- (c) Pain of coronary occlusion rarely radiates to the back.
- (d) Signs of falling blood pressure and cardiac failure may rapidly ensue.
- (e) Electro-cardiography can quickly determine a coronary infarct in cases of doubt.

These points may be of value in elucidating the problem where the two conditions may simulate each other or co-exist, a fact which has received much attention of recent years.

Summary

1. A short account of the medical and surgical history of biliary disease has been given.
2. A discussion of the etiology has been briefly presented under the headings—infection, cholesterol metabolism, and mechanical, chemical and toxic factors.
3. A review of the symptomatology, physical signs, and clinical laboratory data and their diagnostic value has been made.
4. A series of the chief differential diagnostic problems met with in practice has been presented in which appendicular disease, peptic ulceration, pancreatic disease, and coronary occlusion have been shown to give rise to the greatest difficulties.

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THE CLINICAL DIAGNOSIS OF CHRONIC GALL-BLADDER DISEASE

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Symptoms

Chronic cholecystitis usually presents itself as gastritis, flatulent dyspepsia or indigestion. In the past these terms satisfied us as definite entities, but not so now; we want ocular demonstration or some more definite proof before we accept them as the true diagnoses. Chronic cholecystitis is more common in women than men, and affects those in middle life or in the 50's. Women that are fat are more affected than those that are thin, also those that have taken little exercise and have been indulgent as regards food are more likely to be affected than the thin ascetic type. But no age, except perhaps young children, can be looked upon as exempt. The dyspepsia of chronic cholecystitis, despite the difficulties of diagnosis, has certain features which can often be recognised by a careful history, or at least one can, by this means alone, be suspicious that the gall-bladder is not in a healthy state. The indigestion of chronic cholecystitis is often an epigastric discomfort, a fullness or a slight nausea which comes on after food—and often after the most carefully prepared and simple meal. It is often quite irregular in the time at which it comes on, and, unlike gastric and duodenal ulcer, is not

at all related to any kind of food except fats, fatty foods, and certain foods which have been twice cooked. Such items as fried fish, rissoles, eggs, especially hard boiled, cheese and cheese dishes may disagree, whereas ordinary plain cooked food in moderate amounts will not disagree; even beef (but not pork), salads and fruit can be taken with impunity. It often happens that certain meals may disagree while others may not; a meal in congenial company may not disagree, whereas one taken perhaps alone, and therefore more hurriedly, may produce fullness. This *fullness*, or "wind," produces much discomfort; it may come on early or late after a meal, and produces a desire to belch, which only gives momentary relief. Intestinal flatulence is not common. Pain is not one of the more usual features, it is rather discomfort, but when it can be so described it is commonly located in the right hypochondrium, or sometimes may be occasionally in the right shoulder, and neither the pain nor the discomfort is relieved by alkalis or vomiting, though sometimes by a small amount of neat spirit. Occasionally the pain may be a true biliary colic located to the right hypochondrium with sweating, and even collapse.

The bowels are not as a rule much affected, but a slight constipation is more usual than diarrhoea. No treatment by purgation to assist the emptying of the lower bowel has any effect on the indigestion unless it be the cholagogues and those drugs that act on the gall-bladder—such as small doses of calomel and magnesium sulphate.

These symptoms of dyspepsia are not necessarily constant. They may appear, for instance, after a cold, and then may be absent for several months, and a holiday in congenial surroundings often allays a bout of discomfort. Vomiting, if it occurs, is not characteristic; it may only be mucus, perhaps some semi-digested food, seldom a large amount of bile. There tends, however, to be more mucus than usual in the vomit.

Sometimes the attacks occur at intervals and gives rise to "bilious attacks"; attacks of vomiting with or without headache, in which the patient is prostrate and must remain in bed.

Fever is not a very conspicuous element in cholecystitis, but the patient occasionally shows an occasional rise to 100°. Such rises of temperature are more commonly observed in hospital than when the patient is ambulatory, but they are a valuable sign when present.

