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THE

LIVER IN JAUNDICE

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Fervens difficili bile tumet jecur.

HORATIUS.

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THE following pages are reprinted from the *British Medical Journal.* They are an attempt to set forth concisely the state of our present knowledge of the morbid anatomy of the liver in permanent obstruction of the bile ducts.

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THE LIVER IN JAUNDICE.

By jaundice is meant a yellowness of the skin. It is a name drawn from the French word *jaune*. By the Greeks the disease was called icterus. In most modern books, the fanciful etymology of Pliny the Younger (*Nat. Hist.*, lib. xxx, cap. xi) is given. A certain yellow bird was called icterus; and the sight of this by one jaundiced was death to the bird, but recovery to the man. If Aretæus, as seems more probable, lived after Pliny, he was likely to have had this derivation in mind when he says the name icterus "is derived from certain four-footed and terrestrial animals, called ἴκτιδες, whose eyes are of this colour" (*On the Causes and Symptoms of Disease*, book I, chap. xv). This animal, the ἴκτις, was the yellow breasted marten, and appears to have been kept by the Greeks in their houses for the same purpose as we keep cats, viz., that of killing mice. The object of comparison would thus be close at hand. As to Pliny's derivation, it seems highly improbable that a means of curing the disease should be known before the disease itself had a name. The name used by the Latins, *morbus regius*, has also a common and faulty explanation. It is so called, not on account of the royal diet and regimen needed by jaundiced patients, but on account of the resemblance of the yellow colour of their skin to gold, the *rex metallorum*.

It is my object in these papers to describe those changes in the liver which follow an obstruction to the flow of bile into the duodenum. These morbid appearances divide themselves into two heads: 1, the changes met with in the bile-passages; 2, those met with in the parenchyma of the liver itself. The former of these will first be considered.

The first effect of an obstruction in the bile-ducts is a dilatation of the duct behind the obstruction. Should the obstruction be in the common duct, it is the gall-bladder which suffers at first. Its walls are easily distended, and it may, therefore, become enormously dilated. One of the most dilated gall-bladders on record was met with by Cline (reported by John Andree, *Considerations on Bilious Diseases*, Hertford, 1788,

p. 18). A tumour gradually formed in the belly of a boy, aged 16. Fluctuation was clearly felt, and the swelling was tapped. More than twenty ounces of a bilious fluid were let out. The boy died in seven days; and, on examination, the gall-bladder was found to contain two quarts of bile, and stretched from the liver to the pelvis. Van Swieten likewise (*Comment.*, sect. 950) found in a boy, aged 12, the gall-bladder of immense size, holding eight pounds of a thick bile. The greatest amount of fluid in the gall-bladder that Frerichs has seen (*Klinik der Leberkrankheiten*, Braunschweig, 1861, Band II, p. 447) is eighteen ounces. I have never seen the gall-bladder distended so much as this, although it is not uncommon to find it as long as six, seven, or eight inches.

Usually it is filled with a dark viscid bile. But if the gall-bladder be much distended, and any obstruction to the flow of bile through the cystic duct take place, as often happens when gall-stones are the cause of jaundice, the bile becomes absorbed, and its place taken by a colourless fluid, which is either viscid or limpid. In one of Van Swieten's cases, the taste of the fluid was saltish; and he also, in another case, mentions its coagulation by heat. This *hydrops vesicæ felleæ*, as it is called, was first noticed by Glisson (*Anatomia Hepatis*, Hagæ, 1681, end of cap. xxxix), and by Regnerus de Graaf (*Tract. Anat. Med. de Succi Pancreât. Naturâ et Usu*, Lugd. Bat., 1671), who also noticed the absence of bitterness in the fluid.

