Original Articles.

GALL-BLADDER INFECTION IN TYPHOID FEVER,

With the Report of a Case in which Tapping the Gall-Bladder Resulted in Cure.[1]

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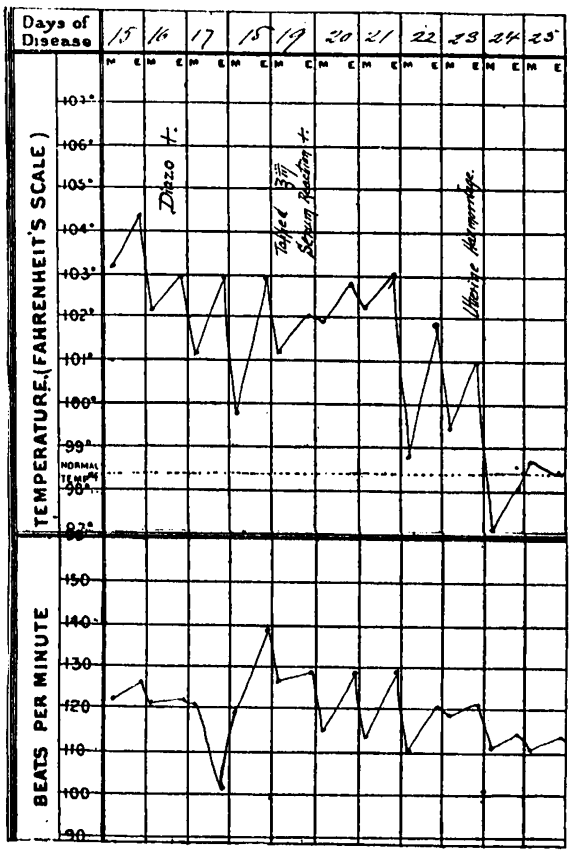
Inflammation of the gall-bladder, sometimes resulting in ulcerative perforation or in rupture from distention with consecutive peritonitis, has long been noted as an occasional complication in fatal cases of typhoid fever. The clinical evidences of this condition have usually been masked by the general abdominal symptoms of the disease so that the localization of pain or tumer in the region of the gall-bladder and the recognition of this appendage as the immediate source of danger have not been practicable. Therefore, most of the recorded cases, some forty in number, have been post-mortem discoveries; or, if the state in question has oftener been surmised at the bedside, it has seldom been the subject of accurate observation or of surgical interference. There are a few instances, however, in which this localized inflammation presents such striking symptoms that its seat and nature can be determined and thus impending danger may be averted. Such an instance affords the basis for this paper, in which I will relate the history of a case of typhoidal cholecystitis and then refer to the literature bearing upon this subject and the deductions to be drawn therefrom.

A woman, aged thirty, entered the Boston City Hospital in the third week of typhoid fever, with dry, brown tongue, palpable spleen, rose-spots and distended abdomen. Anorexia, vomiting and constipation had been prominent symptoms. Widal's serum test was positive, but not immediate; clumping of bacilli and loss of motility in fifteen minutes. Leucocytes, 9,600. Typhoid deafness. Toward the end of the third week she complained of increasing abdominal pain that became localized in the right hypochondrium, where a tumor four inches in diameter developed, extending from the costal border toward the umbilicus. This tumor caused a visible swelling, was very tender, absolutely dull on percussion, and descended on full inspiration. At the time of admission, a week earlier, the liver dulness had been normal, and there was no special pain in this region. Now the patient's condition showed partial collapse, and as suppurative distention of the gall-bladder was thought to be present, my surgical colleague, Dr. George W. Gay, saw her in reference to an early laparotomy because rupture of the gall-bladder seemed imminent. Her state was regarded as unfavorable to the success of a capital operation, therefore I at once tapped the gall-bladder at a point one inch below the costal margin and four and a half inches from the umbilicus. Three and a half ounces of sero-purulent fluid were withdrawn, pale in color, looking more like urine than bile. The aspirating needle moved up and down with the action of the diaphragm. No gall-stones could be felt with the point of the needle. After its withdrawal a pad and swathe were applied to prevent the escape of septic fluid into the peritoneal cavity. The relief to pain was immediate. The next day all urgent symptoms had disappeared, and they did not return. The pulse fell from 140 to 120, and defervescence followed in five days. The gall-bladder gradually retracted; convalescence ensued; and when the patient returned for observation a month later, nothing abnormal was found in this region. (A photograph and chart were presented, together with a specimen of the fluid withdrawn. The chart is herewith produced.)



The following report was made by Dr. R. M. Pearce, assistant to Dr. Councilman in the Pathological Laboratory of the City Hospital:

The fluid is of a pale yellowish color, watery consistency and fecal odor, with considerable fine, yellowish sediment, in which fine reddish-yellow granules could be seen. Specific gravity, 1.016; albumin, one per cent.

