An Address

ON

SOME ASPECTS OF CHOLELITHIASIS.

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THE surgery of cholelithiasis has two objects: it is concerned primarily with the health or the rescue of the individual patient; it is now concerned also with an attempt to discover the causes of the condition, so that its prevention may, in some degree at least, become possible. Research, no less than therapy, is an aim of all the methods of surgery.

In an investigation of cases of cholelithiasis the conclusion has been reached that two factors are of chief importance in respect of causation: infection, and an increase in the cholesterol content of the blood.

Infection may be derived from any source—from the teeth; from the facial sinuses; from any part of the alimentary canal; from the urinary system; from other foci within, or without, the abdomen. Theoretically there is no infection which cannot, when uncontrolled, gain access to the blood and so find its way to any part of the body. The infections so arising find their way to the gall bladder by several routes. If they are alimentary in origin they may ascend from the duodenum along the common duct; they may reach the liver, through the portal circulation, and thence descend with the bile. They may be borne by the blood, or by the lymph stream; or may attack the gall bladder by direct invasion from a neighbouring organ. The immediate effect produced upon the gall bladder varies in different instances. If contaminated bile is the direct source of the infection the mucosa is first attacked, and the inflammatory changes pass outwards through all the walls of the gall bladder. If the disease is blood-borne, little clumps of organisms are first seen in the submucosa, and a crowd of leucocytes surrounds them. The inflammatory process thence extends inwards to the mucosa and perhaps outwards to the peritoneum. The infection of the gall bladder found in typhoid fever seems to start with great frequency in this fashion. If the invasion occurs through the lymph stream or by direct contiguity, the serosa is first infiltrated by organisms, which make their way slowly inwards towards the mucosa. Sections made of the gall bladder have demonstrated quite clearly these several paths of infection. In cases of multiple gall stones infection is invariably present in the gall-bladder wall. The view has been expressed that infection is the consequence, and not one of the chief causes, of the development of calculi. Such evidence as I have been able to gather seems to indicate quite indisputably that infection always precedes the deposit of stones. Indeed, our search now inclines to the recognition of infection in the gall bladder during the period before the stones are formed. The most frequent agent of infection in the gall bladder is the *Bacillus coli*. It is found in all stages of cholelithiasis, from the earliest to the most advanced. Table I shows this unmistakably. In many cases of cholelithiasis a history of other forms of *B. coli* infection, especially of the urinary tract, may often be elicited. Women are afflicted with gall stones at least twice as often as men. They are apt to suffer from bacilluria; and in the periods of pregnancy pyelitis or cystitis of *B. coli* origin is no uncommon event. There would appear to be a connexion between the infections of the urinary tract and those of the gall bladder. Walton in particular has emphasized the truth of this observation.

The infection which sets going a process of calculus formation must be mild and is often recurrent; it waxes and wanes. If it is severe an acute cholecystitis develops, and gangrene or perforation may occur. As this acute infection subsides it may leave a crippled gall bladder incapable alike of secreting or of discharging its contents; and stasis

TABLE I.—RESULTS IN 100 CONSECUTIVE CASES FROM WHICH CULTURES OF THE GALL BLADDER WALL WERE GROWN.

A.—Showing the Relation between Degree of Lesion and Type of Infection.

	Streptococci.	B. coli.	Double Infection.	B. pyocyaneus	Other Infection: B. lactis, Staphylococcus, Pneumococcus.
Early lesion	5	19	1	1	14
At acme	1	7	2	—	5
Subacute cholecystitis ...	2	14	2	1	8
Chronic cholecystitis ...	—	2	—	—	2
Empyema of gall bladder	—	4	—	—	4
Total percentage ...	8	46	5	2	33

B.—Showing the Organisms found on Histological Examination of the same Cases.

	In Mucosa.	In Peritoneum.	All through.	Total.
Streptococcus	4	6	—	10
Pneumococcus, etc....	17	13	3	33
B. coli	20	25	5	50
B. pyocyaneus...	2	—	—	2

and a milder sepsis may then together lead to the growth of stones. If the infection is mild there appear to be pauses in the growth and activity of the organisms, for after cholecystectomy the bile may be found sterile, and the walls of the gall bladder, though crowded with organisms, may show only an attenuated growth, or even none, on culture. The incidence, the abeyance, and the recurrence of infection are shown by the existence of several generations of stones in the gall bladder, each generation having stones of the same size—larger if of older date, smaller if more recent. Three generations are often found.