Signs

The aspect of the patient seldom gives any help. The complexion may be sallow; jaundice is a rare sign; the tongue may be a little furred. The main thing to look for is Murphy's sign, a tenderness in the right epigastrium which is marked when the patient breathes and the liver descends, coupled with, almost invariably, some rigidity of the right rectus muscle. Superficial tenderness may sometimes be elicited; it is common to find that on pinching the skin and superficial fat that it is more sensitive on the right than on the left side. Hyperaesthesia of the skin is sometimes found in a definite area between the level of the xiphisternum and the umbilicus in the 8th and 9th dorsal segments in the nipple or anterior axillary lines. It is seldom more than 2 or 3 inches across, but when present is easily marked out with the head of a pin, and is constant from day to day while the symptoms persist. With deeper palpation if the patient will permit it, it may be possible to make out the outline of the gall-bladder, though as a rule it cannot be felt. One patient of mine, whom I see occasionally with attacks of indigestion and vomiting, had on one occasion a well-defined gall-bladder the size of a small egg, which, however, ultimately subsided. This patient in the times of peace used to find that she was better if she took the juice of half a lemon with the principal meals, a measure which probably acted by its power to cause emptying of the gall-bladder.

Differential Diagnosis

1. *Gastritis*.—It is not always easy to separate gastritis from cholelithiasis; there is the same fickleness of appetite, the same discomfort after meals, and indigestion attends all foods—not necessarily those that are fatty. The tongue is furred and indented by the teeth. In gastritis, however, there is usually some indication of the cause, the patient habitually disobeys the rules one makes for preserving the digestion, there may be obvious sepsis in teeth, tonsils or throat, and the swallowing of septic secretions may be a factor. A careful history of the mode of taking alcohol, whether it is too much, too concentrated (cocktails, aperitifs), and whether it is taken with or apart from meals. In all these cases, however, the radiological outline of the gall-bladder is normal, and the appearance of the stomach in a barium meal may

show coarse rugae of the mucus membrane. The same symptoms and signs of gastritis may be seen in a patient with indigestion from a chronic grumbling appendix. In a patient suspected of gastritis, examination with the gastroscope is a considerable help and may be desirable.

2. *Gastric and duodenal ulcer.*—The point to make sure of is that though from time to time the discomfort and pain of ulcer occasionally diminish, even when untreated, and tend to be worse at certain times of the year, they are moderately constant in the regularity of onset from day to day; the pain comes on regularly after a meal, and certain foods always tend to produce discomfort, whereas in cholecystitis the indigestion, except for the inability to digest fats, is less constant and more fickle. A good radiologist, however, seldom fails to demonstrate the signs of an ulcer. But the presence of signs of ulcer need not be taken as ruling out cholecystitis, for in cases where there has been a previous perforation of an ulcer, especially of the duodenum adhesions, may have interfered with the function of the gall-bladder and be the cause of a mild cholecystitis.

3. Attacks of *vomiting* may occasionally be due to mild cholecystitis. A middle-aged lady of active habits and not one that one would suspect of cholecystitis used to have occasional attacks of vomiting while out doing her morning shopping. The only physical sign was a definite Murphy's sign. She did not have any more after she had been put on a regular dose of a cholagogue (Calomel gr. 1/10). Such attacks may be mistaken for *migraine*, which often goes under the loose expression "sick headache."

4. *Attacks simulating coronary thrombosis.*—The pain of coronary thrombosis occasionally is abdominal in its distribution, and the pain of cholelithiasis with colic may closely simulate it. The collapse, low blood pressure with its circulatory concomitants, may make the diagnosis a matter of extreme difficulty. Even the electrocardiograph may show the features usually associated with a coronary thrombosis. An X-ray, however, designed to show up the gall-bladder, would fail to show the normal filling and the excision of the gall-bladder, if such were done, would cause a restoration to normal of the electrocardiograph more rapidly than after a coronary thrombosis.

5. *Arthritis of the spine* is another condition which rarely may be mistaken for gall-bladder disease. The pain is in the same segmental area, and the segmental tenderness may superficially simulate the tenderness of a gall-bladder affection, even producing a false Murphy's sign; but the history of the discomfort would not be so closely related to digestion, and an examination of the spine would quickly reveal some abnormality and pain on movement or on jarring.

Special Methods of Investigation

Radiology.