Fresh examination, microscopically, shows much bile pigment, numerous cholesterin crystals, pus cells and epithelial cells, most of the latter being granular and some fatty.

Sediment stained with Löffler's methylene blue shows pus cells, epithelial cells, and numerous short, thick bacilli with rounded ends, occurring singly and in pairs, and usually in the pus cells, arranged in clumps around the nucleus.

Cultures show round, flat colonies with elevated centres, of pale white color, almost transparent; microscopically, short, thick bacilli with rounded ends and very motile. No other bacilli.

Cultures from dilutions, planted on potato, produced invisible growth; in litmus milk no reddening or coagulation; in sugar gelatin no gas production. Flagella stained.

With serum from a known typhoid case characteristic clumps, with loss of motility, were produced. The same reaction was produced with the patient's own serum.

Diagnosis: Typhoid bacillus.

December 7th, 3 P. M. A guinea-pig was inoculated subcutaneously with one cubic centimetre, and one cubic centimetre intra-peritoneally of forty-eight-hour bouillon culture.

[1] Read before the Association of American Physicians, May 4, 1897.

A large, subcutaneous abdominal abscess developed, which burst and discharged.

December 20th, 1 P. M. Pig killed. Autopsy showed general edema of abdominal tissues; marked enlargement of inguinal and axillary glands; large slough, two centimetres in diameter, at seat of inoculation; fluid in abdominal and pleural cavities; marked enlargement of mesenteric and retro-peritoneal glands; spleen enlarged, reddened, follicles distinct; Peyer's patches enlarged; intestinal tract otherwise normal. No changes apparent in other organs.

Dr. S. W. Ellsworth, house physician, used pure cultures of the bacilli found in this fluid in further clinical tests for Widal's reaction, as follows:

With the serum from eight cases of typhoid fever the characteristic clumping and loss of motility were quickly obtained.

With serum from one case each of malaria, pneumonia, phthisis and rheumatic fever the results were negative, as they also were in further testings of the serum from these cases with a pure culture of typhoid bacilli from a spleen.

The records of the Boston City Hospital, so far as I am aware, contain but three other cases of this complication in typhoid fever, and these occurred in the same family, as reported by Dr. C. Ellery Stedman in the third Series of City Hospital Reports, 1882.[1]

They are, briefly, as follows:

CASE I. A girl, aged thirteen, died on the 24th day with symptoms of peritonitis. At the autopsy the usual lesions of typhoid fever were found, and in addition adhesive inflammation in the region of the gall-bladder, which was glued to the colon at the junction of the ascending and transverse portions. The fundus of the gall-bladder was ulcerated and ruptured, and there was a pint and a half of yellowish serum in the abdominal cavity. No gall-stones.

CASE II. A girl, aged six, sister of the above, died of typhoid fever on the 28th day, and the post-mortem examination showed extensive peritonitis, with a pint of sero-purulent fluid in the abdominal cavity. There were three perforations of the gall-bladder and extensive ulceration of its inner surface.

CASE III. Male, aged sixteen, brother of the above, developed a tender, rounded tumor in the region of his gall-bladder in the second week of typhoid. This gradually subsided, and the patient made a good recovery.

LITERATURE.

In examining the history of this subject during the past sixty years we find some forty cases recorded in which destructive inflammation of the gall-bladder during typhoid fever has attracted attention as a matter of special interest, usually after death. Few of the earlier, and almost none of the later, works on medicine give it more than a passing mention, and the unusual localization of the lesion so *bizarre*, as it was termed by a French writer, has until recently found no satisfactory pathological explanation.

Louis in his work on "Typhoid Fever"[2] states that "changes in the bile and gall-bladder are much more frequent in the course of the typhoid affection than in that of other acute diseases." He cites three fatal cases in which cholecystitis, unrecognized during life, had supervened. In two the gall-bladder was filled with a "transparent, aqueous, diaphanous or urinous liquid" and in one case the cystic duct was obliterated.

Similar cases are mentioned by Andral, Grissolle, and by other writers in the French journals since 1835, to which reference is made at the end of this article.

In the German writings before 1890 are several communications based upon the discovery of post-mortem typhoidal lesions of the gall-bladder, but I will mention only the observations of Rokitansky and Frerichs and Hölscher's autopsy records.

Rokitansky[3] speaks of fibrinous exudations of a "diphtheritic" character as occurring within the gall-bladder and ducts in typhoid fever, cholera and pyemia, their existence being indicated by no symptoms during life and only determined by post-mortem examinations. This is not an adequate description of the process under discussion.

Frerichs[4] on the other hand, found the gall-bladder filled with a turbid, ash-colored, albuminous fluid, of neutral or feebly alkaline reaction, in three cases of typhoid fever and one of typhus. In two cases bile-pigment and biliary acids were entirely absent; in the other two small quantities of these substances and some leucine were found. The lining membrane of the gall-bladder and ducts was softened and pale. There were no gall-stones, and no jaundice or other hepatic affection was present.

