On congenital obliteration of the bile-ducts / by John Thomson.

Congenital Obliteration of the Bile-Ducts.

John Thomson, M.D.

ON

CONGENITAL OBLITERATION OF THE BILE-DUCTS.

BY

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PREFACE.

THE following pages are reprinted from the *Edinburgh Medical Journal*, and are founded on a thesis which was presented on graduation at the University of Edinburgh.

Cases of the class here dealt with seem to have received less attention than they deserve, alike from physiologists, pathologists, and clinical observers, considering the great variety of interesting problems which they present.

Nothing like a complete *resumé* of previously recorded cases of this lesion has ever been published before; and the author ventures to hope that the facts here gathered together may prove of interest not only to those who, like himself, are chiefly concerned with the clinical aspects of the cases, but possibly also to scientific workers more qualified to estimate their full significance.

When we find Nature herself practising "experimental pathology," it is well worth our while to investigate, as fully as we can, the conditions under which she works and the results of her experiments.

J. T.

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ON CONGENITAL OBLITERATION OF THE BILE-DUCTS.

WE find, scattered about in medical literature, a comparatively small number of cases which are usually described under the title "congenital obliteration, or absence, or malformation of the bile-ducts." These cases present a distinct series of symptoms, and may profitably be studied as a group by themselves.

The main clinical facts, stated very briefly, are as follows:—

The parents of the children seem healthy people, and yet in many cases it is found that they have previously had one child, or several children, similarly affected.

The children themselves are either jaundiced at birth, or they become so within the first week or two of life; otherwise they are healthy and well-nourished. In some cases, there is a discharge of normal meconium followed by colourless motions; in others, the fæces are devoid of colour from the very first. The urine is deeply bile-stained. The jaundice is of a dark greenish tinge, and lasts till death; and the motions remain colourless. A certain proportion of the children die from umbilical hæmorrhage within the first fortnight; and, of those who survive this period, a large number suffer from spontaneous hæmorrhage from other situations. The liver steadily enlarges, and the spleen also. After living some months, the children become more or less emaciated. Fits often supervene, and death ensues in the end in a state of exhaustion from some trifling intercurrent disease.

At the post-mortem, the liver is usually found much enlarged, of a very tough consistence—due to biliary cirrhosis—and of a dark green colour, owing to the presence of numerous masses of inspissated bile in the small bile-ducts. In the great majority of

cases there is complete obliteration of some part or hepatic, common or cystic ducts, or of the gall-bladder, very few exceptions, implication of the bloodvessels or in the neighbourhood is conspicuous by its absence.

What is the etiology and pathology of these cases?

How are the various symptoms to be explained?

In the present paper an attempt has been made to ir data we have wherefrom to form an opinion on tions, *firstly*, by accumulating all the available detai published cases (along with those of an original case), a by looking at them in the light of other clinical fact results of recent experimental investigation.

It may be objected that the reports of individual ca from miscellaneous sources, which must form the basi investigation, are often defective, and possibly sometin and misleading; but then we must remember that ou drawn from this source are not to be regarded as forr which is no stronger than its weakest link, but that resemble a line of stepping-stones, by means of whi individually they are not all very reliable, one may s to a satisfactory conclusion,—always provided one does to put too much weight in places not able to bear it.

We shall first give the facts of our own case; then pr examination of other published cases of congenital ob the bile-ducts, and of cases of fatal infantile jaundice w ducts; and, lastly, we shall consider the pathology a etiology of the condition.

I. Case of Congenital Obliteration of the Bi

Geo. Morrissey, aged 3 months, seen first on 6th

Other Children.—One, a girl about 10, is alive an
Three have died in infancy—two of "bronchitis," a
"worms." None of them were ever jaundiced or suf
hæmorrhages, and none of them had any symptoms of
syphilis.

Pregnancy.—During the whole time of her pregnancy t
was insufficiently fed, and lived largely on fruit given
friendly greengrocer.

Labour.—The mother says that she was under chlorof
hour and a half, and that instruments were used "becaus
came."

At birth, the child seemed perfectly well, and was
jaundiced. After about ten days, he gradually became y
has been so ever since. He never had any hæmorrhage
umbilicus. He was given the breast only, and throve
till five weeks ago when the whooping-cough began. The
always dark and stained his clothes yellow. During p
first week, he passed several dark green stools ("like thos
new-born babies"), but after that time the motions bec
coloured. They have never had the slightest yellow
tinge. About a week ago some dark blood was seen in th
and about the same time there was bleeding from the n
nose. The bowels have always been freely opened thr
times a day; the child has never been subject to vom
has had no fits. During the last week or so, he has be
so feeble that he makes scarcely any noise when he cr
has never had any symptoms suggestive of congenital
He has been given grey powders and cough-mixture, bu
improved at all.

Present Condition.—The child is tolerably well-nouri
very weak and languid. The scalp is dry and scaly, the

There is a small umbilical hernia. The abdomen is otherwise normal.

Thorax.—Tolerably well-formed. Heart and lungs seem normal. Slight bronchitis.

Treatment.—The whooping-cough and bronchitis were treated in the usual way, and a few doses of grey powder were given without any effect.

Further Progress.—18*th July.* The child has been getting steadily weaker, and has lost flesh markedly. During the last few days, the stools have been very dark from the presence of blood.

20*th July.*—Rapidly getting thinner and weaker. Motions still contain much blood. On the inner side of each calf there is a small hard nodule about the size of a pea; these are not tender, and the veins round about them are enlarged. The jaundice has varied in intensity from time to time, and is now distinctly less deep than it was a week ago. The urine is dark greenish-yellow, and turbid from the presence of much amorphous deposit. No albumen, no tube-casts found; a few coloured blood-corpuscles.

21*st July.*—Died quietly at 7.30 A.M.

Post-mortem performed at 11 A.M. on 22*nd July* (had to be done hurriedly and under considerable restrictions).

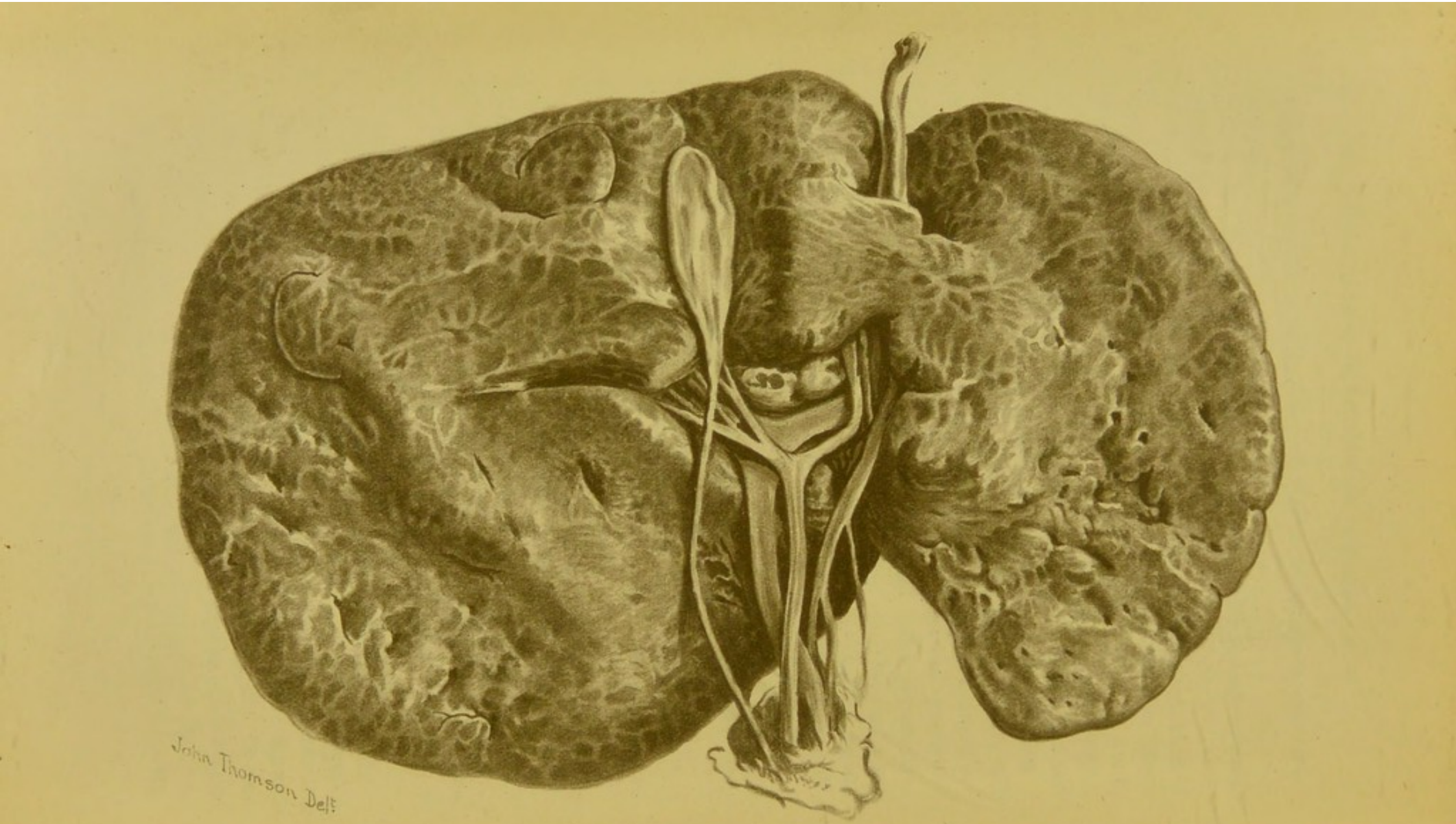
Child emaciated, skin deeply jaundiced, rigor mortis passed off, abdomen distended with gas. Reddish-brown fluid oozing from nose and mouth.

