ORIGINAL ARTICLES

"ACUTE CHOLECYSTITIS."*

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In response to your request for some remarks about acute cholecystitis, I shall not attempt a description of the disease, but simply discuss some of the topics that come into the physician's mind when he is at the bedside with his patient.

Etiology: Nearly all cases of cholecystitis are due to the presence of micro-organisms. It is true that a traumatism may cause some inflammatory trouble, but this quickly subsides unless some microbe avails itself of the diminished resistance in the tissues to aggravate and prolong the disease; and it has been shown experimentally that toxines alone may cause irritation of the bladder wall, even haemorrhagic in character, but in a very short time the process becomes microbic so that practically all cases of cholecystitis are associated with the presence of micro-organisms.

The microbes most frequently found in the inflamed gall cyst are the typhoid bacillus, the colon bacillus, the pneumococcus, varieties of streptococci and staphylococci, and, just as in affections of other tissues, there may be mixed infections where two or more organisms are present.

At first we would be inclined to imagine that the most frequent route for the infection to travel was directly up the ducts from the intestines, but there are reasons why this should not be the case. (1) The duodenum is generally free from bacteria during health, a fact that explains to some extent why colon bacillus infection is not more frequent, although we must admit that this may not hold true in disease. (2) The periodical discharge of bile into the intestine flushes the ducts and offers a mechanical obstruction to the ingress of microbes. (3) The comparative powerful contraction of the sphincter of the diverticulum of Vater presents another obstacle.

Since specific micro-organisms have been found in the general circulation in typhoid fever, pneumonia and various other diseases, it appears perfectly possible that these agents may be carried to the gall bladder and give rise to trouble, indeed this opinion has the support of experimental evidence, but the more frequent route is the portal circulation in which bacteria that have escaped the destructive influence of the intestinal epithelium, leucocytes, and lymphnodes, penetrate the walls of the ducts or gall bladder that have already been damaged by the toxines of the disease. This injury to the tissue wall seems to be essential before bacilli within the gall bladder can cause any harm, because typhoid bacilli are almost constantly present in the gall bladder in fatal cases of typhoid fever, while cholecystitis is not a very frequent complication of this disease. In all probability the healthy mucous membrane lining the gall bladder is as resistant to bacilli, reaching it directly from the intestines, *via* the large bile ducts, as is the healthy bronchial mucous membrane to inhaled organisms, and it is only when the endothelium is injured by traumatism, biliary stagnation, or toxines and microbes attacking it from subendothelial tissues that the micro-organisms in the gall bladder can inflict any injury. This may explain why colon bacilli are frequently found in both healthy and diseased gall bladders, and why a cholecystitis due to the bacillus typhosus may not arise until ten or even twenty years have elapsed since the attack of typhoid fever.

The relation between cholecystitis and gall stones is a matter of considerable interest both from an etiological point of view and also in regard to treatment, because the symptoms of cholecystitis are not infrequently mistaken for those of cholelithiasis; surgeons have felt chagrined and patients have been rendered very indignant because an operation for the removal of gall stones has failed to discover any calculi. Gall stones are composed of cholesterin, calcium and bile pigment, alone or in combination with one another. At one time the view of Naunyn that the cholesterin in the calculi was obtained only from the endothelium lining the gall bladder was generally accepted, but this has been disproved by Bacmeister who has demonstrated that cholesterin is precipitated from the bile itself by chemical changes resulting from the action of the bacillus typhosus, the bacillus coli communis or other micro-organisms, and although endothelial particles from the gall bladder wall are not essential to the process, it is considerably hastened by their presence. This applies to pure cholesterin stones but not to those composed of lime and cholesterin, for in his opinion lime salts are an almost exclusive product of the secretory cells of the gall bladder. "As an amount greater than normal must be furnished to participate in the formation of gall stones, their presence signifies a catarrhal inflammation of the mucous membrane of the gall bladder." While therefore it is true that cholelithiasis maintains a mechanical irritation that permits the infection of the gall bladder and a consequent acute or subacute cholecystitis, it is nevertheless equally true that cholecystitis is responsible for the majority of cases of cholelithiasis with the result that the close relationship between the two often leads to symptoms being attributed to one condition which really belong to the other. There can be little doubt that the reputation enjoyed by many drugs in the treatment of gall stones is due to the fact that they relieve the cholecystitis but not that they dissolve the calculi.