Frerichs also gives the following description of a case that recovered:

A female, aged twenty-six, on the 13th day of a typhoid fever had attacks of vomiting, and two days later a very painful, pear-shaped tumor was found in the right hypochondrium in immediate connection with the liver above. It gave a muffled, tympanitic percussion tone. There were no signs of biliary obstruction. Leeches and cataplasms were applied. The vomiting ceased altogether; nausea continued for many days. Pain and tension diminished, and the boundaries of the tumor contracted until, in the fourth week, convalescence ensued, although the gall-bladder could be felt for a long time.

There is a noticeable similarity between this history and that of my case, except that the withdrawal of the fluid enabled us to determine both its source and cause by methods that were not formerly available.

In Hölscher's[5] 2,000 typhoid autopsies marked hepatic degeneration was found in more than ten per cent. of the cases. In 22 only jaundice was present, and in but five was purulent inflammation of the gall-bladder discovered. In a single case there was perforation with circumscribed peritonitis.

Courvoisier,[6] in his elaborate work on "The Pathology and Surgery of the Biliary Passages," records 10 fatal cases of typhoid cholecystitis, two with gall-stones and phlegmonous infiltration of the gall-bladder walls, and seven with sero-purulent exudate, occasional ulcers and necrotic areas. In four cases of perforation no gall-stones were present.

Among English authorities Budd[7] relates a case which came under his care in 1849:

CASE. A female, aged eighteen, entered King's College Hospital in the second week of typhoid fever. During the third week she lay delirious, on her back, with legs drawn up, and gave signs of pain when the region of the liver was pressed upon. "On the 19th day," says Dr. Budd, "when I made pressure on the belly to the right of the epigastrium she uttered a loud shriek. I now discovered a fulness in that part of the belly, and inferred that there was inflammation of the gall-bladder or that an abscess existed in the liver." Chills and vomiting followed, but the patient

lived two weeks longer. There was no jaundice. Autopsy showed a distended gall-bladder, an inch and a half below the liver-margin, with recent peritoneal adhesions to the surrounding parts. It contained considerable puriform fluid and fourteen gall-stones, one of which completely blocked the cystic duct. They consisted of a cholesterine with nuclei of inspissated bile. The liver itself presented no unhealthy appearance. Extensive ulceration of Peyer's patches.

Budd remarks that "suppurative inflammation of the gall-bladder seems especially liable to occur when by any cause the cystic duct is permanently closed."

He regards the purulent and ulcerative inflammations of the gall-bladder in typhoid as similar to the appearances observed in the violent remittent fever that prevailed with great fatality among the British troops on the Island of Walcheren in 1809, in the fever of Sierra Leone and in yellow fever.[8]

Murchison, Harley and Hale White make special reference to the cholangitis and cholecystitis that may attend typhoid fever.

Murchison[9] states that in this disease "fatal peritonitis may result from ulcerations of the gall-bladder proceeding to perforation." He cites the case of a youth who on the 15th day was seized with symptoms of peritonitis and died within twenty-six hours. The cause of death was perforating ulcer of the gall-bladder which had allowed bile to flow into the peritoneum.

This author further says: "The lining membrane of the gall-bladder is very liable to become inflamed in enteric fever without producing any marked symptoms during life. This inflammation is sometimes catarrhal, with pus formation; at other times, according to Rokitansky, it is diphtheritic. Thirdly, it may take the form of ulceration, as in cases recorded by Andral, Jenner and Trousseau, and the process may end in perforation and fatal peritonitis. In a large proportion of cases when the disease has lasted three or four weeks the bile is thin, watery, almost colorless, of low specific gravity, 1.010 to 1.016 instead of 1.026 to 1.030."

Murchison mentions several other cases by different authors as well as in his own practice.

Harley,[10] after commenting upon the usual hepatic degeneration in typhoid, says that he constantly found the bile thin, watery and of low specific gravity, giving slowly and faintly the characteristic reactions when tested with the mineral acids or by Pettenkoffer's test. It was sometimes excessively acid, and in one case, examined twelve hours after death, had a strong smell of sulphuretted hydrogen. Harley's view of these biliary changes is that the hepatic secretion becomes vitiated either by prolonged vascular congestion or through "the effect of some morbid agent carried by the portal vein from the intestinal surface into the liver," which may, at an early period in the disease, cause torpidity of that organ and more or less complete cessation of its functions.

Although our own authors have not made such extensive reference to the biliary complications of typhoid fever as the writers to whom I have referred, they mention the danger to life that may arise from suppuration within the gall-bladder; and beside the cases of Dr. Stedman previously quoted, I have found a few others.