Thorax.—Heart and pericardium normal; pleuræ normal, with the exception of numerous hæmorrhages from one to three lines in diameter under the pulmonary layer on both sides. Lungs partially collapsed, partially emphysematous, and both show on section numerous small hæmorrhages. A good deal of bronchitis.

Abdomen.—Peritoneum normal, no adhesions or roughness, no ascites.

Liver much enlarged (the greatest diameters being $6\frac{3}{4}$, 4, and 2 inches), weight 13 ozs.[1] General contour not much changed. Colour very dark olive-green, with fibrous bands of a yellow tint passing over the surface in all directions. Surface somewhat irregular, like that of morocco leather (on a larger scale). Capsule not apparently thickened, edges hard and rather sharp, consistence

[1] That is a good deal more than twice the normal weight, *vide* Birch-Hirschfeld, Gerhardt's *Handbuch d. Kinderkrankh.*, Bd. iv., Abth. ii., p. 668.



CONGENITAL OBLITERATION OF THE BILE-DUCTS.

extremely hard and tough. The surface of a section has a dark olive-green colour, and is crossed by numerous greenish-yellow trabeculæ. A considerable amount of dark green fluid flows from the cut surfaces.

(Plate I. is from a drawing, and shows the morocco-like surface of the organ, as well as the condition of the gall-bladder and ducts.)

The hepatic ducts are not to be found in their usual form, but in their place there is a transverse sinus about $1\frac{1}{4}$ inches in length and $\frac{1}{3}$ inch in diameter. On its lower surface it presents two little sacs bulging downwards (one of which has been opened in the drawing). Its walls are thick and fibrous; its lumen is lined with a smooth membrane, and communicates by numerous openings with the dilated and thick-walled ducts in the interior of the liver. There is no communicating duct between this sinus and the cystic duct, and no distinct band of fibrous tissue can be found connecting the two. The gall-bladder is rather small; it is flaccid and wrinkled, and contains about 20 minims of a brownish watery fluid, like thin mucus. The cystic duct is small (perhaps $\frac{2}{3}$ the normal diameter); it can be followed right down into the centre of the pancreas, and its lower two-thirds, or so, which is of the same calibre as the upper portion, is all there is to represent the common duct.

Owing to the hurried nature of the post-mortem, the portion of the duodenum containing the papilla was left *in situ*, but there can be little doubt that it would have been found pervious, because fluid could be readily squeezed from the gall-bladder down as far as the middle of the pancreas where the duct was severed.

The bloodvessels are quite normal. The connective tissue round the vessels and ducts is possibly a little thickened, but certainly shows no evident traces of past inflammation, and there is no roughness or other abnormality of the peritoneum covering it. The pancreas and the portion of duodenum removed are normal. The lower parts of the bowel contained much blackened fæces. The spleen is large, measuring $3 \times 1\frac{3}{4} \times \frac{7}{8}$ inches; it weighs $1\frac{1}{2}$ ozs. It is dark in colour, with a distinctly yellowish tinge, and is very tough. The Malpighian bodies are indistinct. The kidneys appear normal.

Microscopic Examination:—

Liver.—Several pieces of the right lobe were hardened in Müller's fluid, and several in spirit; and they were cut, stained, and mounted in the usual way.

On using a low power, one is struck at once by two things, —firstly, the section is traversed by a very coarse network of fibrous tissue, which is continuous with the lower layers of the capsule, and generally includes several acini in each of its meshes; and, secondly, the tissue looks as if peppered over with little dark spots. The largest of these are found to correspond in distribution with the strands of the fibrous network, while the smaller are most numerous in the inner zones of the hepatic lobules. On closer examination of the section we find the following conditions:—

The *capsule* is somewhat wavy in outline, and is thickened, but very irregularly. In some places it differs little, or not at all, from the normal in this respect, while in others it is six or eight times the usual thickness. It is thickest where it is joined by large branches of the interacinous network, and these places generally bulge somewhat on the surface. It contains numerous large vessels and sinuses filled with blood, and in its inner layers are many bile-ducts distended with green or brown masses of inspissated bile.

The *fibrous network*, already mentioned, is formed by broad bands of fibrous tissue which pass inwards from the capsule, and branch round the lobules. Generally the meshes include from 1 to 6 acini in each (mostly 1, 2, or 3), and these are more or less distorted in shape owing to the compression they are exposed to. In some places, what appears to be only a portion of a lobule is all that occupies a mesh. The knots, so to speak, of the network are represented by masses of fibrous tissue arising from an enormous increase of the connective tissue normally present in and around the portal spaces, while the connecting strands occupy interlobular spaces. The network is by no means a complete one, and there are numerous small islets of connective tissue at points in between the lobules, and sometimes wedged into the substance of them, as it were. In stained specimens, the fibrous bands are usually more deeply coloured along their outer margins, owing to the presence of numerous proliferating cells. This fibrous tissue, like that of the capsule, contains numerous dilated bloodvessels and bile-ducts. The arteries appear to be increased in number as

well as in size, they are tortuous in their course, and some of those seen on section seem to have thickened muscular walls. The bile-ducts are also tortuous and have thickened walls, and many of them contain large masses of inspissated bile. As to their distribution here, it is not so easy to make out as in the layers of the capsule, but they seem to be more numerous, on the whole, towards the periphery of the bands than in their centre.

In many places at the junction of the liver-lobules and the fibrous tissue, one sees most beautifully the arrangement of the liver-cells into parallel rows, and the formation out of them of new bile-ducts.

The *hepatic lobules* vary much in size, and also, as already noted, in shape, owing to the compression they are undergoing.

The microscopic characters of the liver-tissue vary very considerably in different portions of the organ, and even in different parts of the same section.

Firstly, A large proportion of the lobules are composed of very normal-looking cells, arranged in the usual way. The nuclei of these are well formed and colour well, and, indeed, in certain areas they absorb the carmine out of the picro-carmine stain in a very remarkably distinct way, and seem larger than usual, as if in a state of unusual activity.[1] In these acini one finds no intra-lobular cirrhosis at all.

Secondly, Many of the cells even of the normal-looking lobules contain vacuoles, and some of these are so large that the cell seems transformed into a vesicle, and the nucleus is not to be seen. Many, if not all, of these vacuoles are merely the spherical spaces left from the oil having been dissolved out of fatty globules during the hardening process. Most of them do not stain with osmic acid at all, but in a few it brings out a black crescent or radiating crystals.