An excellent example of this is in the following case of Mrs. D., age 38: I first saw her upon March 12, 1910. For many years she had suffered severe attacks of pain in the right hypochondrium and epigastrium which radiated downwards to both iliac regions but were most distressing on the left side. She had gone for months without any trouble, in fact she was perfectly free from pain during an interval of nearly six years, but it returned two years ago and gradually increased in severity so that instead of being present only for a few minutes, or at most two or three hours, it was now constant with occasional paroxysmal attacks, during which she was nauseated and could not retain food in the stomach. Her weight had fallen from 120 pounds to 87 pounds. The liver was large and tender, the gall bladder was distended below the umbilical line and very tender to pressure. Upon March 21st she was admitted to the Children's

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Hospital, where, in addition to local applications, the medication consisted of two drachms of the Elixir of Succinate of Iron three times daily together with a capsule containing Euonymin gr. ss. and Extract Cascara Sagrad and Pil. Rhei Comp. aa gr. IISS every night. She improved rapidly and left the hospital at the end of three weeks when she was perfectly free from pain but still had tenderness on pressure over the gall bladder, and had gained six pounds in weight. Four weeks later she began to suffer again from severe paroxysmal pains, which came on at intervals for four days and during this time she passed more than forty gall stones. Upon May 31 she was much more comfortable but still had tenderness over the gall bladder, with pain in the bowels from gaseous distension. In this case we have an example of a drug that allayed the cholecystitis and the patient's suffering so that she believed herself cured but did not have any solvent effect on the calculi.

In this connection Bain's experimental work upon the treatment of cholelithiasis should be remembered. He has shown that when gall stones are placed in the healthy gall bladder of dogs they disappear in about six weeks, while if a culture of bacilli coli communis is injected into the gall bladder and at the same time its walls are scraped so as to produce an infectious cholecystitis the stones do not dissolve. This not only bears out what was said a few moments ago about the influence of cholecystitis in producing calculi, but as Bain remarks, it indicates that in the treatment of gall stones we should endeavor to render the gall bladder healthy rather than attempt to dissolve the stones in situ by giving solvents which act upon the stones outside the body.

Symptoms. It is not possible to differentiate with certainty between the catarrhal, suppurative and gangrenous forms of cholecystitis; as in appendicitis, we can only infer the existence of one or other from the intensity of the symptoms. The number of adhesions about the gall bladder that are found at surgical operations and at post mortem examinations warrant the suspicion that mild attacks of cholecystitis are by no means uncommon and that they are so evanescent as to be overlooked by the patient, or that we ourselves on account of the absence of colic, jaundice or distended gall cyst, have misinterpreted the symptoms presented by the patient.

In the majority of cases the temperature is but moderately, if at all, increased, in fact, variations in the pulse rate are of more prognostic value than is the presence or absence of fever.

Pain and tenderness are important symptoms but vary in their distribution so as to make errors in diagnosis easily possible. The pain may be of a steady, dull aching character, possibly when the serous covering of the gall bladder is affected, but more frequently it is paroxysmal in character, resembling that of gall stone colic. It is most frequently felt a little way above the umbilicus and to the right of the median line, but at other times it is in the epigastrium, the right iliac fossa or diffused over a considerable area of the abdomen, or it may be referred to the right shoulder or a point below the right scapula. Occasionally the tenderness can only be elicited by dipping the fingers below the margin of the liver and pressing upwards towards the gall bladder. Full inspiratory movements are suddenly arrested by the production of severe stabbing pain similar to that experienced in diaphragmatic pleurisy, so that the real nature of the attack is not infrequently overlooked and the patient is supposed to be suffering from the latter disease. We cannot see many of these cases without wondering what causes the pain and why it is so erratic in its characteristics.