There are not many analyses of the colourless fluid found in the gall-bladder or ducts on record. J. C. B. Bernard (Reil's *Archiv*, 1799, Band III, p. 477) seems to have been the first to examine the fluid very attentively. He found the fluid transparent as water, of the consistence of white of egg, and tenacious. Heat, alcohol, and acids did not cause coagulation, but only a flocculent precipitate. The fluid was unaltered by mineral alkali or carbonate of vegetable alkali. Albert Schaefer (*De Hydrope Ductuum Biliarium*, Diss. Inaug. Turici, 1842, p. 9) found in the fluid of the bile-ducts the same chemical and physical characters as in the plasma of the blood. Frerichs (*op. cit.*, p. 449) found the fluid alkaline, transparent, and containing mucous corpuscles. There were no bile-pigments or bile-acids. Nitric acid caused a slight cloudiness; acetic acid made the fluid gelatinous and thick. In another case, he found a great quantity of albumen. Casali (Virchow's *Jahresbericht*, f. 1869, Band I, p. 287) has also lately found much the same state. But Ritter (*Comptes rendus*, 1872, tome lxxiv, p. 813), however, states that certain colourless fluids from the bile-passages gave no reaction of bile-pigment, yet contained the rest of the biliary constituents. This statement needs

to be investigated by further observers, as the general experience of physicians is that both bile-pigment and bile-acids are absent. I have recently had the opportunity of examining this colourless fluid in two cases, and could not detect the presence of bile-pigments or bile-acids on the repeated and careful application of Gmelin's and Pettenkofer's tests.

The presence of a colourless fluid in the gall-bladder and the bile-ducts was formerly looked upon as evidence that the liver had ceased to secrete bile. Indeed, a recent writer (W. Moxon, *Transactions of the Pathological Society of London*, 1873, vol. xxiv, p. 129) is still plainly of this opinion. But, to my mind, the evidence seems rather the contrary. It should be remembered that it was the large ducts which were seen to be filled with this colourless fluid, and that nothing is said of the state of the smaller ducts, of the interlobular and capillary ducts. These continue to receive the bile poured into them by the liver-cells, but the bile does not reach the large ducts, because the small ducts are shut off from the large, either by plugs of this tenacious fluid or biliary gravel. In a case which I recently examined at St. Bartholomew's, the large ducts were perfectly colourless; but, by gently pressing the liver, a yellow fluid could be made to issue from the small ducts. Also, by careful dissection, the small ducts could be seen to be stained yellow.

Precisely the same inference may be drawn from Oskar Wyss's experiments (*Archiv der Heilkunde*, 1867, p. 469). He made biliary fistulæ in dogs, and then poisoned them with phosphorus. He found that though very little or no bile flowed out of the fistulæ, the dogs, notwithstanding, became jaundiced. Here, then, seemed to be evidence that the liver ceased to secrete bile. On dissecting the livers of these dogs, the large ducts were found indeed unstained, and containing a colourless mucus, but the openings of the smaller ducts into the large were plugged with a thick mucous secretion which hindered the flow of bile into the larger tubes. Ebstein (*Archiv der Heilkunde*, 1867, p. 506; and 1869, p. 379) has noticed also the same plugging of the fine ducts in patients who became jaundiced after poisoning themselves with phosphorus.

The ducts outside the liver become dilated. It is common to see them as large as, or even larger than, the middle finger. In man, I have never seen them tortuous; in animals, it is not uncommon to see this appearance when the ducts have been tied near the duodenum. The size which these ducts may sometimes attain is enormous; so that at first sight they may be mistaken for tumours connected with the liver. There is an old case of Traffelmann (quoted by Schenk, *Observationes Medicæ*, Lugdun., 1644, lib. III, sect. ii, p. 405) often quoted, and

invariably misquoted. In the body of Daniel, Archbishop of Mainz, who died in 1582, the bile-ducts were found filled with gall-stones, and dilated "*instar utriculi*". Morgagni (*De Sedibus et Causis Morborum*, Epist. XXXVII, sect. xlvii), quoting this, changed the *utriculi* into *ventriculi*, and this error has been followed up to the present day by every writer who has mentioned the case.