On looking over the sections with a low power, one notices here and there smudged-looking patches which have not taken on almost any stain. These areas shade off almost imperceptibly into the surrounding tissue, and are not bordered by a line of deeply staining cells. Under a high power, they are found to be composed more or less entirely of cells which have become distended with colourless fluid until they are quite globular and much larger (2–4

[1] See Hamilton, *Journ. of Anat. and Physiol.*, xiv., 1879, p. 185.

times) than normal. It looks as if the vacuole had gone on enlarging till all the cell-contents, including the nucleus, had disappeared, and a simple bladder resulted. The exact localization of these areas is not always easy to determine; in some cases they occupy a segment (a quarter or so) of the circle formed by the lobule, but often their position is less distinctly defined. They seem usually free from bile-masses, even although these may be plentiful in the adjoining liver-tissue. Some of these patches appear shrivelled and small, as if in process of being absorbed and replaced by a sort of cicatrix. It seems possible that some of the islets of fibrous tissue, before alluded to, may have arisen in this way, and if so, this would account for the apparently intralobular situation of some of them.

It is very difficult to ascertain the cause of these appearances; but, judging from their situation and surroundings, one is inclined to think that they must be due in some way to the pressure exerted by the newly-formed connective tissue. It is, however, possible that the state of stagnation of the bile may in some unexplained way have to do with their causation. These areas, especially when the process is far advanced in them, are certainly strikingly similar in appearance to those figured by Beloussow in his article "On the Results of Tying the Ductus Choledochus in Animals,"[1] which he regards as little patches of localized gangrene brought about by the bursting of over-distended bile-capillaries. He found, however, that it was only during the earlier days after the operation that this appearance was met with, and that a week or two later they were replaced by fibrous cicatrices. Pick also, in his paper on the same subject,[2] gives a somewhat similar figure of a necrotic area.

Thirdly, There is a morbid change which resembles that just described in some ways and differs from it in others. Under the capsule—especially marked near the sharp edge of the liver—there is a homogeneous-looking zone which scarcely colours at all with stains. It stretches along parallel to the capsule without regard to the limits of the individual lobules, and is bordered by a richly nucleated, brightly-staining line. There are very few fragments of bile seen in it. On closer inspection this turns out to be apparently

[1] P. N. Beloussow, *Arch. für Experiment. Pathol.*, xiv., 1881, p. 200.

[2] Ernst Pick, *Zeitschr. f. Heilkunde*, xi., 1890, 2 and 3, p. 117.

an area of coagulation-necrosis, in which the cells are breaking down by atrophy and fatty change, and are being absorbed. Its situation and distribution suggest that it is probably caused by the compression exerted by the thickened capsule and other newly-formed fibrous tissue. In the part which is beginning to be affected, we find the nuclei much increased in number and very deeply stained. There are also many vacuoles. As one passes from the more healthy surrounding tissue towards the centre of the morbid area, these vacuoles increase in number and size, the nuclei rapidly lose their power of absorbing colours, and the cells become atrophied or fattily degenerated and break down. In the parts most affected, the cellular structure is difficult to make out. In thin sections, from which the cellular debris has been shaken out of this area, one sees that there is a delicate network of inter-cellular fibrous tissue left.

Fourthly, One of the most noticeable features of the sections is the large number of little masses of inspissated bile scattered about over them. These plugs are found, as already noted, distending many of the small bile-ducts, the largest of them being seen in those ducts which are among the fibrous tissue. Of the smaller ones, the majority are found in the inner two-thirds of the lobules, and the number of them in many places is very great. In this situation we find, on looking closer, that by far the largest number of these little fragments are not, as one might perhaps have thought at first sight, *in* the liver-cells, but lie between them, constituting, in fact, casts of the bile-capillaries, and many of those which are cut lengthways have a branched configuration.

A few of the cells, however, do seem really to contain fragments of this material inside them. We find some, for example, which have a stained nucleus and tolerably healthy-looking protoplasm, and in it one or two small round green masses. These latter, by their shape, size, and position, remind one very much of the intra-cellular bladders which Pfeiffer and Kupfer [1] have described as occurring in the cells of the rabbit's liver after injections with Prussian blue, and they may possibly be casts of similar cavities here.

Where larger fragments occur, the cell in which they are seems usually more or less free from stain, and without a visible nucleus. In many places, one finds several different-sized masses lying

[1] Hermann's *Handbuch der Physiologie*, Th. i. p. 226, 1883.

together inside what looks like a cell-wall, with only a little granular unstained matter about them, as if the damming back of the bile into the inside of the cell had caused dissolution of the ordinary cell-contents. This may probably account for the number of cells which seem to have disappeared from the inner zones of those lobules in which the bile-plugs are most numerous, the absence of which gives those areas such a ragged look under a low power.

It is difficult to see why these fragments of bile should be localized so markedly in the inner zones of the lobules. Wyss, in his observations on the histology of obstructive jaundice (in adults),[1] found that when the obstruction had only existed a short time, the cells in the inner zone were diffusely stained with bile; but that when it was of long (three years) duration, bile-plugs were met with at the periphery of the lobules. In our sections there are only a few cells that present the diffuse granular pigment described and figured by Wyss, and the cells thus affected are usually ones which form part of the wall of a bile-capillary which is distended with bile.

Spleen.—Sections of the spleen show the ordinary appearances of chronic hypertrophy of that organ.

Kidneys.—Sections of one kidney were also examined, and showed a few very fine bands of young fibrous tissue running inwards from the capsule—a very slight amount of interstitial nephritis. In other respects the organ seemed normal.

II. Other Published Cases.

The following list contains all the cases which I have been able to find reported in which the diagnosis of malformation, obliteration, or absence of the biliary passages was confirmed by a post-mortem examination. In Tables I. and II., the clinical and pathological details of these cases are tabulated for comparison.

1. West.—*Diseases of Infancy and Childhood*, eighth edition, p. 649.
2. J. H. Morgan.—*Path. Soc. Trans.*, xxix., p. 137.
3. Eustace Smith.—*Disease in Children*, third edition, p. 718.

[1] O. Wyss, Virchow's *Archiv*, xxxv., p. 553.

4. Henoch.—*Lectures on Children's Diseases*, New Syd. Soc. Transl., vol. i., p. 28.
5. C. Murchison.—*Diseases of the Liver*, third edition, p. 422.
6. Wickham Legg.—*Bile, Jaundice, and Bilious Diseases*, p. 641.
7. H. Ashby.—*Pendlebury Hospital Abstracts*, 1883, p. 59.
8. H. Ashby.—*Ibid.*, 1886, p. 73.
9. Glaister.—*Lancet*, 1st March 1879, p. 293.
10. S. Wilks.—*Path. Soc. Trans.*, xiii., p. 119.
11. Harley.—*Diseases of the Liver*, p. 299.
12. Nunneley.—*Path. Soc. Trans.*, xxiii., p. 152.
13. Roth.—Virchow's *Archiv*, xliii., p. 296.
14. }
15. } C. Binz.—Virchow's *Archiv*, xxxv., p. 360.
16. }
17. Donop.—*De Ictero speciatim neonatorum*, Berlin Dissertation, 1828, p. 18.
18. C. Lotze.—*Berliner klin. Wochenschrift*, 1876, No. 30, p. 438.
19. Heschl.—*Wiener med. Wochenschrift*, 1865.
20. }
21. } Hennig.—*Jahrbuch für Kinderheilkunde*, ix., 1876, p. 406.
22. Freund.—*Ibid.*, p. 178.
23. Oxley.—*Lancet*, 1883, ii., p. 988.
24. Cursham.—*London Medical Gazette*, 1840, vol. ii., p. 388.
25. Lomer.—Virchow's *Archiv*, xcix., p. 130.
26. }
27. } Schüppel.—*Archiv für Heilkunde*, xi., p. 78, 1870.
28. E. Gessner.—*Ueber congen. Verschluss der grossen Gallengänge*, Diss. Halle, 1886.
29. }
30. } Köstlin.—Canstatt's *Jahresber.*, iii., p. 293.
31. } A. D. Campbell.—*Northern Journal of Medicine*, Aug. 1844,
32. } p. 237.
33. Anderson.—*Boston Med. and Surg. Journal*, Jan. 2, 1850, p. 440.
34. } A. A. Gould.—*Boston Med. and Surg. Journal*, Sept. 6, 1855,
35. } p. 109.
36. H. W. Dean.—*Trans. Amer. Med. Assoc.*, vol. ii., 1858, p. 304.
37. J. Blake White.—*American Journal of Obstetrics*, Jan. 1888, p. 48.

