ON JAUNDICE
AND ON
PERFORATION OF THE GALL-BLADDER
IN TYPHOID FEVER

BY
FRANCIS HAWKINS, M.B. EDIN.,
PHYSICIAN TO THE ROYAL BERKSHIRE HOSPITAL

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CASES of jaundice with typhoid fever, arising either during its course or during convalescence, are not frequently met with. Such a condition is in fact *rare*; hence Sir William Jenner¹ writes, "Jaundice is a *very* rare symptom in typhus and typhoid fever, so rare that I cannot call to mind a single case in which I have observed it." Murchison² says "I have met with jaundice in four cases of enteric fever." Osler³ writes, "Jaundice is a very rare complication; . . . it was present in only 1·1 per cent. of the Munich autopsies." Frerichs⁴ says, "In ileo-typhus jaundice is only observed in exceptional cases." Louis⁵ quotes two cases, Andral⁶ one, and Liebermeister⁷

¹ 'On Fevers and Diphtheria,' *vide* foot-note, p. 353.

² 'Diseases of the Liver,' p. 456.

³ 'Principles and Practice of Medicine.'

⁴ 'Diseases of the Liver' (New Sydenham Society), vol. i, pp. 172 and 215.

⁵ 'Recherches de Fièvre Typhoïde,' 1841, vol. i, pp. 118 and 367.

⁶ 'Clinique Médicale' (trans. by D. Spillan), 1836, p. 613, case 1.

⁷ 'Cyclopædia of Medicine,' by Ziemssen, vol. i, p. 158.

writes, "Icterus occurs less frequently during typhoid fever than in many other febrile affections, as, for instance, pneumonia." In searching through literature I can find but nine¹ cases recorded as illustrative of this complication. From the facts thus obtained I find that as regards *age*, no case has been observed in any patient under eighteen years of age; it may, however, occur at any age above this up to fifty-four. As to *sex*,² males are much more liable to develop this symptom than females, only one case occurring in the latter. *The time of the occurrence*³ of jaundice varies; thus in the case recorded by Andral the countenance was yellow on the "third day." In other cases jaundice was noted respectively on the "fifth day," "the fourteenth," at the "acme of the fever," the "twenty-sixth day," "twenty-ninth," on the "thirty-eighth day," and, in one case, during a relapse.

Associated symptoms.—Delirium, violent in some instances. Vomiting of bile, in one case continuously for five days. Diarrhoea was observed in some cases, but in two the condition of the bowels was described as being "confined." In one case green-coloured evacuations were noted, but in others the stools were pale or clay-coloured. Bile was present in the urine in most instances, and in one, in addition, "albumen." In one case the urine was passed involuntarily. Other symptoms noted were "epistaxis" so profuse as to require plugging of the nostrils, bloody expectoration in one case without any signs of pulmonary complication. Pneumonia was noted in another case, but

¹ Murchison, 3 cases. Jenner, p. 445 ('On Fevers,' &c.), mentions the case of a soldier in a native regiment at Sierra Leone, and adds, "... it is probable that in some countries jaundice does occur in typhoid fever, &c." Frerichs, 2 cases. Louis, 2 cases. Andral, 1 case. Liebermeister quotes the following: "Griesinger reports ten attacks of jaundice in 600 typhoid fever patients." Hoffman, 10 cases in 250 post-mortems. "In the Hospital at Basle, icterus was observed twenty-six times in 1420 cases."

² In the 26 cases in the Basle Hospital, fourteen were males and twelve females.

³ Murchison mentions that in two of his cases the jaundice appeared during the "primary fever;" both cases died.

the jaundice preceded it by several days. Parotid bubo in one case. Thrombosis of femoral vein (left) in one case, and erysipelas of legs in another. It is of interest to note that in no one case is it recorded that hæmorrhage from the bowels occurred.

As to the condition of the liver in these cases. In instances where any mention has been made it has been stated that there was tenderness on palpation over the hepatic region, and physical examination would tend to show diminution of the hepatic area; in one case it is noted that "hepatic dulness disappeared entirely."