When infection, from whatever source derived, reaches the cavity of the gall bladder, where an excess of mucus is quickly secreted and produces stagnation, the process of calculus formation may begin. An examination by x rays of the gall bladder after removal shows that, as a rule, the smaller the stone the larger the proportion of cholesterol that it contains—the smaller stones, that is, are almost translucent. As they grow larger calcium begins to be deposited upon a spot here and there; the area covered increases, and finally the complete closure of a cholesterol nucleus in a calcium capsule may be seen. In other instances the calcium seems to infiltrate the stone, stealing in towards the centre. In still others the nucleus of the stone is a dark spot of calcium and cholesterol is deposited around it. The calcium is no doubt derived in part from the mucus secreted in excess and in part from the inflammatory fluids poured into the gall bladder when the infection has aroused a great response. We do not at present know why in one case cholesterol is the chief constituent of gall stones, and why in another calcium is the component. The connexion between a preponderance of cholesterol in the stones and a high cholesterol content of the blood is clearly suggested by our experience to be presently mentioned, and calcium is doubtless an evidence of a subdued, though persistent, local infection, and perhaps, too, an evidence of a deranged calcium metabolism of which in this connexion I know nothing. The infective origin of multiple gall stones can hardly be disputed; and the aphorism I ventured to express many years ago, that "a gall stone is a tombstone erected to the memory of the stones within it," remains true. These buried organisms are not always dead. I have found typhoid organisms viable twenty-eight years after the occurrence of typhoid fever; and Finney relates a case in which living typhoid organisms were found in the centre of gall stones thirty-five years after an attack of enteric fever.

So far I have spoken of multiple gall stones. On occasion we find not many stones but one only. A solitary stone is composed of pure cholesterol; it is not caused by infection, though it may set infection going by becoming impacted once or oftener in the cystic duct. It causes no "inaugural" symptoms. No evidence of its existence is given until it suddenly becomes lodged in the pelvis of the gall bladder and occludes the cystic duct. This event rarely takes place until the stone is of the size of a nutmeg. The stone is irregular and warty on the surface, like beeswax in appearance, almost translucent; and on section shows a characteristic appearance of spokes radiating from the centre. When the stone is larger calcium may be deposited between these spreading lines, or upon the surface. The solitary cholesterol stone, then, is not caused by infection, but results from a condition of hypercholesterolaemia. The diagnosis of "solitary cholesterol stone" is easily made when one remembers that none of the prodromal symptoms of cholelithiasis are present. The first symptom is an agonizing attack of pain coming quite suddenly, seizing the right half of the abdomen, piercing through to the shoulder blade, spreading across the epigastrium, and producing infinite unrest, difficulty in deep breathing, sweating, and prostration, until, in an instant, relief comes. The stone is released as quickly as it was engaged. When such events are repeated infection in the gall bladder is a necessary consequence.

The question of the cholesterol content of the blood is one for close examination in all suspected cases of cholelithiasis. With the skilful help of Dr. Cecilia Shiskin 280 patients suffering from various abdominal diseases requiring operation have been examined (Table II). Of

TABLE II.—HYPERCHOLESTEROLAEMIA IN RELATION TO DIAGNOSIS.

A.—Types of Disease.

Type of Disease.	Hyper-cholesterol-aemia.	"High Normal."	Total.
	Per cent.	Per cent.	Per cent.
Gall bladder cases	65.0	23.0	88.0
Gastric and duodenal cases ...	16.4	11.2	27.6
Other diseases	22.9	13.0	35.9

B.—Details in 280 Cases.

Nature of Case.	Cholesterol in Blood.			Total.
	Below 0.160 per cent.	160 to 0.200 per cent.	Over 0.200 per cent.	
Gall bladder disease— (a) Stone	12	29	60	101
(b) Cholecystitis, etc. ...	4	6	8	18
Gastric ulcer	8	13	5	26
Duodenal ulcer	26	10	5	41
Jejunal ulcer	5	—	1	6
Carcinoma (gastric, pancreatic)	8	2	4	14
Chronic appendicitis	5	9	2	16
Acute yellow atrophy	1	—	—	1
Hydatid cyst of spleen	—	1	—	1
Abdominal adhesions }	22	12	11	45
Visceropptosis				
Pernicious anaemia	1	—	—	1
Splenic anaemia	3	—	—	3
Haemolytic jaundice	7	—	—	7
Total	—	—	—	280

these, 101 were cases of cholelithiasis. Cholesterol is a member of the important group of substances known as lipoids. It is an invariable constituent of all active cells of the body, both in its free form and in combination as ester.

In disease it may occur in abnormal amounts in various organs, tissue fluids, and calculi. It is present in the blood in very variable quantities. The normal amount may be stated as 0.160 per cent., and in older people as rather more than this. For purposes of classification (Fig. 1) we regard

Less than 0.133 per cent. as indicating hypocholesterolaemia.
Between 0.133 and 0.160 per cent. as being normal.
Between 0.160 and 0.192 per cent. as being high normal.
Above 0.192 per cent. as indicating hypercholesterolaemia.