38. Danforth.—*Chicago Medical Journal*, 1870, p. 110.
39. Sir Everard Home.—*Philosophical Transactions*, 1813, p. 156.
40. } James Blundell.—Elliotson's *Human Physiology*, 1840, p.
41. } 101 (*note*).
42. L'hommeau.—*Bulletins Soc. Anat. de Paris*, 1842, xvii., p. 52.
43. Jenkins.—"On Spontaneous Umbilical Hæmorrhage," *Trans. Amer. Med. Assoc.* vol. xi., 1858.
44. A. R. Simpson.—*Edin. Med. and Surg. Journal*, 1860–61, p. 1045.
45. J. M. Hobson.—*Path. Soc. Trans.*, 1882, p. 183.
46. Paul Meyer.—*Berliner klinische Wochenschrift*, 19th April 1886, p. 255.
47. Walter Thomas.—*New Zealand Medical Journal*, April 1891, p. 161.
48. Dr Cnopf.—*Münchener Med. Wochenschrift*, 21st April 1891.
49. Dr Cnopf.—*Ibid.*, 28th April 1891.

To complete this list, I should mention that Dr West[1] refers to two other cases he has seen, in addition to those he gives details of—that Prof. Virchow[2] mentions his having seen one case—and that a case has been published by Michel[3] and one by Lobstein,[4] of which I have not been able to get any particulars. Trousseau[5] also refers to some cases mentioned by Porchat in his thesis (1859), and I have not been able to find out whether these are among those I have tabulated. Lastly, Witzel[6] has published an account of a child with congenital obliteration of the bile-ducts in addition to a large number of other developmental abnormalities.

We shall now proceed to analyze the tabulated cases (see Table I.)

1. *Rarity of Occurrence.*—Whatever the causes are which combine to produce this lesion, it is evident that they are only very rarely found in combination, for all the reported cases do not amount to sixty in number.

[1] West, *Diseases of Infancy and Childhood*, eighth edition, p. 649.
[2] Virchow, *Gesammelte Abhandlungen für wissenschaftl. Medicin*, p. 858.
[3] Michel, *Correspondenzblatt d. Würtemberg. ärztl. Vereinigung*, Stuttgart, H. 33, p. 261.
[4] Lobstein, see Meckel's *Pathologische Anatomie*, i., p. 606.
[5] Trousseau, *Clinical Medicine*, New Sydenham Soc. Transl., vol. iv., p. 317.
[6] O. Witzel, *Centralbl. für Gynæcologie*, 1880, p. 561.

TABLE I.

No. of Case.	Reported by	Health of Parents.	Other Children.	Age at Death.	Sex.	If Premature.	Labour.	State at Birth.	Signs of Syphilis.	When Jaundice began after Birth.	Meconium.	Motions.	Progress of Jaundice.	State of Nutrition.	Position of Hæmorrhages, if present.	Ascites.	Spleen.
	J. T.	No syphilis.	None affected.	3½ months.	M.	No.	Prolonged; forceps.	Healthy.	None.	About 10th day.	Normal during 1st week.	Clay-coloured after 1st week.	Seemed to get rather less.	Wasted gradually.	From nose, mouth, and bowel.	No.	Large.
1	West.	.....	.....	6½ months.	F.	.....	.....	.....	.....	3rd day.	Apparently, during 1st day.	White after 2nd day.	Increased from 3rd day to 3rd week.	.....	.....	Yes; 1½ pint.	Much enlarged.
2	Morgan.	Good; no syphilis.	One died of (?) congenital heart disease.	9½ weeks.	M.	.....	.....	Healthy.	None.	10th day.	Said to be normal.	"Without bile;" sometimes contained greenish-brown matter.	Began gradually.	Good.	Subcutaneous, and from stomach.	No.	.....
3	E. Smith.	Good.	None affected.	4 months.	M.	.....	.....	Robust; healthy.	None.	A week.	2 dark stools.	Hard and white.	Varied in intensity.	Gradually wasted.	.....	No.	Not enlarged.
4	Henoch.	.....	.....	5½ months.	...	.....	.....	.....	None.	Present at birth.	.....	Dry, milk-white.	Got greener.	Wasted to a skeleton.	.....	No.	.....
5	Murchison.	.....	.....	5 months.	F.	.....	.....	Healthy.	.....	A few days after.	.....	Perfectly white; very offensive.	Increase, then decrease.	Wasted.	Subcutaneous, and from nose, stomach, and bowel.	.....	.....
6	Wickham Legg.	.....	None affected.	5½ months.	F.	.....	.....	.....	Snuffles.	Present at birth.	.....	"Like curds and whey."	Increase, then decrease.	Wasted.	Subcutaneous, and from the bowel.	No.	Much enlarged.
7	Ashby.	.....	.....	4½ months.	M.	8th month.	Tedious.	.....	No snuffles or rash.	About a week.	.....	Loose; grey and white.	.....	Gradually wasted.	.....	No.	.....
8	Ashby.	.....	.....	4 months.	M.	.....	.....	.....	.....	Present at birth.	2 dark motions.	Perfectly white; offensive.	.....	Fairly nourished at first.	.....	.....	Enlarged.
9	Glaister.	Both bilious.	7, of whom 4 died of jaundice.	62 hours.	M.	No.	"Dry."	Healthy.	None.	On the evening of 1st day.	During 1st day.	Clay-coloured.	Steadily increased.	.....	Under conjunctiva.	.....	.....
10	Wilks.	.....	.....	6 weeks.	M.	.....	.....	.....	.....	A fortnight.	White.	White.	.....	.....	.....	.....	.....
11	Harley.	.....	Several.	3 days.	M.	No.	Easy.	Healthy; not robust.	None.	Present at birth.	Pale, creamy.	Pale, creamy.	.....	.....	.....	No.	.....
12	Saunsley.	.....	.....	6 months and 21 days.	M.	.....	.....	.....	.....	Present at birth.	White; sometimes contained green lumps.	Light ash-grey; sometimes contained green lumps.	.....	Greatly emaciated.	.....	A small quantity of yellow serum.	.....
13	Roth.	.....	.....	4½ months.	M.	.....	.....	Healthy.	Abscesses, and P.M. conditions thought to show it.	Present at birth.	.....	.....	Steadily increased.	Emaciated.	Into tissue of left lung.	.....	Twice usual size.
14	Binz.	Father syphilitic; mother very healthy.	Sister of next.	2 days.	F.	No.	.....	Apparently quite healthy.	None.	2nd day.	Several very small evacuations.	.....	.....	.....	.....	.....	.....
15	Binz.	As above.	Brother of last.	24 hours.	M.	No.	.....	Pretty well developed; cyanotic	None.	During 1st day.	.....	.....	.....	.....	.....	.....	Very big.
16	Binz.	Father healthy; mother delicate; no syphilis.	Some healthy.	27 days.	M.	No.	.....	Healthy.	None.	3rd day.	.....	Colourless, clayey; very offensive.	Rapid increase.	.....	.....	.....	.....
17	Dowp.	Mother healthy.	.....	More than 7 weeks.	M.	.....	Easy.	Healthy.	.....	Within 24 hours.	.....	Partly greenish or yellowish, partly ash-coloured; almost no smell.	Steady increase.	Emaciated steadily.	From bowel and from leech-bites.	.....	.....
18	Lotze.	Father treated with mercury; mother anæmic.	.....	In 8th month.	...	.....	.....	.....	Not the slightest.	In first weeks.	.....	Light yellowish-grey, free from bile during last fortnight.	Became deep.	Very emaciated.	.....	.....	.....
19	Heschl.	.....	.....	In 7th month.	...	.....	.....	.....	.....	Present at birth.	None passed.	Whitish or greyish; offensive.	.....	.....	From bowel.	.....	Large.
20	Hennig.	.....	.....	5 days.	...	.....	.....	.....	.....	.....	.....	Quite colourless.	Increased steadily.	.....	.....	.....	.....
21	Hennig.	.....	.....	A few days.	F.	8th month.	Breech presentation; narrow pelvis.	.....	.....	Soon after birth.	.....	Three brown motions.	.....	.....	On face at birth.	.....	.....
22	Freund.	Mother healthy.	Other twin was jaundiced and recovered; 3 others.	3 months and 3 days.	M.	.....	.....	Healthy.	.....	A few days after birth.	Quite white.	Quite white, like curds.	Increased rapidly.	Extremely emaciated.	.....	.....	.....
23	Oxley.	.....	.....	More than 6 weeks.	F.	.....	.....	.....	.....	.....	.....	Like white curd.	.....	Emaciated.	.....	No.	.....
24	Cursham.	.....	.....	7 weeks.	...	.....	.....	.....	.....	Present at birth.	None.	White.	.....	Emaciated.	.....	No.	.....