Dr. Daniel Ayres[11] in 1846, described "A Case of Perforating Ulcer of the Gall-Bladder complicating Continued Fever."

Case. A young hospital interne, during convalescence from typhoid fever, was taken with acute pain in the right hypochondrium and died of peritonitis. At the autopsy a perforating ulcer at the fundus of the gall-bladder was found and the abdominal cavity contained ten ounces of biliary fluid, serous in character. The ducts were patent and there were no gall-stones.

Ayres mentions the cases of Budd and Louis, which were then recent, and, after alluding to their analogy in this respect with yellow fever and other diseases of tropical climates in which inflammation and ulceration of the gall-bladder may occur as a sequence to biliary derangements, he concludes that "perforation generally supervenes upon a previously diseased state of the gall-bladder and very rarely appears in the course of acute diseases without such a cause."

An interesting case is reported by Dr. William Pepper,[12] and is quoted by Frerichs as bearing upon this subject:

Case. A man, twenty-six years old, had a prolonged bilious fever, and came under the care of Dr. Pepper six months later with severe pain and a tumor in the right hypochondrium which gradually extended as far as the crest of the ilium. It was tapped, and a few ounces of muco-purulent fluid were withdrawn. After death the gall-bladder was found enormously distended by two quarts of semi-purulent fluid. The walls were ulcerated, and the cystic duct was completely closed by exudate. No gall-stones were present. There were two small abscesses in the right lobe of the liver.

The most comprehensive study that had then appeared (in 1876) is contained in the Paris Thesis on "Cholecystitis in Typhoid Fever," by Hagenmüller.[13] Eighteen cases from French and German reports are collected. In four cases there was slow recovery; in the others, death from peritonitis, the affection of the gall-bladder having been unrecognized during life. Hagenmüller's conclusions were that typhoidal cholecystitis, apparently so rare, will be more frequently observed when attention is awakened to the subject; that it results from the propagation of the intestinal inflammation to the gall-bladder, owing to low systemic conditions; that the diagnosis must be based upon the localization of pain in the right hypochondrium or in some cases upon intumescence of the gall-bladder; and that fatal peritonitis may result from perforation or from simple extension of the inflammation to the peritoneum by contiguity. In but two cases were gall-stones found, and rarely did the inflammation involve the liver substance.

During the past decade only has it been possible to apply the methods of bacteriological research to these obscure lesions and to trace the gall-bladder infection directly to the typhoid bacillus.

In 1890 Gilbert and Girode[14] reported the first case of suppurative cholecystitis caused by the invasion of typhoid bacilli, as demonstrated microscopically and by cultures. In 1893 the same authors presented a further communication relating to the same subject.[15]

Case. A woman, aged forty-five, during a moderately severe typhoid fever had symptoms referable to the gall-bladder, pains and a swelling in that region. With convalescence the swelling diminished, but after a considerable interval the symptoms returned, and on re-admission to the hospital, five months after the termination of the typhoid attack, cholecystotomy was performed. The gall-bladder contained pus which

gave a pure culture of typhoid bacilli, and there was also a small calculus.

E. Dupré in a comprehensive thesis on "The Biliary Infections"[16] gives two cases (Observations VII and IX) in which he had made pure cultures of the typhoid bacillus from the gall-bladder. The first was that of a man, forty-six years old, who died on the 16th day of his fever. Although the gall-bladder presented no apparent pathological changes, pure cultures of Eberth's bacillus were obtained. The second observation relates to a woman, forty-five years old, who died from an operation for gall-stones, performed six months after recovery from typhoid fever. The discovery of typhoid bacilli in both gall-bladders led the author to think that this infection was more common than was supposed.

In 1892 Guarnieri[17] found an infection of the biliary passages, liver and spleen by the typhoid bacillus in a case that presented no intestinal lesions.

Chiari's[18] report of a case of destructive cholecystitis, in which the pathogenic organisms of typhoid fever were found, was one of the first on this subject.

CASE. A boy, twelve years old, after six weeks' illness with typhoid fever, died, apparently of a terminal pneumonia. At the autopsy the classic intestinal lesions of typhoid fever in a convalescent state were found, also broncho-pneumonia. The gall-bladder was full of pus and had several necrotic patches on the walls. Externally was a fibrinous exudate with adjacent peritonitis. The biliary ducts and duodenum were normal. The cause of death was cholecystitis, which had provoked peritonitis. Typhoid bacilli in pure culture were found in the pus and in the gall-bladder walls.

The author regarded his case as second to the one reported by Gilbert and Girode.

Chiari[19] made a further report to the International Medical Congress in Rome, giving the results of his examinations of 22 patients who died of typhoid fever. In three only were the typhoid bacilli absent from the gall-bladder. In 15 they were the only kind, and the number was often very great. Inflammation of the gall-bladder had occurred in 13 cases, in 12 involving only the mucous lining, in one the whole wall and causing a secondary peritonitis by extension. Chiari concludes that the occurrence of typhoid bacilli in the gall-bladder is the rule in typhoid fever, and that they increase and may remain there a long time; finally that they may cause gall-stones and relapse.

