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Diagnosis gallbladder disease

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THE DIAGNOSIS OF GALL BLADDER DISEASE

This thesis is respectfully submitted to the faculty of the University of Nebraska College of Medicine as a partial requirement for a degree of Doctor of Medicine.

--- J.I. Limburg

April 26, 1935

Omaha, Nebraska.
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DIAGNOSIS OF GALL BLADDER DISEASE
ANATOMICAL CONSIDERATIONS

This paper dealing with the diagnosis of gall bladder disease must necessarily include a few words on the anatomy of the liver, gall bladder, and ducts.

The liver arises in the form of a diverticulum or hollow outgrowth from the ventral surface of that portion of the gut which afterward becomes the descending part of the duodenum. This diverticulum is lined by entoderm, and grows upward and forward into the septum transversum, a mass of mesoderm between the vitelline duct and the precardial cavity, and there gives off two solid buds of cells which represent the right and left lobes of the liver. The solid buds of cells grow into columns or cylinders, termed the hepatic cylinders, which branch and anastomose to form a close network. This meshwork invades the vitelline and umbilical veins and breaks up these vessels into a series of capillary-like vessels termed sinusoids, which ramify in the meshes of the cellular network and ultimately form the venous capillaries of the liver. By the continued growth and ramification of the hepatic cylinders the mass of the liver is gradually formed. The original diverticulum of the duodenum forms the common bile duct, and from this the cystic duct and gall bladder arise as a solid growth which later acquires a lumen. The opening of the common duct is at first in the ventral wall of the duodenum; later, owing to the rotation of the gut, the opening is carried to the left and then dorsalward to the position it occupies in the adult.

The bile ducts commence by little passages in the liver cells which communicate with the canaliculi which are termed intercellular biliary passages. These passages are merely little channels or spaces left between the contiguous surfaces of two cells, or in the angle where three or more liver
cells meet, and they are always separated from the blood capillaries by at least half the width of the liver cell. The channels thus formed radiate to the circumference of the lobule, and open into the interlobular bile ducts which run in Glisson's capsule, accompanying the portal vein and hepatic artery. These join with other ducts to form two main trunks, which leave the liver at the transverse fissure, and by their union form the hepatic duct. The walls of the biliary ducts consist of a connective-tissue coat, in which are muscle cells arranged both circularly and longitudinally and an epithelial layer, consisting of short columnar cells resting on a distinct basement membrane.

The excretory apparatus of the liver should be considered as being part of the liver and no discussion of the gall bladder is complete without mention of the duct system. The excretory apparatus of the liver consists of the hepatic duct formed by the junction of the two main ducts, which pass out of the liver at the porta; the gall bladder, which serves as a reservoir for the bile; the cystic duct, or the duct of the gall bladder; and the common bile duct, formed by the junction of the hepatic and cystic ducts.

Two main trunks of nearly equal size issue from the liver at the ports, one from the right, the other from the left lobe; these unite to form the hepatic duct, which passes downward and to the right for about 4 cm., between the layers of the lesser omentum, where it is joined at an acute angle by the cystic duct, and so forms the common bile duct. The hepatic duct is accompanied by the hepatic artery and portal vein.

The gall bladder is a conical or pear-shaped musculomembranous sac, lodged in a fossa on the under surface of the right lobe of the liver, and extending from near the right extremity of the porta to the anterior border of the organ. It is from 7 to 10 cm. in length, 2.5 cm. in breadth at its widest part, and holds from 30 to 35 c.c. It is divided into a fundus,
body, and neck. The fundus, or broad extremity, is directed downward, forward, and to the right, and projects beyond the anterior border of the liver; the body and neck are directed upward and backward to the left. The upper surface of the gall bladder is attacked to the liver by connective tissue and vessels. The under surface is covered by peritoneum, which is reflected on to it from the surface of the liver. Occasionally the whole of the organ is invested by the serous membrane, and is then connected to the liver by a kind of mesentery.

The cystic duct about 4 cm. long, runs backward, downward, and to the left from the neck of the gall bladder, and joins the hepatic duct to form the common bile duct. The mucous membrane lining its interior is thrown into a series of crescentic folds, from five to twelve in number, similar to those found in the neck of the gall bladder. They project into the duct in regular succession, and are directed obliquely around the tube, presenting much the appearance of a continuous spiral valve. When the duct is distended, the spaces between the folds are dilated, so as to give to its exterior a twisted appearance.

The common bile duct is formed by the junction of the cystic and hepatic ducts; it is about 7.5 cm. long, and of the diameter of a goose quill.

It descends along the right border of the lesser omentum behind the superior portion of the duodenum, in front of the portal vein, and to the right of the hepatic artery; it then runs in a groove near the right border of the posterior surface of the head of the pancreas; here it is situated in front of the inferior vena cava, and is occasionally completely imbedded in the pancreatic substance. At its termination it lies for a short distance along the right side of the terminal part of the pancreatic duct and passes with it obliquely between the mucous and muscular coats. The two ducts unite and open by a common orifice upon the summit of the duodenal papilla, situat
at the medial side of the descending portion of the duodenum, a little below the middle and about 7 to 10 cm. from the pylorus. The short tube formed by the union of the two ducts is dilated into an ampulla, the ampulla of Vater.

**GENERAL DISCUSSION**

It has been roughly calculated that over twenty-percent of all the adults presenting symptoms referable to the digestive tract have pathology in the gall bladder.

The diagnosis of cholecystic disease is often not easy. A typical clinical pictures are very confusing to the clinician and frequently it is impossible to make a definite diagnosis. Since the introduction of the Graham Cole method of visualizing of the gall bladder, a renewed interest has been stimulated in an attempt to make an earlier diagnosis of cholecystic disease. This method of examination has proved itself to be a great aid to the diagnostician. Much has been claimed by certain writers for the value of Meltzer-Lyons method of studying the biliary fluid by means of a duodenal tube. Many who have given this test a fair trial feel that its value can be seriously questioned.

Without question the most important single diagnostic procedure is the securing of a careful history dating back to the first appearance of digestive disturbance or pain. The patient often needs considerable prodding in order to remember the mild pains of digestive upsets that occurred a number of years before. Complete freedom from distress of any kind may be present for years after the initial attack.

The symptomatology of gall bladder disease has its origion either in the over-distended gall bladder itself or by reflex or direct action of the diseased gall bladder on the adjacent organs, notably the stomach, pancreas, and intestinal tract. "Reverse peristalsis syndroms" plays a
very prominent part in the production of the discomfort. These symptoms are nausea, vomiting, belching, bloating and pyrosis. Although these are present in many states causing digestive disturbances, including that large group called functional indigestion, it is believed by many authorities that this syndrome is often an early finding in cholecystic dysfunction.

It is difficult to find any particular food that uniformly cause these patients distress. Fats are said to be eaten with difficulty. The patient is always searching for a cause, and usually ascribes it to something that was eaten in a previous meal. I do not believe it has been proven that any particular food or foods are capable of producing an attack. The only physical findings that seem to be of any importance are tenderness, palpation of the enlarged gall bladder, and jaundice. Of these, tenderness is by far the most frequent and most important sign. When present it is an extremely valuable finding, but its absence should not mislead the clinician in his search for gall bladder disease. When ordinary palpation fails, tenderness can often be elicited by having the patient sit up and lean forward; then, with the physician behind, the examining fingers can be pressed deeply under the ribs.

Palpation of the gall bladder is extremely difficult unless there is gross pathology such as empyema or cancer. When it is palpable, it always means that a pathological condition is present. Jaundice, contrary to ordinary beliefs, is not of frequent occurrence. Some authors state that jaundice occurs in only eight per cent of cases of gall bladder disease. The gall bladder must be considered as an integral part of the hepatoenteric systems. We must think of the liver as one unit and the intestinal tract as the other unit, and the two associated by connecting links which the French call the hepatoenteric circulation. This conception
is vitally important, as it emphasizes the complete dependence of one link of the chain on the other portion, the afferent chain connecting the digestive tract to the liver and the biliary tract, the great efferent chain. The liver, like the kidneys, is in a large degree the excretory organ. The biliary tract is the transit system for bile, and the gall bladder is a diverticulum in the course of this transit system. It certainly plays no very active part in upper abdominal digestion. The lack of the organ in many animals and the comparatively unimpaired digestion which occurs in individuals who have been submitted to cholecystectomy bear out this view.

