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CHOLECYSTITIS STRESSING THE INDICATIONS
FOR MEDICAL AND SURGICAL TREATMENT

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INTRODUCTION

There is an old saying that dead men tell no tales, but autopsy protocols are often silent witnesses to many pathologic complications that might have been avoided had either the primary disease been treated earlier or had the treatment instituted been based upon better judgment. Thus it is with the treatment of cholecystitis.

In the past, it has been the tendency of the surgeon to treat all cases surgically, whereas the internist has tended to treat all cases medically. This form of treatment was adequate in many instances; however, in others it exposed a lack of the attending physician's knowledge concerning the best method of treating the problem with which he was confronted.

Statistics show that the mortality in gallbladder surgery is due in the main to operations performed upon stoneless gallbladders, and it is a sad admission that gallbladder surgery leaves a large percentage of patients with symptoms requiring further advice and treatment. On the other hand, many cases of cholecystitis have been exposed to a medical regimen with disastrous results from

complications which might have been avoided with early surgical interference.

The majority of patients in any general medical clinic present as their chief complaint gastro-intestinal symptoms; and in recent years, it has been more and more recognized that their underlying pathology rests in the biliary tract. As the result of many surgical and pathological studies, there seems to be no doubt that gallbladder disease is the commonest organic cause of digestive symptoms. Extensive studies of autopsy material show that cholecystitis is present in 60 per cent of people over 40 years of age, and gallstones are present in about one out of every five. It is twice as frequent as peptic ulcer and gastric cancer combined and may be accepted as the commonest and most important condition from both a diagnostic and therapeutic standpoint that comes to the attention of the internist. Although the majority finally come into the hands of the surgeon, it is the physician who, as a rule, sees these patients first and upon whom rests the responsibility of making an accurate diagnosis and advising a proper line of treatment.

The treatment of gallbladder disease, therefore, is neither all medical nor all surgical but will for a long time be divided into three groups; those cases which are strictly medical, those which are only surgical, and a third group that cannot at once be classified.

It is the purpose of this thesis to discuss cholecystitis in all its forms and particularly to differentiate between those cases which should be treated medically and those which should be referred to the surgeon. The indications and contraindications to surgery in cholecystitis and the present day medical regimen have been discussed at length.

HISTORY

Probably the earliest evidence of Cholecystitis is to be found in the early Egyptians as proven by the unearthing of an Egyptian mummy, the Priestess of Amon who died 1000 B.C., with a gallbladder full of stones. Many authorities still maintain, however, that the Egyptians were not troubled with this infection. (20)

Galen, in 170 A.D., stated that loss of appetite was due to undigested substances, bilious humours, or phlegm which were present in the stomach. He believed nausea was induced when the cardia took on a bitter character due in turn to a preponderance of bile in the stomach. Galen noted also that jaundice was the result of obstruction to the bile duct, inflammation, or tumors and was not a disease but rather a symptom. (52)

The first physician to describe gallstones was apparently Gentile da Foligno, who was born in the latter part of the thirteenth century. He carried out numerous public dissections and during one of them discovered "a stone tending to green" in the duct of the gallbladder at its mouth. (43)

Regarding the symptoms of Cholecystitis, in the middle of the fifteen century Antonio Benivieni records the case of a noble woman who was troubled many times during the day with a pain arising in the neighborhood of the liver and on that account consulted very many doctors. "After she had departed this life, we took care to open the body of the dead. And in the sloping membraneous part of the liver stones of different shapes and colors were found collected. For some were round: others angular: others quadrate, according as posture and chance had worked, also marked with red, yellow and white spots. Now this pronounced the cause of death we considered it vain and useless to dispute concerning obscure things." (43)

It is very striking that the early European medical writers seem to have had little knowledge of gallbladder disease either in human beings or domestic animals. There is particularly no mention made of anything which could be considered gallstones until the sixteenth century. Hoppe-Seyler believes that the remarkable absence of comment on gallstones by the early European anatomists must signify that they were much less common in those days than they are now, perhaps due to the different methods of

living. Sydenham is frequently credited with discoveries that have thrown light on the pathology of gallstones. As a matter of fact, however, he considered gallstone colic as a symptom of hysteria and described its occurrence in female subjects who were suffering from other forms of hysterical seizures. (29)

Thomas Vicary, in 1548, reveals a bit of his knowledge of the anatomy of the gallbladder system as indicated in the following quotation:

"Nowe to speake of the Gal, or the chest of the Gal: it is an official member, and it is spermatike and senowy, and hath in it a subtil wyl; and it is as a purse or a pannicular vesike in the holownesse of the Lyuer, about the middle pericle or lobe, ordeyned to receyue the Cholerike superfluties which are ingendred in the Lyuer. The which purse or bagge hath three holes or neckes; by the fyrste, he draweth to him from the Lyuer the choler, that the blood be not hurt by the choler; by the seconde necke, he sendeth to the bottome of the stomacke, Choler to further the digestion of the stomacke; And by the third neck, he sendeth the choler regularly from one gutte to another, to clense them of their superfluties and drosse; and the quantitie of the purse may conteyne in it halfe a pinte." (69)

He describes Choler as a hot, dry, yellow humour, contained in the gallbladder and used for the fermentation of chyle, bringing it to perfection.

Jean Fernel, in 1581, states that obstruction, calculus, fullness and emptiness attack the gallbladder. The obstruction is either of the duct by which the bile is led away from the liver, or of that by which it is discharged from the gallbladder into the intestine. In both, the bowels are obstinate and sluggish, feces whitish, the urine reddish and thick so that it frequently becomes dark, the bile diffused with the blood throughout the whole body disfigures the skin with jaundice. In the former, moreover, the gallbladder is entirely empty; in the latter it is distended by the large amount of bile, and is oppressed by various symptoms of great importance. He describes a black calculus that commonly forms in the gallbladder but which is light and floats in water. A predisposing factor to gallstone formation is discovered in his description of a certain old man very prone to anger who after death was found without bile and without a gallbladder, in whose place a large calculus had formed. With continued jaundice and the appearance of diarrhea, he commonly detected innumerable calculi expelled like peas or barley grains. (43)

Wilhelm Fabry, "the father of German surgery", in 1560 described in detail two enormous sized stones

found in a gallbladder. (43) Francis Glisson, of the same period, tells of stones in the biliary tract and of the inflammatory changes produced in the walls of the ducts; he seemed to think their origin was related to the intestine since stones were found in the gallbladders of oxen fed upon hay or straw in the winter, which were not present when they ate grass in the springtime. (27) Morgagni states that biliary stones occur in the aged for in the flourishing time of life the juices are thinner, more briskly agitated, and less prone to concretion than in the decline of life. (50) Felix Platter, 1646, speaks of calculus and sand in the liver and its bladder causing severe dull pains in the hypochondrium. (43) Matteo Colombo, the celebrated anatomist of the middle sixteenth century, describes stones of various shapes, various colors, and of varied number found in the gallbladder.

Coates has noted the frequent occurrence of gallstones in people past middle life and suggests that they are often found in the gallbladder after death without their existence having been suspected during life. The cause of their formation is obscure; and they are formed by the deposition of the constituent of the bile, chiefly cholestearine, and next to

that bile-pigments, but also lime and magnesia salts in varying proportions. He states that stagnation of bile in the gallbladder at least predisposes to gallstone formation, thus also explaining their occurrence in the older age group where gallbladder actions are sluggish. In the center of gallstones there is frequently a nucleus composed of remains of epithelium or mucus; the single gallstones are composed almost purely of cholestearine, are oval in shape, somewhat nodulated on the surface, and have a glistening appearance not unlike that of a sugar-plum. (18)

Some thirty years previously, 1855, Dickson described attacks of gallbladder colic. He noted that concretions may be voided in icteric stools without inconvenience or suffering, but in general a little before the time of passage the subject underwent an attack of acute symptoms, usually with an accompanying jaundice. (19) The treatment of cholecystitis at this time consisted first of venesection, to be carried out with a freedom and boldness proportional to the urgency of the symptoms. If the stomach would bear it, tincture of opium was used instead of morphine. Fomentations or warm mustard poultices were applied

over the whole abdomen, but especially to the pit of the stomach. (19)

In 1915, George of Boston announced that one could demonstrate a gallbladder which was abnormal; and in the following year, he assumed that whenever a gallbladder was visualized it was pathological. Following this period, he and Leonard elaborated on the indirect signs of gallbladder disease which constitute the basis for the present day determination of most forms of pericholecystitis. The actual development of cholecystography was done by Graham and Cole in 1924. Earlier, in 1871, von Bayer discovered a group of compounds called the phthaleins; but it was not until 1901 that Abel and Rowntree, in the hope of finding a serviceable hypodermic purgative, studied the phthaleins and showed that certain ones were excreted through the liver and others by way of the kidney. From these experiments and the work of Graham and Cole there has arisen a test of gallbladder function which has revolutionized gallbladder roentgenography. (60)

Thus we may conclude from the history of the biliary tract system that although gallstones were discovered many, many years ago their relationship to cholecystitis

has only recently been developed. Perhaps the close relationship of the gallbladder to the liver has led many of the early anatomists to transfer gallbladder symptoms to liver pathology, thereby overlooking cholecystitis as such. Diagnostic methods were unknown until the advent of cholecystography not over twenty years ago.

ANATOMY

From the ventral floor of the fore-gut of a 2.5 mm. embryo there develops an outpocketing, into the splanchnic mesoderm of the ventral mesentery, known as the hepatic diverticulum. This is lined with entoderm and develops just cranial to the yolk stalk. Bile capillaries are formed from the end of this diverticulum whereas the interlobular ducts, hepatic duct, and ductus choledochus are the stem portions of the original hepatic diverticulum; the gallbladder and cystic duct represent a special offshoot of the early diverticulum. (2) This solid system of cells soon develops a lumen and with the rotation of the gut is carried into the position acquired in the adult. Occasionally, we find a congenital atresia of the bile ducts resulting in early fatality.