There are several questions of interest that suggest themselves in connection with these various reports, clinical and pathological:

(1) How do the germs reach the gall-bladder?

(2) Have they a special predilection for previously damaged gall-bladders or those containing gall-stones?

(3) Is it probable that typhoid fever may cause gall-stones?

(4) What are the means available for diagnosis and treatment?

CHANNEL OF INFECTION.

The sterility of normal bile is not questioned so long as the ducts are pervious and the flow is free, but when there is disease of the biliary passages by which the bile current is checked, micro-organisms from the duodenum find easy access to the gall-bladder. Charcot and Gombault after tying the common duct in animals found that the bile above the ligature was infected by bacteria within a short time. Numerous other observations have confirmed this, and Létienne[20] examined the bile immediately after death in forty-two patients who died of various diseases finding micro-organisms in twenty-four, or more than half. The bacterium coli commune was often observed, but there seems to be no reason why this germ should not always invade the gall-bladder after death. Naunyn[21] found it in the fluid removed during life in several cases of recent cholecystitis.

Whether in typhoid fever and in other infectious diseases there may be a stagnation in the bile-current and a vitiation in quality, as suggested by Harley, that allow the ready invasion of intestinal germs, or whether this may be preceded by a catarrhal cholecystitis engendered by the passage of the typhoid bacilli through the portal circulation, cannot be easily determined. Both channels are open. It has been shown experimentally by Pisenti[22] that the amount of bile secreted is diminished from one-half to two-thirds during septic fever in animals, and the same tendency may be assumed to be present in some degree during typhoid fever.

As to infection through the blood-stream, it is held by Sherrington[23] that "though the blood be teeming with micro-organisms none can escape through the normal hepatic tissues, and it is only when the latter have been damaged by toxins in the blood, formed by the life of the bacteria, that the tissues allow the germs to pass through them." Experiments by Blachstein[24] and others showed that after the intravenous inoculation of animals with the typhoid bacillus the gall-bladder in numerous instances was infected ten or twelve days later. In two rabbits these organisms were found to be very active in the bile after very long periods, from three to four months.

It is a matter of common observation that the bacilli of typhoid are voided with the urine, which they must reach, according to the observations of Flexner,[25] through the glomerular capillaries, and there appears to be sufficient proof that the hepatic secretion is contaminated in a similar manner through the portal circulation. The suggestion of Chiari that germs may pass directly through the intestinal wall to the gall-bladder cannot be substantiated although the fecal odor is probably thus imparted.

Therefore we must conclude that infection of the gall-bladder takes place by the passage of micro-organisms through the biliary ducts with the supplementary agency of a contaminated blood-current.

RELATION OF GALL-STONES TO ETIOLOGY.

Recent studies (Naunyn,[21] Courvoisier,[6] Brockbank,[22] Mayo Robson[26]) leave no doubt that gall-stones render the biliary ducts and gall-bladder more receptive to infecting microbes, especially if either the common or the cystic duct is obstructed. The presence of calculi in a typhoid-fever patient would undoubtedly favor the occurrence of accidents from severe gall-bladder infection, and this is substantiated by the post-mortem evidence in some of the cases previously cited, since about one-fourth of the patients who died with typhoidal cholecystitis were found to have gall-stones. But in the great majority of cases no calculi were present and no evidences of previous local lesions. Moreover, several were in childhood, more in the adolescent period of life, when gall-stones

are comparatively rare. Therefore it may be assumed, in view of Chiari's discovery of Eberth's bacillus in the gall-bladder at nearly all his typhoid autopsies, that the pre-existence of gall-stones is not an essential feature in the infective process.

TYPHOID INFECTION AS A CAUSE OF GALL-STONES.

There is more ground for the supposition that typhoid fever, through gall-bladder infection, may be an important factor in the etiology of gall-stones.

Bernheim[27] suggested this sequence, stating that he had seen three or four times veritable accessions of biliary colic in the course of typhoid fever in subjects who had never had such attacks before. "May not typhoid fever," he asks, "produce alteration or stagnation of bile and thus determine the formation of gall-stones?"

The prolonged vitality of the typhoid bacillus within the body is well known and is instanced by the two cases previously cited, in which pure cultures were obtained from the gall-bladder in patients who came to operation for calculous cholecystitis five and eight months respectively after the termination of the fever.

A similar report by Chautemesse[28] relates to a case of grave typhoid with slow convalescence. Six months later, after an interval of perfect health, biliary colic appeared for the first time with icterus from obstruction. Surgical operation. Gall-stones. Pure culture of typhoid bacilli from the gall-bladder.

