A British Medical Association Lecture

ON

BILIARY INFECTIONS:

WITH SPECIAL REFERENCE TO DIAGNOSIS.

BY

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ACCURATE diagnosis and appropriate treatment must ever rest on a sound knowledge of pathology. In the case of some abdominal maladies diagnosis and treatment would appear to have advanced somewhat hastily beyond the controlling limits of ascertained pathological fact: not so in biliary infections. To the frequency of such infections all pathologists and surgeons will bear witness. We are only beginning to realize how much chronic ill health is attributable to such infections and how many fatal complications may supervene in the neglected cases. Our aim should be to prevent the development and establishment of such chronic infective processes in the biliary tract, and, where this is not possible, to reach an early diagnosis and recommend appropriate treatment before complications have developed and irretrievable damage has been done.

ANATOMY, PHYSIOLOGY, AND PATHOLOGY.

Certain points in the anatomy, physiology, and pathology of the biliary tract require emphasis, as they form the essential basis for a correct interpretation of symptoms.

Anatomy.

The striking feature of the biliary duct system is that large diverticulum the gall bladder, with its thin wall containing elastic tissue and a small amount of unstriated muscle fibre, its narrow eccentrically placed outlet, the spiral fold of mucous membrane in its duct, its generous blood supply, and its free lymphatic drainage. The main bile ducts are thin-walled and possess but a thin layer of unstriated muscle, except at the lower end of the common duct, where there is an aggregation of circular muscle fibres, sphincteric in function, as first described by Oddi. The intimate relationship of the main pancreatic duct with the bile duct is important, but not more so than the free anastomosis between the lymphatics draining the gall bladder and ducts and those of the head of the pancreas. The nerve supply of the biliary passages is a complex one and goes far to explain the diversity of symptoms met with in biliary disease. It consists of sympathetic fibres from the coeliac plexus corresponding to the lower six thoracic segments of the cord, fibres from the vagus, and occasionally sensory fibres from the phrenic. Herein lies the explanation of the pain and constricting sensations round the lower ribs, the gastric symptoms, and the shoulder pain met with in gall-bladder affections.

Physiology.

The secretion of bile with its contained pigments and bile salts and its cholesterin in colloidal emulsion is a continuous process. Between meals, however, little bile escapes into the duodenum, and it is the storage and concentration of bile in the gall bladder during the fasting period and its ejection following the succeeding meal that form the characteristic and significant features of the biliary mechanism. Whilst the lining membrane of the bile ducts secretes a fluid which dilutes the bile, the gall bladder has remarkable powers of absorption and concentration. It is no mere passive cul-de-sac, the storage capacity of which is measured by its size; on the contrary, it is an active concentrating chamber in which the bile may be concentrated ten times within twenty-four hours. In this absorptive function lie its virtue and its danger, for, when infection supervenes, not only does its inspissation of content tend to favour concretion formation, but the absorption of toxic products may lead to poisoning of the other tissues, notably the heart muscle. The synchronous emptying of the gall bladder with relaxation of the sphincter of Oddi, produced by stimulation of the sympathetic or of the central end of the vagus

and shown to follow the introduction of concentrated magnesium sulphate into the duodenum, is not so perfect a co-ordinated action as was at one time believed, and it is probable that the gall bladder empties much more from outside pressure consequent on respiratory and other efforts than from an active contraction of such unstriated muscle as is present in its walls.

Pathology.

Infection reaching the biliary passages might be expected to lodge and obtain a foothold more readily in the gall bladder where stasis is a physiological property than in the conducting channels, and this is notoriously the case. Further, the gall bladder has been shown to be one of the seats of election for the lodgement of certain forms of bacteria which may gain entrance to the blood.