Of modern instances, the most extreme dilatation seems to have been reached in a case recorded by Halliday Douglas (*Monthly Journal of Medical Science*, Edinburgh, 1852, vol. xiv, p. 97). In a jaundiced girl, aged 17, a fluctuating tumour could be felt on the right side nearly as low as the ilium. Thirty ounces of fluid were taken away by tapping. On examination after death, a sac was found on the right side of the belly, over the front wall of which the duodenum passed as a flat band. The sac contained within a few ounces of half a gallon of a yellow fluid. The walls of the sac were dense and fibrous, one-twelfth to one-eighth of an inch in thickness. At the upper part of the sac, the dilated openings of the hepatic and cystic ducts were seen. The hepatic duct within the liver was much dilated. Todd, also (*Dublin Hospital Reports*, 1817, vol. i, p. 328) found in a girl of 14, the hepatic and common ducts so enormously dilated that they contained more than a quart of bile, and formed a sac which reached from the porta of the liver to the os sacrum. They lay behind the duodenum, pancreas, and root of mesentery, and covered the anterior surface of the right kidney and the greater part of the left. The cause of the dilatation was a scirrhous state of the pancreas. Frerichs (*op. cit.*, Band II, p. 444) also gives a drawing of an immense dilatation of the common ducts.

Within the liver, the ducts also become dilated. But they do not enlarge so greatly as outside. The proper parenchyma of the liver prevents this. In all the cases which I have yet met with, the dilatation has been uniform or cylindrical. Virchow (*Die krankhaften Geschwülste*, Berlin, 1863, Band I, p. 254) has described the saccular or cystic dilatation. The cyst is at first filled with bile; later on, this becomes thick; the bile decomposes and deposits cholestearin, bilifulvin, and hæmatoidin. These dilatations chiefly affect the bile-ducts near the surface of the liver; further, the liver-tissue around them atrophies, so that they lie close under the liver-capsule. These dilatations may be as large as a cherry or walnut; they may closely resemble a small echinococcus cyst, only they have no membranous wall. Leyden (*Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 119) says that these saccular dilatations usually become separated from the gall-duct by chronic inflammation of the surround-

ing liver-tissue. Their contents become watery, thin, or tenacious. Their origin is then doubtful. If they dry up, it is, indeed, difficult to distinguish them from dried up echinococci, unless hooklets or laminated membranes be found. Monneret (*Traité élém. de Pathologie interne*, Paris, 1864, tome i, p. 660) describing these dilatations, has compared them to the saccular dilatations which the bronchi undergo, a comparison which can scarcely be approved of, as the causes in the two cases are altogether different; in the liver, a pent up secretion causes the widening; in the lung, it is most commonly caused by disease of the surrounding lung-tissue.

Friedreich (*Archiv für patholog. Anatomie*, Band XI, 1857, p. 466) has described a cyst, which, he inclines to think, resulted from a dilated gall-duct. In the contents, he found well marked ciliated epithelium. I believe no similar case exists on record. The epithelium of the gall-ducts is ciliated in some of the lower animals during fœtal life; and in some it persists even during the whole of life.

I have also not met with any similar case to that of Boisment, which is quoted by Abercrombie (*Diseases of the Stomach, etc.*, London, 1837, third edition, p. 331). The liver had the appearance of a large undulating cyst. The appearance was found to depend upon a remarkable distension of all the biliary vessels with dark coloured bile, and was accompanied by wasting of the proper substance of the liver. The affection seemed to depend upon a singular obstruction of the common duct by a membranous band which passed over it.