The attempt to visualise the gall-bladder by X-rays is the most important method of confirming the diagnosis. Two nights before such X-ray examination an aperient should be given; the next day, at about 5 p.m., a meal free from fats, butter or milk should be taken. At 6 p.m. 4 grams of tetra-iodo-phenolphthalein (opacol*) should be taken with half a tumblerful of water. No food should be taken until the examination has been completed the next morning; this ban, however, does not extend to drinks of water. A normal gall-bladder will show up as a pear-shaped shadow; an abnormal gall-bladder may not show up at all. A normal gall-bladder should empty in two hours after a fatty meal has been taken. The interpretation of the results, however, requires circumspection; not all gall-bladders that fail to fill are abnormal. One investigator, Liel, found that 26 per cent of organically sound gall-bladders failed to fill in duodenal ulcer; therefore it is always necessary to rule out the presence of such an ulcer by a barium meal and "follow through." Most radiologists as a routine take a preliminary X-ray to exclude other shadows that might interfere. Poor filling, however, of a gall-bladder on repeated examination means abnormality. Radiologically a small proportion of normal gall-bladders may contain stones and the mucous membrane be abnormal.

The Bile-Drainage Test.

The patient being in a fasting condition, a Ryle's tube is passed until it is in the duodenum (as told by the condition of the aspirated contents which should be neutral or alkaline and contain bile). Three oz. of 10 per cent magnesium sulphate are then taken, and the contents of the duo-

* Supplied by May and Baker.

denum aspirated at 15 minute intervals for one hour. Each sample is centrifuged and the deposit examined microscopically. Crystals of cholesterol, pus cells or red blood cells indicate that the mucous membranes of the gall-bladder is unhealthy.

The Liver Function Tests.

It may be necessary to get some indication from special tests as to whether the function of the liver substance itself is normal or abnormal; there are several tests that can be used.

1. *The icteric index.*—Serum or plasma diluted if necessary with saline is matched against an arbitrary standard of potassium bichromate. Normal blood gives 4–6 units; up to 15 units is latent jaundice, and above 15 units there is visible jaundice.

2. *The laevulose test.*—50 grms. of laevulose are used for the test given in the same way as glucose for the glucose tolerance test. Laevulose has no effect on the blood sugar in normal persons. When, however, there is liver insufficiency a rise occurs resembling the normal blood sugar curve after glucose ingestion. The duration and height of the rise is proportionate, roughly to the degree of hepatic insufficiency.

3. *The hippuric acid test.*—The bladder is emptied between two meals and the patient is then given 4 grms. of sodium benzoate in 200 cc. of water flavoured with peppermint; he empties his bladder one, two, and three hours after, and the whole of the specimens are saved for estimation of the hippuric acid. No food should be taken during the test, but water is allowed should he desire it. Benzoic acid is converted in transit through the liver into hippuric acid, and the result is expressed as the percentage of sodium benzoate ingested. Normally 80 to 100 per cent of the hippuric acid will be found in the urine within 4 hours. In abnormal cases of liver disease the excretion is much slower.

4. *The sucrose test.*—No food is taken after 8 p.m. The next morning at 9 a.m. 20 cc. of blood are collected and the patient is then given a drink of 100 grms. of sucrose (Cane sugar) in 300 cc. of water flavoured with tincture of orange. Further samples of blood (about 1.5 cc.) are taken at 30, 60, 90, 120 and 150 minutes later, and the urine is collected before and 90 minutes after the drink. The amount of glucose and laevulose is estimated in each sample of blood, and the tests for the same are applied to the urine passed. In normal adults the blood glucose rises quickly to a maximum of 160 mgm. in about half an hour, and then falls slowly to the end of 2½ hours. The blood laevulose does not rise so quickly (to about 10 mgm. in 1½ hours), and then is sometimes a delayed fall, but in all cases the values fall to under 6 mgm. at the end of the 2½-hours period.

The writer would like to acknowledge the great help he has received in the biochemical details from Mr. G. A. Higgins, B.Sc., of the Biochemical Laboratory of the Radcliffe Infirmary; the details of the sucrose test and other of the data were the subject of a paper by him and Mr. J. R. P. O'Brien, B.Sc., an account of which was read at a meeting of the Physiological Society at Manchester in July 1942, and which is now in course of preparation for publication.

THE SURGERY OF GALL BLADDER DISEASE

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Long ago a lecturer told a class of medical students that the three most important qualifications of a successful surgeon were "Judgment, Judgment and Judgment."

To no sphere of surgery is this axiom more applicable than to that of the treatment of the gall bladder.

The edifice of surgical judgment is based on the solid foundation of exact anatomical knowledge; its walls are laboriously built with the bricks of experience and crowned with the dome of understanding.