The experiments of Rosenow have shown how certain strains of streptococci injected into the blood stream may infect the wall of the gall bladder in preference to all other tissues. Typhoid bacilli may continue to live in the gall bladder for years after the primary intestinal infection. The colon bacillus, carried to the liver by the portal circulation, may escape in the bile or by way of the hepatic lymphatics and so reach the gall bladder, where, under certain conditions, it finds a favourable habitat. Graham has demonstrated the frequent association of a hepatitis with a cholecystitis, and has brought forward considerable evidence to show that the infection spreads from the liver to the gall bladder, either directly or through their free lymphatic connexions. Anything which causes an unusual degree of biliary stasis will favour the inception of biliary infection. Thus we find that persons in middle life who have begun to put on weight, to take less exercise, and to allow their abdominal muscles to become merely a casing for their omental fat, are peculiarly liable to biliary infection and stone formation. The association of biliary infection with pregnancy and the puerperium is known to all. Three factors probably contribute to this special liability. First, biliary stasis; secondly, increased cholesterol content in the blood and bile; and thirdly, and I think of most importance, constipation, with *B. coli* infection of the portal blood, a cholecystitis developing along with or independently of a *B. coli* pyelitis of one or both kidneys. The portal of entry of the organisms invading the gall bladder may be a recognizable focal infection, such as a root abscess of a tooth or an appendicular infection; in many cases, however, the primary source will be sought for in vain. That biliary infection is an essential and inevitable precursor of gall-stone formation is, I consider, unproven. The single cholesterol stone may quite possibly be an aseptic gall stone. It is unlikely to remain indefinitely so. Sooner or later the lowered vitality of the gall bladder consequent on repeated obstruction of its outlet will permit of infection settling in its wall, and we get a cholecystitis secondary to stone. All evidence points, however, to the other sequence—infection, then gall-stone formation—being infinitely the more common one.

CLINICAL PICTURE.

We are now in a position to approach the subject from the purely clinical standpoint. It may be stated at once that the diagnosis of a biliary infection, especially when associated with gall stones, can usually be made by ordinary clinical methods—that is, by a careful and painstaking history and a purposive physical examination. Moynihan first laid emphasis on the importance of recognizing the inaugural symptoms of biliary infection. In the majority of cases the patient's complaint is of stomach trouble. The gastric symptoms are of two kinds. Most frequently the complaint is of a flatulent type of dyspepsia—of discomfort and distension coming on shortly (half an hour) after food, relieved by belching up wind. The patient may on occasion have to loosen the clothing in the endeavour, often vain, to get relief. This discomfort is worse after certain kinds of food, particularly fats, pastry, and vegetables. In other cases, however, the discomfort is delayed for an hour or more after food, when acid eructations and heartburn indicate that a gastric hyperacidity is present. Such symptoms should always suggest biliary trouble, and if the patient be a stout middle-aged multiparous female they form strong

presumptive evidence of gall-bladder mischief. So obsessed may the patient be with the stomach symptoms that, unless asked directly, she may fail to tell of definite attacks of colic, lasting for some hours, or of soreness under the right costal margin, lasting for days. As in the majority of cases the infection and calculus formation are mainly confined to the gall bladder, jaundice is not likely to be a symptom. The absence of a history of jaundice must never be taken as evidence against the presence of gall-bladder disease.

The seat of pain in the inaugural stages of gall-bladder disease is very varied. As a rule it is referred to the "pit of the stomach"; not infrequently it is more pronounced on the left than on the right side, and, as it is often accompanied by palpitations, may suggest cardiac disease. The aching in the right shoulder and right side of the neck may suggest rheumatism, or when down the right arm, neuritis. In the majority of cases, however, it is referred to the right costal margin and round the lower ribs on the right side to the lower angle of the right scapula. It is a notable fact that in quite 15 per cent. of cases the pain is felt as low down as the iliac fossa on the right side, so as to raise suspicions of appendicitis, suspicions not always unfounded, for coincident appendicular disease is by no means rare. Some patients will seek advice for pain in the right breast, when the absence of local pathology will render the gall bladder suspect. Any of the above symptoms should lead to a close cross-questioning of the patient as to a history of short attacks of severe pain, for a surmise may become a certainty if such a story be obtained.

