1933

Cholecystitis

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CHOLECYSTITIS

SENIOR THESIS

UNIVERSITY OF NEBRASKA

COLLEGE OF MEDICINE

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CHOLECYSTITIS

Gall-bladder disease did not occupy such a prominent part in the early medical writings as it does in those of the present day. However, in Hippocrates (fourth century B. C. (460-370? B. C.)) and in Galen (second century A. D. (131-201 A. D.)), it is true there are a few brief communications on pain in the hepatic region, and on icterus as a result of constipation without fever, but these descriptions are, according to Hoppe-Seyler, very inadequate as compared to their precise and exact communications on renal colic. In view of the fact that the old Greek physicians were good clinical observers, and at the same time thorough students of anatomy, the above author feels forced to conclude that gall-stones and gall-bladder disease were less frequent in those days than they are in modern times. The reason for this can not very well be given, but the mode of life may have had something to do with it. The food was simpler and physical exercise was an important factor throughout the lives of these people.

The earliest knowledge of gall-bladder disease came thru observation of biliary calculi. Gentilis of Foligno, in the fourteenth century, is said to have found stones for the first time in the gall-bladder and cystic duct of a corpse that he was embalming. Antonius Benivenius in the sixteenth century was the first to associate the clinical

symptoms of gall-bladder disease with gall-stones. He describes gall-stones that were seen in the case of a woman who had been a sufferer from pain in the abdomen. They were found both in the gall-bladder and in a sacculated cavity on the surface of the liver. He assumed that the death of this patient was caused by these stones. Fernelius, also in the sixteenth century, describes gall-stones and the symptoms which they produce. According to Hoppe-Seyler this latter author seemed to be familiar with the fact that occlusion of the ductus choledochus leads to a swelling of the gall-bladder, a white discoloration of the feces, and the passage of dark urine, and that in occlusion of the hepatic duct the gall-bladder is empty. He also associated a stagnation of bile with calculus formation, especially stagnation due to occlusion of the cystic duct. He states that the symptoms of this condition are frequently so indistinct that the disease cannot be diagnosed.

As we follow thru the literature, various men are found to have made contributions to the study of gall-bladder pathology. As has already been mentioned, gall-stones occupied the attention of all the early observers. It was not until the last century that disease of the gall-bladder apart from cholelythiasis has assumed an independent role.[2] 32 Rolleston's work, "Diseases of the Liver, Gall-Bladder and Bile Ducts", published in 1905, was one of the first comprehensive discussions on diseases of the gall-bladder. Graham, Cole, Copher and Moore in their book, "Diseases of the Gall-Bladder

and Bile Ducts"[13], have given us the most complete review of the late work on gall-bladder function both in normal and pathological conditions. With this latter work as a background, a review of the more recent articles up to the present time enables one to arrive at very logical conclusions as to the mechanism of disease in the gall-bladder.

PHYSIOLOGY OF THE GALL-BLADDER

There are many problems relating to the functional activities of the gall-bladder which are still obscure in spite of the great amount of experimental work that has been done along this line, although much has been learned from the findings of cholecystography since the introduction of this method of study by Graham and Cole in 1924.

The general conception of gall-bladder function would come under two headings, one probably the older of the two, is that the gall-bladder is a store-house for bile. The other, that it serves to concentrate the bile, making it more effective when expressed into the duodenum. Both of these conceptions are correct, but an additional and broader understanding may be obtained from a consideration of Moynihan's summary or classification, which is as follows:

"1. The chief function of the gall-bladder is excretory.

"2. The mucosa of the gall-bladder absorbs fluid and other substances from the hepatic bile, which it reduces to one-sixth or less of its original volume.

"3. Fluids and other substances absorbed are carried off by the lymphatics and by the capillary circulation.

"4. The mechanism by which the gall-bladder is emptied is complex; muscular contractions, variation in abdominal pressure, milking of the common duct by duodenal peristalsis, the 'sprengel air pump' action of bile as it descends from the liver flowing past the opening of the cystic duct,

elastic recoil, may all play a part in this act.

"5. The quantity of bile leaving the gall-bladder in the course of 24 hours is very small.

"6. The functions of the gall-bladder as an adjuvant of alimentary digestion are slight, and operative experience suggests that they are almost negligible.

"7. The part played by the gall-bladder in the general economy, by virtue of its powers of absorption is unknown. There is suggestive evidence that it is concerned with the movements or the metabolism of cholesterol."

The bile is secreted by the liver at varying rates and except for the amount which is utilized during periods of digestion, is stored in the gall-bladder till needed. The quantity of bile which passes to the gall-bladder is much greater than the volume of the gall-bladder which, however, by its concentrating action is able to take care of the excess. Rous & McMaster demonstrated the concentrating power of the gall-bladder conclusively. These men made a quantitative study of the ability of the gall-bladder to concentrate the pigments of the bile. They collected the bile secreted by the liver of dogs in two portions, one portion comprising the bile which had passed into the gall-bladder, while the other portion was not allowed to enter the gall-bladder. Analysis showed that the proportion of pigment in the bile from the gall-bladder was sometimes ten times as great as that in the bile which had not entered the gall-bladder.

The rapidity of the development of jaundice was shown by Mann and Bollman to be influenced by the absorptive function of the gall-bladder. They found that if the common bile duct was tied and the gall-bladder left intact, jaundice did not appear for thirty-six to forty-eight hours following the ligation, while if the gall-bladder was removed at the same time that the common duct was ligated, jaundice appeared in from three to six hours. It is this ability of the gall-bladder to concentrate bile that permits its visualization after the administration of the phenolphthalein-iodine combination. The lymphatics, capillaries and venules of the gall-bladder all seem to take an active part in absorption. In addition to the absorptive power of the gall-bladder, it secretes mucous which mixes with the gall-bladder bile. The extra hepatic ducts are also said to secrete a thin mucous.

The regulation of the flow of bile into the duodenum was formerly thought to be controlled wholly by the sphincter of Oddi. Recent authors, however, lean toward the idea of control by tone of the duodenal musculature, since the bile duct runs for some distance obliquely through this muscle layer. The discharge of bile into the duodenum seems to occur chiefly during the relaxation phase of the peristaltic movement. Phillips gives five factors in the mechanism of emptying the gall-bladder.