TABLE I.—*Continued.*

No. of Case.	Reported by	Health of Parents.	Other Children.	Age at Death.	Sex.	If Premature.	Labour.	State at Birth.	Signs of Syphilis.	When Jaundice began after Birth.	Meconium.	Motions.	Progress of Jaundice.	State of Nutrition.	Position of Hæmorrhage, if present.	Ascites.	Spleen.
25	Lomer.	Father syphilitic.	9 others healthy; 1 abortion.	Still-born.	—	6th or 7th month.	.....	Macerated.	Distinct (bones, etc.)	.....	.....	.....	.....	.....	.....	Much sero-sanguinolent fluid.	.....
26	Schippel.	Mother syphilitic.	1st child.	On 3th day.	F.	4-6 weeks premature.	.....	Poorly developed.	Distinct (eruptions, etc.)	2nd day.	.....	.....	.....	.....	.....	A little greenish fluid.	Twice normal size.
27	Schippel.	Mother apparently healthy.	1 healthy.	8½ days.	F.	37th week.	.....	.....	.....	5th day.	.....	Quite white.	Increased.	.....	From bowel.	A little clear yellow fluid.	Thrice normal size.
28	Gessner.	Apparently healthy.	7 healthy.	14 weeks.	M.	.....	Easy.	.....	.....	Immediately after birth.	None.	Whitish grey.	Increased steadily.	.....	Subcutaneous.	.....	.....
29	Klotlin.	.....	.....	4 weeks.	M.	.....	.....	Healthy.	None.	3 weeks, along with abscess.	.....	Partly yellow, partly greenish.	Increased gradually.	Good.	.....	.....	.....
30	Klotlin.	.....	.....	6½ months.	F.	.....	.....	Healthy.	.....	About 6 months, along with erysipelas.	.....	Continued coloured.	.....	Wasted steadily.	.....	.....	.....
31	Campbell.	.....	.....	10th day.	F.	No.	Tedious.	Large and well developed.	.....	2nd day.	.....	Constantly light-coloured.	.....	.....	Umbilical.	.....	.....
32	Campbell.	.....	.....	6 months.	...	No.	.....	Healthy.	.....	Day after birth.	.....	.....	Became deep.	Emaciated.	From stomach.	.....	.....
33	Anderson.	.....	One other child had jaundice and hæmorrhages, but recovered.	12 days.	F.	.....	.....	Apparently healthy.	.....	.....	.....	Clay-coloured.	.....	.....	Subcutaneous and umbilical.	.....	.....
34	Gould.	Healthy.	Brother of next.	11 days.	M.	No.	Easy.	.....	.....	.....	None.	Copious; destitute of bile.	.....	.....	Umbilical, and from bowel.	.....	.....
35	Gould.	Healthy.	Sister of last.	7 days.	F.	No.	.....	.....	.....	6th day.	One motion of normal meconium.	.....	.....	.....	Umbilical.	.....	.....
36	Dean.	Healthy.	.....	4 days.	M.	No.	.....	Seemed quite healthy.	.....	2nd day.	.....	.....	.....	.....	Umbilical.	.....	.....
37	White.	.....	Some.	On 12th day.	...	No.	Natural and short.	"Seemed physically sound."	.....	9th day.	Apparently passed as usual.	.....	Got very deep.	.....	.....	.....	.....
38	Danforth.	.....	.....	72 hours.	...	.....	.....	.....	.....	30 hours.	.....	.....	.....	.....	.....	.....	.....
39	Home.	.....	.....	Several months.	...	No.	.....	Usual size.	.....	.....	.....	Regular.	.....	Emaciated.	.....	.....	.....
40	Blundell.	.....	.....	4 or 5 months.	...	.....	.....	.....	.....	.....	.....	White, like spermaceti.	.....	Throve tolerably and grew rapidly.	.....	.....	.....
41	Blundell.	.....	.....	4 or 5 months.	...	.....	.....	.....	.....	.....	.....	As above.	.....	As above.	.....	.....	.....
42	L'homme an.	.....	.....	3 months.	...	.....	.....	.....	.....	.....	.....	.....	.....	.....	Into gall-bladder, as well as "elsewhere."	.....	.....
43	Jenkins.	Good.	.....	4 days.	M.	No.	.....	Apparently healthy.	.....	2nd day.	.....	.....	.....	.....	Umbilical.	.....	Enlarged (weight 2 oz.)
44	Simpson.	.....	.....	About 6 weeks.	...	.....	.....	.....	.....	None mentioned.	.....	.....	.....	.....	.....	A teacupful of yellow serum, with fibrinous flocculi.	.....
45	Hobson.	No syphilis.	5 healthy.	10 weeks.	M.	.....	.....	.....	None.	Present at birth.	Some dark meconium passed after birth.	Absence of bile.	.....	.....	From stomach (fatal).	.....	.....
46	Meyer.	No history of syphilis obtained.	3 healthy; 1 abortion.	4½ months.	F.	.....	.....	.....	None.	2nd day.	.....	Clay-coloured.	Increased before death.	Steadily emaciated.	.....	.....	Enlarged.
47	Thomas.	Apparently very good.	4 had died jaundiced before 9th day.	12 days.	...	No.	Easy.	.....	.....	2nd day.	.....	.....	Steadily increased.	.....	.....	.....	.....
48	Caspf.	Mother healthy; had been scrofulous.	1st child.	7½ months.	M.	.....	Easy.	Very delicate.	None, except swelling of the epiphysis of one tibia.	3rd day.	.....	Thin greyish-yellow.	Could not get deeper.	Very badly developed and nourished.	Subcutaneous, and from bowel.	A litre of clear yellow fluid.	Enlarged.
49	Caspf.	Both healthy.	2 others healthy.	3 months.	...	.....	.....	.....	.....	2nd day.	.....	Quite colourless.	.....	.....	.....	.....	Small.

2. *Health of Parents.*—The main point of special interest with regard to the parents' health is the question whether they were suffering from syphilis. The evidence has, of course, to be received with considerable reservations so far as it is negative. In twenty-nine out of the fifty cases, nothing is said about the parents that can be held to bear on this particular. In fifteen it is said that they were "healthy," and, in at least four of these, it is expressly stated that there was no history of syphilis discoverable. Mr Morgan seems to be quite certain on this point with regard to the case which he has reported. In four instances, one parent was certainly syphilitic (or had been), and probably also in a fifth. Therefore out of the ninety-six parents of these fifty children we have evidence of syphilis in five only. It certainly deserves attention that in several cases one or both parents suffered severely from some digestive derangement. It is scarcely likely that this fact can have any etiological importance, but this has been suggested as possible.[1]

3. *Other Children.*—About the other children we notice three things:—

(*a.*) In several instances there had been a large family of healthy children before the patient was born.

(*b.*) In no case is it mentioned that any of the other children had shown signs of syphilis.

(*c.*) Although in several cases the patient was the only child affected in a large family, there is evidently a very remarkable tendency for the disease to occur in more than one child of the same parents. For example, among our fifty cases we find that there twice over occur two cases in the same family (Nos. 14 and 15, 34 and 35). In another instance (No. 22) a pair of twins was jaundiced, and one of them recovered. Then in Anderson's case (No. 33) another child of the same parents suffered, we are told, from both jaundice and hæmorrhage, but recovered; and again, out of seven children in the same family, as Glaister's case (No. 9), four had died jaundiced, and two were less severely jaundiced and recovered; and in the case reported by Thomas (No. 47), four previous children had died with exactly the same symptoms. In the two cases before alluded to, which Dr West

[1] Binz, Virchow's *Archiv*, xxxv., p. 360, and Glaister, *Lancet*, 1st March 1879, p. 293.

mentions without giving particulars, there was also a marked family history of infantile jaundice. It is interesting to note that in the cases of fatal infantile jaundice which have been found post-mortem to be accompanied by pervious bile-ducts, occurrence of the disease in several members of a family is an equally characteristic phenomenon (*v. infra*).

4. *Character of the Labour.*—This is important, because injury or exposure at the time of birth might be the exciting cause of peritonitis, and therefore is of possible etiological importance in connexion with our subject. We find, however, that there is nothing in the statistics of the table to suggest that the character of the labour can be thought of importance. In those few cases in which the labour is said to have been tedious or otherwise abnormal there is nothing in the date of the onset of the jaundice to indicate any probability of injury at the time of birth being the cause of the disease.