Hypercholesterolaemia is found in cases of arterio-sclerosis, chronic nephritis, diabetes, the later months of pregnancy, and in cholelithiasis.

Of 101 cases of cholelithiasis (proved by operation) 66.4 per cent were females. The average cholesterol value

FIG. 1.

was 0.217 per cent.; 65 per cent. of cases showed hypercholesterolaemia; 23 per cent. had high normal values; 11.5 per cent. had normal values; and 2 cases only showed hypocholesterolaemia—one patient was a man aged 76, the other suffered from an acute empyema of the gall bladder. In both a low value was therefore to be expected.

It is interesting to compare these figures with those obtained in cases of gastric and duodenal ulcer. Twenty-six cases of gastric ulcer were examined; the average cholesterol value was 0.167 per cent.; 27 per cent. of the cases showed hypocholesterolaemia; 50 per cent. gave normal values; and 23 per cent. hypercholesterolaemia. Forty-one cases of duodenal ulcer were examined: the average value was 0.149 per cent.; 36.6 per cent. of the cases showed hypocholesterolaemia; 51.2 per cent. gave normal values; and 12.2 per cent. showed hypercholesterolaemia; and in some of these arterio-sclerosis was noted.

The diagnostic significance of an increased cholesterol content of the blood is therefore important. Over 75 per cent. of patients in whom hypercholesterolaemia was found were suffering from cholelithiasis. The blood examined after operation shows that after all operations of magnitude there is a fall in the cholesterol content. This fall is followed slowly, as a rule, by a rise which may carry the content up to or beyond the normal. A condition of

hypercholesterolaemia may then persist unless measures are taken to reduce the accumulation of cholesterol. To this end a careful supervision of the dietary is necessary. I have followed Chauffard in this matter, and I now give to all patients after operation the following chart.

DIETARY.

This régime seeks to achieve three objects: to avoid any digestive disturbance; to decrease, or at any rate not to increase, the cholesterol content of the blood; and to prevent intestinal infection which might give rise to infection of the biliary tract.

Forbidden.

Fat and eggs.
Stews and fried foods.
Sweetbreads and liver, goose, duck, kidneys, black pudding.
Pork, game, high or spiced dishes, oily fish, soft roe, caviare.
Cooked butter.
Peas, cabbage, raw vegetables.
Strong cheeses.
(Sweets made with eggs may be taken.)
Avoid aerated waters, alcoholic beverages, beer, and liqueurs. Take alkaline drinks and a drink of hot water at the end of each meal.
Frequent small meals, rather than a few heavy meals, should be taken.

Advocated.

Skimmed milk.
Soups made with milk, vegetables, rice, semolina, tapioca.
White meats, lean meats, boiled, grilled, or roasted.
Salt-water fish, containing little fat or oil (for example, sole, whiting, turbot, brill), and river fish, provided they are fresh and not fried.
Cereals.
Potatoes, mashed or in their jackets, turnips, endives, spinach, artichokes, asparagus, vegetables in purées, rice, vermicelli and macaroni.
Mild cheeses.
Fruit—after three months.

The greater frequency of cholelithiasis in women may be in some measure due to their blood condition. Dr. Cecilia Shiskin has found that just preceding and during the first day or two of menstruation the cholesterol content is high (Fig. 2); and that during pregnancy this value steadily augments (Fig. 3) until in the ninth month it is approximately double the normal.

We did not derive much help in diagnosis from an examination of the stomach contents by the Rehfuess method. Out of 77 cases we found complete achlorhydria in 17, hypochlorhydria in 3, a low normal in 14, a normal in 18, a high normal in 8, and hyperchlorhydria in 17. The "types," of course, were not significant. The only point here which needs comment is that which concerns the rather large proportion of cases in which achlorhydria was present. In all these the administration of dilute hydrochloric acid after operation (30 drops in a tumblerful of water once or twice daily at meal times) is necessary. The rate of emptying the stomach in these cases was: rapid in 27; normal in 34; delayed in 16. The normal period for emptying after the test meal is from one and three-quarters to two and a half hours.

FIG. 2.—Effect of menstruation on cholesterol contents of bloods. (Shiskin.)