Twenty-five years ago the diagnosis of gall bladder disease was confined to those cases with biliary colic and sharply circumscribed pain in the upper right quadrant. Today, owing to modern methods and by a more perfect correlation of surgical and medical material, the refinement of biliary tract diagnosis has approached that stage where it is possible to assume that many forms of gall bladder disease do not present this classical picture.

Gall bladder disease rarely exists alone. There is an abundance of clinical and surgical evidence to prove that the liver is usually implicated. Many authors have emphasized and proved beyond a doubt that liver disease is a common association of biliary tract disease. Some men go so far as to contend that there is lymphatic drainage both ways, from the gall bladder to the liver and vice versa.

METHODS OF DIAGNOSIS

Gall bladder diagnosis two decades ago consisted in a well taken history and a careful examination. Today it consists of the same procedure amplified by methods which throw more or less direct light on gall bladder function and pathology. We have at our disposal the following methods:
(1) HISTORY (2) PHYSICAL EXAMINATION (3) X-RAY EXAMINATION (4) DUODENAL INTUBATION (5) A STUDY OF BLOOD SERUM, notably the Van den Bergh reaction, the icterus index, blood cholesterol and so forth.

HISTORY

Let us consider for a moment the history. A history of biliary colic or sharply defined upper right-sided pain more or less circumscribed to the biliary region and in the right upper quadrant is encountered in the majority of cases.

Pain in gall bladder disease is due to two factors: first, acute inflammation of the gall bladder per se, and second, muscular spasm set up by the presence of a calculus in the duct. The pain in cholecystitis varies according to whether or not there is a stone attempting to pass along the cystic duct. When there is a stone, the pain is generally localized to the region of the gall bladder, or if there be contiguous peritonitis, adhesions, or bands the pain may be diffused over the right side and even to the chest or to the left side. If the liver and gall bladder are much enlarged downward, the pain may extend down to the iliac fossa and even down to the lower extremities. When there is a stone in the neck of the gall bladder or in the cystic duct, the pain radiates also to the area beneath the inferior angle of the right scapula. This corresponds to the level of distribution of the eighth dorsal segment from which the gall bladder derives its main nerve supply. In uncomplicated cases, pain is not felt in the right acromial or clavicular regions, but in the right hypochondrium or in the epigastrium alone.

In a review of the literature, we have arrived at the conclusion that pain in gall bladder disease is as variable as the pain in appendicitis. In other words, the pain may vary from the anginal type to one resembling
that of a retroversion.

METHODS OF PHYSICAL EXAMINATION

In the physical examination, nothing is more suggestive of gall bladder disease than residual tenderness at or near the tip of the ninth costal cartilage and more pronounced on upward pressure. A tumor of the gall bladder is (1) empyema; (2) hydrops, usually associated with stone in the cystic duct; (3) carcinoma; and (4) an occasional gall bladder filled with stones. Rigidity of the upper right rectus, cutaneous hyperesthesia localized to the gall bladder area are of value.

Duodenal intubation is now a standard method of biliary tract investigation, and will later be discussed in more detail.

For the successful treatment of any disease it is an absolute preliminary requisite that we have a sound diagnostic conception of the disease to be treated. If adequate diagnosis is required to work out the beginning details of the comparatively easy diagnostic picture of acute mastoiditis or acute appendicitis, how much more difficult does differential diagnosis become when we find ourselves dealing with relatively vague pictures of chronic digestive disorders which have not progressed to the classical syndromes or clear cut clinical entities? These are days when we are beginning to realize the importance and value of making complete diagnostic surveys of all patients, but particularly those presenting long continued symptoms of ill health, and no diagnostic survey is complete without a most careful study of the gastro-intestinal tract, and not alone by means of the roentgen ray or simple test meal analysis. The cause of much chronic invalidism will be found to lie here.

Much has been said recently in criticism of the tendency in medicine of today to develop diagnosis by means of endless charts, curves, graphs
and laboratory formalae, and to sit back and admire such handiwork, perhaps at the expense of failure to make skillful use of the five senses employed to such advantage by our medical forefathers. Certainly neither one of these extremes is alone correct. They should be wisely combined, each with a consideration of what can be gained by the other, but with a neglect of neither. Surely the doctor of two or three generations ago, if his medical education had not grown with the times, would be unable to successfully compete with the best of today if his whole dependence lay in the skillful use of his five senses.

In palpating for gall bladder tenderness it will be found that the right upper rectus is slightly more resistant normally than is the left upper rectus perhaps on account of the lower position of the right lobe of the liver. This is a normal and physiological difference similar to the slightly increased percussion dulness of the posterior upper pole of the right lung as compared to that of the left lung. The usual point of gall bladder tenderness will be found in the upper third of a line drawn between the ninth rib and the navel. It thus very closely merges with the usual point of duodenal tenderness which lies at about the middle point of this line.

In examining for tenderness in the region of the gall bladder or gall ducts bimanual thumb pressure should always be employed at some stage of the examination. For this the patient should be lying on his back with the head and neck slightly raised and the knees comfortably flexed over a pillow, or with the soles of the feet comfortably placed on the bed. The examiner, sitting on the right side of the patient, places the thumb of each hand in each hypochondrium at the tip of the ninth ribs with the palm and
fingers more lightly grasping at the costal margins. With the patient nicely relaxed, after each successive deep inspiration the thumbs at expiration are more and more firmly pressed up under the costal margins. When the gall bladder or gall ducts are the seat of inflammation, even of slight degree, after the thumb has been firmly pressed upward on expiration, a further full inspiration will not only elicit pain, but will interfere with the free respiratory movement of the diaphragm on the right side. When there are acute inflammatory adhesions or some localized peritoneal irritation there will also be brought out, as a rule, some protective rigidity and spasm of the upper right rectus muscle.

Another common way of eliciting gall bladder pain is for the examiner to stand on the right side of the patient, but facing his feet, and with the fingers of the left hand tightly grasping and pressing under the right costal margin in the neighborhood of the ninth rib the patient is instructed to take deep respirations, and at the end of a deep inspiration the examiner smartly strikes the knuckles of the left hand with the closed fist of the right hand. This maneuver will almost invariably bring forth an exclamation of pain or distress from the patient possessing an inflamed gall bladder. In certain instances in which the upper right quadrant is in a state of intense muscle rigidity and spasm it may occasionally be necessary to put the patient in a tub full of hot water which will so help to relax the abdominal muscles as to make palpatory examination more easy.

Another maneuver for eliciting gall tract tenderness when the gall bladder or ducts are inflamed is by ulnar concussion described by Riesman. This consists of having the patient take and hold a full inspiration when the examiner strikes in turn both the upper right and the upper left quadrant with the ulnar edge of the hand. The examiner learns to differentiate
gastric from gall tract inflammation by comparing the subjective response
to localized tenderness on the part of the patient in the left upper quad-
rant with that in the right.

X-RAY EXAMINATION

Roentgenography is especially valuable as a diagnostic aid in de-
termining the extent and location of pathologic changes found in the gall
bladder and adjacent organs. The sympathetic nervous system, through the
superior and inferior mesenteric ganglia, receives fibers from the right
kidney and ureter. Also from the stomach, duodenum and the right colon
and gall bladder. This causes much difficulty in detecting which organ may
be responsible for pain situated in this region. As an example, kidney and
ureteral lesions are found frequently with pronounced gastro-intestinal
symptoms, particularly of nausea and vomiting. Cholecystitis, with or with­
out cholelithiasis, may simulate closely duodenal or gastric ulcer and
diseases of these organs may simulate gall bladder disease.