"(1) dilution and interchange of bile", an idea also expounded by Graham and Cole.

"(2) elastic recoil of the gall-bladder.

"(3) contractions of the gall-bladder itself.

"(4) variations in intra-abdominal pressure.

"(5) possibly a gall-bladder hormone which may in some manner affect the first four factors."

Copner, Kodama & Graham beleive that the factor of dilution and interchange of bile is of great importance in emptying the gall-bladder. This is accomplished by the entrance of unconcentrated bile from the hepatic ducts into the gall-bladder which results in a gradual washing out of the concentrated gall-bladder bile. The above men found that, if the hepatic duct of a dog was ligated and the cystic and common duct were left intact, the gall-bladder did not empty itself at all readily after a fat meal, as was shown by the persistence of the gall-bladder shadow after the injection of tetra-iodo-phenolphthalein.

That elastic recoil plays a part in emptying the gall-bladder is borne out by Boyden, who found that the response of the gall-bladder to food containing fat was greatest when it was distended. Such finding would be expected when one considers the large amount of elastic connective tissue in the gall-bladder wall. Variations in the intra-abdominal pressure due to muscular exertion and respiratory movements probably play only a minor role in the emptying of the gall-bladder. As to the action of the muscle tissue in the wall of the gall-bladder, there has been some question as to its

effectiveness. Rhythmic changes in pressure in the gall-bladder nave been recorded, which are believed by several investigators to be due to contractions of its wall. How much of a role these contractions play in the emptying of the gall-bladder it is impossible to estimate.

Based on the hypothesis of a reciprocal activity between the gall-bladder and the sphincter of the common duct, Lyon and Meltzer have instituted a non-surgical drainage of the gall-bladder. There has been a great deal of criticism of this theory, but some recent work by Potter and Mann and McMaster and Elman would seem to support Meltzer's hypothesis. These men found that after the ingestion of food there was always a sudden decrease in the resistance to the passage of bile into the intestine, which was accompanied by a synchronous increase in the pressure within the gall-bladder.

The decrease in resistance to the passage of bile into the intestine could very well be explained on the assumption that the flow is regulated by the tonicity of the duodenal muscle. Under this hypothesis there would be a rhythmic relaxation of the terminal end of the common duct preceding each peristaltic wave. The contraction of the gall-bladder, however, must be explained in another way. The possibility that some hormone is present either in the secretion of the gall-bladder itself or in the secretion of the duodenal and jejunal mucosa has been considered for some time. And re-

cently Clay and Oedberg have succeeded in obtaining a purified extract from the duodenal mucosa which when injected intravenously causes the gall-bladder to contract, and to exert pressure on its contents and at the same time excites secretion on the part of the pancreas. With this evidence of hormonal activity the hypothesis of reciprocal action on the part of the sphincter of Oddi and contraction of the gall-bladder could be discarded for that of a relaxation of the duodenal end of the common duct, with peristalsis and a hormonal stimulation of the gall-bladder.

CHOLECYSTITIS

Cholecystitis or inflammation of the gall-bladder is the disease of the gall-bladder most frequently encountered. This, like inflammation in any organ, may be eitner acute or chronic in type, and cholecystitis of either type often is associated with inflammation of the bile ducts and with the presence of stones in the gall-bladder.

Acute inflammation of the gall-bladder may be catarrhal, suppurative, phlegmonous, or gangrenous in character, depending upon the virulence of the infection and the resistance of the organ to the invading bacteria. It may occur in the course of any acute infection, such as typhoid fever, and is frequently associated with gall-stones. It may occur at any age, but is seen most frequently between 40 and 60. However, there are cases reported of cholecystitis in children and it is known to occur in elderly people as well.

Phillips[28] divides the etiological factors in cholecystitis into two groups, (a) predisposing and (b) exciting factors. Under predisposing factors are those conditions which lower the resistance of the gall-bladder and render it more liable to infection. These are: "(1) conditions which cause stagnation of bile in the gall-bladder, such as visceroptosis, tight lacing, and abdominal distention or pregnancy, which may impede the movements of the diaphragm; (2) a previous attack of cholecystitis, after which the microorganisms have remained

latent in the wall of the gall-bladder, but are capable under suitable conditions of causing a relapse, or the presence of gall-stones; for a pure cholesterol stone may form without any previous inflammation of the gall-bladder. McEachern and Gilmore[23] are not fully in accord with this statement, but its presence favors the production of a subsequent infection; (3) injury to the gall-bladder, which by reducing its resistance, may allow microorganisms that reach the gall-bladder to become active; (4) the absence of HCl in the gastric contents, which favors microbic activity in the intestine and thus favors infection of the gall-bladder; (5) a previous general infection such as typhoid fever or pneumonia; (6) the presence of foci of infection elsewhere in the body such as infected teeth, tonsils or sinuses." It is impossible to evaluate definitely the part each of the above factors plays in the etiology of cholecystitis. But an effort to eliminate those possible should be made before the onset of a chronic cholecystitis.

There are several routes by which infection may be carried to the gall-bladder. There is an ascending route from the duodenum, thru the common and cystic ducts into the gall-bladder, and there is a descending route by way of the hepatic artery or portal vein to the liver, from which the bacteria are carried by the lymphatics or by the bile to the wall of the gall-bladder. It is also possible for the gall-bladder to become inflamed by the spreading of

an infection thru its wall from an inflammation of a contiguous organ.

An ascending infection is said to occur rarely except in those cases in which there is an obstruction of the common duct at its entrance into the duodenum, because normally the bile passages do not contain bacteria, even though the contents of the duodenum may be rich in them. An obstruction of the lower end of the common duct capable of causing an ascending infection might be due to the presence of a stone in the ampulla, to cicatricial stenosis, or to an acute inflammatory edema resulting from duodenal catarrh. An obstruction high in the common duct is not likely to cause infection of the gall-bladder and if cholecystitis is present in such a case, the infection is more likely to be of the descending variety.

Descending infection of the bile passages and gall-bladder can take place as a result of infection in almost any part of the body. It might follow an osteomyelitis, a dental or tonsillar infection, influenza, a furuncle, carbuncle, puerperal fever, appendicitis, typhoid or scarlet fever or some other general systemic infection. However, infected areas drained thru the portal system would seem especially liable to cause infection in the liver with subsequent spread to the gall-bladder.