It is generally conceded that, like the stomach and intestines, the gall bladder is not sensitive to ordinary painful stimuli, and it is questioned whether the painful sensations are ever really felt in the nerves of the viscus itself, or whether an abnormal stimulus in the viscus is transmitted to the cord and there diffuses to adjacent pain nerves so that the painful sensation is felt not in the viscus but in the cutaneous distribution of these secondarily stimulated nerves; or it may be that, since the normal distribution of nerves to the several parts of the body is in harmony with promoting the functional activity of that part and protecting it from injuries to which it may be exposed, there is no necessity for the viscera being endowed with sensibility to the same tactile and painful stimuli as the body surface since they depend upon the abdominal and thoracic walls for protection against external agents. Perhaps, however, it is possible that abnormal processes going on in the viscera may give rise to abnormal stimuli which are capable of producing pain in the viscera themselves. Although the existence of true visceral pain in response to special stimuli is still a matter of doubt, there cannot be any question that the sensation is diffused to adjacent nerves in the cord and gives rise to cutaneous pain and sensitiveness in the area of their distribution; hence we find the radiating character of the pain and the tender nodes upon the body surface.

We notice two kinds of pain in cholecystitis, the paroxysmal and the continuous, and both of these are due to increased tension. In acute cholecystitis there may be some swelling or other condition causing narrowing of the lumen of the bile duct; this will tend to produce accumulation of bile or inflammatory exudate in the gall bladder and a spasmodic contraction of its muscular wall in an attempt to expel it, similar to what takes place when feces accumulate in the intestine, hence the paroxysmal pain. The continuous pain on the other hand is due to the increased tension produced by infiltration of the gall bladder wall itself. The radiation of pain in many cases can only be explained by the presence of adhesions between the gall bladder and other organs. It is very common in cholecystitis to have pain in the region of the appendix and this may be due to a variety of causes. (1) There may be an associated appendicitis arising from a simultaneous infection, or, as has been suggested, the infecting micro-organisms in a cholecystitis may be derived from an inflamed appendix. (2) The gall bladder is sometimes so enlarged as to reach into the right iliac fossa and give rise to the appearance of a perityphlitic abscess. (3) There may be adhesions between the gall bladder and the peritoneal covering of the intestine giving rise to intestinal disturbance most acutely felt in the region of the ileocecal valve. The following case is fairly typical of the appendicial pain found in these cases. In

September, 1909, Mrs. W., aged fifty, consulted me regarding pain in the region of the transverse colon and gall bladder, and informed me that some years ago she passed several biliary calculi. The area of hepatic dullness was normal but there was marked circumscribed tenderness over the gall bladder. Cholecystitis and cholelithiasis were diagnosed. Under treatment the distressing symptoms disappeared and the patient regained her usual health. On May 13th, 1910, after considerable excitement and fatigue, she was attacked with headache, nausea and vomiting; pain and tenderness in the upper right abdominal quadrant with a maximum over the gall bladder, also diffuse pain and tenderness in the right iliac fossa, including McBurney's point, but the most intense tenderness was in the skin over the crest of the ilium. The fever disappeared in twenty-four hours and the pain was much mitigated. In six days the pain had entirely subsided, there was not any tenderness in the iliac region, but distress was severe whenever the gall bladder was palpated. Evidently this was an acute exacerbation of a chronic case of cholecystitis with local parietal peritonitis over the enlarged gall cyst, and the pain was transmitted downwards in the cutaneous nerves, as a result of the peritonitis, to the crest of the ileum and iliac region. The absence of special tenderness over McBurney's point made it improbable that the appendix was involved.

The following case is also of interest: A. J., age 42, a laborer, complained of fever and nausea together with severe pain in the right hypochondrium which was aggravated upon any attempt to take even a moderately full inspiration. No marked enlargement of the gall bladder could be detected but there was extreme tenderness on palpation over it. In a few days the acute symptoms disappeared, but more or less pain and tenderness persisted over the gall bladder and increased in severity whenever the stomach was distended by a full meal or when the patient bent over forward. As this condition did not improve after about four weeks the patient was referred to a surgeon with a diagnosis of cholecystitis and cholelithiasis and the suggestion that surgical exploration of the gall bladder was probably the best course to pursue. It was with some chagrin that a few days later a message was received from the surgeon to the effect that I had made an error in diagnosis and had mistaken a case of chronic appendicitis for diseased gall bladder; that he had removed the appendix after finding some adhesions as evidence of old inflammatory process, that he believed the gall bladder to be healthy because while the patient was still under the anesthetic, he had introduced his finger into the abdominal cavity through the incision in the iliac region and reaching upwards failed to discover that it was particularly enlarged or contained biliary calculi. The patient returned to me within one month of his operation still complaining of pain over the gall bladder but refusing further operation, and from time to time I saw him during the subsequent three years still suffering from his attacks of pain but without his appendix. In this case I blame myself that knowing the frequent co-existence of appendicitis and cholecystitis, I did not make a more thorough examination in the vicinity of the ileocecal valve to discover whether there were any signs of the appendix having been injured in former attacks, and thus have been in the position to prepare the patient for the possibility of a double operation, and I blame the surgeon that with the history and diagnosis given him he should have satisfied himself with such a crude examination.