cholelithiasis in all cases except those in which the solitary cholesterol stone is present. Our endeavour should be to recognize the presence of the infected gall bladder before the stones have had time to form. The symptoms to which I drew special attention in 1908¹ as "inaugural" are amply sufficient to indicate the existence of cholecystitis. They are symptoms referred by the patient to the stomach. The complaints are of a fullness, weight, distension or oppression in the epigastrium, coming as a rule within half or three-quarters of an hour after meals, relieved by belching, and dismissed almost on the instant by vomiting. These sensations are elicited with remarkable constancy by certain articles of diet, especially those containing greasy or acid material. There is a sensation of tightness, which, if unrelieved, may become acutely painful; by it the patient is made restless, and from it he obtains relief by bending the body forwards, by flexing the right thigh on the abdomen, or by loosening all garments which press upon the waist. There is often a complaint of acidity or heartburn, and in the act of belching there may be bitter and acid regurgitation. Many patients notice that quite suddenly there may be a great gush of saliva into the mouth. While discomforts last there may be a "catch in the breath." When a deep forced breath is taken an acute stabbing pain may be felt on the right side, of such severity that the act of respiration is suddenly checked. Faintness, nausea, sweating of the face and neck, and a sense of great prostration may be followed by vomiting. There may be a slight sensation of chilliness and of shivering, especially in the evenings; "goose-flesh" is mentioned repeatedly in the clinical histories as a very disagreeable experience. Upon all these symptoms, which may exist for years, a series of attacks of colic may be imposed. Our efforts, however, should now be directed to the recognition of the pre-calculous stage of the disease. Recently, with the very skilful co-operation of Dr. L. A. Rowden, this aspect of our work has received close attention.

The radiological evidence of a pathological gall bladder

FIG. 3.—Changes in cholesterol contents of blood with the progress of pregnancy. (After Shiskin.)

may be direct or indirect. There are times when stones are quite clearly seen in the x-ray photograph, and there are times when the gall bladder shows an opacity greater than that of the stones which lie within it, when what may be called a "negative shadow" is seen. The appearance of the shadows of stones is variable. When the stone consists chiefly of calcium the shadow is very opaque. When the stone is composed largely of cholesterol and a surface deposit only

of calcium is present a "new moon" shape, or a "wedding-ring" shape may be recognized in the shadow. Sometimes a mosaic pattern is found, and is due to the overlapping of shadows when stones are superimposed one on another.

The indirect effects produced by disease in the gall bladder are due either to pressure or to traction. A greatly enlarged gall bladder must make room for itself in the abdomen, and it does so by pushing aside the stomach or the duodenum or the colon. The outline of these displaced viscera, when they are filled with an opaque meal, is changed in greater or less degree from the normal. A "half-shadow" is seen in place of the usual shadow. When, on the other hand, the gall bladder after contracting attachments to these viscera begins to shrink it drags them away

DIAGNOSIS.

The diagnosis of cholelithiasis does not, as a rule, present much difficulty, for the formation of stones in the gall bladder, and those attempts at migration which cause hepatic colic, are terminal events. Cholecystitis precedes

and a conspicuous distortion in their shadows is then seen. A large pouch may form in the duodenum, or the colon be so hitched up to the gall bladder that no effort can displace its shadow.

It may be taken, I believe, as indisputable that a gall bladder which is clearly visible on ordinary radiological examination (apart, that is, from inflation of the peritoneal cavity) is pathological. The following table has been drawn up by Dr. Rowden.

TABLE III.—*Radiological Evidence of a Pathological or Calculous Gall Bladder.*

Direct Evidence.

1. Shadow of stones—
 - Opaque and solid;
 - "New moon" shape;
 - "Wedding-ring" shape;
 - "Mosaic" due to overlapping.
2. Shadow of gall bladder—
 - Every clearly visible gall bladder is pathological.

Indirect Evidence.

1. Pressure effects on—
 - (a) Duodenum;
 - (b) Pyloric part of stomach (half-shadows).
2. Traction effects—
 - (a) Pouching of duodenum;
 - (b) Displacements of duodenum;
 - (c) Displacements of colon;
 - (d) Fixity of duodenum or colon.

It is to be hoped that, by a combination of the several methods of inquiry I have mentioned—inquiry into the clinical history, into the cholesterol content of the blood, and into the radiologist's evidence—an accurate diagnosis of "pre-calculous" cholecystitis may become more frequently possible. When the knowledge gleaned from these sources is correlated with that gained by a chemical and bacterial examination of the gall bladder and its contents, then some clue as to the prevention of cholelithiasis may happily be discovered. I have now had the opportunity of removing a number of gall bladders in what I think may truthfully be called the "pre-calculous" stage; and a number of patients are being treated by large, intermittent doses of urotropine in the hope that they may be enabled to escape the attention of the surgeons.

When stones have formed in the gall bladder the morbid changes are generally extensive and well advanced. It is certain that the walls of the gall bladder are deeply infected, and the muscular layer destroyed; in many cases the infection has spread from the gall bladder to parts around, as is indicated by significant adhesions. Hepatitis in an early or advanced stage is often, though by no means always, present, and the pancreas is not seldom affected. In a large proportion of cases a condition of chronic appendicitis is found, and to all appearance is often of an older date than the disease in the gall bladder. In a small proportion of cases ulceration of the duodenum, or of the stomach, or of both, may be found also. The research work of the surgeon has shown the close affinity, the common causation, or the etiological relationship between these several diseases.