The gallbladder itself is a thin walled, musculo-membranous, pear-shaped sac lodged in a fossa on the under surface of the right lobe of the liver, extending from near the right extremity of the porta to the anterior border of the organ. It is 8 to 10 cm. in length, 2.5 cm. in breadth at its widest part, and holds from 30 to 50 cc of bile. Normally, the

gallbladder is a slate blue color and is slightly translucent, with a thin tracery of small blood-vessels on its surface. It is ordinarily covered by peritoneum on the under surface of the liver except on its upper aspect where it is united to the fossa of the liver by thin, loose, areolar tissue. Occasionally it is completely covered by peritoneum with a mesenteric attachment to the liver, and sometimes it may even be completely imbedded in the liver substance. The fundus is the lower, wider part whereas the upper part which joins the cystic duct is called the neck (collum) and the intermediate portion is known as the body (corpus). The gallbladder and bile-ducts lie in Morrison's pouch, or the subhepatic space, bounded above by the under surface of the right lobe of the liver, below by the transverse colon and mesocolon, externally by the parietes down to the iliac crest, and internally by the peritoneum covering the spine. This space can be adequately drained with a lumbar incision. (29)(32)

The fundus of the gallbladder is directed downward, forward, and to the right; anteriorly it is in relationship to the anterior abdominal wall and

posteriorly to the transverse colon. The body comes into relationship above with the liver, below with the transverse colon and posteriorly with the descending portion of the duodenum. The neck pursues an S-shaped curve inward toward the portal fissure. The anatomical position of the gallbladder with surrounding structures readily explains the adhesive processes which often make surgical procedures very difficult and hazardous. (29)(32)

The cystic duct is about 3 or 4 cm. in length and passes backward, downward, and to the left from the neck of the gallbladder to join the common hepatic duct. The mucous membrane of this duct is thrown into from 5 to 12 crescentic folds, the so-called valves of Heister.

Microscopically the gallbladder is found to consist of mucosa, a fibromuscular coat, a subserous coat and serosa. The mucous membrane is thrown into tufts or folds covered by a single layer of columnar epithelial cells which secrete mucous. The fibromuscular coat is composed of elastic tissue in which are imbedded bands of smooth muscle tissue. Hendrickson's studies leave no doubt that there are three muscle layers which are plexiform and interlaced in

arrangement and which, by their action, produce a simultaneous reduction of the organ in all its dimensions. (60) The hepatic, cystic, and common bile ducts all possess a mucosa composed of a single layer of columnar epithelium which contains mucous glands, a submucosa of thick connective tissue, and an outer plexiform arrangement of smooth muscle. These glands furnish a thin fluid which tends to dilute the bile. (5) The sphincteric arrangement of the muscle fibers around the common bile-duct in its duodenal portion is referred to as the sphincter of Oddi after an Italian who described it in 1886.

The common bile duct is formed by the junction of the cystic and hepatic ducts, is approximately 7.5 cm. long, and has the diameter of a goose-quill. It descends behind the superior portion of the duodenum, in front of the portal vein and to the right of the hepatic artery. At its termination it lies to the right of the pancreatic duct and unites with it to form a dilated ampulla (Ampulla of Vater) just before entering the medial side of the descending portion of the duodenum a little below its middle. (29)(32)

The gallbladder system derives its blood supply

from the cystic artery, which is a branch of the right hepatic artery, which in turn is a branch of the celiac artery arising from the descending aorta. The arteries penetrate the wall of the gallbladder and divide in the fibro-muscular coat near the subserous layer; branches are given off to the mucosa, in which a fine network is found, and to the subserous and serous coats. The veins run in the fibromuscular coat and drain into the portal vein. (29)

The lymphatics of the gallbladder have been well explored and an accurate account established. The large lymph vessels running over the gallbladder bring lymph from the liver and coats of the gallbladder; they follow the inner side of the cystic duct and end in mesenteric lymph glands. (29) The lymphatics of the biliary system not only drain to the lymph glands at the hilus of the liver but also along lymph channels leading into the liver substance. Some vessels unite and drain into a gland at the neck which is sometimes referred to as the sentinel gland since it is often enlarged in cases of cholecystitis and of major importance surgically. (13) There is a network of lymph channels in the subserous layer which empty into the larger vessels mentioned above;

this network is very irregular and the channels vary markedly in size and shape. The submucous sets of lymphatics are seen to lie in the connective tissue just under the mucous membrane, and they are rarely seen to run up into the folds. An important point to remember about the gallbladder lymphatics is that they have a very intimate anastomosis with those of the liver. The lymph from the hepatic, cystic, and upper part of the common ducts drains into the hilar glands whereas the lower end of the common duct drains into glands in the region of the head of the pancreas.

The nerves of the gallbladder and extra-hepatic ducts are derived from the same source as those which go to the liver, arising chiefly in the plexus hepaticus which surrounds the portal vein and hepatic artery. Nerve fibers pass chiefly to the muscular elements of the biliary passages and are dependent upon the sympathetic system. In the gallbladder muscle wall there is a plexus of nerve fibers designated "the principle plexus" which might compare anatomically with Auerbach's plexus in the intestine. This plexus contains cellular elements belonging to several types which furnish motor fibers to the media and wall of the vessels and other fibers which form a secondary

plexus in the mucosa; this in turn sends fibers right up to the epithelium and may very reasonably be considered as sensory. (29)

Anatomical variations are rather common, and many of them are of great importance from a surgical standpoint. Complete absence of the gallbladder is uncommon; however, in many animals the gallbladder is normally absent. Vasa aberrantia, or aberrant ducts, are not rare and can be seen to subdivide and anastomose without ever coming into relationship with any liver lobules. Duplication of the gallbladder is occasionally seen and has been subdivided into four main groups: (1) cleft gallbladders, (2) diverticular bladders, (3) ductular bladders, and (4) trabecular bladders. (29) The cystic duct may be seen to join the hepatic duct at an angle, may run parallel with the hepatic duct, or may wind spirally around the hepatic duct before uniting with it. Accessory ducts of varying sizes are often present. Occasionally the right hepatic artery arises from the aorta, the renal artery, the gastric or the inferior mesenteric artery; and not infrequently an accessory cystic artery is present crossing in front of the bile ducts.

In summarizing, then, the anatomy of the gallbladder has three important features in the physiologic consideration:

1. An excellent lymphatic system.
 2. A mucosa arranged in such a manner as to bring the contents into intimate contact with as much surface as possible.
 3. A weak, diffuse, but very adequate muscular coat.
- These features anatomically best fit the gallbladder for absorption. (44)

PHYSIOLOGY AND PATHOLOGY

The chief function of the gallbladder is devoted to the concentration and storage of bile; subsidiary functions are the reduction in the alkalinity of the bile and the equalization of pressure within the biliary duct system. (5)

Gallbladder bile is approximately ten times more concentrated in total solids than bile freshly collected from the hepatic duct. Water and inorganic salts are absorbed through the lymphatics and blood vessels of the gallbladder wall; however bile pigments, bile salts, and cholesterol are not absorbed to any appreciable degree under normal circumstances. (41)

Inflammation of the gallbladder reduces or abolishes its concentrating power. The gallbladder mucosa also adds to the viscosity of the bile by the secretion of a thick mucinous material. The ducts, on the other hand, do not concentrate bile and, in fact, are known to secrete a thin watery fluid which rather dilutes the consistency of the bile. This clear colorless fluid secreted by the mucosa of the ducts is seen in pathological conditions such as obstruction of the bile duct whence it is termed "white bile". It contains no pigment, bile salts, or cholesterol and bears practically no resemblance to bile. (5)

Without the ability to absorb fluid and reduce the bulk of the bile the power of the gallbladder to equalize pressure within the biliary duct system would be negligible, since the amount of bile secreted in twenty-four hours is some twenty times greater than could be contained in the gallbladder. The loss of this pressure equalizing power is probably a factor leading to the dilatation of the bile ducts which is so frequently seen following removal of the gallbladder.

Contractions of the gallbladder wall itself are responsible for the expulsion of its contents via the cystic and common ducts into the duodenum. The times of emptying are related to gastric digestion. During fasting it remains distended with bile, although the sphincter guarding the common duct is relaxed, plainly indicating that the viscus is competent to retain the bile without the aid of the sphincter of Oddi. The sphincter can normally withstand a pressure of 100 to 120 mm. of water, whereas the pressure developed by contraction of the gallbladder is approximately 250 mm. of water. It is probable, however, that relaxation of the sphincter of Oddi occurs as part of a coordinated mechanism when the bladder wall contracts, and the bile is not merely forced through. The duodenal

muscle surrounding the oblique intramural portion of the common bile duct is capable when contracted of offering a resistance of over 750 mm. of water; and since this is much higher than the pressure exerted by contractions of the gallbladder, the flow of bile is completely blocked during contractions of the duodenal muscle but squirts into the duodenum during a period of relaxation. (60)

The most effective stimulus for the discharge of bile is a meal of fatty material, particularly egg-yolk or cream, however some degree of digestion of the fat must occur before evacuation results. The effect of meat upon the discharge of bile is much less than that of fat, and pure protein such as egg-white and carbohydrate food is almost without effect. The products of fat digestion, hydrochloric acid of a strength comparable to that in the chyme, or magnesium sulphate cause evacuation of the gallbladder when placed in the duodenum. (60)

That there is a nervous mechanism controlling evacuation of the gallbladder has been well established by experimental excitation of the vagus or sympathetic nerves resulting in contractions of the gallbladder. Experiments attempting to demonstrate the precise

actions of the extrinsic nerves upon the gallbladder movements have given very conflicting evidence. This in turn may depend upon intrinsic nervous plexuses in the walls of the biliary structures. Nevertheless, nervous mechanisms are not essential to gallbladder activity; this is evident from the fact that the reaction to the introduction of fat into the duodenum occurs after all nervous connections between the biliary and gastro-intestinal tracts, and between the former and the central nervous system have been severed. That gallbladder contractions can occur under such circumstances suggests a hormonal or humoral mechanism. Ivy obtained an acid extract from the mucosa of the upper part of the intestine which caused contraction of the gallbladder when injected intravenously. Acid itself is without effect when injected as are also fats and its derivatives. These substances, therefore, which are excitatory when placed in the duodenum or fed act apparently by causing the production or liberation of a hormone in or from the intestinal mucosa called cholecystikin. It closely resembles secretin and is free from histamine and other vasodilator substances.(60)

The gallbladder shows spontaneous rhythmical contractions which occur at the rate of from two to

six per minute and tonic contractions which last from five to thirty minutes or more. The rhythmical contractions are capable of producing a pressure change of from 250 to 300 mm. of water which is about the maximal pressure at which bile can be secreted by the liver. Rhythmical contractions of the common bile duct have also been demonstrated. (5)

Gallbladder disease frequently gives rise to derangements of other organs and particularly the stomach producing anacidity or hypoacidity, and increased motility of the pyloric part of the stomach. Ivy and Fishbach have proven experimentally that mild stimulation of the biliary tract inhibits gastric motility and lowers gastric tone which is probably conducive to gastric flatulence and belching. Cardiac irregularities may result through reflexes initiated from the gallbladder or bile ducts. (5)