It is in cases of this type that roentgenology in the hands of a com­
petent roentgenologist manifests itself as a most valuable procedure, for
by a process of elimination the correct solution of the problem can usually
be made. But the mere taking of roentgenograms often contributes nothing to
the diagnosis. This particularly applies to the lesions of the gastro-in­
testinal tract and often a correct diagnosis can be made by a skilled
fluoroscopist. In many instances the films do not demonstrate the lesion
definitely. The development of this branch of medicine through new methods
and improved technic has brought about a change in the operative schedule
in hospitals and the frequent necessity for exploratory operation a decade
or so ago is no longer prevalent.

The roentgenographic diagnosis of a specific lesion may not always be
a solution of the problem, for quite frequently more than one organ may be involved. For example, a patient with a diseased appendix may also have a duodenal ulcer or a gall bladder lesion.

The dye test is of unquestioned aid in the differential diagnosis of gall tract disorders. Never the less, several conditions must be kept in mind lest the shadow of a supposed gall-stone or an absence of gall bladder visibility tempt an over anxious surgeon. A renal calculus in a lateral film will definitely determine the location of the stone. Calcified mesenteric glands likewise cause suspicious shadows. Gas bubbles many times present shadows which are most suggestive of calculi. However successive films at subsequent hours will rule out this possibility. Occasionally in a hypermotile stomach the capsules will be so rapidly ejected into the intestine that the dye will pass beyond the gall bladder. This is not a common occurrence and with careful observance of the schedule for administration at least a portion of the dye should reach the gall bladder. Cholecystography is but a new link in the diagnostic chain and with its use a much more precise knowledge of the diseased gall bladder is made possible. We would emphasize this fact, that it should not replace the other methods of diagnosis.

In 1924 Graham and his associates found that when calcium tetrabromphenolphthalein was injected into the veins it was excreted chiefly with the bile, and thus it was possible to depict the gall bladder in the roentgenogram. Sodium tetrabromphenolphthalein was then used as it was found to be as efficacious and much less toxic than the calcium salt. Improvements on the drug and its method of administration followed rapidly after this preliminary work so that now examiners prefer to administer it orally.

The technique employed by Kirklin at the Mayo Clinic has proved
satisfactory. The patient is instructed to eat the usual amount of supper at 6 P.M., but without eggs, cream, butter or other fats, and, during or immediately after the meal, to take the iodine compound. This is dispensed to him in a single dose of 4 Gm, dissolved in 30 cc. of distilled water, and he is directed to mix it with a glassful of grape juice. Laxatives are forbidden, but next morning he is required to cleanse the large bowel with a soapsuds enema. Breakfast is omitted, although water, black coffee or tea is allowed. At 8 A.M., approximately fourteen hours after the dye was taken, the first set of roentgenograms is made with the patient thoroughly immobilized in the prone position and the rays directed through the back. At 10 A.M. the second (sixteen-hour) set of films is exposed. The patient is then instructed to eat as desired at the noon hour, but to include with the meal a glassful of milk and cream or its equivalent in other fats as preferred. An hour after the meal the third, or twenty-hour, set of roentgenograms is made.

Kirklin emphasized two of the foregoing technical features: (1) administration of the dye with or immediately after a full meal from which fats are excluded, and (2) complete immobilization of the patient during roentgenography. If the drug is taken after a light meal, or after digestion is well under way, nausea and vomiting are likely to ensue; if fats are included in the initial meal the shadow of the gall bladder is likely to be faint or absent. Movement, however slight, during roentgenography, will often obliterate evidence of stones or papillomata.

In broad terms, a normal cholecystogram is characterized by a definite, homogeneous, regularly contoured shadow of the bile that is impregnated with dye in the gall bladder, which changes in size and density at successive periods. Usually the shadow is denser at the sixteenth hour than at
the fourteenth hour; at the twentieth hour, the fat meal having been taken in the meantime, the shadow most often will be considerably reduced in size and may disappear. As a general rule, the shadow will be slightly larger at the second period than at the first. This sequence as to size and density is not inflexible; the shadow may be most dense at any of the three periods and it may be largest at the first period. In short, no arbitrary standard can be set either for density or size. However, variation of size is an indication that the elasticity of the cystic wall is preserved, and if at any period the shadow is sufficiently dense to be visible it can be assumed that the faculty of concentrating bile has not been lost. The shadow should always be homogeneous in the sense of not having persistent thin areas or dense spots. Neither the general form nor the position of the shadow has significance; in persons of the enteroptotic habitus the shadow is likely to be slender and situated low and toward the median line; in persons of broad habitus the shadow is usually rounded and seated high laterally.

Abnormal responses to the test comprise absence, faintness, mottling, gross deformity, and unchanging size and density of the gall bladder shadow. The most common abnormal manifestation is failure of the gall bladder to cast a shadow in any of the serial roentgenograms. If the routine has been carried out as prescribed and without technical lapses, the total lack of a shadow is a highly dependable sign of disease, for it indicates either that the drug has failed to enter the gall bladder, or that the latter has been unable to concentrate the dye impregnated bile sufficiently to produce a shadow. Marked faintness of the shadow may be accounted for on similar grounds. Mottling may be caused by stones, or, occasionally, by intracystic neoplasms. Stones with a high calcium content produce areas of
(15) intensified density within the shadow, whereas cholesterin stones appear as areas of rarefaction. It has been recently shown that papillomata, adenomata or other new growths are manifested as transradiant areas within the shadow. Frequently shadows of a stone are demonstrable without any shadow of dye, but by cholecystography a somewhat larger percentage of stones can be revealed than by former methods, and the diagnosis can be made with greater assurance if the gall bladder is depicted. Deformity of the shadow, if pronounced, as in the case of hour-glass contraction, sharp angulation or marked distortion, may be due to pericholecystic adhesions from ancient or current disease, but deformity without other abnormal manifestation is a hazardous basis for diagnosis.

The rarefied mottled areas produced by cholesterin stones or papillomata may be imitated by collections of gas in the bowel. Shadows of dense gall stones require distinction from those of calcified lymph nodes, renal calculi, pancreatic stones, calcification in the ribs, cartilage or transverse processes, and opaque material in the bowel, any of which may be exhibited within the shadow of the gall bladder. However, the localized transradiant or opaque areas produced by gall stones tend to maintain a constant form and situation in all films, whereas those due to other causes are likely to change in one or another respect.

It is obvious, then, that cholecystography is primarily a test of function at the time of examination, and only in exceptional cases is a means of demonstrating disease directly. X-Ray reports are usually confined to three forms: (1) normally functioning gall bladder, (2) poorly functioning gall bladder (when the shadow is persistently faint), and (3) non-functioning gall bladder (when a shadow of the viscus does not appear). Evidence of stones may be associated with any of the three varieties, and
is so reported.

Notwithstanding the high dependability of cholecystography as shown by statistics, it would be a grave abuse of the method to recommend or discourage operation on the basis of this test alone. A patient is not merely a contribution to a statistical table but a subject with complex elements which cannot be tabulated; he should be considered independently of all others by the surgeon and clinician, who should grant to the cholecystographic opinion only that weight which it deserves in the particular circumstances.

INTUBATION

As has been before-mentioned, intubation of the duodenum is used routinely by some men as a diagnostic measure while other men equally proficient deprecate its usefulness. Perhaps some of the criticism of this procedure can be explained by Lyon's statement, "I have often regretted that for the purpose of my own understanding of gall tract diagnosis it has been necessary to make a diagnostic medical drainage so highly technical, time consuming and laborious". This necessarily militates very distinctly against its adoption and wide application by the profession in general.