TREATMENT.

When the diagnosis of cholecystitis has been made, or the existence of stones within the gall bladder confidently asserted, the question as to the most appropriate treatment will arise. In the days to which we look forward with hope, and some expectation, it is possible that a recognition of earlier stages in the disease may enable us to prevent, or to delay, those advanced or terminal stages with which our therapeutic activities are now chiefly engaged. By the time that stones have developed, medical treatment can do nothing more than ensure a degree of clinical silence; it does not seem able to retard a steadily progressive pathological change. For the experience is not infrequent which shows that an inhibition of the symptoms of the disease, or more rarely their complete relief, may be witnessed, when in later days it is recognized that morbid processes have been steadily developing in the walls of the gall bladder; and perhaps cancer at last reveals itself.

The conditions which make it necessary to decide against surgical relief must be extremely few. I have often hesitated in days gone by as to whether the condition of a patient's heart would forbid the operation I was otherwise inclined to advise. But, under the tuition of Sir James Mackenzie, before he left Burnley, and after, I learnt that the removal of a diseased gall bladder was in many cases a sure method of giving relief to the heart. Glycosuria is often an effect of cholecystitis, and disappears after an operation which has not been too long delayed. Nephritis, too, need cause no anxiety if deliberate preparation for operation is made to extend over many days. The danger in the operative treatment of cholelithiasis comes from delay, which has led to infection of the ducts, and of the liver, to the "cholecystic heart," and so forth. Yet the dangers of operation are very small. In the last ten years of my private work, including all cases—malignant cases, cases of stone in the ducts, in the ampulla, in every stage of activity—the gross mortality is 3.1 per cent. Hysterectomy, gastrectomy, colectomy, gastro-enterostomy, and splenectomy are included among the operations performed at the same time as the operation upon the gall bladder or bile ducts. In over half the number of cases the appendix was removed; in many it had been taken at an earlier operation. Some of the cases had been operated upon two, three, four, or more times before I saw them. The mortality is still too high; but it is almost certainly less than the mortality from cancer of the gall bladder alone, in cases not submitted to operation. There is, however, more than the death rate to consider. Operation is not only safer than continued medical treatment, it is also far more merciful. The agonies of hepatic colic are sometimes considerable; they are repeated on occasions which are perhaps very close together; they are sudden and unexpected in their incidence; and no sooner is one attack over than a dread of the next is felt. An operation for cholelithiasis is not always without pain, even when the nerves are blocked with quinine and urea; yet no patient will admit that the pain of the operation is equal to that experienced in one attack of colic. The surgery of cholelithiasis is difficult, sometimes extremely difficult. I held it to call for greater technical skill, and to present more problems for immediate accuracy of judgement, than any other branch of surgery; and the after-treatment too has its own grave problems.

If I might presume to offer any advice to the surgeon who has no great or continued opportunities for practical work, I would suggest to him never to do gastro-enterostomy in the absence of a demonstrable lesion which requires it; and to leave the surgery of the gall bladder alone. The fact that in my own work nearly one-quarter of the patients suffering from cholelithiasis have been operated upon before is an argument, not against the surgical treatment of the disease, but against an attempt by the inexperienced or untrained operator to deal with conditions which may tax all the energies and call out all the reserves of even the most proficient. Surgery is not only a craft, though craftsmanship of a high order is essential. It is a profession to which a man should feel not only complete devotion but also a sense of special dedication. Its practice requires the most flawless integrity in thought and act. It is not lightly to be undertaken by any who have not first surrendered to an iron discipline of training by the masters of their art. No one acquainted with the truth can deny that far too many operations nowadays are done by those who, having perhaps a measure of success in the trivial cases (none are trivial to a patient!), rashly embark upon procedures which they are not fully competent to undertake. And the good repute of surgery is wounded.

CHOLECYSTECTOMY.

In the surgical treatment of cholelithiasis when the stones lie only in the gall bladder, cholecystectomy has displaced cholecystostomy. I feel confident that this decision, which is almost universal, is sound and finds an ample warrant in the bacteriology and morbid anatomy of the gall bladder. The results of drainage of the gall bladder were often good, but they were bad in too large a proportion of cases: for

stones recurred, carcinoma sometimes developed, and the symptoms of an infected gall bladder persisted. Removal of the gall bladder was at first found difficult; the mortality was certainly a little higher, and the complications which ensued, due no doubt to lack of technical experience, were occasionally disastrous. But surgery is growing out of the indiscretions and the sins of its youth. Cholecystectomy rightly performed is as safe as drainage of the gall bladder, and the after-results are far more satisfactory.