The pain in the shoulder is probably due to the relationship between the phrenic nerve and a branch to the subclavius muscle.

It not infrequently happens that the patient suffering from cholecystitis cannot adopt certain positions without inducing pain and this is probably due to traction upon adhesions to the parietal peritoneum, or the pressure of other organs upon the diseased gall bladder. Thus when the patient lies upon his side there may be a dragging pain due to the weight of the liver making traction upon the adhesions and it is especially liable to occur where the abdominal walls are lax and do not give the normal support to the viscera.

The tenderness of the inflamed gall bladder to pressure is a prominent symptom and is somewhat difficult to explain when we are confronted with the fact that the healthy gall cyst is apparently insensitive to ordinary painful stimuli. Probably it is analogous to what was observed by Mackenzie in his well known case of bowel resection. He had to operate for the relief of umbilical hernia in a patient who refused to be anesthetized. After the abdominal cavity had been opened the rest of the operation was performed painlessly. Dr. Mackenzie says: "I was able to detach adhesions from the liver and bowel, to resect a piece of bowel and mesentery, and to stitch these structures without the patient experiencing the slightest sensation. But I found that he occasionally groaned with pain when I was not touching him, and watching to see the cause I found that the upper part of the resected bowel, which was laid on one side in a warm aseptic cloth, occasionally passed into peristalsis, contracting from a wide tube into a thick fleshy rod; when this happened the patient groaned with pain. I asked him where he felt the pain and he passed his hand invariably over the umbilical region. I started the peristalsis several times by slightly pinching the bowel, and each time the patient felt the pain. Here before my eyes was the cause of the pain, and the seat of origin of the pain was at least twelve inches away from the part in which the pain was felt." The argument is that pain in visceral disease is of a reflex character, the apparent impulse arising in the viscus and passing to the cord where, on account of its intensity or abnormal character, the stimulation extends to neighboring centers and from these, sends a sensory impulse to the brain, so that the resulting sensation is referred by the brain, not to the viscus, but to the peripheral distribution of the sensory nerve. This is described as a viscero-sensory reflex and its object in such cases as the present is to call into play such structures as Nature has interposed for the protection of the viscus and hence we find the abdominal muscles over the gall bladder thrown into a state of tonic contraction and constituting another symptom or sign found in diseases of the abdominal viscera.

It is not always possible to palpate the gall bladder because unless there is some degree of obstruction of the cystic duct, the distension may be comparatively slight. As a rule, however, the lining of the cystic duct is swollen so that the inflammatory exudate cannot pass through it and consequently the gall bladder may be felt as a pear shaped mass generally movable from side to side, but occasionally

fixed in position by peritoneal adhesions. A condition, however, may arise that not only makes it impossible to feel the enlarged gall cyst but has led to errors in diagnosis. I refer to paralysis of the intestine caused by extension of peritonitis from the gall bladder to the intestine. This may give rise to local distention of the intestine so that the gall bladder cannot be detected by the most careful palpation, or the distended loop of intestine may lie across the neck of the gall bladder and give rise to a tympanitic area between the head of the tumor and the margin of the liver, but the fact that it moves up and down with the respiratory movements should make us suspicious of its real character. When the paralysis affects the hepatic flexure of the colon, the bowel is liable to become obstructed and distended, but the extreme tenderness upon palpating over the right hypochondrium indicates to some extent the origin of the trouble.