To insure an understanding of this technic, a discussion of the types of bile is necessary. Four sterile bottles labeled "A", "B", "C" and "D" are handy. All duodenal glassware should be labeled "D" after the duodenal tube is in place, the duodenum is gently douchèd with 75 cc. of magnesium sulphate by gravity instillation, and immediately withdrawn by syphonage, and the proximal end of the tube connected with the first sterile drainage bottle labelled "A". If it has been already proven that bile has escaped from the common duct, through an unphysiological sphincter into the
duodenum, we obviously cannot carry out a segregation of the usual three types of bile, and the tube is then attached to the sterile bottle labelled BC", indicating that our first bile recovered is a mixture of gall bladder and liver biles, both being expelled from the common duct.

In all normal and in certain pathological gall tract cases the drainage sequence is very much of the same type, and is usually as follows: Shortly after the magnesium sulphate solution reaches the fasting duodenum there occurs a relaxation of tonicity in the duodenal wall, and within a few seconds to three minutes the normally closed ampullic sphincter described by Oddi, likewise relaxes, and within approximately this same period bile begins to tinge the magnesium sulphate solution which is being recovered by gravity syphonage from the tube. When this bile tinged magnesium sulphate solution has been withdrawn, and is being replaced by a light golden-yellow bile, the tube is connected with the first sterile drainage bottle labelled "A". This "A" bile, since it is the first obtainable from the closed sphincter, must be bile lying within the common duct, and later becomes slightly diluted with bile from the cystic and hepatic ducts, with perhaps a few drops of gall bladder bile.

Drainage is then continued until the bile deepens to a darker shade of golden-yellow to yellow-brown with a viscosity between that of syrup and a thin molasses. This is a mixture of the first portion of gall bladder bile mixed with the last of the common duct bile, and still further diluted with liver bile. At this point the tube is disconnected from the sterile bottle labelled "A" and attached to a sterile bottle labelled "B", and the drainage continued. The color gradually deepens and the fluid becomes more viscid as the purer gall bladder bile is being discharged, although it must be understood that this too is being constantly thinned.
out slightly by admixture with liver bile.

With a gall bladder possessing a normal muscular wall, and under a normal tension, this type of bile averages from 1 to 2.5 ounces, and is discharged under one magnesium sulphate stimulation in from ten to fifteen minutes, when it is gradually, although sometimes quite abruptly, replaced by a very much lighter and thinner lemon to straw colored bile than either of the first two types. This is called "C" bile and believed to be freshly secreted and expelled liver bile. When this transition takes place a connection is made with a third sterile bottle labelled "C" and the drainage continued over a long period as we may desire.

The amount of "A" or duct bile averages from 5 to not more than 30cc, and is discharged rather rapidly within approximately five minutes. The "C" bile from the liver may continue to drain for a long time, even up to several hours, and several ounces may be secured if drainage is continued over a two or three-hour period. There are many interesting phenomena concerned in the method of delivery of these several biles. They vary in the manner of return and the velocity of their discharge, whether it be intermittent drops, sudden spurts, or a steady, even flow.

Olive oil and 10 per cent solution of peptone are also effective gall bladder evacuating stimulants.

In all normal gall tracts all three of these different colored bile fractions should be perfectly clear and transparent and contain no microscopical cytology in the uncentrifuged specimen. In certain pathological cases in the earlier stages and of lesser severity, the gross colors of these bile may be identical with those of the normal, but there may be an increased sliminess or increased viscosity due to partly dissolved mucous which may adhere to the glass observation window, and, in addition, there
will be a small but appreciable amount of flocculent particles which can be readily picked out of the uncentrifuged specimen with a 1 cc. pipette and which microscopically present certain cytological features.

In certain pathological cases the gross appearance of the bile may be very close to the normals except for an increased sliminess and evidence of catarrh in the shape of mucopurulent flocculations. The microscopical cytology of these flocculi, together with the positive bacteriological evidence in fresh spreads, later checked up by cultural growth, is the only clinical method that offers any possibility of definitely diagnosing the early gall tract lesion.

Quantitative expression of the flocculi in regard to diagnosis is therefore very important. Beyond the occasional floccule which occurs in normal cases, the presence of large numbers of them is indicative of catarrh. When the flocculi covers from 1/8 to 1/4 of the bottom of the bottle and microscopically show only mucus strands with pus cells and exfoliated epithelial cells, it is taken to indicate a relatively mild catarrh and scored as plus 1; where 1/2 of the bottom of the bottle is covered by flocculi it is considered that the patient has a moderately severe catarrh and scored as plus 2. Where the catarrhal or inflammatory state is a severe one the flocculi and mucus slime will cover 3/4 or all of the bottom of the bottle and this is scored as plus 3 or 4. Whether this catarrhal inflammation is duodenal or gall tract or a combination of the two is differentiated by whether the mucus flocculi are or are not bile stained and by a microscopical study of the individual cells, differentiating the columnar from the cuboidal or oval. As a general rule the latter are to be interpreted as being derived from the duodenum. These flocculi may appear as fine and feathery, or as thick clumps or granular
or shaggy masses. Sometimes where the viscosity or mucosity of the duodenal fluid or the bile may be so great that the mucoid flocculi cannot sink down to the bottom of the bottle, they will remain suspended or festooned down at various levels.

In all the cytological examinations the extent and severity of the catarrh can be quantitatively estimated by the numbers of flocculi left unexamined in the specimen bottle when compared with the amounts used in one or more microscopical spreads; remembering that one or two drops from a pipette will practically supply a cover slip preparation, and give an enormous amount of cytological evidence. Therefore it will be seen that the cytological evidence is of real importance only when considered from the quantitative estimation. A classification of A plus I to plus 4 usually covers this.

It is most important that flocculi in bile be examined very promptly as cytological evidence from all points within a gall tract properly drained will show rather deep bile staining of all microscopical elements.

The portion of the tract that is afflicted pathologically is determined by the specimen bottle which contains the pathology, such as in cholecystitis alone the "A" bottle will contain numerous flocculations which will cease to appear or become distinctly less numerous as the gall bladder bile is being expelled.

DIFFERENTIAL DIAGNOSIS BY MEANS OF INTUBATION

Failure to recover "B" bile in a diagnostic study makes one think of the following differential possibilities:

I. Obstruction of the cystic duct due to the following causes:

A (I) The mucous membrane of the cystic duct may be in a state of
inflammatory edema.

(2) It may be choked by impissated mucus or by very fine gall sand.

(3) Impacted stones.

(4) May have occurred localized irritation of the racemosed glands at the neck of the gall bladder.

B. (I) Adhesions involving the cystic duct.

(2) Angulations of cystic duct by pressure or otherwise.

(3) Stricture of cystic duct.

C. (I) By pressure exerted upon the cystic duct from without, as by

I. Neighborhood tumors.

2. An enlarged lymphatic gland lying along the cystic duct.

II. The cavity of the gall bladder may contain relatively little or no recognizable bile in the event:

A. That its entire capacity may be filled with multiple calculi of varying sizes.

B. Or a large solitary stone around which the gall bladder has contracted.

C. Or the gall bladder may be in a state of complete atrophy or fibrosis.

III. The bile contained in the gall bladder may be so ultrastatic and of such tarry consistency as to be too thick to flow of itself, or the gall bladder musculature may have become to weakened to force it through the cystic duct.

IV. Adhesions angulating the gall bladder in such a manner as to prevent discharge of its bile.

Empyema of the gall bladder is easiest to diagnose directly by medical drainage provided the gall bladder is mechanically able to discharge a specimen of its contents. Lyons says, On several occasions I have been.
able to recover an ounce or more of practically pure pus from patients who, at operation, were found to have an empyema of the gall bladder. Indeed I have been able to successfully drain several such cases and have brought about such a relative symptomatic recovery that operation has still been declined on the part of these patients, and I am convinced that where it is possible to prove by medical drainage that the pus can be evacuated by way of the duodenal tube this method may be substituted as an alternative in cases in whom surgery is contraindicated, and may take them over temporary surgical contraindications until they can be better prepared to stand the operative risk.

