removed at a previous operation and the current surgical procedure was performed primarily because of suspected choledocholithiasis.

No cases of stricture or malignant obstruction of the common duct were included. All patients were operated on at the Mayo Clinic between January, 1946 and January, 1949. They presented nothing unusual, so far as the factors of age, sex or associated diseases are concerned. In 70 cases, stones were found in the common bile duct; in 30 cases no stones were found. Diagnoses in the latter group included cholelithiasis, stone in a stump of a cystic duct, biliary dyskinesia, pancreatitis, unexplained abdominal pain and hepatitis.

Bile collected by aspiration of the common duct was placed in a sterile cotton-stoppered tube. Bacteriologic examination, carried out in the laboratories of the Section on Bacteriology, consisted of streaking a portion of the specimen over the surface of (1) a nutrient blood-agar plate and (2) an eosin-methylene blue plate. In addition, 1 to 3 cc. of the bile was added to a tube of brain broth. These media were incubated at 37° C. for a minimum of 48 hours, at the end of which they were considered sterile if there was no growth. If any of the inoculated media exhibited growth, proper bacteriologic procedures were employed to identify the organisms present.

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RESULTS OF CULTURE OF
CHOLEDOCHAL BILE

Bile From Patients With Stone in Common or Hepatic Ducts. In 53 of the 70 cases in which stones were found in the common or hepatic bile ducts, culture of bile taken from the common bile duct produced a growth of organisms. Positive results of culture were obtained in approximately three of four cases (75.7 per cent). Review of the organisms found revealed a wide variety of bacteria, occurring either alone or in various combinations. In two thirds (66.1 per cent) of cases in which culture produced growth, a single type of organism was found; in about a third of cases (33.9 per cent) multiple organisms were present. In all, 11 different bacteria were isolated from the group in which growth was produced; they included *Escherichia coli*, *Aerobacter aerogenes*, *Streptococcus faecalis* and species of *Proteus*, *Corynebacterium*, *Pseudomonas* and *Micrococcus*, as well as green-producing, hemolytic, nonhemolytic and anaerobic streptococci.

Escherichia coli was found more often than any other organism both by itself and in association with other bacteria (Table I). It was found in a total of 69.8 per cent of the 53 cases in which positive results of culture were obtained. In 44 per cent of cases *Escherichia coli* occurred alone, and in 25.8 per cent of cases it was found in combination with one or more other types of bacteria. *Aerobacter aerogenes*, *Streptococcus faecalis* and *B. proteus sp.*, respectively, were the other organisms most frequently encountered.

Bile From Patients Who Did Not Have Stones in Common or Hepatic Ducts. In 30 cases stones were not found at the time of exploration of the common or hepatic bile ducts. In 15, or half of these cases, culture of bile taken from the common duct produced organisms. Eight different types of organisms were encountered in the

group of specimens from which growth resulted. These organisms were similar to those produced from the specimens of bile from patients who did have stones in the bile ducts. Again, *Escherichia coli* was the organism found most frequently. It was present in a total of six of the 15 cases in which results of culture were positive, and in four of these it was the only organism present. A green-producing *Streptococcus* was present in four cases. *Aerobacter aerogenes* was found in three cases and *Streptococcus faecalis* in two cases; others

TABLE I.—*Bacteria Found in Choledochal Bile in 53 of 70 Cases in Which Stones Were Present.*

Organism*	All Cases in Which Organism Occurred		Organism Occurred Alone	
	Cases	Per Cent	Cases	Per Cent
<i>Escherichia coli</i>	37	69.8	22	44
<i>Aerobacter aerogenes</i>	13	24.5	5	9.4
<i>Streptococcus faecalis</i>	10	18.9	2	3.7
<i>B. proteus sp.</i>	3	5.6	1	1.9

* Seven other organisms encountered less frequently.

were found once. In 11 of the 15 cases (73.4 per cent) only one organism was isolated, a somewhat higher percentage than obtained in those cases in which stones were present. In four cases multiple types of bacteria were found.

RELATIONSHIP OF PREVIOUS OPERATION ON BILIARY TRACT TO INCIDENCE OF INFECTION IN CHOLEDOCHAL BILE

A total of 54 of the 100 patients in this series had undergone an operation on the biliary tract prior to the one at which a specimen of choledochal bile was obtained for culture. It is of interest to note that results of culture of bile were positive in 81.5 per cent of this group. On the other hand, positive results of culture of bile were obtained among only 52.1 per cent of those for whom no operation previously had been performed on the biliary tract.