It is not uncommon to find large ducts opening into hydatid cysts and abscesses. A large cyst will not, in all probability, be due to a dilatation of the duct. The contents are of little help, because hydatids often hold masses of red hæmatoidin exactly corresponding to those spoken of by Virchow above. The diagnosis will really depend upon the structure of the wall. The laminated structure of the hydatid membrane is diagnostic. The question of diagnosis from abscess is much more difficult. It depends chiefly upon two points: whether any obstruction in, or general dilatation of, the bile-ducts exist; and whether the lining membrane of the gall-duct can be traced around the walls of the abscess. Joffroy (*Comptes rendus des Séances de la Société de Biologie*, année 1869, p. 218) gives the following rules. In abscess, secondary to rupture of the bile-duct, there is often no limiting membrane, or, if there be, it is not lined with columnar epithelium, and the contents of the abscess do not show columnar epithelium, but liver-cells in process of disorganisation. The collections of pus found in saccular dilatations of the bile-ducts, on the other hand, are always bounded by a membrane

formed by the dilated bile-duct, which, in some places at least, retains its epithelial covering; and columnar epithelium is also found with the pus : liver-cells are never found.

The amount and extent of the general dilatation of the ducts depend upon the degree of obstruction and the length of time which it has lasted. If the obstruction be complete, of course the dilatation will be great. In some cases, the dilatation does not reach the interlobular ducts. I am doubtful, from my own observations, if the capillary ducts ever become varicose, as Oskar Wyss (*Archiv für Path. Anatomie*, 1866, Band xxxv, p. 553) and H. Meyer (Stricker's *Medicinische Jahrbücher*, Wien, 1872, p. 133) have described. I have never seen such an appearance in man; or in animals whose bile-ducts have been ligatured. The walls of the bile-ducts become thickened, even to the naked eye. Under the microscope, this thickening resolves itself into a great overgrowth of the fibrous coat, in which abundance of new lymphatic elements are to be seen, precisely similar to those observed in ordinary cirrhosis.

Many observers have been unable to find any epithelium lining the walls of these dilated bile-ducts. I doubt if this statement be universally true. In three cases which I have lately examined, in which the large ducts were dilated to the size of a man's little finger—in one case from disease of the head of the pancreas, in the other two from gall-stones—I was certainly unable to find any epithelium on the larger ducts, which measured ten millimetres when cut across. In those measuring only four millimetres, I found abundance. One source of fallacy must be guarded against. All washing or wiping of the ducts must be avoided. For, in a case of complete obstruction to the ducts by a hydatid tumour, followed by great dilatation, I found abundance of epithelium in all the preparations taken from the ducts immediately they were opened; but none could be found in the specimens taken after a stream of water had been poured on the ducts or their surface wiped with a sponge.

In those cases which I have hitherto examined, the left branches of the hepatic duct have always been much more dilated than the right. This appearance is probably due to the left lobe of the liver being less bulky than the right, and thus offering less resistance to the dilating tubes.

The catarrh which is set up by the long continued obstruction sometimes goes on to suppuration of the duct; and a mixture of pus and mucus is found in the biliary canals. In another form, the suppuration becomes local and abscesses form. This result of ob-

struction seems to have been first noticed by Cruveilhier (*Anat. pathologique*, livr. 12, pl. 4 and 5; tom. ii, livr. 40, pl. 1) and Frerichs (*Hannov. Annal.*, 1845, Heft. i and ii, quoted in Canstatt's *Jahresbericht*, 1845, Band i, p. 81). The abscesses are usually multiple, near the surface of the liver, and, when cut across, their contents are seen to be a mixture of pus and bile. They are rarely larger than a hazel-nut in size. They greatly resemble the secondary abscesses seen in pyæmia.