The total diagnostic impression from a medical drainage of the gall tract is then developed from close study of the data found and recorded on the biliary drainage sheet, interpreted in the light of the history and physical examination, and should embrace the findings which occurred in the stomach, the question involved in a delayed duodenal transit time due to the various causes, and a direct study of the bile and the manner of its discharge, the promptness with which "A" and "B" biles appear, suggesting normal tonus, subtonus or hypertonus of gall bladder musculature; and whether or not more than one stimulation with magnesium sulphate or olive oil has been required; the velocity and character of the discharge of "C" bile; the gross appearance of the several biles; their color, consistency, viscosity, transparency, turbidity, flocculations, mucus, etc; and especially the careful examinations into the cytology, freshly examined while still warm (epithelium, whether bile stained, its suggested source, pus, leucocytes, crystals, concretions, amorphous salts, red blood corpuscles, mucus, bacteria and inflammatory debris; into the chemistry of the bile (cholesterol, calcium, pigments, lecithin, fat, effervescence on acidification);
and into the bacteriology by culturation of each of the segregated samples of bile.

In answering the following question: "of what real diagnostic value is medical drainage?" we must consider the following points:

1. It gives us definite information as to the patency of the ducts. If A, B and C biles are found, we can be reasonably sure there is no great obstruction to the ducts. If after several drainages no "B" bile is found, an obstruction at, in or around the cystic duct may be found.

2. Microscopical blood, and no bile on stimulation with magnesia sulphate, in conjunction with other physical signs, aids us in the diagnosis of malignancy.

3. Real dark "B" bile means biliary stasis. Enteroptosis can be placed under this heading.

4. Dark bile, with positive cultures, aids in the diagnosis of the type and location of our infection.

5. Gall bladder sand may aid in the diagnosis of stones.

6. In cholecystectomy with recurrent symptoms, we can determine as to the patency of the ducts, and whether or not infection is still present.

7. It is another means of locating foci of infection.

8. It aids in the diagnosis of typhoid carriers.

9. It can be used as an aid in the diagnosis of pancreatitis.

10. It is an aid in the visualization of the duodenum. A distorted duodenal curve denoting evidence of peri-duodenal adhesions.

11. It aids in diagnosis of certain types of headaches.

12. It assists in diagnosis of all lesions producing pain in the upper right quadrant.
(24)

PRODUCTS OF INTUBATION MAY SUGGEST STONES

Drs. Louis M. Rousselot and Louis Bauman presented a note stating that during the past ten years there has been a gradual accumulation of evidence by various investigators tending to show that the association of cholesterol crystals in duodenal bile and gall stone disease is more than a coincidence.

Lyon, Hollander, Rateer and Chester Jones all felt that the presence of many clumps of cholesterol crystals probably signify the presence of gall stones. Recently Bockus presented a large, carefully studied group of cases and concluded that the presence of cholesterol crystals or calcium bilirubin pigment or both in bile obtained by a duodenal tube was positive criteria for the diagnosis of gall stones.

Similar studies have been repeated and somewhat elaborated at the Presbyterian Hospital recently. A technic has been adopted that greatly simplifies and hastens the passage of the duodenal tube. All intubations are checked as to position by using the fluororoscopic table. The indentification of the crystalline elements and calcium bilirubin pigment in the bile sediment is not difficult.

It was specifically stated that this test was not done routinely on all cases of biliary tract disease but is reserved for those cases in which the diagnosis is vague and in which there is no confirmatory x-ray evidence. It is used almost routinely in jaundice cases to establish the presence or absence of bile in the duodenum.

The following conclusions were reached:

(1). The failure to obtain concentrated "B" bile after two or more drainages is suggestive of intrinsic disease of the gall bladder.

(2). The absence of cholesterol crystals or calcium bilirubin pigment
in concentrated "B" bile is fairly strong evidence against the presence of stones.

(3) The finding of cholesterol crystals or calcium bilirubin pigment in dilute "A" bile or "B" bile is almost pathognomonic of the presence of gall stones.

**BLOOD CHEMISTRY IN DIAGNOSIS**

In speaking of jaundice, we must mention an etiological classification; and so McNee's classification is here given:

(1). **Obstructive:** in which there is a mechanical obstruction to the extrahepatic bile ducts with resultant absorption of bile pigments.

(2). **Intra hepatic:** (toxic or infective) in which there is an inability of the parenchymal liver cells to excrete the bile pigments in a normal manner.

(3). **Hemolytic:** in which there is an excessive destruction of red cells so that bilirubin forms more rapidly than normal with consequent retention in the blood stream. It is also called hematogenous jaundice. An excess of bilirubin in the blood is called bilirubinemia.

All normal blood serum contains a certain amount of blood pigment (bilirubin). It was Hymans Van den Bergh who first demonstrated that such traces of bilirubin in the serum are derived from extrahepatic sources. Bilirubin is derived from the disintegration of the hemoglobin of the red blood cells (normal consumption which is physiological) and from the cells of the reticule-endothelial system, especially those of the bone marrow and splenic pulp. The polygonal cells of the liver do not play any part in its formation. They simply excrete this pigment in the bile. For the purpose of analogy we cite the excretion of those halogen dyes which are used in gall bladder visualization. Van den Bergh also was first to point out
that the amount of bilirubin in the serum becomes immediately increased when certain disturbances of the liver are present or when intensified decomposition of the blood occurs. A "direct" reaction is obtained with the blood of a patient only when the bilirubinemia results from the retention of bile in consequence of some mechanical obstruction. An "indirect" reaction is obtained with the blood of a patient if the bilirubin is not excreted by the liver, but remains in the circulating plasma because of increased decomposition of the blood or altered hepatic function. This is the so-called "hemolytic" icterus in contrast to "mechanical" or obstructive icterus above described.

An increase in the amount of bile pigment in the circulating blood (above the normal amount) is a forerunner of jaundice. By tests we can predict that jaundice will develop long before the yellow flag of jaundice appears on the skin and before the sclera becomes discolored and before bile appears in the urine or before we get the classical clay-colored stools. We can thus predict "latent jaundice" with reasonable certainty. These tests are also useful to ascertain the progress or decline in any case of jaundice already developed. Thus, when frequent records of this test are kept graphically they will reveal a "serum pigment curve". In obstructive jaundice, as the obstruction lets up the "curve" sinks lower and lower. A rising "curve usually means increasing obstruction. To the surgeon contemplating operation, a rising curve is interpreted as signifying that operation should be delayed because experience has taught him that a rising curve is a sign that hemorrhage will be profuse if operation is performed in such cases. The various tests for icterus index, namely, Leulengrachts' and Bernheim's colorimetric tests for bilirubin have now given way to the
Van den Bergh test which is both quantitative and qualitative.

RELATIONSHIP OF HEART AND GALL BLADDER DISEASE

There seems to be conclusive evidence that a definite relation exists between certain cases of gall bladder disease and heart disease. Surgeons occasionally use the phrase "cholecystic heart" with the idea that the gall bladder pathology bears a casual relation to the heart condition and symptoms. Graham recently accented this relation when he wrote, "We have observed brilliant results in cases of heart disease following cholecystectomy after it had been determined that there was a pathological gall bladder. We know of suspected cases of angina pectoris receiving complete and permanent relief following cholecystectomy after it had been determined that there was a pathological gall bladder".

Acute cholecystitis seems to have less disturbing influence as a rule on the cardio-vascular system. However the great pain incident to a paroxysm of biliary colic seems more definitely to upset the circulation.

GALL STONES AND HEART DISEASE

The presence of gall stones is probably to be regarded as a by-product and an end result of inflammation or disease of the gall bladder. Cholecystitis does not include cholelithiasis, the latter usually intimates the former. Whether inflammation is the sole element or even the chief element in influencing the heart and just how much part stones may play, are factors difficult to separate and evaluate. The gall bladder is not an organ to be medically or surgically despised. While not much good may come of it, certainly much evil may proceed from it, though one author recently referred to it as "a relatively unimportant appendage". When diseased, it rarely lives unto itself alone. It must be kept in mind, then that when
a diagnosis is made of angina pectoris and the patient considered to have only angina pectoris, whereas the angina pectoris is but a symptom related to and caused by a chronic cholecystitis.