There is considerable discussion as to whether the bacteria reach the gall-bladder by way of the blood stream,

the lymphatics, or by way of the bile ducts themselves. All three avenues are possible and each plays a part under conditions especially adaptable to that mode of transfer. As for the bile, in all cases of bacteremia, microorganisms are carried down to the gall-bladder from the liver by the bile, but it is only occasionally that cholecystitis results. In typhoid fever a large proportion of, if not all cases, have typhoid bacilli in the gall-bladder, but only occasionally does cholecystitis result. Moreover, as Phillips points out, in cholecystitis the bacteria are found in greatest numbers in the deeper layers of the wall of the gall-bladder, so that the infection would seem to be carried there either thru the blood stream or the lymphatics, as the bacteria would not penetrate so deeply into the wall if they merely came into it by contact with the mucosa.

The hematogenous origin of cholecystitis and the selective affinity of streptococci from the tonsils for the gall-bladder has been emphasized by Rosenow. And it is believed that some cases of cholecystitis may be accounted for in this way. However, the association of cholecystitis with inflammation of the appendix or of other organs drained by the portal system is more common and would seem much more probably for there is direct communication between the blood supply of the appendix and the gall-bladder. The lymphatics on the other hand are thought by some, notably Graham and Peterman, to be a more important pathway for infective bac-

teria. There is a very intimate lymphatic connection between the liver and gall-bladder through the attachment of the gall-bladder to the liver. And Judd believes that cholecystitis rarely exists without hepatitis and that hepatitis usually precedes the cholecystitis. Graham and Peterman have shown that in cases of cholecystitis associated with abdominal infection, hepatitis precedes the cholecystitis, and the gall-bladder is infected secondarily thru the lymphatics. The infection first is brought to the liver by the portal vein or rarely, perhaps, by the hepatic artery. Following this a hepatitis results and then because of the extensive anastomosis between the lymphatics of the intra-hepatic and extra-hepatic biliary systems a direct extension of the infection into the wall of the gall-bladder takes place.

The degree of inflammation revealed by an acutely infected gall-bladder depends upon the severity and duration of the infection. In the wild forms of the disease the gall-bladder is distended and reddened, its wall is somewhat thickened and edematous, and the mucous membrane is congested, may have a villous or velvety appearance and shows an abnormal amount of mucous in its surface. The reddened mucous membrane may show numerous yellow specks containing cholesterol ester. These form papillomatous projections out from the mucosa and lend to it the strawberry appearance which has resulted in the term strawberry gall-bladder. This condition is not a true inflammation, but is associated with a

dysfunction of the gall-bladder. McEachern and Gilmour[23] believe it to be a sequel of cholecystitis with a failure of normal absorption of cholesterol on the part of the gall-bladder. "The serous coat of the gall-bladder may appear dull because of the presence of fibrin on its surface, and it may be adherent to adjacent structures. The cystic duct is narrowed or even may be closed by the swelling of its mucous membrane. The gall-bladder contains cloudy, bile-stained fluid with an excessive amount of mucous, except in the cases in which the cystic duct is closed, when, with the bile pigment absorbed, the contents of the gall-bladder become quite clear. The gall-bladder may be enormously distended and may or may not contain stones. The lymphatic glands which are related to the cystic and common ducts are enlarged and if there have been recurrent attacks of acute inflammation these glands may be so hard as to simulate a malignant condition." (Phillips: Diseases of the Liver & Biliary Tract)

The simple catarrhal stage of cholecystitis may progress to the suppurative form or so-called empyema of the gall-bladder. This is associated nearly always with an obstruction of the cystic duct due, as a rule, to the presence of an impacted stone. In cases of the suppurative form of cholecystitis the gall-bladder is considerably swollen and tense, and in some cases may be gangrenous. The contents of the gall-bladder are purulent, and in the early stages of the disease are yellowish or brown in color, but if the

empyema has been present for several days the bile pigment will have disappeared, and the contents will have the color of ordinary pus. If the condition is due to the impaction of a stone in the cystic duct, many other stones may be present in the gall-bladder. The regional lymph glands may be greatly enlarged and occasionally contain pus. There are more extreme degrees of cholecystitis known as phlegmonous and gangrenous cholecystitis but these merely mark a more advanced gradation of suppurative inflammation of the gall-bladder. The important factors concerned in the production of these severe forms of cholecystitis are the virulence of the invading organism, the blocking of the cystic duct and the gangrene which results from the blocking of the blood supply by thrombosis. It is also possible that torsion may shut off the blood supply to the gall-bladder with a resulting gangrene. This is said to be very rare, however.

Histo-pathological changes occur in all layers of the gall-bladder wall. The mucous membrane shows varying grades of inflammation and may be lost in some places, but it is seldom completely destroyed even in the severer forms of inflammation of the gall-bladder. The muscular layers may be severely inflamed, infiltrated and edematous and the same may be true of the subserous layer beneath the peritoneum. In these latter cases a localized peritonitis occurs. The amount of pathology depends upon the severity of the infection and following some of the more severe inflammations of the gall-bladder contractions and distortions of the organ amounting

to almost obliteration may result.

The symptoms of acute cholecystitis vary greatly with the severity of the infection. It is very probable that some of the milder cases are overlooked, the condition being diagnosed as dyspepsia or indigestion. In other cases in which the disease accompanies some acute infection, the symptoms of the latter, as for instance the stupor and the abdominal distention that so frequently accompany typhoid fever, may obscure entirely the symptoms of inflammation of the gall-bladder.

In well-marked cases of cholecystitis, as in cases of other infections, the onset of the symptoms is quite sudden and is sometimes accompanied by a chill. Chills occasionally occur at the onset, but as a rule they are not severe. The temperature varies from 100-102° F. in the usual case to 104-106° F. in extreme cases. The rise in temperature is accompanied by symptoms of intestinal irritation, anorexia, nausea and vomiting. Pain is a prominent symptom in most cases. It is continuous and aching in character and localized in the right upper quadrant.