5. *State of the Child at Birth and Prematurity.*—The state of the infant at birth confirms the above impression, for in none of the cases (with the exception of two evidently syphilitic ones, Nos. 25 and 26) does anything morbid, except the yellow colour of the skin, seem to have been noticed.

Prematurity is mentioned five times. In none of these cases was jaundice present at birth.

6. *Sex.*—It has often been pointed out that this condition affects more boys than girls, and our table bears this out. Out of thirty-four cases in which the sex is mentioned, twenty-one were boys and thirteen girls.

7. *Symptoms.*—

(*a.*) *Onset of Jaundice.*—The exact period of the onset of the jaundice seems to have varied very much in different cases. Turning to our table we find that this fact is not mentioned in 10 cases.

that jaundice was present at birth in			9	„
„ it appeared on the day of birth in			5	„
„	„	„ second day „	9	„
„	„	„ third day „	3	„
„	„	within a week of birth in	4	„
„	„	within 1 or 2 weeks after birth in	6	„
„	„	after a fortnight or more in	3	„

The exact period of onset is, of course, a point with regard to

which there are several sources of error. For example, the presence of ordinary icterus neonatorum might obscure the precise date of appearance of the more severe form of discoloration; or want of light or attention might easily lead to its presence being overlooked for several days. Still, taking such difficulties fully into account, there can be no doubt, after studying the reported cases, that in a considerable proportion of them there was no jaundice present until several days after birth, and that the period of onset varies very much in different cases. Also, it is plainly stated in many cases that the jaundice was very faint at birth (or when first seen), and rapidly became more intense—which change suggests that the symptom was not of long standing.

These facts lead one to infer that something or other occurring at or about the time of birth has some relation to the onset of the coloration in many cases.

What period of time should elapse between the obstruction of the bile-duct and the appearance of jaundice in an infant, we do not know. Wickham Legg[1] is of opinion that the time for an adult is twenty-four to forty-eight hours. Murchison[2] says that in patients with biliary colic the yellow discoloration is observed twelve to twenty-four hours after the subjective symptoms have occurred. Little help can be got from observing the time which ligature of the common duct in the lower animals takes to produce jaundice, because this varies widely not only with the different genus operated on, but with the individual animal, and also apparently with the individual operator. In dogs it takes from a few hours[3] to three days,[4] in cats from ten to twenty days,[3 5] and in guinea-pigs it does not come on at all.

We should naturally think it possible that the action of some external agency, such as violence or cold at the time of birth, might be to blame for the appearance or aggravation of the jaundice soon after it, but this, as already seen, finds no support from facts.

The enormous change which the circulation in the liver undergoes about the time of birth constitutes the most probable ex-

[1] Wickham Legg, *loc. cit.*, p. 257.

[2] Murchison, *loc. cit.*, p. 380.

[3] Charcot and Gombault, *Arch. de physiologie*, iii., 1876, p. 273.

[4] Frerichs, *Klinik der Leberkrankheiten*, 1858, Bd. i., p. 99.

[5] Wickham Legg, *St Bartholomew's Hosp. Rep.*, 1873, vol. ix., p. 161.

planation of the relation between the onset of jaundice and that event.

It seems very difficult to understand how a child who for months of intra-uterine life has had no bile reaching its intestines (as indicated by entire absence of colour in the fæces from the first) can be born and remain for many days unjaundiced; still this seems to have been so in Wilks' and Freund's cases (Nos. 10 and 22). Jaccoud says that in cases of long-continued obstructive jaundice when the colour passes off, this is due to the fact that the liver may under these circumstances cease to secrete bile. Can it possibly be that the cells of the child's liver, which had long ceased to secrete bile, owing to the permanent blocking of their ducts, are so stimulated by the sudden change in their circulation that their natural function begins again ?

(*b.*) *Character and Progress of Jaundice.*—Even when it is absent or only slightly marked at birth, the jaundice always becomes extremely deep sooner or later, and often is of a greenish tinge. It is sometimes noticed to vary a little in severity from day to day, but on the whole it gets steadily worse until it is as deep as it can well be. Towards the end it has sometimes been observed to become a little paler.

It is interesting to observe that in several cases (Nos. 18, 21, 29, and 30) where there is said to have been a certain amount of communication by at least one duct between the liver and the intestine (see Table III.), the jaundice was as marked as in the other cases where the common duct was entirely obliterated. These cases, in fact, form a sort of link between those of complete obliteration and the other cases of jaundice with similar clinical histories, in which pervious ducts are found at the post-mortem (*v. infra*).

(*c.*) *Urine.*—In Dr Nunneley's case (No. 12) it is stated that there was no bile-pigment in the urine. In all the other cases where the urine is described, there was apparently much bile-pigment in it. No other abnormality is noticed.

(*d.*) *Meconium.*—Meconium is to a large extent made up of matters derived from the vernix caseosa which the fœtus in utero swallows along with amniotic fluids,[1] but it also contains intestinal

[1] Zweifel, *Arch. f. Gynæcol.*, vii., 1875, p. 474.

epithelial cells and mucus, and its dark green colour is derived from the bile. It begins to be formed early in intra-uterine life, and in a three months' fœtus, according to Zweifel, both bile-pigment and bile-acids may be detected in it. It gradually accumulates in the intestine until the whole of the lower bowel is distended by it, and at birth it amounts to from 60 to 90 grammes.[1] The meconium, which is found lowest down in the bowel at birth, and which has therefore presumably been longest there, has the darkest colour, while that near the cæcum is considerably paler. So far as I know, meconium is never met with without its usual very dark green colour—even light green—except in cases in which there is severe organic disease of the liver or bile-ducts.

When we turn to Table I. we find that in ten out of the fifty cases it is either expressly stated, or else implied, that ordinary meconium, or something similar in appearance, was passed during the first few days.

Some of the infants who passed ordinary meconium were born jaundiced, but in others the discoloration was not noticed for a week or more after birth. With the exception of Köstlin's cases (Nos. 29 and 30), which indeed differ in several points from the others, it seems that in none of the cases was the dark meconium followed by even one motion of normal yellow fæces; the stools at once assumed their cream-colour or clay-colour, even if the jaundice did not come on for some days later. This looks as if the disease was always in a state of considerable advancement at birth.

What is the significance of the occurrence of normal meconium in some of the cases, and of perfectly colourless motions from the first in others? When normal meconium is passed it proves that the way from the liver-cells to the bowel must have been open for some time after meconium began to be made, and it therefore excludes the possibility of the obliteration of the duct having been due solely to an arrest of development. Where the discharge is colourless from the very beginning, it points to a very early occurrence of the obstruction. Some reasons might be urged against so early an origin for the lesion, but the entire absence of colour cannot be otherwise satisfactorily explained. We cannot think it possible, for example, that bile passed into

[1] Vierordt, Gerhardt's *Handb. d. Kinderkrankheiten*, second edition, vol. i., Abth. i. p. 330.

the bowel can become decolorised in time, as bile shut up in the gall-bladder sometimes does;[1] for, if so, we should have this occurring also where the liver and ducts were normal. Nor can we reasonably suppose a morbid condition of the liver to have existed before, of such a nature as to give rise to colourless bile like that secreted in congenital syphilitic cirrhosis.

(*e.*) *Motions.*—In about twenty of the cases the motions seem to have been white, greyish, or cream-coloured from the beginning, and in most of the others they became so immediately after the meconium had been passed. In a few, however, we are told that the motions sometimes contained coloured matter at a late stage of the case. These may be divided into two distinct classes,—*firstly*, those in which there was not complete obstruction to the flow of bile from the liver to the duodenum, such as cases 18, 21, 29, and 30, in which a varying amount of yellow, green, or brown matter was observed; and, *secondly*, a few in which green matter was passed along with the grey or white fæces, although the obstruction to the bile-duct must have been quite complete at the time; for example, Mr Morgan's case (No. 2), in which the motions contained greenish-brown matter after a dose of grey powder; and two other cases (Nos. 12 and 17) in which green lumps were seen, and in which no mention is made of their following the administration of mercury.