Especially interesting as bearing upon this point is the communication of Dr. Dufourt, of Vichy,[29] on "The Rôle of Typhoid Fever in the Etiology of Biliary Lithiasis." Nineteen patients with gall-stones had their first attacks of colic after severe typhoid fever. These attacks came on as early as the second month after the fever in two cases; in the third month in six cases; in the fourth month in three; and in the fifth month in one; while the remaining five dated their first symptoms at ten months or later after recovery from the fever. Such cases may be classed with the so-called "hepatic typhus" of French writers.[30]

Whether the micro-organisms may cause a chemical precipitate in the gall-bladder from which cholesterine calculi are formed, or whether the bacilli themselves act as nuclei, is a matter for further study, but stagnation of bile, an important factor in stone formation, may be assumed to be present in typhoid fever. Naunyn states that he has found micro-organisms in the centre of a few bilirubin-calcium calculi, but this is very exceptional.

REINFECTION AND RELAPSE.

Chiari thinks that the possibility of re-infection through the intestine by bacilli from the gall-bladder should be considered. The occurrence of relapse in typhoid is an arbitrary matter and inexplicable. The belief that it is caused by the resumption of solid food *per se* is untenable. In certain cases the gall-bladder becomes a stagnant reservoir of typhoid bacilli, so to speak, under conditions favorable to prolonged and virulent activity. Therefore it is by no means impossible that an increase of food, by exciting a stronger flow of bile, may send back to the intestine a new growth of organisms which in turn cause those exacerbations and relapses that are often attributed to errors of diet.

PATHOLOGICAL CHANGES.

The pathological changes that have been noted involve the gall-bladder, the ducts and the peritoneum. The cholecystitis may be catarrhal with an exudate which at first is mostly serous. In other cases it is entirely purulent. Ulcers, often multiple, are found chiefly at the fundus, but they may cause perforation at the neck or elsewhere. Abscess involving the wall alone has been observed and in some instances the gall-bladder is destroyed by gangrenous inflammation.

In many cases the ducts have been free, with little evidence of cholangitis. In others impacted gall-stones were found, and jaundice is mentioned not infrequently. It cannot be supposed that great distention of the gall-bladder occurs without obstruction, although this may not be apparent after death if rupture has taken place. Brockbank[31] states that "the cystic duct is curved like the letter S in its course between the neck of the gall-bladder and its junction with the hepatic duct, and pressure on it from a full gall-bladder, whether the fulness be caused by calculi or fluid only, will, at times, obliterate its lumen and induce further collection of the secretion of the wall of the gall-bladder with consequent dilatation of the latter."

When this obstruction is the result of pressure or of inflammatory thickening, the cystic duct may again become patent. But when the duct becomes impervious and takes "the appearance of a fibrous cord," the lumen is entirely obliterated by adhesive inflammation.

In many of the cases cited it has been noted that the fluid confined within the gall-bladder was pale, semi-serous, of low specific gravity, and lacking the usual appearances and chemical constituents of bile. This change, by which the gall-bladder secretion replaces the bile, goes on somewhat rapidly after the stoppage of the cystic duct.

A localized peritonitis may be induced by contiguity even when there is no perforation, and if rupture occurs later the escaping fluid may be limited to the right hypochondrium by adhesions between the liver, abdominal wall and transverse colon.

CLINICAL AND DIAGNOSTIC FEATURES.

In turning to the clinical aspect of gall-bladder infection it is apparent that, although we must believe that many or most cases of typhoid fever present bacteriological evidence of such infection, the symptoms caused thereby are seldom of importance; but on the other hand, the inflammation may reach such a degree of severity that life is cut off without warning of the local danger. In more than half the cases recorded, either through the latency of the symptoms, or on account of typhoidal stupor, nothing unusual was observed. Thus the gall bladder may become distended or perforation may occur without detection.

The subjects are mostly young, and childhood is not exempt from this complication. Several cases under ten years of age have been reported.

Those instances in which this condition can be determined during life present fairly diagnostic symptoms. They are: pain in the region of the gall bladder and under the scapula; a palpable, very tender swelling that is dull on percussion, sometimes pear-shaped and visible, giving a doubtful fluctuation, described in one instance, as like that of a tense hydrocele. "In gall-bladder inflammation," says Mr. Mayo Robson,[32] "there is almost invariably a tender spot a little above

and to the right of the umbilicus, or, to be more exact, at the junction of the upper two-thirds with the lower third of a line drawn from the ninth rib to the umbilicus."

If perforation occurs, these symptoms are merged into those of collapse and general or local peritonitis, of which the source can only be inferred from its manner of development and the previous history.