In simple catarrhal cholecystitis the gallbladder is usually distended, its walls are tense and swollen, and the mucous membrane congested with desquamation or superficial ulceration and polymorphonuclear and lymphocytic infiltration. (28)(7) In the subacute type the villi stand out as yellow specks and give the lining the appearance of a strawberry. Complete or

partial blocking of the cystic duct predisposes to suppurative inflammation in which the mucosa of the gallbladder is covered with a mucopurulent or purulent exudate and shows patches of exfoliation or gangrene. The muscular coat is infiltrated with leukocytes, and the serous coat dulled with a deposit of fibrin; empyema of the gallbladder may result. This process may develop into a gangrenous cholecystitis with extensive necrosis of the wall; should perforation of the gallbladder occur, local or generalized peritonitis would result. (15)(16)(21)

Microscopically, in acute cholecystitis there is an infiltration of polymorphonuclear leukocytes, areas of hemorrhage, edema, and some destruction of the overlying epithelium. (29)(10)

In suppurative cholecystitis, the gallbladder is most frequently adherent to other viscera by thick, fibrinous adhesions and may be partially covered by omentum. (29)

In chronic cholecystitis, there is a low-grade inflammatory reaction commencing in the outer part of the wall and gradually spreading throughout the gallbladder. The gross appearance varies considerably; the lumen may be normal, dilated, or contracted, the wall is usually thickened and fibrosed; the bluish

color of the thin-walled normal gallbladder is lost; and the surface may be opaque or may be yellow owing to an accumulation of subserous fat. As a result of contraction of the fibrous tissue, the surface may become reticulated and scarred so as to present an interlacing network of fine bands which show through the atrophic mucosa with great distinctness. The mucosa will be seen to be papilliform in some but in advanced cases will be found to be unusually flattened. The microscopic appearance is one of chronic inflammation with inflammatory foci most marked in the outer part of the wall. There are definite groups of lymphocytes and occasionally large numbers of plasma cells and eosinophils as well as more diffuse infiltration. The folds of the mucosa are thickened owing to edema but the epithelium is usually intact.

(10)(29)(11)(9)

In the strawberry gallbladder, yellow specks are present on the red mucosa giving a very typical picture of a ripe strawberry. (29) Boyd is of the opinion that this yellowish material is an ester of cholesterol and is similar in nature to the lipid occurring in the adrenal cortex and the corpus luteum of the ovary. He believes that cholesterol is

normally absorbed from the gallbladder, and if something interferes with the normal absorption the strawberry gallbladder results. The most probable factor in preventing normal absorption being chronic infection, this type gallbladder is placed in the group due to a chronic cholecystitis. (10)(11)(9)

ETIOLOGY

The etiology of gallbladder disease is a problem which has engaged the clinician and research worker alike; and although much work has been done in an attempt to prove the source of infection found in cholecystitis and gallstones, the exact relation of the infection to gallstone formation is still in dispute. Evidence is gleaned from the surgical removal of the gallbladder on the operating table, from the bacteriological studies of the excised gallbladder, from the experimental production of cholecystitis in animals, and finally from a more or less characteristic clinical picture. The mechanisms by which gallbladder disease can be produced may be classified as infection, metabolic disturbances, and mechanical factors and will be taken up in detail later.

It is generally accepted that an intramural focus is the commonest starting point of the actual gallbladder inflammation, but there is by no means the same agreement as to the origin of the causative bacteria. (54) Rosenow has done much to prove the frequency of intramural infection and is responsible for the hypothesis of "elective localization"; he

suggests a bacterial embolus of peripheral origin and lays stress on the specificity of certain streptococci. (62) Prior to the work of Rosenow, it was generally believed that the intestinal bacteria were chiefly responsible for cholecystitis.

Cholecystitis occurs most commonly during the fourth decade or later; however many of the cases first recognized later in life had their origin in childhood, possible as cases of supposed catarrhal icterus, or of acute indigestion of some sort. (29) In 612 routine postmortem examinations, Mentzer of the Mayo Clinic found pathological evidence of cholecystic disease in 66 percent of the cases. The large number of people afflicted with gallbladder disease but presenting very few, if any, symptoms can be appreciated by the fact that only 8 per cent of the 612 patients had a primary diagnosis of cholecystitis. Gallbladder infections occur more frequently in females than in males in the ratio of about two to one. This may be due in part to the hypercholesterinemia and the biliary stasis which accompanies pregnancy; it is unusual for a woman who has borne four or more children to escape cholecystitis. Osler

states that 90 per cent of women having gallstones have borne children. (53)(29)

There are theoretically only four possible routes of gallbladder infection, namely:

1. Blood-stream infection--systemic or portal.
2. Lymphatic infection--liver or some other organ.
3. Via the biliary passages--downwards from the liver or upwards from the duodenum.
4. Direct spread from an abdominal viscus.

Each will be taken up in detail with results of experimental work in evidence of these routes as possible infectious pathways to the gallbladder.

Blood-stream infection is generally believed to be the most likely route of infection of the gallbladder, strong evidence in its favor being the frequency with which, in cases of cholelithiasis, the gallbladder wall is infected while the gallstones and fluid contents are sterile. Organisms may come from far distant foci such as infected teeth or tonsils and pass via the cystic artery to the gallbladder. The majority of organisms causing gallbladder infections are of an intestinal nature and probably reach their destination via the portal system, which would exclude the liver as an efficient bacterial filter. (54)

One explanation of lodgement in the gallbladder is an assumption of a specific affinity for the gallbladder on the part of some organisms such as for certain streptococci. (62) It has also been suggested that the gallbladder may be in a state of lowered resistance at the time the organisms are circulating allowing for their enlodgement. Since gallstones are primarily aseptic and metabolic in origin, they may be responsible for the lowered resistance of the gallbladder.

The importance of infection of the gallbladder from the liver through the lymphatics has been strongly emphasized by Graham. (29) Anatomically, the natural direction of lymph flow is from the gallbladder to the portal fissure; and there is therefore no recognized route of flow from the liver to the gallbladder, thus theoretically a spread of bacteria from the liver to the gallbladder would necessitate a reversal of the normal direction of lymph flow. The experimental evidence does not provide support for the lymphatics as a route of infection, and it cannot at present be regarded as important.

Spread of infection downwards from the liver via the biliary passages after injecting relatively large

doses of bacteria either portally or systemically leads to excretion in the bile in 25 per cent. (54) The excretion does not begin immediately but is quite definite in 24 hours and maximal in about 48 hours. Therefore, biliary excretion cannot be excluded as a possible route of infection. Experiments prove that ascending infection from the duodenum along the lumen of the bile duct must be a rare occurrence.

Occasional cases have been reported in which infection of the gallbladder has occurred by direct extension from an inflamed organ in the neighborhood, but there is no evidence that organisms can spread in a similar way from non-inflamed viscera so that this route need not be considered further. (54)

The causes of biliary tract disease and the nature of the deranged physiologic processes, as far as they affect the gallbladder, are quite generally conceded to be: (1) Biliary infection, (2) Biliary stasis, and (3) Metabolic disturbances. These will now be taken up each in turn in detail.

Biliary infection - bacteria pass from the blood stream through the cells of the liver into the bile and reach the wall of the gallbladder where they cause inflammatory changes as well as in any or all

parts of the biliary vessels. Therefore, a hepatitis is the first pathologic change created by such an invasion and may be present without cholecystitis and may persist long after the secondary cholecystitis has been cured. (41) Bacteriological investigations of the gallbladder in cases of cholecystitis have been made in two ways, by cultures of the contained bile or other fluid content, and by cultures of the ground-up wall of the organ, the latter being the most acceptable method. (39) Rosenow was the first to emphasize strongly the desirability of making cultures from the wall and not merely from the contents of the organ since there is no assurance that the bacteria responsible for the disease always gain access to the lumen. (62)

The prevailing type of bacteria found in the wall was a streptococcus; whereas *Bacillus coli*, *Bacillus welchii*, staphylococcus, fusiform, and diphtheroid bacilli were also cultured from this locality. These streptococci have an elective localization when injected intravenously into animals, and their number is proportionate to the degree of gross and microscopic change. (29)(62) Many cases of cholecystitis have been preceded by typhoid fever,

and it is now generally agreed that these organisms migrate via the systemic and portal systems to the gallbladder where they take up their abode without producing actual clinical symptoms of the infection, thus that individual becomes a "typhoid carrier".

It appears, then, that there are two great groups of bacteria found, one resembling those found in the various foci of the head and the other resembling organisms found chiefly in the bowel. The latter group resists bile, thrives in varying degrees of temperature, and is probably the more important of the two groups. (59)

Biliary stasis - in any condition in which the gallbladder is partially collapsed and its refilling prevented, the concentration might go on to precipitation and theoretically to gallstone formation. Some such conditions are: (a) Too often repeated stimuli to emptying as with frequent meals and overfeeding, (b) Insufficiency of the sphincter of Oddi from atony preventing refilling, (c) Pressure from without as in pregnancy, and (d) The above factors plus infection. (41) It has been noted that the type of individual in which stasis is most pronounced on cholecystographic examination, namely, the

viscerototic, is not the type in which biliary disease is most frequent. (29)

Bisgard concludes that stasis plays an essential and fundamental role but not the active one in the production of cholecystitis and stones. Apparently it merely creates circumstances favorable to the damaging activity of pancreatic enzymes and of bacteria. In other words, cholecystitis results from stasis plus either the reflux of pancreatic secretions or infection or a combination of the three. (8)

Metabolic disturbances - an upset in the metabolism of lipid material and cholesterol may readily result in the formation of calculi, the majority of which are cholesterol, less commonly pure pigment calcium calculi, and least commonly mixtures of these substances. (41) Newman, Rosenthal, and Licht within the last few years have called attention to the necessity of maintaining a proper bile-salt-cholesterol ratio if stone formation is to be prevented; the bile salts hold cholesterol in solution by forming a water soluble addition compound. The pathogenesis of faceted gallstones has been described as due to the absorption of bile salts which occurs in the infected

gallbladder; the cholesterol is left behind and supposedly precipitates and affords a nidus for gallstone formation. (58) In some cases, there is little doubt that the presence of calculi has preceded a true cholecystitis and there is much evidence that the mechanical and possibly the chemical irritation of the gallstones aggravates an existing cholecystitis. (29)

Acute cholecystitis rarely develops alone; more frequently it is part of a general cholangitis or results from the trauma of gallstones. The association of acute cholecystitis with appendicitis is of interest in the light of recent theories which suggest that lesions in the appendix exert a reflex influence upon the gallbladder and sphincter of Oddi. (15)

Chronic cholecystitis may follow the acute form or may be slow and insidious from the onset by infection with an organism of low virulence such as the streptococcus viridans, Bacillus typhosus, or the colon bacillus.