When cholecystitis is associated with stones in the gall-bladder the pain may be cramp-like and colicky and require large doses of morphine for relief. Occasionally the pain may be referred to the back, especially to the region of the tip of the right scapula and to the right of the lower dorsal vertebra. In rare cases it may be referred to the precordium or upper left quadrant of the abdomen. If there is

a localized peritonitis around the gall-bladder the pain may be referred to the tip of the right shoulder as a consequence of the irritation of the terminal branches of the phrenic nerve. The pain is most acute during the first 2 - 3 days,, after which it begins to subside so that as a rule it disappears within a week or ten days.

Jaundice may occur and when it does its presence indicates that there is some obstruction of the hepatic or common duct by stones, or by the extension of the inflammatory process from the gall-bladder to the ducts. Jaundice may also occur as the result of an associated hepatitis which has been shown to occur in practically all cases of cholecystitis and is characterized by inflammation around the intra-hepatic bile ducts.

Examination of the patient generally reveals no marked impairment of health, tho he may have lost considerable weight as a result of the gastro-intestinal disturbances which are usually associated with the cholecystitis. Tenderness over the gall-bladder and rigidity of the right rectus muscle are present, the latter symptom may be so marked as to make it impossible to determine whether or not the gall-bladder is enlarged.

When the cystic duct is obstructed, the gall-bladder may be enormously distended so that it can be felt as a large, cystic, pear-shaped tumor extending into the right flank or even down toward the pelvis. The liver is sometimes en-

larged, tho as a rule to no great degree, and tenderness can be elicited by pressure at the right of the 11th and 12th dorsal vertebrae. Cutaneous hyperesthesia may also be present in the 8th and 9th dorsal segments.

If there is marked irritation of the peritoneum, around the gall-bladder, there may be severe vomiting with signs of intestinal obstruction, which probably is due to paralysis of the bowel resulting from irritation of the hepatic flexure of the colon. The respiration may be jerky and because of the pain, more or less restricted on that side. The respiratory sounds at the base of the right lung may be diminished in intensity. The laboratory will show a leucocytosis of 12-25,000 cells with a relative increase in polymorphs.

Roentgen-ray examination in cases of acute cholecystitis is of very little value, tho it may be of some advantage if the patient is seen after the acute stage has passed. Lyon's method of biliary drainage may be useful as the findind of pus and detritus in the "B" bile aids in establishing the diagnosis. In considering a case of possible acute cholecystitis a number of other conditions must be ruled out. In a typical case in which fever, localized tenderness and rigidity over the gall-bladder are present, the diagnosis is not difficult. On the other hand, in atypical cases, the condition must be differentiated from inflammatory conditions above the diaphragm and conditions in the right side of the abdominal cavity.

Among those conditions which are sometimes confused

with acute cholecystitis may be mentioned: (1) gall-stone colic, (2) acute appendicitis, (3) acute pancreatitis, (4) diaphragmatic pleurisy with or without pneumonia of the lower lobe of the right lung, (5) hydronephrosis, (6) floating kidney, (7) ovarian cyst, (8) distended bladder with diverticulum, (9) omental cyst, (10) lead colic, (11) gastric crises of tabes, (12) coronary thrombosis, (13) herpes zoster.

In gall-stone colic the pain is usually more severe than that caused by cholecystitis, and it is not accompanied by fever. However, the two are very frequently associated.

Acute appendicitis readily can simulate acute cholecystitis in certain atypical cases, as in the not-so-infrequent retrocecal appendix in which the appendix is situated high up in the abdomen, having failed to descend in the course of development, or in cases in which the tip of the appendix is turned upward and is adherent at a point near the gall-bladder.

Acute pancreatitis is usually mistaken for acute cholecystitis. However, in acute pancreatitis the prostration is as a rule more marked, the temperature higher and the tenderness more nearly in the mid-line.

Pneumonia and pleurisy on the right side of the chest may cause symptoms simulating those of acute cholecystitis. The pain in diaphragmatic pleurisy is often referred to the abdomen, but a careful examination of the chest usually will establish the diagnosis. Also the respiratory rate is much

increased in pneumonia and there is limitation of expansion on the affected side. In pneumonia pressure on the affected side relieves pain, often the patient lies on that side, while in cholecystitis the pain is increased by pressure.

Hydronephrosis and floating kidney can be differentiated readily from acute cholecystitis by means of a pyelogram. In the case of an ovarian cyst the examiner can trace its attachment to a point within the pelvis, and the same is true in the case of a diverticulum attached to a distended bladder.

Lead colic and gastric crises of tabes are not accompanied by fever. Also a history of exposure to lead, basophilic stippling of the red cells and a lead line on the gums will serve to establish the diagnosis of lead poisoning, while a neurological examination and history will reveal or exclude the presence of tabes.

In addition to the above-mentioned conditions there are serious heart complications, such as angina pectoris and coronary thrombosis, which may give rise to pain in the upper abdomen. And because of the hepatic engorgement in coronary thrombosis there may be tenderness and rigidity of the upper right quadrant of the abdomen. With coronary thrombosis the patient is gravely ill, the pain is so severe that even morphine has little effect, the pulse is small and rapid, and the sounds faint. There may be a pericardial friction rub and the blood pressure is low.

The treatment of acute cholecystitis depends upon the

severity of the condition. In the milder forms the patient is kept in bed. Relief from the local symptoms may be obtained by the use of hot fomentations over the entire upper part of the abdomen. These should be changed frequently and kept hot by covering them with oiled silk or paraffin paper over which a hot electric pad or hot water bottle is placed. When the pain is very severe a hypodermic injection of morpnine should be given. The bowels should be kept open by the daily morning administration of magnesium sulphate. Lyon recommends the non-surgical drainage of the gall-bladder by means of the administration of a 33% solution of magnesium sulphate thru a duodenal tube. Many observers, however, believe that they get as good results by the oral administration of magnesium sulphate. Lyon's method of gall-bladder drainage has fallen into considerable disrepute since its introduction in 1923, but at the present time (1933), investigators seem to be giving his work more generous consideration. (Twiss[37], John Russell) The diet should consist of liquids or easily digested carbonydrates.

Cases of suppurative cholecystitis or of hydrops of the gall-bladder should be treated by surgical operation. Cholecystostomy or cholecystectomy may be done for cholecystitis. The latter is the operation of choice except in the case of very aged or debilitated individuals. Also in cases of empyema of the gall-bladder it is sometimes better to do a two-stage operation, drainage being established in the first stage, and the gall-bladder removed in the second.