The conditions to be excluded in diagnosis, in the more latent stages, are impacted feces, hydronephrosis, cyst, displaced kidney and appendicitis; and, when rupture of the gall-bladder has occurred, intestinal perforation. The distended gall-bladder gives more pain than either of the first three affections. A displaced kidney is movable, and the appendix is seldom found in the right hypochondrium. Collapse and peritonitis from rupture of the gall-bladder, as before mentioned and as observed in numerous cases, may be indistinguishable from these conditions when due to intestinal perforation. Marked leucocytosis would be suggestive.

PROGNOSIS.

The prognosis is unfavorable if the gall-bladder has become much distended or if deep ulceration has taken place, unless the symptoms can be promptly relieved. The local dangers in addition to those from the fever itself are very great. Among the cases that I have found reported one-quarter only got well, including those of post-typhoid cholecystotomy in which Eberth's bacilli were discovered at operation. Without doubt many cases of typhoidal cholecystitis recover spontaneously and go unobserved or unrecorded. But it is equally probable that others die in whom this state is unsuspected.

TREATMENT.

The indications are to relieve pain by opiates and local applications, hot or cold, to avert perforation if possible by absolute quietude or tapping the gall-bladder, and if rupture occurs or appears inevitable to resort to the promptest surgery.

I know of no case similar to mine in which typhoidal cholecystitis, as determined both clinically and bacteriologically at the height of the fever, has required immediate intervention. There may be others. Fortunately a simple tapping relieved pressure, opened the cystic duct and allowed escape for the sero-purulent fluid.

Had re-accumulation occurred, in the absence of peritonitis, expectant measures or tapping again would have been indicated, as the acute typhoidal state is a very unfavorable one for radical surgery.

In case of perforation and septic peritonitis, however, laparotomy should be performed as affording almost the only chance, but probably a better one than after intestinal perforation at the same stage of typhoid fever, because the inflammatory processes may be limited to the right hypochondrium, and the gall-bladder is a less vital part.

Such operations will be rare; but if done in the declining stage of the fever or during convalescence, the prospect of success is less unfavorable. A case of this kind, thus far the only one, I believe, was reported in the *Lancet* two years ago by Mr. Monier-Williams and Mr. Sheild.[88]

CASE. A female, thirty-one years old, on the eleventh day of typhoid fever had sudden, severe abdominal pain with semi-collapse. The pain was limited to the upper half of the abdomen, and was thought to be due to an intestinal perforation. The patient recovered from this complication, and became convalescent in the fourth week. The temperature was normal for a fortnight, when, at the end of the sixth week, there was another sudden, severe accession of pain and tenderness in the right hypochondrium at the hepatic flexure of the colon. Here a dull tumor appeared, the size of an orange. Again a diagnosis of probable intestinal perforation was made, and the condition was regarded as nearly hopeless. The next day there was slight rallying from collapse and a worse abdominal condition. Operation was decided upon. Median incision, extending later to the right, showed turbid fluid in the right hypochondriac region chiefly, but no perforation of the intestine. The gall-bladder was deeply inflamed, of a dark plum color, thickened, adherent and tightly distended. Near the neck was an ulcer the size of a three-penny piece, with a small perforation through which oozed the contents. The gall-bladder was opened and emptied of an ounce and a half of thick, offensive pus. There were no calculi. The patient made a good recovery. No satisfactory bacteriological examination was made.

From this study the following conclusions are drawn:

(1) The gall-bladder in typhoid fever is often infected by Eberth's bacillus, seldom by other organisms (streptococcus, bacillus coli communis).[84]

(2) Fatal cholecystitis may result, the inflammation often involving the ducts (cholangitis), less frequently the hepatic parenchyma (abscess).

(3) Gall-stones predispose to this complication, and on the other hand there is ground for thinking that typhoid fever may determine the formation of calculi in predisposed subjects.

(4) The gall-bladder may be a focus for systemic re-infection.

(5) Diagnostic symptoms sometimes indicate the necessity for evacuating the gall-bladder by tapping or cholecystotomy.

ILLUSTRATIVE CASES.

1. Recovery. Leudet (Hagenmüller, *op. cit*).

Female, thirty-six years. Fourth week, pyriform tumor in right hypochondrium, disappearing in ten days, reappearing at intervals during seven weeks. No jaundice.

2. Recovery. Griesinger (Hagenmüller, *op. cit*).

Female, age twenty. Sixth week, peritonitis, slight icterus. Painful tumor to right of umbilicus. Swelling of liver. Collapse. Convalescence. In eighth week sudden return of tumor, with chills, icterus, vomiting. Later, two more relapses. Recovery fifth month.

3. Recovery. Laveran (Hagenmüller, *op. cit*).

Man, age twenty-three. Painful symptoms and tumor in region of gall-bladder in sixth week.

4. Martin-Solon (*Bull. Fac. de Méd. de Paris*, 1820–21, VII, p. 370–375).

Patient died of peritonitis, and twenty-five ulcers of gall-bladder were found. Previous illness not clearly typhoid fever. *Enterite* (?).