SYMPTOMS

Since inflammation of the gallbladder reveals itself in many forms, the clinical picture will likewise be varied. As in other conditions, an effort should be made to establish a diagnosis in the early and relatively mild cases in order to forestall the late effects as much as possible not only in the gallbladder but in other organs as well.

In acute cholecystitis the onset is usually sudden, sometimes with a chill. Evidences of peritonitis supervene early consisting of pain in the right upper quadrant of the abdomen, muscular rigidity and tenderness more pronounced in that region, vomiting, leukocytosis, and fever. The pain is usually of a continuous aching character of a severe type; it may be cramp-like with severe paroxysms. The pain is often referred to the back particularly in the region of the angle of the right scapula and lower dorsal spines. (26) Roughly speaking, the pain is felt in the area supplied by the descending cutaneous branches of the third and fourth cervical nerves and must be distinguished from the infrascapular segmental pain commonly felt in gallstone disease and in some gastric conditions.

Ordinarily the pain begins to subside in about 24 hours; and in a typical case, after about ten days the symptoms are gone. Usually the chills are not severe and the fever is not above 102 degrees Fahrenheit unless there is extensive involvement of the liver coexistent. In a case of acute cholecystitis uncomplicated by stones, jaundice is ordinarily not a conspicuous feature. Respiration is painful and may be restricted on the right side and somewhat jerky. (29) Nausea and vomiting are not uncommon symptoms, and the gallbladder is palpable in approximately 20 per cent. (15)

Symptoms of the suppurative form are more severe than in the simple catarrhal form of acute cholecystitis, prostration is marked, there is often generalized abdominal pain caused by the association of the branches of the celiac axis and the vagus, the spleen may be enlarged, and albumin is present in the urine.

The pulse is not diagnostic, and the rate is usually proportional to the amount of fever present. Leukocytosis of moderate degree may accompany the condition although in over 50 per cent the count will not be greater than 10,000. (16)

An acute gallstone attack may occur at any hour

of the day or night, but they are prone to occur after indigestible fat meals at two or three o'clock in the morning. The pain of gallstone colic is sudden in onset, intermittent or constant, excruciatingly severe so as to require morphine for relief. It may continue for hours or minutes and stop as suddenly as it began. In the aftermath of the attack there is residual tenderness over the gallbladder, perhaps a trace of jaundice, bile pigment in the urine, change in the stool color, and a rising level of serum bilirubin. (60) When a stone is present in the cystic duct the pain instead of being more or less continuous may be paroxysmal and very severe during the paroxysms. (29) Noncalculous cholecystitis may appear just as acutely but rarely with as severe pain, especially during the course of acute bacterial lesions. An attack of acute cholecystitis almost invariably subsides spontaneously. (60)

The symptoms of chronic cholecystitis are again extremely varied. In some cases there are recurring attacks of severe biliary colic, at times followed by jaundice; these are the cases in which stones are likely to be present. In other cases there are spells of vague soreness or discomfort in the upper abdomen,

a little more marked on the right side. In still others, there may be only dyspeptic symptoms or disturbances in other parts of the body as in the joints. Again, the symptoms may be referable largely to pericholecystic adhesions to other organs or due to a carcinoma. The diagnosis is simple in the advanced case which gives a history of recurrent attacks of pain in the right upper quadrant associated with nausea and vomiting; still easier if there have been attacks of jaundice with these recurrent attacks of pain. (29)

The most characteristic symptom of chronic cholecystitis is recurrence of attacks of biliary colic. The pain characteristically begins more or less suddenly in the epigastrium or right upper quadrant of the abdomen and is projected around the right costal border to the right subscapular region. At the onset the patient is frequently nauseated and vomits and there is a picture of extreme distress. The pain may cease as suddenly as it began after a few minutes, but the usual sequel is marked residual soreness in the region of the gallbladder for several days. The colic may or may not be recurrent, and during the interval there may be entire freedom from

all symptoms. The temperature usually remains normal or subnormal during the paroxysm, and the pulse is accelerated. Many patients characterize their distress as a dull, aching soreness under the right costal border which increases in severity upon jolting or jarring or by eating a full meal. (16) This distress may have been diagnosed as neuritis or neuralgia for years.(41)

Digestive disturbances of one sort or another are present in chronic cholecystitis. Epigastric fullness after meals with bloating and gaseous eructations is extremely common and may be the most troublesome symptom of the disease. Some patients will not tolerate fried or greasy foods, and others, coarse vegetables; but many find that mere overloading of the stomach with any type of food seems to cause distress and may precipitate an attack of colic. Jaundice is not a common accompaniment if the gallbladder alone is infected, but there may be transient jaundice as the result of associated hepatitis or cholangitis; this jaundice leaves as the attacks subside. (16)

The symptoms of chronic cholecystitis and cholelithiasis are practically identical, and clinical

examinations often fail to demonstrate whether gallstones are present or not. Many patients complain merely of vague digestive disorders, flatulence, belching, acid eructations, and a sensation of weight or oppression in the upper abdomen. Palpitation and precordial oppression may be due to flatulence or to absorption of toxins from the gallbladder. Ingestion of food does not give relief. There may be intervals of varying length in which the patient is free from symptoms. These are followed by attacks of pain, chilliness, and a slight rise of temperature, thought to be due to reinfection or to spasm of the gallbladder caused by the irritation of calculi. (15)

Constipation, dizziness, headache, cardiovascular phenomena, biliousness, nervous disorders, and fatigue are all not uncommon symptoms of chronic cholecystitis. He is that type of individual who fatigues easily, sleeps poorly, and shows a distinct aversion to fat. Furthermore, he is inclined to neurasthenic, melancholic, hypochondriacal, and psychotic manifestations, many of which are directly linked up with faulty metabolism or the result of a systemic toxemia. (60)(61)

DIAGNOSIS

Most patients with positive cholecystic disease, probably 80 per cent, present symptoms that are clear and unmistakable. In order to make an accurate diagnosis, however, there are five methods that must be correlated, i.e., a careful history, a thorough physical examination, laboratory tests, cholecystography, and biliary drainage. The last two procedures are complimentary with the exception of early disease of the biliary tract where biliary drainage gives the most information and where the history is often confusing and vague, the physical examination negative, and the cholecystogram reported as normal.

The case history still remains the most valuable diagnostic measure and should be carefully taken, delving not only into the present but into the past as well. The physical examination may be entirely negative since positive findings depend upon the stage of the disease and the complications present. (41)

Right upper quadrant tenderness, the tender liver (Murphy's sign), Robson's point sensitiveness, a painful cystic tumor, posterior ninth rib tenderness, and a Head's hyperesthesia area may all or severally appear. (41)

In gallbladder disease many phenomena are elicited:

1. Inspection may reveal swelling or abdominal distention.
2. There may be localized tenderness clearly confined to the gallbladder area.
3. Tenderness which is accentuated by pressure, upward, inward, and outward suggests gallbladder disease; while tenderness which is accentuated by downward and inward pressure suggests the possibility of duodenal or pancreatic pathology. When the liver is enlarged and readily palpable, it is possible to distinguish liver tenderness and gallbladder tenderness; however sometimes both organs will be tender and differentiation difficult.
4. Rigidity either before pressure or induced by palpation is always suggestive of possible gallbladder involvement. A sharp, prodding movement or striking with the ulnar surface of the hand may elicit tenderness otherwise unrecognized.
5. A palpable gallbladder is an occasional clinical finding such as in hydrops and calculous cholecystitis in which the gallbladder may become as large as a grapefruit, simulating carcinoma.

6. The French describe gallstone fremitus, presumably due to rubbing of stones upon one another; but this condition is a rare entity. (60)

Palpation of the abdomen in many cases of chronic cholecystitis will give but little information of value, but a sudden jab of the fingers upward under the right costal margin just as the patient has completed a deep inspiration will often elicit tenderness which may otherwise be missed. (29)

The Lyon-Meltzer method of duodenal intubation is to the study of the biliary tract what gastric analysis is to the study of the stomach. It is the most logical way to study the contents of the biliary tract and is in a sense a study of the physiology or physiopathology of the tract in contradistinction to the x-ray studies which largely throw light on the anatomy of this part of the digestive tract. It is possible by deductive reasoning to determine the presence of pathological alterations by means of duodenal intubation. Before the study of the biliary contents, our conceptions of biliary tract disease were largely confined to the alterations which occurred in the stool where only gross changes such as a lack of fat digestion are recognizable. (60)

The purpose of the Lyon-Meltzer technic of duodenal intubation is to segregate the specimens from the different parts of the biliary tract. After a variable amount of yellow-colored duodenal contents has been obtained, 20 to 30 cc. of a warmed, previously filtered, 33 per cent solution of magnesium sulphate is gently injected through the tube in the duodenum. This is injected slowly and within a few minutes it is possible to extract a yellow-colored, limpid liquid which is called the "A" fraction. Lyon believes this to be from the common duct; it varies in amount from 20 to 30 cc..(42) It becomes darker in color, more viscid, and for a variable period of time this dark bile, known as the "B" bile is obtained. In most instances only small amounts are obtained, and in pathological conditions no "B" bile is present. This bile is believed to come from the gallbladder predominantly. The bile again becomes less thick, more limpid and light yellow in color and is the so-called "C" bile which is supposed to come directly from the liver. (60)

The procedure is entirely negative when there is no evidence of "B" bile; the gallbladder has failed to eliminate any of its contents, and it is assumed

that there is either a blockage of the cystic duct or the gallbladder is filled with a material which it is unable to evacuate. If only a few drops of "B" bile are obtainable, there is either a partial blockage of the cystic duct or the gallbladder is not contracting satisfactorily. If, on the other hand, there is an excessive amount of "B" bile, there is obviously biliary stasis in the gallbladder; and microscopic studies should show excessive amounts of pigment and cholesterol. (60)(61)

An examination of the bile obtained by duodenal intubation will give the trained observer a clear interpretation of what is going on in the biliary tract. It is customary to interpret excess mucus as indicating catarrh; an increase of pus cells as inflammation; an increase of bacteria as infection; an increase of biliary tract crystals as gallstones, potential or formed; and the finding of parasites as infestation.(33) *Girardia* are not infrequently met with and can be readily recognized by their motility and form in fresh specimens. Cultures may also be obtained from the biliary drainings and aid markedly in identifying the etiological agent. (61)

At the present time, we have at our disposal

three approaches to the x-ray study of the gallbladder.