The clinical picture of inflammation of the gall bladder is extremely varied. In the older text books emphasis was placed on the late and most severe evidences of inflammation. Nowadays, however, the desire should always be present to diagnose these cases much earlier than was the custom then. The aim should be to prevent as much as possible the development of the serious and late effects which were formerly the chief foundation of the clinical picture. I will discuss here ordinary cholecystitis under two main divisions acute and chronic.

ACUTE CHOLECYSTITIS

In acute cholecystitis the onset is usually sudden, sometimes with a chill. It occasionally begins during the course of some other disease as, for example, typhoid fever, acute tonsillitis, etc. Pain, chiefly in the right upper quadrant of the abdomen, occurs early and is accompanied by muscular rigidity and tenderness vomiting, leucocytosis and fever. Sometimes the pain is cramplike with severe paroxysms. This is the type of pain which commonly occurs when stones are present. Often, however, it is of a continuous aching character and of a very severe nature. The pain is often referred to the back, especially in the region of the angle of the right scapula and the lower dorsal spine. It is unusual for it to be referred to the right shoulder. Usually when this reference of pain occurs in connection with gall bladder disease peritonitis is present. In typical cases pain is referred to the shoulder blade but not to the shoulder. Generally the pain of acute cholecystitis begins to subside in about
twenty-four or forty-eight hours and usually after about ten days the symptoms are gone. Ordinarily the fever is not high (above 102 F.) and the chills are not severe unless a fairly extensive inflammatory involvement of the liver is also present. Jaundice is usually not present. When present it is usually slight. It indicates an obstruction of hepatic bile which may be due to either stones in the hepatic or common ducts, or, to an inflammatory obstruction of the intrahepatic ducts from edema, infiltration with leucocytes, etc. Graham has shown that apparently in all cases of cholecystitis there is an associated hepatitis which is characterized be an inflammation around the intrahepatic bile ducts, a pericholangitis. If this inflammation is severe enough then some obstruction of the intrahepatic bile ducts will occur. The severity of the jaundice may, therefore, be expected to be variable. The leucocytosis usually varies from about 12,000 to 18,000. Respiration is often painful and may be somewhat limited on the right side.

If the cystic duct becomes obstructed an enlargement of the gall bladder occurs. The most common cause of obstruction of the cystic duct is a stone. In acute obstructive inflammations the gall bladder becomes filled with pus and we have then to deal with an empyema of the gall bladder. In such cases the pain is likely to be paroxysmal and very severe during the paroxysms. If the obstruction of the duct is relieved, either by the passage of the stone or by its falling back into the gall bladder, the pain usually ceases abruptly. If the obstruction persists after the stage of acute inflammation has subsided the contents become less purulent and more mucoid, distend the gall bladder and a hydrops of the gall bladder is then present. Jaundice is not often present in cases of uncomplicated empyema of the gall bladder, and when present it is due ordinarily to an
inflammatory blocking of the intrahepatic bile ducts.

CLINICAL DIAGNOSIS

The diagnosis of acute cholecystitis is usually easy because in the great majority of instances a sudden severe attack of pain in the right upper quadrant most often indicates an acute inflammation of the gall bladder. The presumption of such a diagnosis is greatly strengthened if the patient happens to be middle aged, somewhat obese, and especially a woman who has borne children. There are, however, many other intraabdominal conditions which may give rise to a clinical picture suggestive of acute cholecystitis. For example, perforation of a peptic ulcer may give symptoms which closely imitate those of an acute cholecystitis. The picture is often of a particularly puzzling nature, because if the condition is one of acute exacerbation of a chronic cholecystitis the history of chronic dyspepsia may be very suggestive of a peptic ulcer. Sometimes an x-ray examination after the perforation of an ulcer reveals a collection of gas under the diaphragm.

If it is possible to demonstrate a pneumoperitoneum in this way the diagnosis of perforated ulcer should be made without question. If the patient gives a history of previous attacks of pain like the present one the chances are more in favor of a diagnosis of recurrent acute cholecystitis than of a perforated ulcer. Another condition with which acute cholecystitis is often confused is acute appendicitis. Many patients have been operated on for supposed acute appendicitis who were really suffering from acute cholecystitis. Ordinarily if one exercises care in taking history and in making the examination the differentiation is not difficult because the pain and tenderness of appendicitis are almost always lower than in
acute cholecystitis. Again the history of recurrent attacks is a little more in favor of acute cholecystitis. In certain cases in which the appendix is long and situated with the tip high under the liver it may be impossible to distinguish between the two conditions. Whenever in doubt it is better to operate in order to avoid the possibility of allowing an acute appendicitis to perforate and to develop the long train of serious consequences of such an event. Appendicitis is of course much more common in young adults than is cholecystitis but too much reliance cannot be placed upon age differences. Acute pyelitis and renal colic are both sometimes confused with acute cholecystitis. An examination of the urine is of the greatest importance in order to rule out the possibility of such conditions. The presence of pus or blood in the urine will of course speak in favor of a renal lesion. An x-ray examination of the kidney and ureter should be made in doubtful cases because a stone can usually be demonstrated in that way.

Perhaps the most serious confusion which is made in the diagnosis of acute cholecystitis is that which arises in connection with some of the acute cardiac catastrophes such as coronary thrombosis, angina pectoris, etc. It is particularly important to realize that one of these acute cardiac conditions may imitate closely the picture of acute cholecystitis because if a patient with an acute coronary thrombosis should be operated on, the result of the operation is likely to be disastrous.

Acute cholecystitis is occasionally confused with pneumonia of the right lower lobe and right-sided pleurisy. An examination of the chest should, however, serve to differentiate the two conditions. An x-ray examination of the chest will be helpful in such cases. Other acute abdominal crises such as lead colic, and the gastric crises of tabes dorsalis may
be confused with acute cholecystitis but a careful history and examination should tend to make the differential diagnosis possible. It has sometimes occurred also that a Riedel's lobe has been mistaken for an enlarged gall bladder and a diagnosis accordingly of an empyema of the gall bladder has been made erroneously.

**CHRONIC CHOLECYSTITIS**

Chronic gall bladder disease is so frequent that a very large portion of adult humanity gives evidence, either clinically or pathologically, of this condition. Like many other conditions, chronic cholecystitis seems to be increasing. This apparent increase, however, may be mainly due to the fact there are more people in the world today who have arrived at the age at which chronic cholecystitis is most frequent, and also to the fact that the diagnosis of these conditions has been enormously improved, chiefly by means of the x-ray methods of examination, not only of the gall bladder itself but of the gastro-intestinal canal and also of the right kidney. It is now rather generally accepted that the most common organic cause of dyspepsia is gall bladder disease rather than disturbances of the stomach or intestines.

The recognition of a case of chronic cholecystitis may be extremely easy or it may be so difficult that it can be determined only by a process of exclusion after resort to all the above mentioned modern methods of examination. The easiest cases to diagnose are those in which the condition is most advanced, and in which therefore the symptoms are most extreme. A patient of middle age with the characteristic build who complains of attacks of paroxysmal pain in the right upper quadrant of the abdomen associated with nausea and vomiting is very likely to have chronic cholecystitis, especially if the attacks of pain have no relation to the taking of food, and
if it is referred to the right scapula. The diagnosis will of course be very much strengthened if in addition to these features, jaundice has been present. Much more difficulty is presented in the diagnosis of the less advanced cases. It is very desirable that cholecystitis should be diagnosed in its early and mild forms before it has had time to produce the serious effects which give rise to the classical clinical pictures.