The mode of origin of these little abscesses seems doubtful. Cruveilhier (*Archives générales de Médecine*, 1857, Janvier, p. 54) says that he satisfied himself that they had, in his case, their origin in the dilated bile-ducts. Joffroy (*loc. cit.*) speaks of two kinds: one, a saccular dilatation of the duct, filled with pus; the other, an abscess secondary to rupture of the duct. These two kinds may exist together in the same liver. Both are surrounded by an overgrowth of the connective tissue of the liver, containing nuclear elements. Bamberger also (*Krankheiten der chylopoietischen Systems*, Erlangen, 1864, 2te Aufl. p. 198) makes this division. Leyden, however (*op. cit.*, p. 123) considers that these abscesses may have another mode of origin. In one of his dogs, whose bile-duct had been tied, he found many small and large abscesses in the liver-tissue without any dilatation of the ducts, except of the large ones; and he argues from this that the first beginnings of the abscess must have taken place in the liver-tissue surrounding the abscess. This mode of explanation would seem to exclude rupture of the ducts as a source of abscess. There are some observations by Bristowe (*Transactions of the Pathological Society of London*, 1858, vol. ix, pp. 223 and 286) which support Leyden's view. He found, in a case of obstruction to the bile-ducts, an abscess of the liver, spherical, an inch in diameter, which shaded off into the surrounding tissue. Two considerable branches, somewhat dilated, passed through the substance of the mass. The cause of obstruction was a new growth springing from the inside of the ducts at the junction of the hepatic and cystic. It should also be noticed that there were several ulcers in the duodenum. In another place, speaking of the modes in which hepatic abscesses may be formed, he says that the abscesses were not positive cavities lined by a cyst-wall, but rather indistinctly circumscribed portions of liver-structure in which softening and rarefaction had taken place, and which blended insensibly with the surrounding healthier parts. In this case, the obstruction was a gall-stone.

I have not yet had the opportunity of examining any case of multiple liver-abscess arising from obstruction; and the mode of origin is still very obscure, as so little attention has been as yet paid to the histology

of the disease. In the only case of abscess in the liver following obstruction to the ducts which I have seen, the abscess was a solitary one. It clearly did not arise from a saccular dilatation of the duct, for the cylindrically dilated duct opened into the floor of a depression the size of a walnut, near the surface of the left lobe, and one-half of the duct, not more dilated than before its entry into the abscess, formed part of the floor. In this case, I am inclined to think the abscess was formed by rupture of the duct, seeing that so much of the duct was preserved. The abscess afterwards found its way into the pericardium and pleura. The connective tissue throughout both lobes of the liver had undergone an increase, but especially in the neighbourhood of the abscess, where the growth of connective tissue had left only small groups of highly coloured many-sided cells as remains of the proper parenchyma. This case was read last November before the Pathological Society.

The changes which the parenchyma of the liver suffers in obstruction to the bile-ducts have been very little studied. Oskar Wyss (*Archiv für pathol. Anat.*, 1866, vol. xxxv, p. 553), Leyden (*Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 85), and Heinrich Mayer (*Medizin. Jahrbücher herausgegeben von der k.k. Gesellschaft der Aerzte zu Wien*, 1872, Heft II, p. 133), are almost the only three observers who have paid any detailed attention to this state. The liver at first increases in size; it becomes of a deep bilious or olive-green colour, and is said to be itself jaundiced. Its consistence is increased, and the surface and section are somewhat granular. If the jaundice continue long, the liver wastes.

The changes in the cells and in the connective tissue of the liver may be considered apart. In all cases of long continued obstruction to the bile-ducts, the connective tissue grows. The starting-point of this overgrowth is the place of obstruction itself, and the degree of the overgrowth depends upon the kind of obstruction. Thus the overgrowth is greatest in animals around whose bile-ducts a ligature has been placed. Here the presence of the ligature, and the accompanying disturbance of all the structures in the porta of the liver, cause a rapid and enormous overgrowth of the connective tissue throughout the whole of the gland. In such cases, I have found, on the fourteenth day after ligaturing the ducts, the most intense cirrhosis, so that the liver-structure seemed made up chiefly of connective tissue, with a few dwindled hepatic cells. This overgrowth of the connective tissue begins within a few hours after the operation. (See the author's paper on the Changes in the Liver which follow Ligature of the Bile-Ducts, in *St. Bartholomew's Hospital Reports*, 1873, vol. ix, p. 161.) On the