1. Flat plates or films.
2. Fluoroscopic study (indirect signs).
3. Cholecystography.

Flat plates of the abdomen are made by means of a Bucky diaphragm for the purpose of visualizing the outline of the liver, demonstrating calculi, and occasionally revealing the outline of a gallbladder.

The second method is part of a combined fluoroscopic and serial film procedure used for the general study of the digestive tract. The examiner is able to palpate the right upper quadrant under the screen and can localize tenderness to a given area over the gallbladder. He can note changes in the form of the stomach and duodenum which are suggestive of gallbladder infection. (60)

Cholecystography is considered the greatest single step forward in the last decade in the diagnosis of cholecystitis. (41) It is based upon the principle that when phenolphthalein is either injected into the veins or given by mouth it is segregated by the liver, excreted into the bile, and normally concentrated in the gallbladder to a point at which it is visible on the roentgenogram. Phenoltetraiodophthalein and

sodium tetraiodophenolphthalein are superior to all other substances. (46) The intravenous method of gallbladder dye administration is a safe procedure for all classes of suspected biliary tract pathology; reactions are few and factors of doubt present in the oral method are eliminated. (42)(46) Oral administration of the dye is contraindicated in pyloric obstruction or in obstruction of the common duct.

By this method, we are able to determine the size, shape, and position of the gallbladder and to test its functions, i.e., how it is able to fill, concentrate and empty, as well as to recognize gallstones, especially the non-opaque stones, notably the common cholesterol and bilirubin calcium stones. It is, however, not an infallible diagnostic procedure. A normal gallbladder may appear normal yet because the dye has not been absorbed from the intestinal tract, or parenchymal liver damage may interfere with the proper excretion of the dye into the ducts, or cystic and hepatic duct obstruction may prevent the entrance of the dye into the gallbladder. A similar difficulty may arise when the gallbladder is filled with stones or a new growth. In spite of these possible sources of error, the method provides us with the best way of

estimating gallbladder function. (55)

A faint shadow indicates either that the gallbladder wall is thickened from an old chronic inflammation; it is so packed with stones as to allow only a small amount of dye to enter; there is some interference with normal function of concentration which is especially true in acute cholecystitis; or that it is an acute exacerbation of an old chronic case. Faint shadows indicate an impaired function rather than complete loss of function, as seen in early gallbladder disease wherein the mucosa may be damaged in a manner to hinder the concentration of the bile (65) The success of a diagnosis based on the degree of impaired function demands that a constant and known quantity of dye reach the blood stream; and this can only be achieved by the intravenous method, otherwise it is impossible to compare the density of one gallbladder shadow with another. (60)(61)(65)

In the intravenous method of cholecystography, there should be a beginning visualization of the gallbladder in about four hours, increasing density and alteration in size at eight hours, a maximum size at approximately twelve, and great diminution in size at twenty-four hours. Should the dye be given through the

alimentary tract, visualization is first observed at about the twelfth hour; and from that time on the cycles are exactly the same. There is a wide normal variation of the gallbladder when revealed by this means in regard to its location situation, contents, outline and capacity; however none of these constitute pathological indications if the organ is well visualized, shows a progressive intensification of the shadow, alteration in size, and disappearance of the image shortly after the termination of the starvation period. (29) In those pathological conditions which may be ascribed to a hidden focus of infection, cholecystography will often reveal a diseased gallbladder which is symptomless. Also, it is valuable in the differential diagnosis and particularly in chronic heart disease and angina pectoris. (5)

Many physicians consider cholecystography contraindicated and even dangerous in cases of jaundice. It is, of course, likely to be valueless because the dye generally cannot reach the gallbladder. Simply because gallstones are demonstrable or the gallbladder cannot be visualized, it does not follow a priori that gallbladder disease is the cause of the complaint. (41)

Negative shadows of cholesterol stones should be differentiated from those caused by neoplastic growths, chiefly papillomas and adenomas. Irregularity in the outline of the gallbladder on cholecystography suggests adhesions and sometimes cancer. Biliary drainage will pick up early lesions of the gallbladder more readily than cholecystography, but the two methods should supplement one another. (42) Cholecystography in the early case is of little help as the reports will usually show good filling and emptying response to the dye. Bochs in a study of 148 cases of proven stones found that the cholecystogram demonstrated stones in 29.2 per cent while biliary drainage suggested the presence of stones in 83.2 per cent. (33)

The differential diagnosis of cholecystitis is in itself a major problem but is somewhat simplified by the present day methods of diagnosis at our disposal. In the first place, it is important to make a thorough physical examination to prevent a not infrequent embarrassing mistake. Pay attention not only to the right upper quadrant of the abdomen but to other regions as well, including the rest of the

abdomen, pelvis, vagina, rectum, and prostate.

Beginning pneumonia in the base, pleurisy, intercostal neuralgia, or beginning herpes zoster on the right side may form a question during the early stages.

Coronary artery disease and toxic myocardial disease may simulate gallbladder disease; and therefore, the cardiovascular system should be carefully examined.

Syphilis should be excluded since a visceral crisis in cerebro-spinal lues may be coincidental with an active cholelithiasis. One should not be content with the finding of the first and presumably causative pathology in a patient and assume the case exists in pure text-book form as oftentimes the chances are against this. (33)

Chronic inflammatory lesions of the stomach, especially chronic gastritis, chronic peptic ulcer, gastric carcinoma, pylorospasm, peripyloric adhesions, and duodenitis all may at sometime or other be confused with chronic cholecystitis. Perhaps the most frequent condition confused is chronic appendicitis, and in many cases they are associated.

Visceroptosis may be confused with chronic gallbladder disease and give rise to upper abdominal pain. Dis-

eases of the colon may simulate chronic cholecystitis as for example, carcinoma of the hepatic flexure, as well as spastic colon and mucous colitis. Various conditions of the liver such as cirrhosis and syphilis lead to a wrong diagnosis. Lesions of the right kidney such as pyelitis, pyelonephrosis, hydro-nephrosis, renal calculi, ptosis of the kidney with ureteral kinks may all give rise to right upper abdominal discomfort to be misleading in the diagnosis. The severity of the symptoms in assumed chronic cholecystitis fluctuates markedly often in a manner corresponding to the patient's degree of instability, and often the difference between what is functional and what is organic is next to impossible. (23)(55)

The sympathetic nerves through the superior and inferior mesenteric ganglia are closely linked with the stomach, duodenum, right kidney, ureter, and colon as well as with the gallbladder, a fact not infrequently accounting for confusion in interpreting symptoms of supposed cholecystic disease. (23)

TREATMENT

The treatment of cholecystitis divides itself quite naturally into the two categories of surgical and medical. The method of choice depends upon several factors such as the age of the patient, the type of gallbladder infection manifested, and the stage of the infection. It has been my privilege to review the literature on this subject and herewith set forth the opinions of many noted internists and surgeons, endeavoring to point out the indications and contraindications for such treatment.

The practitioner who turns to the current surgical literature for advice on the management of acute cholecystitis is not likely to receive much help, particularly if his reading is extensive; for paradoxically enough, the more he reads the greater will be his confusion. He will find authorities of equal eminence diametrically opposed in their ideas regarding the optimum time for operation in acute cholecystitis. The average surgeon, however, follows neither school of thought but relies on that sixth sense, commonly known as clinical judgment.

While some surgeons advise immediate operation in cases of acute cholecystitis, whereas others

advance valid arguments for delay, this having been the accepted plan until a few years ago, every case of acute cholecystitis is a law unto itself and must be judged on its own merits. (23)(57)

SURGICAL TREATMENT

The following discourse will review the use of surgery in the treatment of cholecystitis and the indications and contraindications for it. Even though it has been decided by many surgeons to treat cholecystitis with surgery, the question then arises as to when to operate.

The first essential is to determine that it is the gallbladder that is causing the disturbance. If we can be certain of this and can demonstrate stones, or if we suspect fibrous thickening of the wall, or have the history and clinical evidence of recurring colic or icterus, then, no contraindications existing, surgical removal of the gallbladder is indicated. (41)

One must differentiate acute diffuse disorders of the liver which are non-surgical conditions, carcinoma of the ampulla or pancreatic head, and similar borderline surgical conditions, and stones in the extra-hepatic ducts which is an absolute surgical condition.

Calculi, verified by cholecystography, and accompanied by a history of recurrent colic and cholecystitis, as a rule, require surgery. If cholelithiasis is found in a routine examination and the symptoms are slight or absent, or if the patient has had only one attack of colic, a difference of opinion exists as to whether medical or surgical treatment should be employed. If the gallbladder concentrates well, the patient may go on for years with few or no symptoms. (56) Gallstones are purely surgical except in:

1. Silent stones in an advanced senile or sclerotic cardiovascular renal disease.
2. Cases where there is liver damage, severe anemia or disposition to hemorrhage.
3. Coronary disease.
4. Cases where jaundice exists with changing level of bilirubinemia.
5. Presence of an active upper respiratory infection unless controlled.
6. Unexplained hypotension.
7. Large silent stone with evidence of good gallbladder function. (60)

In the very definite, very severe lesions of the

gallbladder such as suppuration, gangrene, perforation, or stone, where frequent or severe attacks of gallstone colic take place, surgery is the only procedure to consider. (12) Whether, in the former group, one should operate during the acute stage, doing a cholecystectomy if possible, whether one should wait until that stage is over, confident that even if perforation does occur the omentum will prevent general peritoneal infection, still is a moot question. Graham, has not advised an operation on an acute gallbladder for four years; and except for the finding of an occasional pericholecystic abscess, has seen only two cases of perforation causing general peritonitis. Most of the surgeons are agreed with this point of view, however some contend that since we cannot diagnose a case of perforation from a gangrene or acute empyema we should advise immediate operation. Brown feels that a few cases unquestionably need immediate surgery and that by having no fixed general rules, by regarding each as an individual problem, by weighing all the factors such as the general condition of the patient, the leukocyte count, the temperature chart, the blood and urine analysis, and an intensive clinical study of the

patient, one can decide whether the acute aspects of the case are subsiding or are becoming progressively worse. In those who are progressing, immediate operation is indicated; but in the former group mortality is likely to be lowered by performing an interval operation after the fulminant acute inflammation has subsided. It must not be forgotten, however, that the symptoms and signs in some of these cases occasionally may be so slight that gangrene and perforation may take place with very few local and no very striking general signs or symptoms. It is a rather wise rule to remember that in abdominal surgery the more severe the symptoms, the more definite the diagnosis and the more obvious the surgical need, the better are the results obtained; hence in gallbladder operations the prognosis is usually quite good. (12)