Result of the cases and duration of the jaundice.—In two cases recovery followed; in one the jaundice developed during a relapse and continued for seven days; in the second case, to quote Murchison, "the jaundice came on suddenly about the acme of the fever; . . . the deep jaundice persisted for some time, even during convalescence." The other cases all terminated fatally. In the case where jaundice appeared on the third day, it remained persistent for six days, when the patient died from pneumonia. When jaundice occurred on the fifth day, the patient died three days later in a state of coma, the jaundice being persistent. The instance where the jaundice appeared on the fourteenth day is of considerable interest, inasmuch as it was apparently persistent for fifty-nine days and then disappeared, and the patient did not die for some two months later. In the other cases death occurred in one fourteen days after the jaundice was first noticed, and on the fortieth day of the disease. In the other two cases the jaundice appeared four days before and remained till death, the patients dying on the thirty-third and forty-second days respectively.

Causes of the jaundice.—Writers who refer to this symptom mention two factors in its causation: (1) a catarrhal process; (2) parenchymatous changes in the liver. In one case cited by Louis the liver is described as healthy, and the bile-ducts pervious." In one of

Frerichs' cases, while the bile-ducts were pervious and the gall-bladder contained a small quantity of thin pale bile, the liver itself was unusually soft, and on section, rounded masses, one to one and a half inches in their transverse diameter, were observed; they were soft, almost pultaceous, and separated from the surrounding tissue by a sharp line of demarcation. In the second case described by Louis the bile-ducts were normal, but there were "*tumeurs purulentes ou non purulentes dans la foie.*" In two of Murchison's cases the liver was found to be small and its secreting cells loaded with oil. In the other case described by Frerichs, he places it under the illustrative cases of "Acute atrophy of the liver," and in his remarks says, "It may be a matter of question whether this case . . . is to be regarded as one of acute yellow atrophy of the liver, or as one of severe (abdominal) typhus, complicated with jaundice." It might be added that in this case there were white submucous deposits in Peyer's patches and the solitary glands, the more extensive the nearer the ileo-cæcal valve was approached.

In conjunction with these facts, the following case of jaundice arising during the course of typhoid fever is of some considerable interest.

A female aged 18 years, a gipsy, was admitted into the Adelaide Ward, Royal Berkshire Hospital, under my care, on January 15th, 1896, suffering from typhoid fever. On the 6th of January she felt sick and had a headache, but did not lie up until the 8th, when owing to weakness she could not get about. Beyond having had pleurisy some twelve months previously, there was nothing to note in her previous history. As regards surroundings, a brother in the same camp was ill with typhoid fever. On admission patient complained of pain in the abdomen and the back, extending down the legs. The condition of the patient was as follows:—She was well built and well developed, with dusky flush over face, pupils dilated, lips fissured, sordes on teeth, tongue moist, but covered with a white fur.

Abdomen.—Tumid ; pain complained of over right iliac fossa ; splenic area increased upwards and to the middle line. Numerous pink, slightly elevated spots, disappearing on pressure, were present, mostly over the right half of the abdomen, also over the front and sides of the chest. The liver was slightly enlarged, but no pain was felt over the hepatic region. Bowels opened three times within two hours ; stools typically typhoidal. Heart sounds normal. Pulse regular, 96. Respirations 44. Râles at bases. Urine, sp. gr. 1030 ; no albumen. Temperature 104°.

Progress of the case.—From January 16th to 21st there was constant pain in the back and legs. The food was frequently rejected. Bowels opened six to nine times in the twenty-four hours. Nocturnal delirium was constant. Fresh crops of spots appeared on the abdomen, chest, left shoulder, forearms, and on the back. The temperature varied from 102° to 104·4°. Respirations were mostly 36 per minute. The *alæ nasi* moved freely in respiration. On the 21st very severe pain was complained of, situated over the right half of the epigastric region and over the right lower axillary and hypochondriac regions ; palpation over the latter region increased the pain. Respirations were now 40 per minute, and there was evidence of dry pleurisy over the right base, axillary, and lower mammary regions. Sickness and vomiting were constant, and the temperature rose to 105·8°. The day following (the 22nd) the conjunctivæ and skin of the upper part of the body were slightly jaundiced, bile was present in the urine, and the stools were frothy and white. On the 23rd the jaundice was much more marked, the pain over the regions before noted was still severe, and now extended around the umbilicus. The region of the gall-bladder was exquisitely tender. The next day the pain was so severe,—and stated to be general as well as local,—that the patient screamed when moved. The jaundice was still marked, and bile still present in the urine. Now for the first time both urine and *fæces* were passed unconsciously. The respira-