Stated in another way, of those patients whose choledochal bile had produced organisms on culture, 64.7 per cent had

undergone a previous operation on the biliary tract, whereas only 31.3 per cent of those whose choledochal bile did not produce organisms by culture had undergone previous operations on the biliary tract. It was found that positive results of culture were obtained less frequently among patients who had undergone previous operations on the gallbladder alone than among those who had undergone a previous operation on the common bile duct. Thus, in 29.9 per cent of 32 patients in the former group results of culture were negative, whereas results of culture were negative among only 13.6 per cent of those who previously had undergone operations on the common bile duct.

COMMENT

Results of culture of choledochal bile removed at the time of operation frequently are positive. Since culture of bile produced positive results more frequently in the presence of stones in the common bile duct (75.7 per cent) than when stones were not present (50 per cent), it might be assumed that infection frequently is a significant factor in the production of calculi in the bile ducts. On the basis of these data, however, such a conclusion does not appear warranted, because it is entirely possible that in some cases infection developed after the formation of calculi. As is well known, choledocholithiasis often causes some degree of stasis of bile, which in turn predisposes to the occurrence of infection. A similar situation sometimes is found in the urinary tract in the presence of stones. If infection were the only factor in the formation of biliary calculi, it might well be expected that the difference in incidence of infection would be greater when stones were present than when they were not present. On the other hand, it is difficult to say that infection never plays a part in the production of choledocholithiasis. Since the organisms found when stones were not present were

virtually the same as those found when stones were present, it seems unlikely that any one type of organism is particularly significant in the formation of stones. The organisms found are of a common variety, such as are encountered normally in the gastro-intestinal tract. Infection in the bile ducts, in the absence of obstruction, appears to be of definitely less clinical significance than when obstruction is present.

It seems to be fairly certain that an operation on the biliary tract predisposes to infection of choledochal bile, whether or not stones are present. This fact, we believe, is of some importance. Although in many cases a mild or low-grade infection in the biliary tree, unassociated with other pathologic changes, may be of no great clinical significance, it hardly seems that it should be ignored.

To proceed further: an obvious suggestion is to administer antibiotic treatment after any operation on the biliary tract, but especially after exploration of the common bile duct, although it is impracticable to determine whether the treatment is effective because of the difficulty of obtaining a specimen of bile for culture after completion of therapy. If, however, such therapy were carried out routinely, at least an effort would have been made to leave the biliary tract sterile after operation. It is true that in the majority of cases such treatment might not be necessary and the patient might obtain an excellent end result even though the treatment were not provided. Yet, in the exceptional case, it might be most efficacious. If a T-tube had been placed in the common bile duct, treatment should be administered only after removal of the tube, because the presence of this foreign body interferes greatly with obtaining and maintaining sterility in the biliary tree.

At present, a number of antibiotic agents are available which have a desirable range of activity and which are excreted in

the bile. Zaslow, Counseller and Heilman^{8, 9} reported interesting results of studies in this regard in 1947. These authors demonstrated, for example, that in the presence of adequate hepatic function and the absence of biliary obstruction, penicillin, after it has been administered intramuscularly, may be found in choledochal bile in concentrations somewhat more than those noted in the blood stream. Under similar circumstances, streptomycin is found in slightly lower concentration in choledochal bile than is present in the blood stream. Likewise, it is known that under similar circumstances both aureomycin and terramycin are excreted in choledochal bile in sufficient concentrations to be effective. After Chloromycetin has been administered systemically, it is found in bile in concentrations too low to be of value clinically. Hence, the use of this particular agent for the treatment of infection in the biliary tree is not recommended.

It would appear that in the usual case of infection of the biliary tree aureomycin and terramycin currently are the antibiotic agents of choice, although penicillin and streptomycin also may be used. It should be remembered that in the presence of obstruction of the common bile duct or appreciable hepatic damage, no antibiotic agent is excreted in the bile in concentrations sufficient to be effective. Selection of the antibiotic agent of choice should be governed, if possible, by the type of bacteria present.

SUMMARY

Bacteria frequently are found in choledochal bile. Bacteria are found more often (75.7 per cent of cases) when stones are present in the common bile duct than when stones are not present (50 per cent). Bacteria are found more often in choledochal

bile if a previous operation has been performed on the biliary tract than if there has been no previous operation. Bacteria are found in choledochal bile somewhat more often if a previous operation has been performed on the common bile duct than if the previous operation was carried out on the gallbladder alone. Infection of choledochal bile was found in a high percentage (87.8 per cent) of cases in which chills and fever occurred in the presence of disease of the biliary tract.

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