Surgeons and internists have found a most perplexing problem in the chronic non-calculous cholecystitis. Operations in these cases are followed by poor results and the outlook for a complete symptomatic treatment following cholecystectomy is definitely less favorable than in cases in which stones are present. Graham puts the unsatisfactory cholecystectomy cases at 40 per cent. (63)

Pathologically two types of non-calculous gallbladders are to be considered. One is the chronic inflammatory type of gallbladder which shows definite edematous and thickened walls and an opaque serous coat. The second type known as the strawberry gallbladder is due to characteristic deposits of cholesterol esters which stud the gallbladder mucosa. Surgery is indicated in these cases when there is no evident and satisfactory improvement under prolonged medical care. (63)

Although he favors early operation, Best mentions that it is a rare occasion when immediate or emergency operation is indicated. In most cases, some hours to several days should be given to observation and adequate preparation of the patient for operation or a higher mortality rate will be the result. (7) Stone and Owings, on the other hand, state that with prompt operation there is a notable saving of time, pain, expense, and danger as compared with the policy of delay. They regard the acute gallbladder lesion whether hydrops, empyema, torsion, gangrene or simple acute cholecystitis, as best treated by prompt operation; and in most cases the operation should be a cholecystectomy. (68)

Glenn advises immediate operation in acute cholecystitis; his mortality in 170 cases irrespective of pathology, age, and other important factors is 3.5 per cent. He states that the real difficulties in operating are encountered in those patients who are allowed to proceed to gangrene and perforation leaving the patient with an extracholecystic abscess or masses of adhesions. As to postoperative complications, there is nothing to indicate that these are influenced by the time at which operation was performed. (26) Smith states that the incidence of empyema, gangrene, and perforation increases as attacks are prolonged; therefore to avoid these pathologic conditions it is wise to intervene early. (66) Zininger, in 54 patients observed for periods of twenty-four hours to twelve days, found that less than two-fifths showed improvement while the remainder failed to improve or got worse. (72) Heuer believes in early operation and presents 153 cases with a 3.2 per cent mortality with 65 per cent operated upon on the day of admission. (36) Graham reports a series of 198 cases of which 20 were operated upon within 48 hours with a 5 per cent mortality; whereas among the remainder the mortality was 6.2 per cent and

complications much more numerous. (31) McKenty thinks that operation in the first 48 hours has a mortality low enough to justify it as a routine measure. Mentzer is an advocate of early operation and states that since he has become bolder in this regard his results have improved. (48)

Pennoyer presented a study of 300 cases from the Roosevelt Hospital where the surgeons prefer to allow the attack to subside before operating; and in order to leave no doubt as to the acuteness of the attack, he included only patients who had a temperature of at least 101 degrees Fahrenheit and a leukocytosis of 12,000 or more. The general mortality was 10 per cent; whereas in the 59 cases operated upon as emergencies the mortality was 25 per cent, representing half the fatalities in the entire series. (56) Graham withholds operation until the temperature is normal unless the condition is becoming worse. (30) After subsidence of the clinical symptoms there is less risk than when intervention is carried out during the acute phase.

It seems quite plain from the above that the question of immediate versus delayed intervention cannot be settled as yet by the statistical method.

Therefore, no rule of thumb can be laid down and each case must be judged on its own merits. There will always be, of course, urgent cases which will require operation at once and contribute disproportionately to mortality. However, if a patient is seen early in the disease and is a good risk, particularly if his symptoms are not severe, a prompt cholecystectomy should not be attended with high mortality and forestalls the dangers of later complications. Patients whose symptoms have subsided are better risks and one should be prepared to intervene promptly if progress is unsatisfactory. Caution is particularly indicated in older patients who furnish a large proportion of the fatalities. (66)

Acute cholecystitis resulting from obstruction of the cystic duct may go on to:

1. Perforation of the gallbladder with leakage of bile into the peritoneal cavity.
2. Small local areas of gangrene and perforation, which usually are encapsulated by gastrocolic omentum.
3. Perforation of the gallbladder into the duodenum and occasionally into the colon.
4. Spontaneous subsidence of the acute inflammation.
5. Extension of the inflammation to pancreas and liver.

6. ~~Expulsion~~ of the stone into the common duct.

The general tendency in most cases of cholecystitis is for the inflammation to subside in a period of a few days; usually by the seventh day the clinical manifestations of the acute inflammatory process appear to have pretty well subsided. (71)

The incidence of gangrene, abscess, and perforation in acute cholecystitis is between 10 and 30 per cent; and the mortalities are mostly in this group. By approaching the case with a surgical attitude and deferring operation only when there is confusion of signs, symptoms, laboratory findings, and appearance of the patient, the mortality for acute cholecystitis may be reduced. Probably about 50 per cent of cases of acute cholecystitis in any series should come to operation to give the lowest mortality for acute cholecystitis. As to appearance, a "stationary loginess of apathy", particularly in the older group seems to be a characteristic of non-subsiding acute cholecystitis. If the differential count reveals staff forms above 10 per cent, one should be suspicious of a nonsubsiding acute cholecystitis. Probably it is safer to favor early operation and operate only upon about 50 per cent

than to favor conservative treatment and operate only after advanced complications have arisen. Best's group mortality was reduced from 13 to 4 per cent by favoring early operation. (7)

Rouse sets down the following contraindications to gallbladder surgery:

1. Gallbladder dyskinesia.
2. Chronic cholecystitis, non-calculous.
3. Neurasthenic cases.
4. Poor surgical risks due to cardiovascular or renal disease.

The biliary dyskinesias comprise a syndrome group of functional gallbladder disturbances. They present all the symptoms of true cholecystitis with evidence of infection or cholesterosis. Due to this functional disorder, stasis of the gallbladder occurs either due to motor inactivity, reversed duodenal peristalsis, or spasm of the sphincter of Oddi. Do not operate on these individuals; even under medical care a number show little improvement. Non-calculous chronic cholecystitis showing poor functioning on the cholecystogram with only a vague history of biliary colic, showing satisfactory response to medical care, should not be imposed upon by the surgeon. (63)

Those patients in whom biliary colic is the outstanding symptom or who complain of more or less persistent pain or discomfort in the right upper quadrant or epigastrium associated with tenderness and varied symptoms of chronic dyspepsia are essentially surgical in their management. (55) This group contains those who have gallstones, varying degrees of biliary tract obstruction, enlargement, distention, and distortion of the gallbladder, the more severe degrees of biliary tract infection, pericholecystic inflammation and adhesions. Those patients whose outstanding symptoms are due to disturbed gastric function with rare to no attacks of pain and inconspicuous tenderness comprise the largest group, who are both difficult of diagnosis and present a therapeutic problem. In it are included the cases that are called chronic cholecystitis, and it is in this group that early operation has proved of little value and at times even harmful. Even though many of these cases ultimately require surgical intervention, practically all of them can be benefited by proper medical treatment which in many instances is so successful that operation can be avoided entirely. In any event, it is wise to delay operation

in this group until all uncertainty as to diagnosis has been cleared up; and in the meantime, medical measures should be carried out to alleviate the gastro-intestinal symptoms and restore the patient's general health so that in the event that surgery be indicated the patient's chances will be greatly enhanced. (55)

Hall believes that there is general agreement as to the following conditions being surgical:

1. Cholelithiasis.
2. The chronic thick-walled gallbladder with deforming adhesions.
3. Malignancy of the gallbladder.
4. Benign tumors of the gallbladder.
5. Obstructions of the cystic or common bile duct by stone, adhesions, or tumor.
6. Cholesterosis of the gallbladder.
7. Acute suppurative cholecystitis.
8. Empyema of the gallbladder. (33)

Carcinoma usually invites surgical exploration in the hope that an operable tumor of the ampulla may be found or that an immediate cholecystogastrostomy, duodenostomy, or cholecystojejunostomy may relieve the jaundice and ameliorate the distressing symptoms.

Where the general condition of the patient is becoming progressively worse, with signs of toxicity, intervening deep jaundice, or prostration, immediate operation is indicated. It is the experience of surgeons that localized areas of necrosis of the gallbladder wall are not infrequent in acute cholecystitis; and fortunately, due to the sealing of these areas by intestine or omentum, a serious complication is averted. Perforations of the gallbladder wall through these gangrenous areas are similarly taken care of, and even walled-off extra-cholecystic abscesses may gradually absorb. (1)

Cases of acute gangrenous cholecystitis must be under constant and careful observation, since timely surgical intervention is required. According to Estes, the only indication for immediate or emergency surgery is the presence of symptoms of perforation with a spreading peritonitis. (21) Alexander, however, does not agree in that he believes even the suspicion of a massive gangrene justifies immediate operation. When there is sudden prostration, high temperature, rapid pulse, and a leukocytosis of 20 to 30,000, there is a strong enough suspicion of gangrene to indicate an immediate operation. (1)

Kruse gives the following indications for operation in biliary diseases:

1. To relieve local symptoms such as biliary colic, dyspepsia, and definite cholecystitis.
2. To combat any distant toxic effects.
3. To anticipate the onset of malignancy.

There are many unfavorable sequelae to surgery such as post-operative adhesions, a common duct stone pushed down at operation, functional disturbances that remain after gallbladder removal, the reactions on an unstable psyche, biliary tract disease primarily established before the gallbladder became involved, secondary dilatation of the bile radicles, destruction of the functional ability of the sphincter of Oddi, increased intestinal putrefaction and fermentation, and lastly mistaken diagnoses. (41)

Brown states quite frankly that chronic cholecystitis is not treated with special success by medical measures; and he feels far safer if first a cholecystostomy is done to see the effect of its long, free drainage or even if a cholecystogastrostomy is done with the object of bringing about permanent drainage. (12)

The choice of operation once the indications

are established is, of course, cholecystectomy. Drainage of the gallbladder, while occasionally required, has been found to be an incomplete and unsatisfactory operation often leading to reoperation. Even in acute empyema, in cases of acute cholecystitis, cholecystectomy has been incomparably the better procedure. (23) In about 20 per cent of cases there are instances when cholecystotomy is justifiable. In these instances the surgeon should perform the operation best suited. (57)

Clinton gives one condition in which he is reluctant to do a cholecystectomy and that is the gallbladder with a myriad of tiny stones with a vague history of mild transient jaundice, since the mortality rate is increased in secondary operations upon the common duct as well as the technical loss of a valuable anatomical guide. (17) Surgeons in England and America believe cholecystectomy to be the operation of choice, whereas in France Cholecystotomy is the popular operation.