It is important to bear in mind that in almost all cases of cholecystitis it is the inflammation and not the stones which is doing the damage to the patient. Diagnostic evidence should therefore be directed to the detection of disease of the gall bladder. The detection of stones is of secondary importance, although of course in a doubtful case the finding of gallstones by any method of examination is reassuring, and enables one more certainly to incriminate the gall bladder as the cause of the patient's symptoms. A presumptive diagnosis of stones can often be made with a fair degree of accuracy if the patient's symptoms are severe and associated with definite paroxysmal attacks of pain followed by jaundice. In the milder cases, however, it is often impossible to make even a reasonably accurate diagnosis of cholelithiasis except by the use of cholecystography which reveal the presence of stones in a large proportion of cases.

ADDITIONAL CLASSIFICATION

Another classification of gall bladder disease which is more comprehensive in its scope will be given here along with some of the differential points.

(I) ACUTE CATARRHAL INFECTIVE CHOLECYSTITIS with enlarged gall bladder must be differentiated from the colon distended with feces, a displaced kidney or a hydropnephrosis, cholecystitis with enlargement of the gall
bladder and paroxysms of pain may closely resemble hydronephrosis with painful crises. At first the enlarged gall bladder is pear-shaped, and later becomes elongated, a floating kidney is more movable than the gall bladder and less fluctuating, and if the gall bladder is pushed backward, it returns when the pressure is removed, whereas a floating kidney remains where placed so long as the patient is recumbent. A floating kidney tends to slip away from the hand while the gall bladder does not. A pyloric tumor is transverse to the axis of the gall bladder and is hard and tender. A tumor of the colon is not so well outlined as an enlarged gall bladder, and is usually transverse to it. A fecal mass can generally be determined by the presence of fecal accumulations elsewhere, and their removal by an enema. In biliary colic the pain is more severe than in cholecystitis, while the tenderness, intestinal distention and enlargement of the gall bladder are more evidence in cholecystitis. Great care must be taken to distinguish cholecystitis from appendicitis and pyelonephritis. In the case of cholecystitis the tumor can be traced from above downward, while in that of appendicitis it may be traced from below upward.pus in the urine may clear up doubt between cholecystitis and pyelonephritis.

(2) MEMBRANOUS CHOLECYSTITIS must be diagnosed by the finding of casts and a history that closely resembles that of gall stones, with which it is usually associated.

(3) SUFFURATIVE CHOLECYSTITIS may resemble subphrenic abscess, duodenal ulcer, or appendicitis in an abnormally located appendix. In the case of cholecystitis, the tumor moves with respiration; duodenal ulcer gives the history of pain a few hours after taking food, and sometimes blood in the stools. A perforated duodenal ulcer and suppurative cholecystitis may be indistinguishable. From appendicitis it must be differentiated along the
lines already laid down. The resemblance of suppurative cholecystitis to pyelonephritis, pneumonia or pleurisy on the right side may be close. If the gall bladder perforates and sets up a general peritonitis this latter must be distinguished from the peritonitis caused by a ruptured appendix or a perforated gastric or duodenal ulcer. The material found on opening the abdomen will clear up the doubt, and the history of the case in its early stage should be carefully inquired into for evidence of one or the other of these condition.

(4) PHLEGMONOUS and GANGLRENOUS CHOLECYSTITIS usually has a history of former attacks of cholecystitis. When there is a localized inflammation in the upper right quadrant the differential diagnosis rests upon the points already mentioned. When the case has assumed the characteristic of a general peritonitis the history of the attack may throw light upon whether the peritonitis is the result of a ruptured appendix, a perforated gastric or duodenal ulcer, a cholecystitis, a pancreatitis, or intestinal obstruction. It is always an extremely difficult task to make a diagnosis of phlegmonous and gangrenous cholecystitis, as distinguished from peritonitis due to other causes, such as those already named.

(5) CHRONIC CHOLECYSTITIS in its clinical manifestations, closely resembles cholelithiasis. The chief diagnostic points are attacks of pain as in gall stones, the presence sometimes of a pear-shaped enlargement of the gall bladder, the absence of pain or tenderness during interval of attacks, and the fact that jaundice is much less likely to occur than in attacks of gall stone colic; if it does, it is usually slight in degree. In chronic ulcerative cholecystitis gall stones are usually present.

DIFFERENTIAL DIAGNOSIS

Palpation of the abdomen will give information of practically no
value in the majority of cases of mild, chronic choledystitis unless one has the opportunity of examining the patient during the time of a recurrent attack of inflammation. In some cases a definitely enlarged liver may be made out. In a case of hydrops, the enlarged gall bladder can usually be found; sometimes in patients with thin abdominal walls, stones within the gall bladder can actually be palpated. Tenderness on pressure of the lower dorsal vertebrae can sometimes be elicited.

There are many conditions which are likely to be confused with chronic cholecystitis. For that reason the differential diagnosis is sometimes extremely difficult, and again mistakes may occur even in cases which seem to present rather typical clinical evidence of gall bladder disease. For that reason, it is better to examine with the x-ray nearly all patients in whom we suspect gall bladder disease. There will be fewer surprises disclosed at operation if greater care is taken to use the more exact methods of examination in association with the ordinary methods of clinical examination.

Chronic lesions of the stomach and duodenum, especially chronic peptic ulcer, are often confused with chronic cholecystitis. The characteristic pain of duodenal ulcer which occurs about two hours after a meal is usually not present in uncomplicated cases of chronic cholecystitis. In the latter condition, the pain is more likely to be paroxysmal when it is severe than when not severe. It is likely to occur without any particular reference to the taking of food. It occasionally happens, however, that the pain in a case of chronic cholecystitis will be relieved somewhat by the taking of food and alkalies, characteristics which are ordinarily thought of only in connection with peptic ulcer. When these characteristics are present in uncomplicated cases of cholecystitis, they are probably due to an existing hyperchlorhydria. When vomiting occurs in ulcer cases,
the pain is usually relieved. In typical cases of cholecystic disease, the pain is not relieved by vomiting. It must be remembered and emphasized, however, that in about 4 per cent of cases of gastric and duodenal ulcer, chronic cholecystitis is present. One should therefore always be on his guard to suspect the possibility of a combined lesion. Other lesions of the stomach also, such as carcinoma, etc., may present symptoms suggestive of chronic cholecystitis. Likewise, cases of diverticula of the duodenum may sometimes present symptoms similar to those of diseased gall bladder. For these reasons, it is a good idea in the majority of cases of suspected chronic cholecystitis to examine the alimentary canal with the barium meal and roentgen ray. Conversely, it is a good idea also to examine most cases of suspected peptic ulcer and of other upper abdominal conditions by means of cholecystography. Larimore and Graham, for example, had two cases in which the symptoms were supposed to be due to diverticula of the duodenum, but which were really due to chronic cholecystitis. The gall bladder was removed in both cases with complete relief of symptoms, and the supposed diverticula were found to be pseudodiverticula.

The various inflammations of the liver often present great difficulty in arriving at a decision as to whether or not the symptoms are due to chronic cholecystitis or to a liver disease independent of the gall bladder. Since the various types of cirrhosis of the liver are often confused with cholecystitis it should be noted that the presence of ascites and of other evidence of portal obstruction, such as enlargement of the spleen and distension of the periumbilical veins should all speak in favor of a cirrhosis rather than of a chronic cholecystitis.
Syphilis of the liver is often accompanied by pain and jaundice, and it may therefore closely imitate cholecystitis and cholelithiasis. If nodules on the surface of the liver can be felt and a positive Wassermann or Kahn reaction is present, the presumption will be considerably in favor of hepatic syphilis. In pylephlebitis and liver abscess pain is usually absent or of a very different type from that of a typical case of cholecystitis. Moreover, the fever and chills in pylephlebitis and liver abscess are characteristic features which are not often present in uncomplicated cholecystitis. Unfortunately, X-ray examination even by cholecystography is often of very little help in the differentiation of cholecystitis from various hepatic diseases because the hepatic condition itself often prevents the development of a well-marked shadow of the gall bladder, even in conditions in which the gall bladder is relatively normal.