The former class requires no discussion, but the causation of the green matter (of non-hepatic origin) in the fæces in the latter class is a matter of some interest and obscurity. The subject does not seem to have been as yet very thoroughly worked out, and I have nothing new to offer in explanation of the facts; but it may be worth while to mention briefly a few facts and statements from different sources bearing on them, and these will suggest various possible explanations of the problem as it presented itself in our cases. *Firstly*, then, although no bile is entering the intestines in the ordinary way, it is *possible* that a slight amount of green or yellow colour may be imparted to the fæces by their being mixed with intestinal mucus which is jaundiced, just as the blood and urine are.[2] This, however, explains very little indeed. *Secondly*, It is now believed that the well-known green stools produced by

[1] Courvoisier, *Casuistisch-statistische Beiträge z. Path. und Chirurg. d. Gallenwege*, Basel, 1890.

[2] Osborne, *Dublin Quarterly Med. Journal*, vol. xv., 1853, p. 106.

the administration of mercury do not depend, as used to be held, on an increased pouring out of bile, but rather on the formation of a peculiar green compound of mercury and sulphur in the alimentary canal,[1] and Radziejewski[2] has produced green stools by giving calomel to a dog with a complete biliary fistula. In Mr Morgan's case, the green matter appeared after a dose of grey powder, so that some such explanation as this would account for it; and as the other cases most probably got mercury also, it might possibly account for them also.

Thirdly, There is another explanation which is quite tenable in some of the cases, namely,—that the colour may be due to micro-organisms. In this connexion I may refer first to L. Hermann's recent experiments.[3] He operated on a number of dogs by separating a loop of intestine entirely from the rest of the gut, sewing up the ends of it, and then establishing the lumen of the rest of the bowel by sewing the cut surfaces together. In those dogs which died after six days, the separated portion of bowel contained a brownish gelatinous fluid; while those which survived the operation several weeks had the loop of gut full of a firm greyish-green mass deceptively like fæces. This greenish material contained innumerable micro-organisms, to the action of which its colour was presumably due. When tested for bile-pigments it gave no reaction. Again, in many cases of infantile diarrhœa the intensely green colour of the stools has been shown by Lesage[4] and others to be due to the presence in enormous quantities of a peculiar chromogenous bacillus, and to have nothing to do with bile. Lastly, I have seen a case where an infant, born with complete obliteration of part of the jejunum and who up to its tenth day had passed only white motions, commenced then to have dark green stools containing large quantities of organisms (micrococci).[5]

(*f.*) *Vomiting.*—In nine of the cases vomiting is mentioned as having occurred, but considering the frequency of this symptom in children this fact does not seem to be of any special importance.

[1] Thudichum, *Lancet*, March 30th, 1889, p. 631.

[2] Radziejewski, *Arch. f. Anat. Phys., u. s. w.*, 1870, p. 37.

[3] L. Hermann, Pflüger's *Archiv*, xlvi., p. 93.

[4] A. Lesage, *Le Bulletin Médical*, 26th Oct. 1887; and *Arch. de physiologie norm. et path.*, 15th Feb., 1888.

[5] See Appendix I.

(*g.*) *Hæmorrhages.*—The occurrence of spontaneous hæmorrhages is one of the most characteristic clinical features in these cases. In twenty-one out of the fifty—that is, in fully half of the cases which lived more than a few days—the fact of hæmorrhage having occurred from some part of the body is noted; and in all probability it may have occurred in some of the others also, although not mentioned, as the records of many of them are so meagre.

The situations of the hæmorrhages mentioned are as follows :—

Subcutaneous	in	7	of the cases.
Subconjunctival	„	1	„ „
Umbilical	„	6	„ „
From nose	„	2	„ „
Vomited	„	4	„ „
From bowel	„	8	„ „
From mouth	„	1	„ „
From lung	„	1	„ „
Into gall-bladder	„	1	„ „
From leech-bite (excessive)	„	1	„ „

A similar tendency to spontaneous hæmorrhage is well known to exist in all cases of continued obstruction of the common duct, sooner or later, and is almost equally characteristic of a number of other very different morbid conditions which are accompanied by jaundice, such as acute yellow atrophy, yellow fever, phosphorus poisoning, etc. The situations above-mentioned are pretty much the same as those from which bleeding usually occurs in those other forms of jaundice, with the exception, naturally, of the umbilicus.

The occurrence of hæmorrhages in a case of infantile jaundice is always of very serious prognostic significance, but they are not invariably followed by a fatal issue. One such case which recovered is mentioned by Anderson,[1] and another is reported by Henoch.[2] Grandidier, in his very comprehensive article on "Spontaneous Umbilical Hæmorrhage in New-born Children,"[3] mentions thirty-five cases of hæmorrhage from the navel in which the children

[1] Anderson, *Boston Med. and Surg. Journal*, Jan. 2, 1850, p. 440.

[2] Henoch, *Lectures on Children's Diseases*, New Syd. Soc. Transl., vol. i. p. 27.

[3] Grandidier, *Journal f. Kinderkrankheiten*, May 1859, p. 380.

were jaundiced, and also had ecchymoses, and of these three recovered. As indicating the close connexion between jaundice and hæmorrhage, it may be mentioned that fully two-fifths of all the cases of spontaneous umbilical hæmorrhage which Grandidier has collected occurred in jaundiced infants.

The *cause* of the hæmorrhages has never been satisfactorily explained, although many suggestions as to their mode of production have been made. The hæmatemesis commonly met with in cases of hob-nailed liver is easily accounted for by local interference with the circulation of the gastric mucous membrane; but in our cases, as also in the various other jaundiced conditions above alluded to, we have subcutaneous and other bleedings which cannot be so explained. We want a theory which will account equally well for all the different hæmorrhages in all the different morbid conditions in which they are found. The following suggestions have been made by different writers:—

i. "*Impoverishment of the blood*" is given by Dr Budd[1] as the probable cause of the hæmorrhagic tendency. Murchison[2] also regards it as due to the blood becoming "impoverished by a diminution in the proportion of the red corpuscles and fibrin;" but he observes that it is particularly seen in conjunction with cerebral symptoms and other indications of blood-poisoning. Frerichs[3] says it is due to some change in the blood and its adhesion to the walls of the vessels.

"Impoverishment" means a simple deprivation or lessening of one or more of the normal constituents of the blood; while the very sudden appearance of the hæmorrhagic tendency often observed would rather suggest the adding of something to the blood than the taking away of anything out of it, which one should have thought would more likely have been a gradual process.

ii. *The action of bile-acids in the blood on the corpuscles* is suggested by Leyden.[4] Wickham Legg objects to this, that if the bile-acids in the blood were to blame we should find hæmaturia, such as, he says, always occurs when bile-acids are injected into the circulation, and this is almost an unknown symptom in jaun-

[1] Budd, *Diseases of the Liver*, second edition, 1852, p. 463.

[2] Murchison, *Diseases of the Liver*, third edition, p. 358.

[3] Frerichs, *Klinik der Leberkrankheiten*, 1858, Bd. i. p. 242.

[4] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 100.

dice. This objection does not appear very forcible, however, when we remember that the experiments referred to were on the lower animals, and not on man, in whom the action may be quite different. Mackay[1] found hæmoglobin always in the urine of rabbits when the ductus choledochus had been ligatured, and exactly the same condition after the intravenous injection of bile or bile-acids.

A more serious objection to this theory consists in the fact that it seems to be only near the beginning of an attack of artificial obstructive jaundice in the lower animals that the blood contains any amount of bile-acids. Mackay found that in the blood of rabbits whose common duct had been tied for more than six days little or no bile-acid could be detected. We should, I think, certainly expect that in this respect man would resemble other animals; and although hæmorrhage is a very early symptom in obstructive jaundice, it is also a very late one.

iii. *A diseased state of the bloodvessels* is said by Wickham Legg[2] to precede and cause the hæmorrhages. He says that Leyden has shown that the bile-acids produce a parenchymatous degeneration of the glands and muscles, and that the bloodvessels are probably affected in the same way. It is difficult to see how this theory can explain the clinical facts at all satisfactorily in the case of jaundice, although a similar one may very probably account for the tendency to hæmorrhage met with in cases of leucocythæmia and some other chronic diseases. The sudden onset of the hæmorrhagic tendency almost simultaneously with the discoloration of the surface of the body, which occurs in so many of the cases, seems alone almost sufficient to disprove the idea that there is an antecedent change in the walls of the vessels. It is a well-known fact that the hæmorrhages occurring in obstructive jaundice are a very early symptom (especially in children[3]); and in several of our cases (*e.g.*, Nos. 35, 36, and 43) the bleeding set in and ended fatally within two or three days of the first appearance of the jaundice. In acute yellow atrophy and in yellow fever,[4] hæmorrhage is a very early symptom also.