tions were increased to 50 per minute, and the breathing was *mainly abdominal*. There was now dry pleurisy on the *left* side as well as on the right. From this date the pain over the epigastric region was better, and ultimately disappeared; at times the patient vomited bile, and the jaundice remained persistent from its first appearance (January 22nd) to the day of death on February 14th, sometimes being more marked than at others. On one occasion, with the exception of the conjunctivæ being yellow it quite disappeared, but returned the day following as marked as before. Bile was almost constantly present in the urine. As regards the pulmonary complications, it must be added that on February 4th dyspnœa became extreme, the face cyanosed, the soft parts were drawn in, and the respirations numbered 56 per minute. The breathing was now *entirely abdominal*; the temperature, which had fallen somewhat suddenly, rose to $105\cdot4^{\circ}$; there was now evidence of pneumonia of the right base, with dry pleurisy over part of the right lung, and all over the left lung. From this time onward the dyspnœa was extreme, the respirations varied from 60 to 80, and eventually the patient died from the pulmonary complications.

As to other points of interest in the case, mention must be made of the—

(1) *Bowels*.—At the first onset of the jaundice the stools were white and frothy, but later on they became more coloured, and on three or four occasions bile was passed by the bowel and the stools were passed unconsciously.

(2) *Hæmorrhage* from the bowels occurred on the 25th of January, and was more or less constant till the 3rd of February, many of the stools consisting of pure blood.

(3) *Delirium* was constant throughout during the night, and frequent during the day.

(4) *Skin*.—On the 29th of January four pomphi appeared on the left leg, subsequently becoming bullous with dark reddish purple margins; at the same time

numerous pink petechiæ appeared on both legs. The bullæ, as also the petechiæ, subsequently disappeared, but the marks where the bullæ had been remained persistent and were distinct at the autopsy. On February 6th a swelling the size of a small Tangerine orange, purplish red in appearance, and extremely tender to the touch, appeared on the left hip. The skin over this showed no tendency to break. Subsequently this swelling entirely disappeared.

The temperature during the first few days varied from 102.2° to 104.4° . On the 21st January (the seventh day after admission) it rose to 105.8° in the evening. The ice-cradle was then used, and in the morning it was 101.4° . Three days later it rose to 105.2° , and two days after this to 105.4° . It then fell gradually, and on the 31st of January (the twenty-sixth day after first complaining of sickness and headache) registered 98.6° , then remained between 100.8° and 99° for four days, when it suddenly rose to 105.2° , and fluctuated between 101° and 104° for four days, then fell to 100.4° , and two days later to 99° . The day following it rose to 103.8° ; then fell to 97.4° ; then rose to 105° , fell to 99.8° , and the patient died within an hour.

Autopsy.—The body was greatly emaciated.

Thorax.—The *left lung* was adherent in all parts, the adhesions broke down fairly easily. The *right lung* was free over the lower lobe, and lymph was present over both pleural surfaces; this free space contained ten ounces of clear fluid. The anterior part of both lungs was markedly pale, and the lungs were in a collapsed condition. There was consolidation at the base of the right lung and a small area at the apex of the lower lobe of the left lung, the latter being in an earlier stage than the former. The cardiac walls were flabby, the right ventricle dilated, and the valves normal.

Abdomen.—The stomach was distended, its lower border reaching down nearly to the umbilicus; adhesions existed between the gall-bladder and the stomach. On reflecting the right half of the abdominal wall the gall-bladder was

found to be adherent to the peritoneum, and around the point of contact was a small circumscribed area of peritonitis. On gently breaking down the adhesions a perforation sufficiently large to admit a No. 10 catheter was noticed in the anterior wall of the gall-bladder, just above that part of the fundus which was adherent to the stomach. The gall-bladder extended for about one inch and a half below the anterior border of the liver; its contents, small in amount, were slightly purulent, its walls thin, a few small ulcers were seen at the fundus, and on the posterior surface was a small area so thin that it was almost perforated. In its neck was one solitary gall-stone resembling in its size, shape, and surfaces a mulberry. The commencement of the cystic duct was not blocked by the gall-stone, which was easily moveable. Unfortunately the hepatic ducts and the ductus communis choledochus were accidentally cut off during the removal of the specimen—the autopsy being performed under difficult circumstances. The liver itself was uniformly enlarged, and on section showed “cloudy swelling;” no bile exuded. There was typical ulceration of the intestine.