It is difficult to state with certainty how often chronic cholecystitis is confused with a chronic inflammation of the appendix. Indeed, as everyone knows, it is very difficult to conclude what degree of chronic change in the appendix may be associated with symptoms. For that matter, the same may be said of the gall bladder, but to a less degree. There are, however, definite cases of a chronically diseased appendix which are relieved by the removal of the appendix. Perhaps it is more important to realize that probably in a majority of cases of so-called "chronic" appendicitis, the symptoms are usually due to something else and often to a chronically diseased gall bladder. A careful X-ray examination made by a skilled roentgenologist is of the utmost help in deciding whether or not there is an actual chronic appendicitis present of a kind which is likely to produce symptoms.

The visceroptotic individual who is never well but yet never quite sick, often has vague distressing pains in the upper abdomen which are
sometimes referred to the region of the gall bladder. Cholecystography will also serve to rule out or establish the diagnosis of cholecystitis with more certainty in such patients than any other method of examination.

Carcinoma of the hepatic flexure has sometimes been mistaken for chronic cholecystitis because of cramplike pain coming on in the upper right quadrant. An X-ray examination with a barium meal should, however, give so characteristic a picture in a case of carcinoma of the colon that this method of examination would serve to establish the diagnosis or to rule it out.

Pyelitis, pyonephrosis, kidney stone, hydronephrosis, etc., may all cause symptoms which are strongly suggestive of chronic cholecystitis when they occur on the right side. Usually, however, they can be excluded by a careful history and careful physical examination, which should include not only an examination of the urine but a roentgen ray examination by pyelography as well. If an enlarged kidney is felt on the right side of course the presumption is greater that a kidney lesion is present than that there is a cholecystitis.

Acute pleurisy, either pyogenic or tuberculous, when it occurs on the right side, may cause pain which is suggestive of cholecystitis. It is usually more likely to be confused with acute rather than chronic cholecystitis. An examination of the chest would serve to rule out the possibility of a pleurisy.

It is the usual opinion that stones which are found in the cystic duct are forced through from the gall bladder. Sweet, however, has produced some evidence which indicates that perhaps in many instances stones are formed in the cystic duct and that they later drop into the gall bladder.
The typical clinical picture produced by this condition is that of the so-called "biliary" colic. This is characterized by a sudden onset of severe pain in the right upper quadrant of the abdomen. The pain is often of the most intense agonizing kind. Associated with it is sometimes a feeling as if the liver were about to burst. The pain occurs in paroxysms with soreness remaining in the intermissions. It is often referred to the right scapula and to the region of the lower dorsal spine. In some cases the pain is most intense in the mid-epigastrium instead of the right upper quadrant and occasionally it is in the left hypochondrium. The pain is sometimes so severe that sudden death has occurred in a considerable number of instances during a paroxysm. This event is more likely to occur in patients whose biliary disease is associated with severe cardiorenal disease. Unless relieved by morphine the paroxysms of pain continue intermittently for several hours. In some cases, however, pain may not be a noteworthy feature, at least it may not occur in severe paroxysms and its onset may not be sudden. Nausea and vomiting are nearly always present during a biliary colic. Tenderness and rigidity of the abdominal muscles are made out on palpation. After the attacks have subsided somewhat it may be possible to palpate an enlarged liver which is tender, and the gall bladder may also be felt to be enlarged. If the stone in the cystic duct has caused obstruction a condition of either empyema or of hydrodrops of the gall bladder ensues, unless the wall of the gall bladder is so scarred with fibrous tissue that it is incapable of distention. Jaundice is seen only in those cases in which the inflammation has extended up to involve the liver, or in those cases in which a stone in the cystic duct is complicated by the presence of a stone.
in the common duct. Moderate fever, leukocytosis and occasional chills are present during the period of colic.

The diagnosis of a stone impacted in the cystic duct, apart from the more general diagnosis of biliary colic, is of importance only in those cases in which a mucous fistula has followed the surgical drainage of the gall bladder and in those cases in which the surgeon at operation is confronted with a distended vesicle.

The presence of a stone in the common duct is nearly always associated with a considerable amount of inflammation, not only in the gall bladder but in the intrahepatic ducts as well. In the majority of instances when the presence of the stone in the common duct is first recognized, the gall bladder has already become greatly fibrosed because of the long-standing cholecystitis. This observation was expressed in the now famous Courvoisier's law. "With obstruction of the choledochus by stone, distention of the gall bladder is rare; the organ is usually shrunken. With obstruction of other kinds, on the contrary, distention is the rule; shrinking occurs in only one-twelfth of these cases". The fibrosis is not limited to the gall bladder but is found also to involve the ducts themselves. This may be so extreme as to cause a stricture. Other complications are the occurrence of fibrotic changes in the liver with sometimes a development of a well-marked biliary cirrhosis.

The diagnosis of a stone in the common bile duct is generally easy when there are present the typical features of repeated attacks of biliary colic followed by deep jaundice, chills and fever. The chief difficulty is in differentiating between a jaundice caused by obstruction of the common duct by stone and an obstructive jaundice of some other cause. When the jaundice is caused by malignant disease, which is uncomplicated by stones,
The symptoms develop insidiously and the picture is in marked contrast with the typical picture of stone in the common duct. Again in malignant disease the jaundice is progressive instead of intermittent and pain is much less prominent than in calculous obstruction. As is shown in the application of functional hepatic tests to diagnosis, the use of phenol tetraiodophthlein as a functional test has proved of great value in differentiating between obstructive jaundice due to stone and that due to malignant disease. When calculi and carcinoma coexist the difficulty in diagnosis very great. It is usually better to make the diagnosis of calculous obstruction and to advise laparotomy because it occasionally happens that cases that were diagnosed as malignant obstruction and perhaps regarded by medical attendants as hopeless, have been found on laparotomy to be due to the presence of a calculous obstruction and, therefore, amenable to surgical treatment. Cases of calculous cholecystitis with cholangitis and hepatitis causing jaundice sometimes resembles the picture of a stone in the common duct so closely that a differentiation can be made only at operation when the opportunity to explore the common duct presents itself. Those cases in which the intermittent fever is conspicuous are sometimes confused with malaria but the leukocytosis, the absence of parasites in the blood, and a long-standing history suggestive of disease in the biliary tract, should serve to favor the diagnosis of calculous obstruction rather than malaria. The various cirrhosis of the liver are sometimes confused with calculous obstruction, but the typical biliary colic and the intermittent chills and fever are usually absent in the former conditions. Sometimes the jaundice associated with acute intoxications of the liver as for example salvarsan poisoning and the condition of so-called "acute" yellow atrophy have been mistaken for acute calculous obstruction of the
common duct. In these conditions of intoxication of the liver the characteristic biliary colic and the intermittent chills and fever are not conspicuous. In hemolytic jaundice the discoloration is not so intense. Bile pigment is not found in the urine. There is but little pain and there is an increased fragility of the red blood cells to hemolysis in salt solution.

There is one type of case which presents rather characteristic features and in which it is very important to establish a diagnosis. If after a cholecystectomy for a calculous cholecystitis the patient has attacks of biliary colic with intermittent jaundice and fever, it is almost certain he is suffering from a stone in the common duct which was overlooked at the former operation. It is possible that in some of these cases a new stone has formed, but it seems to us that most of the evidence is in favor of the idea that the stone was overlooked, unless a long interval has elapsed between the operation and the recurrence of the symptoms. Stricture of the duct from scar tissue will also give a clinical picture which sometimes resembles that of a stone. If the symptoms are due to a stricture which has followed an operative injury to the duct during the performance of a cholecystectomy, there will usually be obtained a history of a profuse discharge of bile after the operation, continuing somewhat intermittently for periods of weeks at a time.

A number of other conditions, which must be mentioned in thinking of the differential diagnosis of the aforementioned conditions are: spatic colon, intestinal allergy, lesions of the sline, hemolytic icterus, slipping rib, the specific infections including parasites, torsion of the gall bladder, acute catarrhal icterus, stone in the hepatic ducts, benign and malignant stricture of the ducts.
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