Chronic cholecystitis, which would sometimes seem to be a more common condition than acute cholecystitis, is truly only a later stage of the acute condition. It is probably largely responsible for the occurrence of gall stones and for their early symptoms. Knowledge of chronic cholecystitis and its importance in the production of gastric symptoms has progressed very rapidly during recent years, especially since the extensive work of Graham and Cole on cholecystography.

Since chronic cholecystitis is a sequel of acute cholecystitis, the sex and age incidence correspond to that of the latter, the proportion of women to men being approximately two to one, and the disease being principally a disease of middle age. Although in some cases the condition exists for a long time before the symptoms become sufficiently marked to bring the patient to the physician.

The etiology, as indicated above, is that for acute cholecystitis and therefore includes the various factors which predispose to gall-bladder disease in general, such as constipation, a sedentary life, and the harboring of foci of infection. In the female, pregnancy is a very potent predisposing factor. The increased abdominal pressure, the resulting lax abdominal wall following pregnancy and the increase in amount of biliary cholesterol during pregnancy are all factors which probably aid in accounting for the greater incidence of cholecystitis and cholelythiasis in women.

In chronic cholecystitis the gall-bladder may be distended with very thick tenacious mucous or in other cases it may be very small and shrivelled. There is catarrhal inflammation with moderate swelling of the mucous membrane and in the cases in which it contains a great deal of mucus, there may be partial occlusion of the cystic duct. The wall of the gall-bladder is usually thickened and indurated and the mucous membrane may be thrown into folds. Adhesions may be formed about the gall-bladder due to extension of the inflammation from the gall-bladder wall. Sometimes adhesions form between the gall-bladder and stomach, duodenum or colon and in cases with many adhesions, the gall-bladder is frequently distorted and contracted.

When there is an associated cholelithiasis, the appearance of the gall-bladder is much the same. In some cases, however, the mucosa may show evidence of ulceration and the gall-bladder contain only very small calculi, suggesting that the inflammatory condition has been the cause of the formation, while in other cases the stones may be larger or there may be one large calculus. In the latter case, the stone probably preceded the cholecystitis and is usually associated with a less intense inflammation of the mucosa and gall-bladder.

Clinically, there is considerable variation in the response of patients to cholecystitis, as well as variation in the severity of the disease in different individuals. In

cases associated with gall-stones, the patients often have recurring attacks of colic, with soreness in the region of the gall-bladder. In some cases there may be only a vague feeling of discomfort in the right hypochondrium, associated with symptoms of dyspepsia which are often very resistant to treatment. There is often a decrease in the amount of HCl in the stomach contents, but the relationship between the two has not been definitely worked out. Piersol and Bockus found the pancreatic enzymes to be diminished in 85% of forty cases of cholecystitis which they studied. This finding could fairly well account for the dyspepsia that occurs so frequently with chronic cholecystitis. Scringer believes that the gastric symptoms can be explained on the basis of nerve distribution. Thus, a stone impacted in the cystic duct may give rise to pain with rigidity of the right rectus muscle, because of the sympathetic connection of the cystic duct with the corresponding dorsal segments. In addition, vagus reflexes may be excited with consequent disturbed function of the stomach or intestine, manifested by eructation of gas, hypermotility, hyperacidity and constipation.

Some of the more remote conditions which occasionally are associated with chronic cholecystitis are arthritis, myocarditis, phlebitis, neuritis, and infections of the urinary tract. Pernicious anemia may be associated with chronic infections of the gall-bladder, but the etiological relationship is doubtful. Probably the two occur together as a coincidence. However, Jones and Joyce offer evidence to demon-

strate that the presence of hemolyzing and of other microorganisms in the wall of the gall-bladder may be a possible cause of idiopathic progressive pernicious anemia.

Physical examination may reveal very little in cases of chronic cholecystitis. There may be moderate tenderness on deep pressure and sometimes the gall-bladder is palpable, but in cases in which the gall-bladder is small, very little information can be obtained by palpation. In many cases the stools show that the food is imperfectly digested; this is assumed to be due to the chronic inflammation of the pancreas which frequently is associated with chronic cholecystitis.

Roentgenographic examination of the stomach and duodenum may reveal some distortion due to adhesions, or the duodenum may be drawn upward and to the right. If the gall-bladder is enlarged, it may impinge upon the duodenum and show its imprint. Cholecystography will reveal whether or not the gall-bladder is functioning. It has been found that a non-functioning gall-bladder as is seen in chronic cholecystitis will not give a shadow after administration of tetra-iodo-phenolphthalein. In the case of cholelythiasis, a stone may be visualized. Lyon places considerable diagnostic value on his method of biliary drainage, but as has been pointed out earlier in this paper there is considerable controversy as to its efficacy.

Chronic cholecystitis can be diagnosed in most cases by means of a study of the clinical features outlined above. However, not infrequently the differential diagnosis presents

many problems because of the various conditions that may give rise to similar symptoms. Among those given by Phillips are: "(1) spastic constipation with mucous colitis, (2) chronic appendicitis, (3) lesions of the stomach and duodenum, (4) carcinoma of the hepatic flexure of the colon, (5) hemolytic icterus, (6) lesions of the spine, and (7) lesions of the kidney."

Any one of the first four of these conditions can usually be diagnosed with the aid of the history, physical examination and a careful roentgenographic study of the gastro-intestinal tract. The last three require a little more extensive investigation to differentiate them conclusively from the other conditions. Hemolytic icterus may be differentiated by an enlarged spleen, increased fragility of the red blood corpuscles and an increase in the amount of bile pigment in the blood, together with its absence from the urine. Also in cases of the familial type of icterus, the history of its occurrence in other members of the family is of aid. Lesions of the spine can best be demonstrated by a roentgenogram and may reveal an arthritis or a Potts' disease. The possibility of a lesion of the kidney can be excluded by ureteral catheterization and the making of a pyelogram.