other hand, if the obstruction be such that the connective tissue around the bile-duct suffers but little, the increase in the connective tissue is also but slight. In a case which I have recently examined, in which the obstruction was caused by the pressure of an hydatid cyst upon the hepatic duct, the increase in the connective tissue was small, and did not pass into the lobules. Further, there was an absence of those lymphatic corpuscles, which are so marked a feature in the new connective tissue after ligature of the ducts and in cirrhosis. I attribute this to the uniform elastic pressure of the fluid in the hydatid cyst, so different in its effects from those of a rough angular gall-stone, one of the most common causes of obstruction. In one of these cases, in which it would appear that the obstruction from the gall-stone was not complete, if the absence of jaundice be taken as evidence on this count, I yet found the connective tissue throughout the liver greatly increased, and containing many new lymphatic elements, so that, at first sight, the section of the liver, seen under the microscope, very strongly recalled a far advanced cirrhosis.

The view that the overgrowth of the connective tissue takes its rise from that surrounding the bile-ducts, is strengthened by the fact that, in all cases of permanent obstruction, the bile-ducts are found greatly thickened. Solowieff (*Centralblatt für die medicinischen Wissenschaften*, 1872, No. 22, p. 337) also found the same morbid overgrowth of the connective tissue in the liver after ligature of the portal vein, as I have found after ligature of the bile-ducts.

This overgrowth of the connective tissue was not altogether unknown to the older pathologists. Albers (*Beobachtungen auf dem Gebiete der Pathologie*, Bonn, 1836, p. 19), in speaking of cases of obstruction and dilatation of the bile-ducts, says the parenchyma of the liver is granular, rough, coloured yellowish brown; and that in one case the liver was really cirrhotic. It appears, he continues to say, that the cellular tissue of the liver is partly atrophied, partly indurated. Andral (*Clinique médicale*, vol. ii, p. 534, 4th edition, Paris, 1839) noticed, in a man whose bile-ducts were much dilated, that the liver was small, deep green, very dense, and granular on the surface and section. These changes Andral seems to attribute to a fall on the right hypochondrium two years before death; but it should be noticed that the man had also been a drunkard.

The changes which the liver-cells undergo are less striking. Leyden (*loc. cit.*), from his experiments, drew too hasty a generalisation that a fatty infiltration of the cells followed all obstructions to the bile-ducts.

This is not universally the case either in man or in animals. In man, I have yet to meet with the case in which fatty infiltration was the most prominent appearance. In some cats who died within a short time of the bile-ducts being tied, I have, indeed, seen this appearance; but I am inclined to attribute it to the liver having been fatty before the duct was tied—a state not at all uncommon in domestic animals.

The chief change in the liver-cells is atrophy. The size of the cells varies from a little smaller than natural, to twice that of a leucocyte when the growth of the connective tissue has been great. When the connective tissue shows less appearance of growth, the cells are less altered; they then preserve very nearly their natural shape and size. In other cases, the shape varies with the size; they tend to become oval or rounded; their outline indistinct. The nucleus is well preserved, shrivelled, or invisible. The contents of the cells seem to be chiefly fat and a few pigment-granules: the fat is rarely in large drops; and the pigment, in the cases which I have observed, not so abundant as the writings of others led me to expect. The arrangement of the cells in rays around the hepatic vein is altogether lost, when the obstruction has existed for any length of time.

One of the most important functions of the liver known to us is the preparation of glycogen. I have made several observations bearing upon the question, whether the liver continues its glycogenic functions when the gall-ducts are completely obstructed. I have found that, in cats, the glycogen disappears from the liver within a few days after the bile-ducts have been tied; and also that, on the fifth or sixth day after ligature of these ducts, irritation of the fourth ventricle is not followed by the appearance of sugar in the urine (*Archiv für exper. Pathologie*, 1874). It would appear, therefore, that within a few days after complete obstruction to the gall-ducts, the liver ceases to secrete glycogen.