It is not uncommon to find a prolongation downwards of the right lobe of the liver in patients suffering from cholecystitis and the formation of this Riedel's lobe, as it is frequently designated, is regarded by some as being secondary to the gall bladder disturbance. I have seen several instances of this formation but as there was no opportunity of discovering when the enlargement commenced and as they all ocurred in women, it has been a matter of doubt whether the two conditions were not produced by a common cause, such as the pressure of corsets rather than in the sequence of cause and effect to one another. The mere fact that the lobe grew smaller as the cholecystitis improved did not help to solve the question, as the treatment for each condition is almost identical.

Treatment: The medical treatment only applies to the catarrhal variety of cholecystitis. Rest in bed, and warm applications to the abdomen will be found of service in most cases. Occasionally it may be necessary to resort to the hypodermatic injection of morphin but from its tendency to cause constipation this should be avoided if possible and an attempt made to attain the same end by the use of poultices or compresses containing laudanum. The medicinal treatment demands that the bowels should be kept clear by means of mild laxatives, and remedies such as salicylate of soda, urotropin and methylene blue have been used on account of their supposed direct action on the gall bladder. My best results have been from the use of sodium glycocholate in five grain doses every night for three or four nights and repeated after an interval of five or six days, this intermittent administration being maintained for some weeks. At the same time dessertspoonful doses of an elixir of succinate of iron, equivalent to five grains of the succinate, were administered. This last remedy does not appear to have the recognition that it merits, possibly because it was vaunted as a cure for gall stones which is very doubtful, as in all probability it has not any direct effect upon the calculi, but in view of Bain's experiments, mentioned in an earlier part of this paper, which showed that calculi could be dissolved in healthy bile, it is possible that in some instances where the succinate of iron relieved the cystitis small biliary calculi may have been dissolved in the bile. I have knowledge of patients who more than twenty years ago were given this remedy on account of paroxysmal attacks of pain in the gall bladder, believed to be due to gall stones, and who have remained free from the attacks since that time. You may remember that in the case of Mrs. D., already mentioned, the patient was rapidly relieved from pain from which she had suffered continuously for months and subsequently passed a large number of gall stones; also that Mrs. H. experienced similar relief and was able to resume her duties within a very few days from the beginning of a severe attack; and the following additional case may be of service in further illustrating the therapeutic value of the remedy:

Case of Mrs. L. W., age 33. Consulted me on January 9, 1909, on account of pain in the right hypochondrium, which had been almost constant for the last eight months and was aggravated by coughing or deep inspiration. She could not lie upon her left side on account of this position producing a dragging pain in the right side. There was no enlargement of the liver nor of the gall bladder but pressure over the latter was painful. Her appendix was removed eighteen months ago. There was not any tenderness over the intercostal nerves, heart and lungs were normal, and the kidney was found in its normal position. The glyco-cholate of soda and the succinate of iron were administered as already described and on February 5, 1909, she reported as feeling perfectly well. I saw her in May, 1910, when she had a bilious attack but there was not any return of the gall bladder symptoms.

Many other cases could be brought forward but those already mentioned are sufficient to illustrate the beneficial results that frequently follow this line of treatment.

All cases of catarrhal cholecystitis do not yield to medical treatment, but many pass on to a chronic stage or rapidly become suppurative. In suppurative, phlegmonous or gangrenous cholecystitis there should not be any delay in adopting surgical methods, and even in cases which have become of a chronic catarrhal nature and cannot be relieved by medication, the question of operative measures should be considered just as in appendicitis, for there is always a strong possibility that calculi will form, and there is also the risk of recurrent acute attacks, any one of which may put the patient in jeopardy. Under such circumstances, the age, general condition of the patient, the severity and frequency of the exacerbations, their influence upon nutrition, must all have careful consideration and aid us in coming to a conclusion. It is not my province to discuss surgical technic, but I would only remind you that these operations can now be undertaken without the dangers consequent upon the use of ether or chloroform, by simply injecting into the abdominal wall in the vicinity of the proposed incision, a half per cent. solution of novocain to every twenty cubic centimeters of which one drop of a one in one thousand solution of adrenalin chlorid has been added. When injected in a proper way this produces perfect anaesthesia of the abdominal wall, and, as the viscera are insensible to ordinary painful stimuli, the gall bladder can be opened and drained without the patient experiencing any discomfort. This being the case there cannot be the excuses that formerly existed for advising delay.