The varied character and wide distribution of symptoms associated with an infected gall bladder are readily explained when, first, we reflect on the different nerve paths along which impulses may travel to centres whence they are referred to the periphery as pain, and, secondly, on the fact that the gall bladder may be a focal infection and toxic absorption from it may involve muscles and joints throughout the body and lead to a definite degeneration of the heart muscle. The "cholecystic heart" is now recognized by many as a clinical entity, and certain cases of muscular rheumatism and of rheumatoid joints have been proved to be dependent on a gall-bladder infection in so far that all rheumatic symptoms have disappeared after cholecystectomy.

Acute Cholecystitis.

Acute inflammation of the gall bladder may present one of two clinical pictures according to whether the cystic duct is occluded or not. In the *simple unobstructive type* the onset is gradual, characterized by nausea, loss of appetite, a rise of temperature, possibly preceded by a slight rigor and by aching pain across the epigastrium and under the right costal margin; acute colicky pain is usually absent. The patient looks ill and poisoned, with a coated tongue and heavy breath, and definite tenderness and rigidity of the upper part of the right rectus muscle are present. Such an attack will usually subside in a few days under expectant treatment. Occasionally, however, a peculiarly virulent infection may lead to gangrene with perforation of the gall bladder, followed by a localized abscess or a generalized peritonitis. Such attacks are undoubtedly very common, but as acute pain is not a striking feature the medical man may not be called in and they pass as "congestion of the liver."

In the other form, *acute obstructive cholecystitis*, so well described recently by Morley, the picture is typical and should be unmistakable. The onset is associated with pain across the epigastric region, radiating round to the back. Tenderness and rigidity of the upper part of the right rectus muscle are almost invariable. A premonitory attack of diarrhoea, associated with flatulence and nausea, is not unusual; vomiting may occur but is not the rule. Some frequency of micturition and pain across the lower ribs behind may lead to an examination of the urine and the discovery of a bacilluria which is probably eliminative in origin, even if due to a coincident pyelitis. The catch in breathing from diaphragmatic spasm may lead to the detection of diminished breath sounds and some crepitations at the base of the right lung—a common finding in acute biliary infections. These secondary manifestations must

not be allowed to obscure the real primary condition, the signs of which are nearly always patent. The rigidity and tenderness below the right costal margin usually prevent the enlarged gall bladder being felt; sometimes, however, it presents as an obvious, tense, rounded swelling. The initial acute pain may suggest biliary colic, and morphine and atropine may be given. When the effect of the drugs has worn off, however, the pain and tenderness persist and the temperature remains up. When seen after the first twenty-four hours the symptoms may at first suggest an intestinal obstruction, for the patient (usually elderly) may complain of a feeling of distension on the right side of the abdomen, an inability to pass flatus, even after an enema, and examination may reveal a dilated caecum. This pseudo-obstruction is due to the adhesion of the hepatic flexure of the colon to the inflamed gall bladder and must not be allowed to deflect attention from the primary seat of mischief. To adopt an expectant attitude in these cases is to run a needless risk, for, whilst in younger subjects the gall bladder may withstand the tension and the obstruction may right itself, in the more elderly gangrene is liable to result with serious consequences. In prompt diagnosis and immediate operation lies the only safe course in these obstructive cases.

Secondary Pancreatic Infection.

My experience has been that in over 9 per cent. of patients showing signs of acute biliary infection there is a coincident subacute pancreatitis. Such patients present a clinical picture which has three main distinguishing features: (1) They look more ill and grey than do those with a simple cholecystitis. (2) They complain of great epigastric distress rather than acute pain. (3) Tenderness is elicited over the whole of the upper part of the abdomen, which may show a definite fullness, and the local rigidity of the right rectus muscle is not so striking as where pancreatitis is absent. When the abdomen is opened in these cases the striking feature is a bile-stained oedema of the cellular tissues over the head of the pancreas with possibly some fat necrosis, but no haemorrhage. The gall bladder, although infected, does not show the same gross changes which we meet with in obstructive cholecystitis, and the pathological findings point to the pancreatic infection as being the immediate cause of the patient's symptoms. The spread of infection from gall bladder to pancreas is probably by way of the lymphatics, at least it is the exception in such cases to find any clear evidence of a cholangitis. Whilst the mortality in such cases is not high—probably not more than 15 per cent.—the convalescence from operation is slow, post-operative complications, including subphrenic abscess, not uncommon, and, in some cases, chronic ill health with glycosuria follows.