Microscopical examination of the liver showed nothing of importance. In the absence of any knowledge of the condition of the choledochus one cannot speak positively as to the cause of the jaundice; still the absence of any bile exuding from the liver on section, and the small amount within the gall-bladder, would lead one to think that the choledochus was not blocked to any appreciable extent; and it is certain that the gall-stone did not cause any obstruction; and had it blocked the cystic duct, that in itself would not produce jaundice if the hepatic duct and the choledochus were patent. A case of some interest in association with this is quoted by the late Dr. G. Budd.¹ A girl, aged 18, died from a severe attack of typhoid fever. At the autopsy fourteen gall-stones were found in the gall-bladder, and one completely blocked the cystic duct.

¹ ‘Diseases of the Liver,’ 1857, p. 197.

The gall-bladder was united to all the surrounding parts by lymph. No jaundice was present. One factor, however,—purulent inflammation within the gall-bladder—which is, according to A. Fraenkel,¹ capable of producing jaundice without any obstruction of the choledochus, was present in this case, and might have been the cause of the jaundice, and while one cannot associate this case in the same category as those of an infective nature consequent upon typhoid fever, pneumonic or relapsing fever, yet it may be claimed that the typhoid fever was the exciting cause, for it is well known that biliary calculi may remain for a long time and yet cause no symptom. A case in point presented itself the other day in a man aged 72, who died from renal disease. A single calculus resembling the one in the case now under review in its size, shape, &c., was found in the gall-bladder at the autopsy; no one symptom of such existed while the patient was under observation, and so far as the history of the case showed, never had done so.

Another point of much interest—not to speak of the age of the patient, eighteen years²—was the presence of local adhesions and perforation of the gall-bladder, which must be attributed, I think, to the gall-stone, for the discharge of such stones through fistulous openings in the abdominal parietes is not uncommon, though I cannot find a single instance recorded of such occurring during typhoid fever. Liebermeister³ cites two instances under his own observation of gall-stones rupturing through the gall-bladder and so causing fatal peritonitis.

This paper commenced with the consideration of the rarity of jaundice, clinically, in typhoid fever, and it must end by mentioning the rarity of perforation of the gall-bladder pathologically in typhoid. That the gall-bladder

¹ 'Centralblatt für innere Medicin,' No. 14, 4th April, 1896, p. 358.

² In an analysis of 395 cases collected by Hein, only 15 were under twenty-five, and only 3 under twenty. Quoted by Murchison, 'Diseases of Liver,' p. 382.

³ Ziemssen's 'Cyclopædia and Practice of Medicine,' vol. i, p. 154.

may be *ulcerated* in this fever has been shown by Jenner ;¹ it would, however, appear to be rare, for only one instance is cited in the 'Transactions' of the Pathological Society,² where Dr. Arthur Voelcker records the case of a man, aged 48, who died on the thirty-ninth day from perforation of intestine ; nine ulcers were found in the gall-bladder, "one of which, on the superior surface, extended into the liver." As regards *perforation* of the gall-bladder during typhoid, no case illustrative of this has been recorded in the 'Transactions,' and Wilks³ and Moxon state, "The gall-bladder . . . has even been found perforated ; we ourselves have never seen this." It would appear therefore, under any circumstances, to be rare. Murchison⁴ mentions one case ; a youth, 19 years of age, died on the fifteenth day of the fever from peritonitis, when the gall-bladder was found perforated. Barthez and Rilliet⁵ cite such an occurrence in a girl aged 12 ; and Mr. Monier Williams and Mr. Sheild record a case in the 'Lancet'⁶ occurring *after* typhoid fever.

In conclusion, it may be mentioned that suppuration of the gall-bladder may occur during typhoid fever. One such case is recorded in the 'Pathological Society's Transactions'⁷ by Dr. Hale White in a youth aged 17. At the autopsy there was general peritonitis around the gall-bladder, matting that organ and the lower edge of the liver and the intestines. The bile itself in this case appeared normal. There were neither gall-stones nor jaundice, the walls of the gall-bladder were very thin, and in some places almost perforated.

¹ 'Fever and Diphtheria,' p. 102.

² Vol. xlv, p. 79.

³ 'Pathological Anatomy,' p. 643.

⁴ 'Continued Fevers,' p. 566.

⁵ 'Traité Clinique et Pratique des Maladies des Enfants,' 3me édit., vol. ii, 1887, p. 612.

⁶ 'Lancet,' March 2nd, 1895.

⁷ Vol. xlii, p. 181.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. ix, p. 51.)