The treatment for chronic cholecystitis especially when it is associated with gall-stones, is preferably surgical removal of the gall-bladder. However, in cases which are not accompanied by definite attacks of colic, the results of cholecystectomy are often disappointing. The reasons for

these unsatisfactory results may lie in the fact that all of the pathological lesions are not removed. In cases of long standing the liver, pancreas, and the bile ducts themselves may be infected and these act as a constant source of disturbance to normal digestive activity. Also, the operation may be followed by an increase in the number of adhesions in those cases in which there has been a preexistent pericholecystitis. In cases of gall-bladder disease, therefore, it is advisable that operations be done without too much delay. An atrophied or non-functioning gall-bladder should be removed, also, because of its likelihood of acting as a focus of infection. Hence, if the gall-bladder is proven to be of no value to the organism, it should be removed because it may represent a mechanism by which more vital structures are reached and broken down.

With those individuals who object to, or are a bit reticent about removal of their gall-bladder, many do very well under medical treatment. Regular hours of work and rest, and the avoidance of over-eating are very important factors in the treatment. Excessive smoking should be prohibited. The diet should consist of frequent meals of easily digestible food, while fried foods, excessive sweets, very coarse vegetables, heavy meats such as pork, and pies and pastries should be avoided. The patient should be careful to get plenty of rest and not eat when tired. It is even recommended that he take a glass of half milk and half cream between meals and at bed-time so that the fat in the cream will assist in

emptying his gall-bladder. He should drink a large amount of water between meals and should take one or two glasses of warm water containing a saline laxative, before breakfast every morning.

Constipation is to be avoided and as an alternative to the saline laxative in the morning, mineral oil at night may be substituted. If there is an associated hyperacidity, an alkaline powder of bicarbonate of soda, bismuth subnitrate and magnesium oxide may be given two hours after meals. If there is a tendency to pylorospasm, relief may be obtained by the use of bromides and belladonna, or olive oil, taken before meals will produce a similar effect.

Lyon's method of non-surgical drainage of the biliary tract may be resorted to here as in the case of acute cholecystitis, but the results of this treatment do not seem to be very promising. His treatment may not be as efficacious in emptying the gall-bladder as a meal containing plenty of fat. McEachern and Gilmour believe that taurocholic acid is the most effective cholagogue known and would place that above the ingestion of fat. If medical treatment is resorted to, various ways of obtaining biliary drainage may be employed, since urgency is not paramount in a condition that is already chronic.

Lyon first employed his method of biliary drainage in the treatment of catarrhal jaundice and obtained what he considered fairly good results. Catarrhal jaundice is a condition especially adaptable to Lyon's treatment, since it is

a result of a mild inflammation of the bile passages both intra and extra hepatic with a resulting edema. The magnesium sulphate solution would tend to reduce this edema and so relieve the condition. In chronic infections, however, the possibility of relieving the obstruction is diminished unless a more radical procedure is undertaken. He has a number of supporters who believe with him that his method of drainage is indicated in cases of early infection of the gall-bladder. He advocates its use as a temporary expedient in cases of gall-bladder disease in which operation is contra-indicated because of serious disease of the kidneys or of other organs. Whether surgical or medical treatment is resorted to will depend largely upon the individual case. However, surgery still remains the standard therapeutic measure in cases of any moment.

In an effort to correlate the somewhat theoretical consideration of cholecystitis with clinical findings, several cases from the literature are herewith presented. The first of these represent the simpler and more pleasant prognostic risks, while the last three represent perplexing and rather discouraging complications.

Case I A Case of Acute Cholecystitis

A woman, age 62, was admitted to Hillingdon Co. Hospital, complaining of abdominal pain and vomiting. She was found to have a large ulcerating cancer of the left breast, and the history of the cancer dated back five years. She had had two operations, and had recently been treated by deep X-ray therapy, which had failed to check the advance of the cancer.

On examination of the abdomen, a lump the size of a lemon was felt in the right iliac fossa. It was tender, tense and cystic; it was dull on percussion and there appeared to be an area of resonance between the lump and the liver dullness. The lump was fixed. The rest of the abdomen moved on aspiration. The patient did not appear to be very ill, and was not in any pain except on palpation of the lump. The temperature was raised to 101° F. in the evening, the pulse rate 110, and the respiration 24. There was no history of jaundice or of kidney trouble. The urine was normal and the bowels quite regular. The patient had vomited twice on the day before admission.

The diagnosis of secondaries in the peritoneum or right ovary (breaking down) suggested itself or possibly an appendix abscess. A laparotomy was performed and the lump found to be an enlarged and acutely inflamed gall-bladder. On palpating the neck of the gall-bladder a stone was felt in the position of the cystic duct. Cholecystectomy was perfored. No stones were felt in the common bile duct. On opening the gall-bladder after operation, a single non-faceted cholesterol stone was

found and the fluid distending the gall-bladder was faintly bile-stained mucous. There was no evidence of secondary deposits in the liver, peritoneum, or the uterine adenexa. The patient made an uneventful recovery from the operation.

Case II Acute Cholecystitis in an 11-year Old Boy.

The boy came to the hospital in the morning with the history of having been awakened about 3 A. M. with pain in his lower abdomen which gradually became more severe and localized just to the right of the umbilicus. At 6 o'clock he vomited some watery material. There had been no epigastric pain and none of the cramplike distress which is characteristic of acute appendix. He had had no urinary trouble and gave no history of previous urinary difficulty. The mother said he had had no food which might cause a gastric upset and the boy had had no diarrhea. Three months previous he had a somewhat similar attack which lasted about 12 hours. His general health had been good. His tonsils had been removed, though his mother said he had had no serious attacks of tonsillitis. Except for measles, there was no history of childhood disease.

On examination, the child was well nourished and quite apprehensive. His respiration was not hurried and he could take a deep breath without difficulty. There was no evidence of pleurisy or pneumonia and it would seem that the pathology was limited to his abdomen. Here it was found that he is very rigid over the right rectus, the most acute point of tender-

ness being just to the right of the umbilicus. He was definitely more tender here than over McBurney's point. While somewhat tender beneath the costal margin, the marked rigidity of the rectus muscle prevented palpation of the liver margin. The temperature was 99.6° F. and his white count 12,000. The urine was negative. Plain X-ray failed to show any evidence of calcified glands or renal stones.