Chronic Grumbling Cholecystitis.

A distinct group of cases may be classed under this heading. In this group the patient suffers from a more or less constant sense of fullness and weight under the right costal margin, instinctively shrinks from any pressure on that region, and feels a sharp stabbing pain on stooping or on stretching upwards with the right arm. If exposed to wet or cold she develops a more pronounced aching in the right lower costal margin, usually attributed to a "chill on the liver." Occasionally a slight tinge of yellow appears in the skin and she is said to be looking liverish. Such symptoms may persist for years, until finally an acute obstructive attack or a pancreatitis supervenes and converts a state of chronic ill health into one of acute and immediate danger. By timely interference in this class of case much chronic disability may be avoided and final disaster averted.

Recurring Cholangitis.

Inflammation of the common and lesser bile ducts is usually secondary to gall-bladder disease and associated with the presence of one or more stones in the common duct. In many cases the clinical picture is too obvious to escape detection. A history of recurring attacks of colic, with rigors, fever, jaundice, and loss of weight, leaves little doubt as to the diagnosis. In other cases, however, the sharp outlines of the classical picture are wanting. No history

of colic is obtained, merely recurring chills with fever, nausea, loss of appetite, a faint tinge of yellow in the skin, and signs of basal pulmonary congestion. As such attacks frequently follow exposure to cold the pulmonary signs are liable to receive undue attention and the primary biliary infection to be overlooked. The marked loss of weight so characteristic of a chronic cholangitis, and due, in some measure at least, to the associated pancreatitis, is apt to suggest malignant disease. Physical examination will reveal little except some tenderness in the mid-epigastric region just to the right of the mid-line, and on the history the diagnosis must be based.

When the patient is seen for the first time when deeply jaundiced accurate diagnosis will be more difficult. Having excluded malignant disease of the liver, advanced cirrhosis, haemolytic jaundice, and the acute catarrhal type, we wish to decide whether the cause is an impacted stone in the common duct or a chronic pancreatitis—for both of which surgery has much to offer—or whether it is malignant disease of the pancreas or bile duct, or, still worse, malignant disease of the gall bladder with secondary glandular involvement in the portal fissure. A history of remissions of fever and of colic will point to a gall stone, a painless progressive course with an enlarged gall bladder to the malignant. In many cases, however, only an exploratory operation will decide the issue. I have found that the general aspect of the patient is the surest clinical guide to a diagnosis in these cases. The clear orange-yellow tint usually gives hope of a non-malignant cause, the grey-green and bronzed give no such hope. Van den Bergh's test has, unfortunately, not proved of great practical value in this class of case, because just in the case where help is most required its findings are indeterminate.

SPECIAL AIDS TO DIAGNOSIS.

X Rays.

Considerable help may be obtained by radiography in doubtful cases, but, whilst positive evidence may be conclusive, negative is to be discounted. Three forms of evidence are available from x-ray examination: First, direct evidence, in the shape of shadows, either of gall stones or of an enlarged and thickened gall bladder, may be obtained. Secondly, indirect evidence, as when after a barium meal a persistent deformity of the duodenum from pressure by or adhesion to the gall bladder is demonstrable. Thirdly, eliminative evidence, where either the definite demonstration of a gastric or duodenal lesion which would account for the symptoms is made, or where no gastro-intestinal lesion is shown and the gall bladder rendered the more suspect. Occasionally where a gall stone is lodged at the lower end of the common duct some barium will enter the duct and outline the stone.

Test Meal.