Patients with simple uncomplicated disease of the gallbladder, without ductal or hepatic involvement, may require but little preparation for surgery; those

with long-standing disease of the gallbladder, with jaundice or a history of jaundice or recurrent infection or obstruction of the biliary tract or liver will require time for surgical preparation. Tests of hepatic function, such as the test with hippuric acid, the rose bengal or the galactose tolerance test, should be carried out repeatedly on all patients who are poor surgical risks. The correction of vitamin deficiencies is particularly important pre-operatively. Fluid and electrolyte balance must be restored in order to prevent dehydration, restore glycogen to the liver, and bring about a favorable exchange between cellular and tissue fluids as well as to promote the dilution and excretion of toxins. Poor renal function is also equivalent to poor surgical risk. (28) Unless surgical indications are urgent, time should be taken to bring the patient to the best condition possible by effecting any necessary weight reduction, by correcting dietary deficiencies, and by treating obvious foci of infection. (51)

In preparing a patient for gallbladder surgery, the first aim should be to keep down the immediate operative mortality to 5 per cent or less, to keep

down the postoperative morbidity to 10 per cent or less, and to keep the operating room or hospital period complications down to minimum. Most patients who die from cholecystectomies die from liver shock, from hemorrhage, from transferred infection, toxemia, assisted by poor anaesthesia and after return to ward or room from avoidable complications such as bronchitis, pneumonia, etc.. (42)

During the first few days post-operatively, opiates or narcotics should be pushed to keep the patient pain-free, mentally and physically relaxed, and to allay nervous tension. If the blood sugar drops below 90 mg. to daily tests, glucose by vein should be given to keep the level to 100 mg. or even more. Fluid by mouth, if the stomach is tolerant, may be started 8 to 12 hours post-operatively beginning with hot water, one ounce each hour, increasing an ounce each time after three or four hours. In 24 hours liquid foods may be started and continued for at least 72 hours. Water metabolism should be balanced by keeping intake and out-put charts. Post-operative nausea, vomiting and upper abdominal painful distension may be relieved by gastro-duodenal lavage and aspiration of toxic gases and fluids. On the fourth

or fifth day post-operatively, small amounts of soft food may be added; but thereafter go slowly in resuming full trays no matter how hungry the patient. The patient should remain in the hospital for 21 days and even four weeks is not considered too long. (42)

Duodenal drainage is beneficial pre and post-operatively as clinical evidence suggests that it removes circulating toxins, bacterial and chemical, from the liver and intestines with marked improvement of the patient. If such toxins are not removed, further resorption of them occurs in the intestinal tract, and thus a vicious circle is produced. (42) Hurst advises the administration of hexamine pre and post-operatively as a biliary antiseptic. He also advocates biliary drainage by the administration of massive doses of magnesium sulphate, particularly following operation. (37)(42)

Alexander gives the causes of the 20 to 25 per cent failures following cholecystectomy as follows:

1. Erroneous diagnosis.
2. Faulty surgical examination and judgment at the time of operation.
3. Overlooked pathology in the gallbladder and ducts even after careful inspection. (1)

One important factor in surgical management is the length of time the patient is kept on the operating table. A period of 30 to 40 minutes will insure survival with reasonable certainty, but if the patient is operated over longer periods shock and mortality are increased. There are few procedures in surgery wherein the length of operation is of more importance. (17)

Operations should not be performed in the face of a rising icteric index. Jaundiced patients should have investigations of the bleeding, clotting, and prothrombin time and should receive vitamins D or K, bile salts, and blood transfusions, if the above tests at any time indicate a bleeding tendency. If the jaundice is obstructive, Courvoisier's law, which states that in the presence of a palpable gallbladder the obstruction is not likely due to stone, may be beneficial in differentiating carcinoma from stone obstruction. (45)

Smith lists the following contraindications to cholecystectomy in the treatment of acute cholecystitis:

1. The presence of peritonitis due to perforation of the gallbladder.
2. Conditions which make it difficult to identify

the important structures in the right upper abdomen.

3. The presence of jaundice caused by obstruction of the common duct.

4. A situation in which the general condition of the patient is so grave that prolonged operation is not justified. (66)

Unless the operative indication seems very definite, especially if the picture is blurred and the symptoms indefinite, and where there is evidence that the symptoms are increased by an unstable psyche, it is wiser to postpone operation sometimes indefinitely, sometimes until all other measures have been proven ineffective. (12)

MEDICAL TREATMENT

The remaining pages of this paper will be devoted to the medical treatment of cholecystitis and the indications for such treatment. Most of the internists are quite in agreement as to the medical regimen in general, however there are slight differences which it might be well to bring to mind.

In the Scott and White clinic, all cases of acute cholecystitis are placed on a medical regimen when admitted; and only those patients who are considered satisfactory surgical risks are advised to undergo surgery after subsidence of the acute phase. (57) Nadler is of the opinion that acute cholecystitis should be treated medically unless preexisting chronic disease with lithiasis is known or is suspected as a result of the clinical course. Usually the attack is mild and subsides promptly at which time a cholecystographic study will detect residual pathology. If not seen until the second or third day and the infection is subsiding, delay operation for a few days, even though stones are believed to be present, in order that preparation for surgery may be carried out. (51)

Kraemer is not of the opinion that patients with acute cholecystitis should be subjected to immediate surgery but should be hospitalized, given no food, glucose in saline administered intravenously by continuous drip, frequent white counts performed, and rectal temperatures taken every four hours. If abdominal rigidity increases, if the white blood count and temperature steadily rise, a cholecystectomy

should be performed. On the other hand, if the temperature declines, the white blood count is diminished, and the patient shows less sign of acute inflammation, medical management may be satisfactory. However, even in these cases, if a cholecystogram reveals stones or a Lyon drainage demonstrates a functionless gallbladder, do a cholecystectomy. (40) Kruse believes that acute situations such as fever, chills, sweats, leukocytosis, and all the other features of an acute cholecystitis with suppuration, imminence of perforation and likelihood of gangrene should not be considered as surgical emergencies. These patients should be carried over this crisis with less danger from complicating hepatitis, a less dangerous and stormy convalescence, and a lower mortality rate. (41)

Acute cholecystitis is often amenable to medical treatment which consists of bed rest, limited fluid intake by mouth, and relief of pain. Morphine and atropine will relieve the pain. Inhalation of amyl nitrite or the oral administration of nitroglycerine will often alleviate the colic. As the patient improves, a high carbohydrate, low fat diet is gradually given. Surgery should be instituted if the patient does not respond to medical measures. (56)

The degree of success in those cases selected for medical treatment will depend upon how early the dysfunction has been detected. Fair, fat, and forty, mother of children, suffering upper abdominal pain and belching gas not only means gallstones but also means late diagnosis; this classical text-book picture of gallstones means a gallbladder that has been diseased for many years. (33) He cites the following conditions as being distinctly medical:

1. Biliary dyskinesia, or dysfunction of the sphincter of Oddi.
2. Simple catarrhal cholecystitis.
3. Obstruction of the cystic duct from catarrh with early cholecystitis.
4. Infectious cholecystitis, secondary to acute infections, such as typhoid.
5. The stoneless gallbladder with chronic cholecystitis with no adhesions or obstruction to the flow of bile into the duodenum.
6. All cases that are too great a surgical risk.
7. Infestation of the duodenum and biliary tract, such as giardiasis and typhoid carriers.
8. Hepatic-intestinal toxemias. (33)

Every gallbladder patient is a medical case whether he

submits to surgery or not. The surgeon can eliminate the end-result, but he does not eliminate the factors which induce it. (60)

Alexander states that although there is some controversy, it is generally accepted that the acute gallbladder infection, with some exceptions, should be handled medically and conservatively. It is only rarely that acute cholecystitis becomes a surgical emergency at the time of the acute attack. (1) He, in turn, divides the chronic cholecystitis cases into three groups:

First, there are the outright gallstone cases with attacks of colic, pain often referred to the back and chronic digestive disturbances. Except in the aged, there is nothing to be gained by deferring operation for months or years. If calculi were removed as soon as discovered, we would see comparatively few cases of acute cholecystitis and fewer common duct stones. The average duration of symptoms before surgery is at present four years.

Secondly, there are the fairly clear-cut cases of chronic cholecystitis with flatulent indigestion, localized pain, and tenderness in the right upper quadrant; a definite percentage have cholecystograms

indicating some abnormality of gallbladder function. This group is entitled to a thorough diagnostic study and a trial at good medical treatment; and if no definite continuing relief is afforded, surgery is indicated.

The third group comes in with vague abdominal discomfort, with pain located somewhere in the right abdomen or epigastrium, chronic indigestion, and frequently constipation. After physician and patient have become discouraged with the amount of relief afforded medically, the patient is often cholecystectomized; and it is this class that so many gallbladder operations fail. With a normal cholecystogram and without definite localizing symptoms of pain and tenderness in the gallbladder region, the diagnosis of chronic cholecystitis should be seriously doubted. (1)

Chronic cholecystitis without stones, diagnosed from symptoms and minor abnormalities of the cholecystogram such as irregularity of contour, distortion or delay in emptying, should be treated medically. Surgery is contraindicated unless medical measures fail. It is this group which is responsible for the failure of surgery to give relief in approximately

one-third of the cases of gallbladder infection. When symptoms of stones are definite, surgery is usually indicated; but if they are absent or slight, treatment is that of chronic without stones. (51) Kraemer states that the diseased, stoneless gallbladder is a medical problem and is in itself a chronic disease. The patient should be informed as to his condition and forewarned that in the presence of upper respiratory infection or gastro-intestinal infections symptoms are likely to recur. The patient should be kept under observation for life and a biliary drainage performed once or twice a year with a cholecystogram every two years both to evaluate the condition of the gallbladder and as a guide to therapy. (40)

Those patients embraced under the popular term of "dyspepsia" with a varied array of gastric complaints plus vague biliary tract symptoms are pre-eminently suited for medical management. Under proper medical care, some of these cases, with only low grade biliary tract infection, are cured; nearly all are definitely improved; however with surgery the results are disappointing and discouraging to both the patient and the physician. Another group in which it is justifiable to delay surgical intervention and

to rely on medical measures comprise those who are bad surgical risks because of age or some associated condition as of the cardiovascular apparatus, kidneys, or central nervous system. It is well recognized that unless the cardiovascular condition is extremely grave, it should not be regarded as a contraindication to gallbladder operation when proper indications exist. (55)