On the basis of probabilities a preoperative diagnosis of appendicitis was made. A right rectus incision was made in the region of most marked tenderness. The appendix was found to be normal -- no Meckel's diverticulum was found, but on exploring up in the gall-bladder region a swollen gall-bladder was found which would not empty. The gall-bladder was removed and a small hard stone was found firmly impacted in the cystic duct. Uneventful recovery -- Etiology unknown.

Case III An Unusual Route of Infection in Cholecystitis

The patient, a stout, unmarried female of 27 years, had complained of pain in the gall-bladder region for some months. She also complained of indigestion, flatulence, and constipation, and occasional pain in the right shoulder region. She had not suffered from vomiting or jaundice.

On physical examination, tenderness under the right costal margin was elicited, but no tumor could be felt. A cholecystogram was done and the gall-bladder found to fill with the dye, and the radiogram after a fatty meal showed normal emptying of the viscus. The temperature and pulse

rate were normal. No stones were seen. A diagnosis of cholecystitis was made.

An operation was performed, and the gall-bladder was seen to have lost its normal blue appearance, and to be the seat of inflammation. In apposition with the gall-bladder were the cecum and an inflamed appendix. Cholecystectomy and appendectomy were performed and the patient made an excellent recovery.

Apparently in this case, due to an embryonic arrest, the cecum and appendix failed to assume their normal position in the abdomen and remained in close proximity to the gall-bladder. Sections of the gall-bladder wall showed that the infection started from the serous and muscular coats and progressed inward and that the mucosa had almost entirely escaped. Section thru the appendix showed it to be the seat of a chronic inflammatory process, as evidenced by the fibrous thickening of its walls, the vessels being infected and the lymphatics infiltrated with inflammatory cells showing the superposition of a recent inflammation.

From the above, it can be assumed that a chronic infection in the appendix gave rise to the acute infection in the gall-bladder wall by direct extension. The superimposed acute inflammation in the appendix is probably the result of a flare-up in the appendix or a "kick-back" from the acutely inflamed gall-bladder.

Case IV Chronic Cholecystitis with Multiple Abscess of Liver.

The patient came in to the hospital thru the emergency ward with the complaint of abdominal pain and vomiting. For the past 2 or 3 years the patient had complained of increasing urinary symptoms, consisting of urgency and hesitancy and about a year before admission, signs of cardiac decompensation developed. His doctor digitalized him and kept him on a maintenance dose of digitalis. Aside from this he had been fairly well until two weeks before admission.

At that time the patient and two other members of the family became sick after eating evidently poor fishcakes, for they all vomited and had abdominal pain for about two days. The other members of the family got well, but the patient continued to have abdominal pain and vomiting. The day before admission he had a good bowel movement and his bowels moved regularily up to admission. The night before admission he ate a hearty dinner. He felt pretty well for about two hours afterwards. Then he was taken suddenly with severe abdominal pain which was constant, more on the right than on the left. Soon he began vomiting and continued to vomit. The doctor gave him morphia, which enabled him to sleep that might. Next morning the pain returned, severe as ever, still in the right lower quadrant. The doctor gave him another dose of morphine and sent him to the Emergency Ward.

On arrival at the Emergency Ward, examination showed a fairly well preserved old man somewhat distressed and dazed

mentally. The heart was enlarged on percussion. There was a harsh apical systolic murmur. There were frequent extrasystoles. The blood pressure was not elevated. The abdomen was rather generally distended. In the right lower quadrant there was marked tenderness and spasm. An indefinite, soft, easily movable mass could be felt in the right flank, just below the level of the umbilicus. The mass was extremely tender and seemed to lie near the abdominal wall. The most striking thing about it was that it could be moved fairly easily. Rectal examination showed that he had a very large prostate.

On admission, the temperature was 104° F. and the white count 24,000. Inasmuch as he had suprapubic distention, he was catheterized and left on constant drainage. The urine obtained by catheterization showed a large number of red cells, occasional leucocytes, a trace of albumin and occasional granular casts.

His condition was too precarious to allow operation, so he was sent to the ward and put on a supportive regime of fluids and glucose by clysis. The maintenance dose of digitalis was continued. An abdominal flat plate was taken on the way to the ward and was negative.

After arrival on the ward the patient's condition steadily became worse. On the second day he became definitely jaundiced. The icteric index was found to be 100. His mental condition became more confused and his breathing more labored. He developed muscular twitchings of the extremi-

ties and was definitely on the downward path. However, it was noted that the mass felt on admission became less distinct after he was on the ward two days, and on the evening before death could not be felt. The most probably diagnosis was a movable distended gall-bladder -- the possibility of a uremia in terminal nephritis had been ruled out by the blood chemistry. The possibility of an appendix abscess was apparently ruled out by the movability of the mass. Autopsy revealed a much dilated, acutely and chronically inflamed gall-bladder, which corresponded to the mass palpated. The reason why it was so low in the abdomen was because there was a marked enlargement of the liver due to one fairly large and multiple small abscesses. There were many senile changes with secondary or terminal lesions, but the cholecystitis and abscess of the liver were undoubtedly the chief pathology and immediate cause of death.

Case V Cholecystitis; Cholelithiasis; Stone in Common Duct.

An Irishman of 70 entered the hospital complaining of pain in the upper right quadrant of one week's duration. For the past year he had been bothered with nausea and vomiting in the morning. His bowels had always been constipated, but were becoming more so. He formerly had a good deal of flatus, but for the past three months had had none. A week before admission he was bloated and had dull non-radiating pain in his right flank and less severe pain in

the right upper quadrant to the mid-line. The pain was nearly constant and severe enough to require morphia for two nights. It was worse in afternoon and evening and had no relation to food. Walking relieved it; soda did not. He vomited once three days before admission. He had had no jaundice or clay-colored or tarry stools.

Under digitalis, enemas and soft solid diet without fats, the patient was more comfortable. The tenderness and distention became less and at the end of two weeks was discharged with advice to continue digitalis, Russian oil and milk of magnesia with limited exercise.

Ten months after his discharge he was again admitted to the hospital. Clinical examination showed a stout slightly jaundiced man showing evidence of loss of weight, having severe attacks of right upper quadrant pain. Sclerae icteric. Eight days after entrance operation was done with a pre-operative diagnosis of cholelithiasis.