5. Husson (*Bull. de la Soc. Anat.*, 1835, p. 104).

Child, eight years. Died at end of third week. Perforated gall-bladder. Cystic duct obliterated and converted into fibrous cord.

6. Dumoulin (*Gaz. Méd. de Paris*, Third Series, Tome III, 1848, p. 551).

Man, age nineteen. Third week, constant nausea and vomiting. Enormous tumor in right hypochondrium, extending to left of umbilicus and into right iliac fossa. Resistance like tense hydrocele. Liver raised. Upper limit line of right nipple. Diagnosis: distended gall-bladder.

Repeated chills suggestive of hepatic abscess. Coma. Death on 16th day. Autopsy: Typical intestinal lesions of typhoid; tumor, size of head, containing two litres of greenish bile; no gall-stones; adhesions with liver, transverse colon, etc.

7. Archambault (*Bull. de la Soc. Anat.*, 1852, p. 90).

Infant. On 30th day, signs of intestinal perforation. Death 12 days later. Perforation of gall-bladder. Localized peritonitis.

8. Barthez and Rilliet (Maladies des Enfants, Vol. II, second edition, 1853, pp. 5, 701).

Girl, age twelve. On 16th day, tumor in right hypochondrium that gradually disappeared. Death on 52d day. Autopsy: Perforated gall-bladder; circumscribed pus cavity between liver, stomach, gall-bladder and colon.

9. Ranvier (*Bull. de la Soc. Anat. de Paris*, 2 S., Tome VIII, 1863, p. 432).

Man, age twenty-eight. Died during convalescence in the fifth week. Autopsy: Limited peritonitis; perforated gall-bladder; right side of abdomen filled with yellowish, opaque liquid; walls of gall-bladder two or three millimetres thick and infiltrated with pus; a small calculus; Peyer's patches in stage of cicatrization. Author says he cannot explain this point of suppurative election, "*si bizarre.*"

10. L. Colin (Études clin. de méd. militaire, p. 197, Paris, 1864).

Soldier. End of third week of rather mild attack; jaundice, gastro-abdominal pain. Death 11 days later. Autopsy: Peritonitis limited by transverse colon, liver and abdominal wall; gall-bladder size of goose-egg, perforated; no gall-stones; ducts pervious; typical intestinal lesions.

11. C. E. E. Hoffmann (Zerstörung der Gallenblase bei Typhus, *Virchow's Archiv*, 1868, XLII, 219–222).

Female, age twenty-five. Sixth week, jaundice. Eighth week, sinuses discharging through abdominal wall. Twelfth week, death. Autopsy: Destruction of gall-bladder; abscess beneath liver, containing 12 gall-stones; lesions of typhoid.

12. O. W. Foot (Enteric Fever, Abscess in Walls of Gall-bladder, *Irish Hosp. Gaz.*, Dublin, 1874, II).

Female, age thirty-two. Died in eighth week. Small abscess between coats of gall-bladder, communicating by a narrow orifice with interior. Extensive adhesions of abdominal wall. One cholesterin calculus, 23 grains.

13. Burger (Typhus abdom. mit Perforat. der Gallenblase in die Bursa Omentalis, *Deutsches Archiv. für klin. Med.*, Leipzig, 1873-4, XII S., 623–630).

Man, age forty-one. Twelfth day, pain and tumor size of apple in region of gall-bladder. Gradual increase in size. Chills. No jaundice. Death from peritonitis in fifth week. Perforation of gall-bladder. Adhesions forming cavity filled with pus. No gall-stones. No abscess of liver.

14. P. L. Legendre (*Bull. de la Soc. Anat. de Paris*, Fourth Series, Tome VI, 1881, p. 193).

Female, age thirty. In second week peritonitis in right upper abdomen. Death 12 days later. Autopsy: Perforation of gall-bladder; pus in peritoneal cavity; three gall-stones.

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EMPYEMA OF THE ANTRUM OF HIGHMORE.

A NEW OPERATION FOR THE CURE OF OBSTINATE CASES.[1]

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IN order to understand the conditions involved in these cases, we must, first of all, give our attention to the necessary anatomical details connected with this region, and then note the pathological changes which may arise, for such an understanding is of indispensable value in the treatment of antral empyema.

ANATOMY.

The Antrum of Highmore is a nearly closed cavity, occupying the whole of the body of the superior maxillary bone, pyramidal in shape, and presents three surfaces, an apex and a base. The apex is directed toward the malar process of this bone, its base corresponds to a large portion of the outer wall of the nasal cavity, and of the three surfaces, the superior forms the floor of the orbit, the anterior presents towards the face, and the posterior presents towards the zygomatic fossa. The posterior surface is the thickest, the base is the thinnest. Of the borders of the pyra-

[1] Read before the Boston Society for Medical Improvement, February 8, 1897.