Biliary infections may be associated with either a decrease or an increase of the free acid in the gastric secretion, but usually the former. Walton has found that in practically 50 per cent. of cases free acid is absent. If, therefore, in a stout subject with suggestive symptoms, free acid is diminished or absent the diagnosis of biliary trouble is supported; on the other hand, Cheney found hyperacidity present in quite a large group of gall-stone cases, so that by itself the test meal evidence is valueless.

Duodenal Tube.

Valuable evidence of the presence of infection in the biliary passages may sometimes be obtained by withdrawing samples of bile through the duodenal tube after the injection of magnesium sulphate into the duodenum. Whilst the accurate location of the infection in the gall bladder or ducts as described by Lyon is usually impracticable, the finding of lymph, pus cells, and organisms in the bile withdrawn gives positive evidence that a biliary infection is present and may thus confirm a tentative diagnosis. Further, the nature of the infecting organism is ascertained, and if active surgical treatment be contraindicated an opportunity for autogenous vaccine therapy is opened up. The course of the infection may also in this way be observed.

and the repeated use of the tube with the introduction of a half-saturated solution of magnesium sulphate into the duodenum is not without therapeutic value.

Test for Bile in Blood Serum.

In many cases of cholecystitis there is a slight biliary obstruction from pressure on the common bile duct. Even when no jaundice is detectable in the skin and conjunctiva, bile pigments may be demonstrated in the blood serum. If 5 c.cm. of blood be drawn into a syringe containing 1 c.cm. of sodium citrate solution to prevent coagulation, the mixture centrifuged and the serum pipetted off, the latter will give with nitric acid the fine play of colours familiar in the test for bile in the urine. If, in the doubtful case, this test be positive, it constitutes valuable evidence of slight biliary obstruction.

Whilst these special aids to diagnosis may play an important role in some cases in making or clinching a diagnosis, they can only supplement, but never replace, the clinical data obtained from an accurate history and a careful physical examination. The latter must ever remain our surest guides to diagnosis, and on them we will mainly rely for the correct interpretation of any given case.

Diagnosis at Operation.

The final opportunity for completing the diagnosis will arrive when the abdomen has been opened. That the opportunity is not always fully grasped is evidenced by the number of cases in which a recurrence of symptoms follows hard on the operation. Little difficulty is found in assessing the pathological changes in the gall bladder. The crux of the problem is the common bile duct, and the diagnosis can never be regarded as complete until this has been exposed and its condition determined. Even should there be no calculus palpable, if there be any thickening or dilatation of the duct it should be explored first with a hypodermic needle and, if the bile withdrawn shows turbidity, by incision and probe.

Failure to detect and remove a stone from the common duct is the usual cause of recurrent symptoms after operation, and, where doubt exists, incision and exploration of the duct should invariably be practised. The condition of the pancreas, the appendix, the stomach, and duodenum must be investigated, as coincident lesions in these organs are by no means rare and may require to be dealt with, that complete recovery may follow. Only with good anaesthesia and a free incision can the complete pathological picture be displayed and adequate treatment be safely employed. Inadequate operation can only bring disappointment to the patient and discredit to surgery. The removal of several hundred gall stones will avail nothing if the one which was the real cause of the trouble be left behind. To remove one or more calculi and leave an infected, thickened, and functionless gall bladder may give the patient some relief but will not result in cure, and is evidence of a failure on the part of the surgeon to appreciate the intrinsic mural character of the gall-bladder infection. Timely pre-operative diagnosis and complete assessment of pathological change at operation are the two essentials for the successful treatment of biliary infections.

PERIARTERIAL SYMPATHECTOMY.*

BY

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THE basis of the theory of periarterial sympathectomy is dependent on the experiments of Claude Bernard, who found that in the rabbit, when the sympathetic nerve in the neck was divided, the arterioles dilated and the ear became hyperaemic; and when the peripheral end of the cut nerve was stimulated, the ear became blanched from constriction of its arterioles.

Attention was first drawn to the useful possibilities of this operation by Leriche of Lyons, who published his

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