The first problem is to decide, in the absence of gall stones, as to those appearances of the gall bladder which justify its removal. What are the signs of a diseased gall bladder? I should say that a gall bladder is infected when it has lost its normal blue colour, or its sheen; when it has lost its suppleness and its walls are thickened by fibrous tissue, or by the deposit of fat, especially along the lines of the vessels; when the cystic gland is definitely enlarged and changed in structure; when adhesions have been contracted to the parts around, especially to the duodenum, or the stomach; or when the cystic duct is thickened and the pelvis of the gall bladder has settled, in a mass of adhesions, firmly down upon the common duct.

In the operation of cholecystectomy there are dangers to be avoided, and there are points to be carefully remembered. The operation begins almost always at the cystic duct. I described this method twenty years ago, and was amused to hear it announced as a novelty, under the title of "retro-grade cholecystectomy," just before the war. In this operation, more, I think, than in any other abdominal operation, the exact position and relation of every structure that is encountered must be clearly defined. If the operation begins at the fundus blood trickles down on to the pedicle where the duct and vessels lie; they become stained and difficult to define clearly, and a rash blind clamping of the pedicle may result in almost irreparable disaster. The cystic duct is first clearly defined; it is almost always adherent to, and lies side-by-side with, the common hepatic duct before these join to form the common duct. When the duct is cleared it may be surrounded by a ligature and divided. It must not be cut flush with the common duct, but divided not less than an eighth of an inch away. If cut closer than this to the common duct it is possible that a stricture may form, and be the source of great difficulties. It is no uncommon thing for the cystic duct to be so tightened in elevating the gall bladder that the common duct is dragged upon and is made to look very like the cystic duct. I have operated upon not a few cases in which portions, sometimes even a length of 1½ in., had been cut out of the common duct. It is an elementary principle that the three ducts at their junction shall be clearly demonstrated. The cystic duct being divided, the cystic artery (there may be more than one) is ligatured, an aneurysm needle, or the cholecystectomy forceps, being first passed round it. I have not infrequently seen a broad forceps applied to the artery, which is then severed; this is a dangerous practice. To clamp ducts or vessels when the gall bladder is being forcibly elevated, and then to cut beyond the grip of the forceps, is a clumsy and perilous method of work. A ligature should be passed round every structure to be severed, and pains taken to make it indubitably certain that nothing but the duct or vessel is embraced. This no doubt sounds very elementary advice; but many patients would have been saved if only it had been understood and observed.

In my gall-bladder operations I was formerly much impressed by two events. Occasionally I would have a long struggle for the life of a patient, or even lose a patient, when I had expected an easy and untroubled convalescence. And occasionally I would find, on visiting a patient in the evening after the operation of cholecystectomy had been performed, that the dressings were saturated with bile. During operations I was struck by the irregular arrangement of vessels, and by the occasional discovery of an anomaly in the ducts. I therefore suggested to my colleague Mr. E. R. Flint that he should examine a series of bodies and endeavour to discover the variations—which were apparently not very infrequent—in the anatomy of the parts concerned in the operation of cholecystectomy. His work² has made matters plain. It is quite evident that

unless unremitting care is exercised it is easily possible to ligature the right hepatic artery instead of the cystic artery. A "cystic artery" that appears larger than normal, or has a "hump" in it, is often the right hepatic artery! Ligature of the right hepatic artery in a patient whose liver cells are already damaged as a result of an infection which is a part of his disease may be a serious or even fatal matter; and an accessory right hepatic duct is present in not less than 15 per cent. of cases. However watchful one may be, the wounding or the division of an accessory right hepatic duct may occur. If this should happen it is hardly worth while to repair the duct, or to anastomose its cut end with the divided cystic duct. But it is essential that a drainage tube should be left in the wound. I have closed the abdomen without drainage after removal of the gall bladder on many occasions; but I never do so now. A small tube does no harm: it leaves no gap in the abdominal wall if the rectus muscle is displaced outwards, and it gives a measure of safety obtainable in no other way.

Many of the patients who must submit to operation for cholelithiasis have been martyrs to their disease for long periods. Stones may have escaped into the common duct, or have passed upwards into the hepatic ducts, and biliary cirrhosis may have developed. The functional activity of the hepatic cells may be greatly impaired. A recognition of this truth must guide every stage in the care of the patient. In the day or two preceding operation as much glucose as possible should be given. During the operation the liver cell must not be made to suffer the burden which chloroform, a deadly drug, imposes upon it. The anaesthesia should, as far as possible, be induced and maintained by gas and oxygen. Hepatic insufficiency and acidosis are difficult conditions to master. Of the former we now recognize two types. There is one in which the amount of bile discharged ceases or is greatly reduced; jaundice deepens ominously; the mind becomes obtuse; vomiting develops; the pulse becomes slower, the patient more and more enfeebled; drowsiness precedes coma, and the blood urea steadily increases; renal failure, consecutive to hepatic failure, is then the cause of death. And there is another in which, after a normal course of from three to eight days, the bile discharged becomes copious, thin, and pale; jaundice does not change perceptibly; restlessness, great prostration, profound muscular weakness, and a peevish irritability are noticed; vomiting is present but is not as a rule severe; blood urea remains low; failure of the liver function is the cause of death.