Another function of the liver, that of secreting the bile-acids, is believed by Golowin (*Archiv für pathol. Anat.*, 1871, vol. liii, p. 433) to be abolished in long continued jaundice. He found that, in dogs in which biliary fistulæ had been made and again closed, the bile-acids could not be discovered in the urine; and he concludes therefrom that, in long continued jaundice, the bile-acids are no longer produced. Further evidence will, however, be required before this opinion can be universally assented to.

Some physiologists appear to believe that the urea and uric acid excreted in the urine are formed in the liver. The experiments of

Gscheidlen (*Studien ueber den Ursprung des Harnstoffs im Thierkörper*, Leipzig, 1871) seem to make this theory more than doubtful. However this may be, in complete obstruction to the gall-ducts I have several times found that, although the urine was much increased in quantity, yet the amount of urea excreted in the twenty-four hours was quite natural.

In some cases of long continued obstruction to the bile-ducts, the liver-cells have been found completely destroyed; nothing but a fatty *detritus* being seen under the microscope, and not a single liver-cell being found in any of the preparations. I have myself seen this appearance only in acute yellow atrophy of the liver. Yet it is noteworthy, that the very first case in which the liver-cells were found to be dissolved was one in which a permanent obstruction to the ducts existed (Thomas Williams, *Guy's Hospital Reports*, 1843, p. 444). The relation, as to cause and effect, which exists between obstruction to the bile-passages and dissolution of the cells, is dubious. I am unable to admit Oskar Wyss' explanation, that the solution of the cells is simply a *post mortem* change. I have frequently kept a liver from a jaundiced patient, even in the heat of summer, without any preservative fluid, and yet been able to recognise the cells many days after death. In one case, where the obstruction to the ducts was complete, and the jaundice had lasted a year, the liver-cells were easily recognised on the seventh day after death, when the liver gave plain signs of putrefaction.

This solution of the cells was attributed by Theodor von Dusch (*Untersuchungen und Experimente als Beiträge zur Pathogenese des Icterus und der acuten gelben Atrophie der Leber*, Leipzig, 1854, p. 36) to the action of the bile upon the liver; but his statement, that the bile dissolves the liver-cells, has been disproved very satisfactorily by Kühne (*Archiv für pathol. Anat.*, 1858, vol. xiv, p. 324). It is true that the bile renders the outline of the cells indistinct, and the cells themselves become difficult to see; but the outline of the cells can always be restored by the addition of some colouring matter to the slide. I have verified these experiments on several occasions; and there is no likeness whatever between the sudden and complete disappearance of the red blood-corpuscle when acted on by bile, and the slow obliteration of the outline of the liver-cell under the same circumstances.

It is still important, however, to keep in view the results of Leyden's experiments (*Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 60) upon the slow absorption of the bile-acids. He found that, after the injection of the bile-acids under the skin of frogs, the liver-cells showed a

marked fatty infiltration; the muscular fibre of the heart a diffused granular appearance. In one case, it is stated that the liver-cells were destroyed. The bile-acids had produced a parenchymatous degeneration of the liver and heart—a common effect of many poisons, such as phosphorus, sulphuric acid, alcohol, etc., and, as I have recently shown, of raising the natural temperature of the body (*Trans. of the Pathological Society*, 1873, vol. xxiv, p. 266). It is quite possible that in these cases, where the liver-cells are found destroyed after death, the long continued circulation of the bile-acids in the blood may have produced their physiological effect, as described by Leyden; and the liver-cells may have thus been dissolved. The appearance of solution of the cells of the liver is, however, not often met with outside acute yellow atrophy; and it would be desirable to have recorded further cases, well authenticated by competent observers.