The gall-bladder was found to be thickened and contained several soft pigment stones. There was distinct evidence of recent acute inflammation of the gall-bladder. There were many light adhesions to the surrounding structures. The common duct was much enlarged and the wall thickened. No stones could be felt in the duct from the outside. The gall-bladder was partially buried in the substance of the liver. It was removed from below upward. It was so adherent that it was opened during this procedure. The common duct was then opened and explored. It contained a small amount of detritus. No

stones were felt. The opening in the duodenum was demonstrated to be patent. The common duct was washed with salt solution and drained with a small catheter. The pathological report was chronic cholecystitis and cholelithiasis. Eight days after the operation the drainage tube came out of the common duct and two days later there was profuse drainage of duodenal contents and marked digestion of the skin. Suction was started and this kept the wound fairly dry and the patient seemed to be getting along all right. But fifteen days p. o. the discharge was thicker and mucoid and the following day the wound opened a little. Four days later the patient was seen to be increasingly irrational and on the twenty-first day p. o. he died.

At autopsy the immediate cause of death was determined to be a broncho-pneumonia in the right lower lobe. However, an anomaly of the common duct -- it emptied lower down into the third part of the duodenum -- had resulted in the retention of a large stone which doubtless was a factor in the reflux of digestive juices and which led to a weakening of the individual, with subsequent pneumonia and death.

Case VI Cholecystitis: Pylephlebitis.

Four days before admission, the patient, a man of 45, suddenly felt a dull griping pain in the mid-epigastrium without any radiation at all. He immediately took bisodol. The pain disappeared within one-half hour. At two o'clock in the morning before admission he had a similar sudden pain.

It was rather dull throughout the day in spite of bisodol, rest and fluids by mouth. He thought he vomited a slight amount of water. His bowels moved with Pluto water. He went to sleep without difficulty. At two o'clock in the morning of the day of admission he had severe epigastric pain which awakened him out of a sound sleep. This pain radiated to the flank, or at least to the mid-axillary line on the left, not to the right at all. It was worse when he was lying on his left side. It lasted until about eleven o'clock in the morning. It was bad enough to make him moan and call a doctor, who gave him hot packs and pantopon with relief. The patient belched a good deal of gas. His bowels moved with an enema given in the afternoon, giving a normal colored stool. At five o'clock in the morning he passed urin and again at eight o'clock. After that time he noted the urin to be rust-colored, i. e., darker than normal. He had a slight chill in the morning, but no sweats and after eleven o'clock there was no chest pain on breathing. He had a slight headache. He was admitted because of the acuteness of his condition.

Physical examination revealed a well-developed and nourished man, a little bit flabby and rather pale, but apparently from indoor life rather than anemia. There was a slight suggestion of icterus in the sclerae. The physical findings were essentially negative, except that if one palpated the right epigastrium or towards the mid-epigastrium, there was produced a pain which was felt to the left of the epigastrium,

over near the nipple line, very much like the pain he had had that particular morning and two days before. As a matter of fact the pain radiated up to about the seventh or eighth rib and there was no local tenderness at all in the sense that he felt pain locally, nothing on the right side, and one could not feel the liver or the gall-bladder. His temperature was 102° F., pulse 120, respiration about 30.

The next morning he still had a temperature, although it had come down a little. The pulse was in the 90's. The respirations were 25. Physical examination was essentially the same, except that there was no doubt about the jaundice. It was evident that there was something wrong with the biliary tract. At that time the white cell count was 31,000. The urin was positive for bile and showed a slight trace of albumin. Otherwise it was essentially negative.

Two days after admission he had an icteric index of 65. Six days later the amount dropped to 10, and the van den Bergh was too low to read. During that time the temperature varied from 99° to 102.5°, with two chills on February 7 and February 9, when the rectal temperature reached 105.5°. The night of February 9, he complained of dull, rather constant pain between the scapulae. He vomited some and felt very sick and sweated a good deal. The jaundice diminished. One could elicit definite pain by pressing over the liver near the epigastrium, but the pain was almost always towards the left side.

A flat film of the gall-bladder and the kidney region was absolutely negative, except for phleboliths. A Grahm test showed no filling of the gall-bladder.

He was carried along for about two weeks till the jaundice cleared up and the patient was feeling better. He was operated and for a period of five days the patient ran an apparently normal p. o. course. There were no chills, the temperature was normal, and the pulse was in the 80's. Routine examination of the chest the second day after operation showed that the diaphragm was well up, but that it moved. It was hard to know whether there was an area of collapse or whether the diaphragm was high, or whether it was a high diaphragm and collapse. Then he began to have chills and fever again. Six days after operation he had the first chill and the next day another. Then the temperature and pulse began to rise and he had the same septic temperature as before. He did not become jaundiced at this time. On February 24th the white cell count, which had dropped to about 11,000, had risen again to 29,000. As soon as he began to have chills again, the possibility of liver infection was considered. There could be liver abscess or cholangitis, pylephlebitis or subdiaphragmatic abscess.

Additional X-rays taken a little later when the patient was running a still higher temperature, suggested partial collapse of the right lower lobe. Because of the continued septic temperature, an effort was made to find out more about the patient. Liver function tests, laboratory tests, and con-

tinued observations were carried out. The only signs that were of importance were the persistent high diaphragm which always moved with respiration and the signs above consistent with collapse of the right lung, or with fluid.

Finally, a tap was done and 75 cc. of straw-colored sterile fluid were aspirated. This sterile fluid suggested subdiaphragmatic infection of some type, possibly liver abscess. At least, operation should be done. A rib resection was done prior to a subsequent exploration of the liver below the diaphragm. For nine days following this exploratory operation the patient ran a septic temperature. The pathology above the diaphragm seemed quiescent and another tap to this area revealed nothing.

Following this the liver was exposed and explored thoroughly without showing any evidence of subdiaphragmatic or intra-hepatic abscess. Six days later the patient became definitely more toxic, the signs in the right chest became more marked, and he apparently had pneumonia by the signs above this area of collapsed lung and fluid. The patient died five days after this third operation, and seven weeks after admission.

Autopsy revealed a series of branching abscess cavities in the portal vein. The right lung was collapsed and the pleural cavity filled with pus. The post mortem findings fitted very well with the clinical history and the location of the pathology explains why the septic processes could not be discovered during life.

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