Another menace, happily infrequent after operation upon the gall bladder or the ducts, is acidosis. Of this one seems to learn little from the textbooks on physiology; yet there are few conditions more necessary for the surgeon to understand.

Acidosis.

(A) Acidosis or ketosis is a condition in which certain acids gain access to the blood and therein threaten to diminish the alkali reserve in consequence of the very urgent necessity that they should be neutralized. The neutralization in the blood is effected chiefly by sodium bicarbonate. As this is accomplished the carbonic acid, whose ratio to NaHCO_3 is constant, would be in excess but for the controlling mechanism which preserves the reaction of the blood at its normal level. Acidosis may therefore be considered as a condition brought about by the excessive withdrawal of bases in consequence of the formation of acids within the body. It is that state of metabolism of which the most constant characteristic is the production in abnormal quantities of "acetone" bodies (hydroxybutyric acid, diacetic acid, and acetone). Even in the most severe degree of acidosis only the slightest alteration in the reaction of the blood is perceptible. The steady maintenance of the normal reaction depends on the presence of certain alkaline salts—the "buffer salts"—of which the chief is sodium bicarbonate, NaHCO_3 .

For a stable blood reaction the ratio between the CO_2 and the NaHCO_3 is maintained at a constant value. When acids are added to the blood they react with the buffer salts, forming sodium salts of the respective acids, and these are excreted in the urine. If, therefore, large amounts of acids are continually poured into the blood, the buffer salts may decrease to a degree which renders it beyond the power of the body to replace them. Their concentration in the blood is therefore reduced below the normal, and, the ratio between CO_2 and NaHCO_3 being kept constant, the carrying capacity of the blood for CO_2 is also reduced, and accordingly CO_2 may accumulate in the tissues. The blood under such conditions will, of course, cause stimulation of the respiratory centre; a more thorough ventilation of the lungs and of the

blood then results in an urgent attempt to prevent further accumulations of CO₂ in the tissues. This hyperpnoea is one of the clinical symptoms of acidosis.

(B) The acids which gain access to the blood are intermediate products in fat katabolism.

(C) The imperfect combustion of fats is associated with, and is perhaps due to the absence, or diminution, of, that product of carbohydrate metabolism which sets alight this combustion.

(D) A primary deficiency in carbohydrates is therefore an essential preliminary fault in cases of acidosis.

(E) This deficiency may be due to an insufficient supply of carbohydrates to the body, such as occurs in cases of, say, pyloric obstruction with copious vomiting, or to an imperfect metabolism of carbohydrates of which there is no lack. The anaesthetic chloroform probably interferes with carbohydrate metabolism by its direct action upon the liver cell.

(F) In cases of carbohydrate deprivation the deficiency may be at once made good by the administration of glucose. This cannot be given in adequate quantities by the mouth to patients afflicted with acidosis, on account of the vomiting which is so persistent. If administered by the rectum its absorption, when considered in relation to the urgency of the patient's need, may appear slow. If it is given subcutaneously the quantity taken up is small, owing to the enfeebled systemic and lymphatic circulations. When administered intravenously there is no reasonable limit set to the amount which can be given. Either a 5 or a 10 per cent. solution may be injected; an isotonic solution contains 4.15 per cent. of glucose. Matas of New Orleans, a surgeon to whom our debt of gratitude is very heavy, was the first to suggest (in 1911) that glucose might be given by continuous instillation. He has recently³ described an apparatus which renders easy the "continuous drip" intravenous administration of a glucose solution maintained at an equable temperature. About 8 pints may be introduced in the period of twenty-four hours; I have once introduced as much as 18 pints. A reaction is seen not infrequently—the patient shivers and then sweats, a miniature rigor occurring; no anxiety need be felt on this account. The cause of the reaction is doubtful; it may perhaps be the too rapid administration of the fluid.

(G) The mere accumulation of glucose within the blood is not, however, all that is necessary. The glucose must be utilized by the tissues. We owe to Thalhimer of Milwaukee⁴ the supremely important suggestion that this may be done by the injection of insulin.

My experience of the method is small, but it is enough to say that a new remedy of considerable importance is now at our disposal. Insulin must not be injected until there is a good store of glucose in the blood lest a hypoglycaemic reaction be caused; not less than 15 ounces of a 5 per cent. solution should have passed into the vein, and unless there is great urgency it is well to introduce an even larger amount, or to have a stronger solution. Lilian Farrar⁵ has used a 20 per cent. solution for intravenous administration. As she points out, glucose is not only a food and source of energy, but also a stimulant to the tissue cells and to metabolism; the liver function is conserved by it and the glycogen store increased.