The two main objects in medical treatment are to minimize the chances of reinfection of the biliary tract and promote free biliary drainage. The first is brought about by keeping mouth, teeth, tonsils, and sinuses in as perfect condition as possible; by avoiding mechanical, chemical or thermic irritants in the diet as well as highly seasoned foods, rich foods, excessively coarse foods, and to avoid constipation or diarrhea so that there is a minimal chance of infection from the colon. The second requisite, promotion of free biliary drainage, is best obtained by the intake of food causing normal gallbladder emptying. Frequent feedings, a proper non-irritating diet with large amounts of those gallbladder emptying foods such as butter, cream, olive oil, and especially egg yolk. These foods, contrary to former opinion,

do not play a part in gallstone formation and are only contraindicated in case of jaundice. All of the salines help, such as a morning dose of phosphate of soda, magnesium sulphate, ordinary table salt, or lemon juice and soda; better still give a smaller dose in hot water shortly before each meal. This procedure helps few, if any, of the acute fulminating lesions, a fair proportion of gallstone colics, and a large number of cases of chronic cholecystitis with or without stones. Brown feels that a large group may be helped by such treatment if the patient is willing to follow the treatment in principle for a long period of time, perhaps indefinitely. Many patients have been comfortable and symptom free for long periods of time with such procedures alone; even cases with demonstrable stones or with definite evidence from x-ray of considerable gallbladder pathology; cases in which there is no evidence of progressive damage to the liver, biliary tract, gallbladder, or pancreas. (12)

Medical management, again, may be considered under the following heads: (1) Prophylaxis, (2) Treatment directed toward the gallbladder and liver, and (3) Treatment of associated organs and

functional disorders of the gastro-intestinal tract.

Prophylaxis is maintained by clearing up all foci of infection, relieving chronic constipation, avoiding all toxic substances, and proper regulation and restriction of diet, exercise, etc.. (55)

Treatment of the biliary tract itself once diseased consists of:

1. Regulating the diet so as to minimize the development of gallstones and lessen the metabolic load on the liver.
2. Disinfecting, if possible, the bile and biliary tract.
3. Promoting biliary drainage.

There is no stereotyped diet suitable for all cases of chronic gallbladder disease, but it must be formulated according to the individual requirements. It is important to know whether the blood sugar, blood urea nitrogen, and blood cholesterol are normal or increased and whether there is any elevation of serum bilirubin; it is equally important to know whether gallstones are present and whether the gallbladder is functioning properly. When there is no jaundice and the blood cholesterol is increased, a diet low in cholesterol and fats should be ordered

in the hope of lessening the formation of stones and aiding fat digestion. If stones are present and the gallbladder still functions, a diet high in fat will induce attacks of severe colic. On general principles, in most chronic gallbladder cases, it is advisable to place the patient on a low fat, low cholesterol diet. Carbohydrates are important in liver damage; and since in most chronic biliary tract disease there is an associated functional or organic impairment of liver cells, chief reliance must be placed on this group of foods to meet caloric requirements and maintain an adequate glycogen reserve. If there is a high urea nitrogen in the blood with suspected damage to the liver cells, the diet should be low in protein but must be present in sufficient amount to supply the body requirements. Disinfection is accomplished by the ingestion of hexamethylenamine but is not considered a satisfactory treatment in view of the effects of biliary drainage. (55) However, Hurst and Knott are convinced that urotropin in large doses is of definite value as a disinfectant of bile. (29) Biliary drainage may be accomplished by the use of certain drugs such as cinchophen, cathartics which possess chologogue properties, bile salts themselves,

or the taking of from six to eight ounces of hot water just before each meal. Although more time consuming and troublesome, the most satisfactory method of promoting biliary drainage is by the duodenal tube method of Lyon. In this procedure, all infected material is at once removed from the body, whereas by cathartics and chologogues, it is merely passed into the bowel from whence absorption may and probably does occur. (55)(60)

Treatment of associated organs and functional disorders of the gastro-intestinal tract is indeed important. Often the most conspicuous symptoms in chronic gallbladder disease are referred to the stomach, and in all cases fractional gastric analyses should be carried out and if any pathology by found adequate measures instigated to give relief. Pancreatic lesions, which occasionally occur supplementary to chronic cholecystitis, react favorably under the same regimen of treatment. Colitis, particularly the irritable spastic colon, is a common accompaniment of cholecystitis; and its successful management will greatly aid in the patient's recovery. (55)(60)(41)

In general, two types of diet are employed,

one stimulating to the gallbladder and the other non-stimulating or sedative. The stimulating diet contains high fat, fruit juices, and meat which promote evacuation of the gallbladder through the elaboration of cholecystokinin. The sedative diet contains a minimum of fat, meat, and fruits to obviate this natural cholagogue action. The stimulating diet is used in the chronic conditions and is not used in acute states or where there is pronounced spasm of the sphincter of Oddi. The sedative diet is employed in acute conditions and where colic denotes spasm of the sphincter; it contains a maximum of carbohydrate to maintain the glycogen stores of the liver at a high level. Both diets should contain ample calories and liberal vitamins. (22)(38)

Elimination by the use of cathartics which relax the sphincter of Oddi and duodenum and permit the free flow of bile produces symptomatic relief, but they are detrimental for they may produce cathartic colitis which in turn may produce a hypertonic reflex gallbladder. Also, the clinical improvement following the use of antiseptics such as salicylates, methenamine, salyrgan, and tetraiodophthalein is not striking; and at present much controversy exists as to their value.(22)

Rafsky feels that these patients should have a liberal diet and not curtail the use of fats unless there is some distinct indication for this procedure. He also believes in the stimulating of fats, meats, and fruit juices where there is inactivity of the gallbladder and the diet low in fats and meats where there is spasm of the sphincter or colic. (56) He states that the diet must be regulated to the needs of the patient, and if hyperchlorhydria or ulcer complicate the biliary tract disease, the ulcer type of diet will prove beneficial. If a lowered acidity, or achlorhydria, should be present give fifteen to thirty minims of hydrochloric acid with the meals diluted in water or fruit juice.

The drugs useful in the medical treatment of cholecystitis may be classified as follows:

1. Those which relax the sphincter of Oddi and reduce the irritability of the pylorus and duodenum.
2. Those which correct disturbances of gastric sensation.
3. Those which stimulate the flow of bile. (chloretics)
4. Those which sterilize the bile passages.

Nitrites and certain derivatives of theophylline are effective in reducing sphincter tone and in most cases

it is advisable to use them daily. Barbiturates plus belladonna or atropine, while not necessarily active in causing relaxation of the sphincter may produce considerable symptomatic relief of dyspepsia and may be prescribed together before meals. The newer antispasmodics, syntropan or trasentin, are more useful since they eliminate some of the unpleasant side effects of atropine. Olive oil or cotton-seed oil will also relieve dyspepsia especially when given before meals. In cases of achlorhydria, hydrochloric acid is prescribed; in hyperchlorhydria, alkaline powders. Bile salts have a choloretic effect. Bilron is thought to produce an increased flow of bile and eliminate the biliary elements. Ketchol and decholin act chiefly by increasing the watery fraction of bile, while actually depressing the elimination of the bile salts. (56)

One accepted treatment for chronic gallbladder disease plus constipation has been daily small doses of epsom salts in water after each meal. The size of the dose recommended is determined by the number of bowel movements during each 24 hour period, two or three being sufficient. (17)

Autogenous vaccine may be made from cultures

obtained from the gallbladder bile but should not be administered until the acute stage has passed. It is particularly of benefit in those cases which are associated with arthritis, myalgia, and in those instances where there is evidence of general intoxication. (33)(60) Bacteriophage may prove to be of value in the treatment of cholecystitis, however it must be injected into the focus of infection which somewhat limits its usage. (60)

Medical treatment should be supervised, controlled and rechecked as to progress by cholecystography and duodenal intubation. The x-ray examination should be repeated under identical conditions. If the gallbladder is not visualized or fails to contract satisfactorily, one must conclude that instead of improvement the condition has become more pronounced. Duodenal intubation with microscopic studies and nature of the color sequence throw light on the physiology of the biliary tract. The clinical improvement of the patient, of course, is the most readily available criterion of the patient's progress under medical treatment. (60)

CONCLUSION

It has been my privilege to explore the current literature on cholecystitis and extract salient facts which have been presented in the foregoing pages. This section will serve to summarize the evidence in view of the present day consensus of opinion.

Therapy seeks to rehabilitate the disordered gallbladder by medical means when physiological alterations with minimal anatomical defects are present; by surgical methods when pronounced structural changes have occurred.

The borderline where medical treatment ends and surgical treatment begins is less easily defined in gallbladder pathology than in diseases elsewhere. In the acute infections of the gallbladder, changing local conditions may, in a few hours, so alter the plan of treatment that operation may be necessary for the safety of the patient. Almost all physicians, internists and surgeons alike, are agreed that the gallbladder containing stones should undergo surgical removal. Where the clinical picture of cholecystitis is a severe one, a very clear cut one, and one with very marked local or general symptoms, surgery is the safest method of approach. In the milder, less

definite and more chronic type of case, it seems better, in view of present knowledge, first to try the simpler and perhaps safer medical measures. Surgery should be undertaken in all cases in which there is not satisfactory response to medical management in a suitable length of time.

Until 1933, the consensus among most surgeons was that it was wise to postpone operating on a patient with acute cholecystitis until the acute manifestations of the inflammation had subsided, providing his general condition improved. However, from this date onward there has been an increasing number of advocates of the early operation treatment.

When to operate has proven to excite much comment; and the soundest judgment, in my opinion, is to have no fixed general rules but rather to regard each patient as an individual problem. Only by weighing all the factors such as the general condition of the patient, the leukocyte count, the temperature chart, the blood and urine analysis, and a clinical study of the patient can one decide whether the acute aspects of the case are subsiding or are becoming progressively worse. It is a rare occasion when immediate or emergency operation is

indicated. In most cases, some hours to several days should be given to observation and adequate preparation of the patient for operation or a high mortality rate will be the result. When surgical treatment is indicated, cholecystectomy is the operation of choice and should be carried out whenever feasible.

Chronic non-calculous cholecystitis should by all means be treated medically as statistics show that surgical treatment is unsatisfactory in some 40 per cent of cases, and at times surgery is even harmful. These cases are responsible for the greater share of mortalities in gallbladder surgery.

In the medical treatment of cholecystitis, the old adage of omitting cholesterol from the diet has been shelved. The two types of diet, stimulating and sedative, are finding wide usage with remarkable results. Biliary drainage is of great importance both diagnostically and in the treatment and is best managed by duodenal intubation.

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