Fisher and Snell⁶ record cases illustrating the value of the insulin treatment in pre-operative and post-operative non-diabetic acidosis.

Vomiting is often the warning symptom of impending acidosis. It is present along with great prostration and a considerable degree of air hunger, and with a sweet "new-mown hay" smell in the breath. The urine gives the characteristic reactions for acetone and diacetic acid.

Lavage of the stomach is the sovereign remedy for relief of the vomiting, which is most distressing. But in acidosis, as in cases of obstruction, or of adynamic distension of the stomach and duodenum, the lavage may need to be repeated so frequently as to be a tax upon the surgeon and a sore trial to the patient. Happily a most excellent method of lavage is made possible by the Jutte tube, or the Levin tube—tubes of about the same size as the Rehfuess tube. If passed through the nostril they may remain for hours without distress to the patient, who may then drink fluids freely.

I have, I fear, wandered discursively over a large field in dealing with the subject of cholelithiasis. There are so many problems that confront us as we cope with this very formidable disorder that it is not easy to choose among them. There is so much still to learn. The relationship of the liver to the spleen, of both to the pancreas, and of all three to the reticulo-endothelial system, and the effect which injury to the liver cell has upon the kidneys, are matters calling for fullest inquiry. Though we seem to know so little of any of these organs, and still less of their interplay, the work of the surgeon which has so marvellously contributed to our clinical knowledge may still hope to prove not unworthy of regard as one of the most fertile of all methods of research.

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Lectures

ON

THE SYMPATHETIC INNERVATION OF STRIATED MUSCLE.*

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LECTURE III.—PART II.

THE PRACTICAL APPLICATIONS (*continued*).

THE CONTROL OF TONE BY THE BRAIN.

THE SELECTION OF PATIENTS FOR RAMISECTION.

I SHALL now consider the reflex arcs concerned in maintaining the two elements of tone, and the scientific principles for the selection of patients for ramisection.

Plastic tone is enhanced in degree in the decerebrate animal. It may appear as a component of postural contraction immediately after the mid-brain is cut across, so that, normally, prespinal pathways are employed by the impulses maintaining it. When decerebration is performed, plastic tone is increased in degree as a result of the release of this prespinal sympathetic reflex arc from higher levels of control. In addition to this, contractile tone is enhanced in value because of the release of a somatic prespinal reflex arc. In animals recently decerebrated this increase of contractile tone selects the antigravity muscles, and their antagonists are reflexly inhibited. The increase in plastic tone rigidly maintains the extended posture, which is endowed by contractile tone upon all four limbs of the quadruped, and maintains the condition of "reflex standing" for long periods of time. When the relaxation from the posture of extension occurs, plastic tone still remains, as is proved by the presence of "lengthening and shortening reactions."

The prespinal reflex arcs subserve the two components of tone of the normal skeletal muscle, and overactivity of these arcs accounts for the phenomena exhibited by the muscle in decerebrate rigidity. It was shown by Sherrington that cutting across the medulla oblongata led to flaccid paralysis of the limbs. More precisely, as Magnus has shown, the limits within which section of the brain stem produces decerebrate rigidity are as follows: The cranial limit is a plane passing dorsally at the level of the caudal limit of the superior colliculus and ventrally in the region immediately caudal to the mammillary bodies. The decerebrate rigidity persists until the level of entrance of the eighth nerve is passed. Obviously, therefore, the nuclei that constitute the cell stations of the prespinal reflexes responsible for decerebrate rigidity lie within these limits.

The work of Thiele in 1905, which is supported by the recent results of Bazett and Penfield,²² indicates that the integrity of the lateral vestibular nucleus of Deiters is essential for the development of decerebrate rigidity. It may be concluded that this nucleus takes part in the completion of one of the reflex arcs, the hyperactivity of which is responsible for decerebrate rigidity. The vestibulo-spinal tract (Fig. 13), which lies in the region of the emerging motor root fibres of the spinal cord mainly on the same side as the nucleus from which it originates, constitutes the descending limb of the reflex arc.

The nucleus of Deiters is a special afferent somatic nucleus, and the reflex arc in which it is incorporated constitutes, therefore, the somatic prespinal reflex pathway. It subserves contractile tone, which has a selective incidence upon antigravity muscles maintaining the body erect.

The question arises whether the nerve cells incorporated in the sympathetic prespinal reflex arc can also be identified. The levels between which section of the brain stem produces decerebrate rigidity suggest that the formative reticularis of the pons supplies the cell station of this arc. The reticulo-spinal tracts of the pons are anatomically of special

* Delivered by Professor Elliot Smith at University College, February 2nd, 1925.