[1] J. C. H. Mackay, *Arch. für Experiment. Pathol.*, xix., 1885, p. 269.
[2] Wickham Legg, *Bile, Jaundice, and Bilious Diseases*, p. 315.
[3] Von Schüppel, Ziemssen's *Cyclopædia* (Eng. Transl.), ix., p. 610.
[4] Fagge, *Principles and Practice of Medicine*, vol. i. p. 258.

In several cases on our table no jaundice was observed until a week or more after birth; and it is interesting to note that no hæmorrhage, umbilical or otherwise, took place in these before the jaundice was seen, although the obstruction of the ducts had certainly been complete in some of them at an early period of intra-uterine life. It is also of interest that in no case does there appear to have been any sign of hæmorrhage having occurred during intra-uterine life.

iv. I have more than once heard it suggested that the obstruction to the outflow of the bile interfered with the hæmocyte-destroying function of the liver, and in this way conduced to hæmorrhages by causing a sort of plethora. This theory cannot, however, be seriously entertained, because there is, as a fact, no increase of the number of these corpuscles in jaundice, but rather the reverse.[1]

v. Another theory comes naturally to one's mind on reading the results of recent pathological research, and certainly, *so far as it goes*, it seems to be much more satisfactory than any of the above. It is that the hæmorrhagic tendency is caused by the presence in the blood, not of bile-acids, but of ptomaines, or some similar organic poisons, formed in the process of ordinary digestion, which the diseased liver is not able to render innocuous, as it would do if it were in a state of health.

The facts suggesting this hypothesis may be briefly stated as follows:—

Firstly, One of the recognised functions of the liver in the animal economy is to render innocuous in some way various sorts of poisons in the blood.[2] Among the poisons which it acts on thus are the organic ones which are formed in the alimentary canal in the process of digestion.

Secondly, It has been found by Roger[3] that this important function of the organ is closely connected with the amount of glycogen it contains, and varies accordingly, so that when the liver contains no glycogen a very much smaller dose of these organic poisons is required to produce a given result than would be necessary if the organ were healthy in this respect. This has been tested in the

[1] J. C. H. Mackay, *loc. cit.*

[2] Lauder Brunton, *Pharmacology and Therapeutics*, third edition, p. 402.

[3] Roger, *Gaz. des Hôp.*, No. 66, p. 525, 1887.

case of animals with artificial cirrhosis of the liver, fatty degeneration, etc.

Thirdly, It has been demonstrated by Legg,[1] and confirmed by Von Wittich, that ligature of the bile-ducts produces disappearance of glycogen from the liver, the retention of bile seeming to interfere with the proper discharge of the function of glycogen-formation in the hepatic cells.

Now, in the disease we are considering, we are, I think, justified in thinking that there is in all probability a diminution of glycogen in the liver, owing to the forced retention of bile in it, and that the organ may very likely, on this account, be letting past its portal some poisonous product of ordinary digestion which, under its usual conditions, it would have summarily disposed of.

The exact method in which a process of blood-poisoning of this sort would act in causing hæmorrhages we do not know; but it is a well-known fact, that many forms of blood-poisoning are accompanied by a tendency to spontaneous bleeding.[2]

(*h.*) *Convulsions.*—In other serious diseases accompanied by jaundice, such as yellow fever, acute yellow atrophy, and phosphorus poisoning, convulsions are a common symptom; and in chronic forms of liver-disease they often occur towards the end. In children who are subject to convulsive attacks we should expect them to be met with often in any disease of this kind; and on looking at the published cases, we find that fits are often mentioned—namely, ten times in the fifty. It is interesting to note that convulsions frequently occur in animals after ligature of the ductus choledochus.[3]

(*i.*) *Emaciation.*—Emaciation always occurs if the child lives long enough, but it is not usually an early symptom. This may be partially explained by the fact that the exclusion of all bile from the digestive process interferes to a certain extent (though not very much[4]) with the assimilation of the fatty constituents of the food which are so important to the infant economy. Probably, however, the emaciation is mainly due to the secondary organic

[1] Wickham Legg, *St Bart. Hosp. Reports*, 1873, ix., p. 178.

[2] For references on this point see Runge, *Die Krankheiten der ersten Lebenstage*, Stuttgart, 1885, p. 117.

[3] J. C. H. Mackay, *loc. cit.*

[4] Noël Paton and J. M. Balfour, *Roy. Coll. Phys. Lab. Rep.*, 1891, p. 191.

changes in the liver-tissue interfering increasingly with the other more important functions of the organ, and with the part it should play in the general metabolism of the body.

(*j.*) *Duration of Life.*—On looking over the table, we find the following details:—Only one child was still-born (and it was premature); of the others,—

11 lived less than a week.
8 „ more than a week but less than a month.
14 „ from one to four months.
16 „ for upwards of four months (two—Nos. 18 and 48—into the eighth month).

Therefore, if we exclude those who died of umbilical hæmorrhage, we may say that a very large majority of the cases lived more than a month. These facts seem to indicate two things,—firstly, that the lesion is one which has not of itself a rapid deleterious influence on the general health; and, secondly, that it is not one which is apt to be accompanied by serious complications (with the exception of the hæmorrhages).

In their recent paper, "On the Composition, Flow, and Physiological Action of the Bile in Man,"[1] Drs Paton and Balfour give it as their opinion that the "bile is to be regarded rather as an excretion than as a secretion playing any essential part in digestion;" and they also find that, "even with the bile excluded from the intestine, no less than about 70 per cent. of the fats" (of the food) "are still used." The fact that infants with complete obliteration of the bile-ducts live so long as they do, seems certainly to corroborate the above opinion to some extent.

(*k.*) *Other Morbid Conditions Present.*—Unequivocal signs of congenital syphilis are stated to have been observed either during life, or post-mortem, or both, in five cases (Nos. 13, 25, 26, 46, and 48), and in one other (No. 6) the occurrence of snuffles is noted.

As already stated, there are no serious complications which are usually met with, excepting the various spontaneous hæmorrhages. The immediate cause of death in the different cases is very various. Apparently the disease causes gradual weakening, and any chance intercurrent affection carries the child off. There does not seem to be a predisposition to any special disease.

[1] Noël Paton and J. M. Balfour, *Roy. Coll. Phys. Edin. Lab. Rep.*, 1891, p. 191.

8. *Post-mortem Appearances* (see Table II.)

(A.) *Peritoneum.*—A large quantity of ascitic fluid was found in two cases (Nos. 4 and 48), a smaller amount in No. 44, and a little effusion in several others—namely, Nos. 26, 27, 12, and 25 (in the last, however, it was probably post-mortem). The presence of adhesions or localized thickenings is noted five times (Nos. 5, 14, 18, 26, and 27).

In two cases (37 and 44) there was recent peritonitis, evidently secondary.

(B.) *Liver.*

(1.) The *size* is generally, but not always, more or less increased.

This point is not mentioned	in 19	of the cases.
The liver is said not to be enlarged	„ 8	„
„ said to be small	„ 1	„
„ „ enlarged	„ 12	„
„ „ much enlarged	„ 9	„
„ „ unequally enlarged	„ 1	„

We find, as we should expect, that enlargement is more frequently noted in cases which lived a long time.

(2.) The *shape* seems usually to be unaltered, even in those cases in which the obliteration is said only to have involved one of the hepatic ducts. In one case, however (No. 25), in which only one duct was obliterated, the corresponding lobe of the liver was shrunken, and showed excess of fibrous tissue with cystic dilatation of the ducts in it, while the other lobe, the bile of which had free exit, was not affected in this way. It is interesting to note that in one of Charcot and Gombault's experiments on animals,[1] in which only one of the hepatic ducts was tied, the resulting cirrhosis was found to affect only the corresponding lobe of the liver.

(3.) The *colour* is most frequently dark green—almost always so when the children have lived long.

(4.) The *consistence* is not alluded to in 30 of the cases. Out of the 20 cases in which it is mentioned, the organ is said to have been tough in 14.

(5.) The *surface* of the organ is only mentioned 12 times; in 4 of these it was smooth, and in 8 finely granular.

(6.) The *bloodvessels* of the liver are described 20 times; in 16

[1] Charcot and Gombault, *Archives de physiologie*, iii., 1876, p. 273, Observation xv.

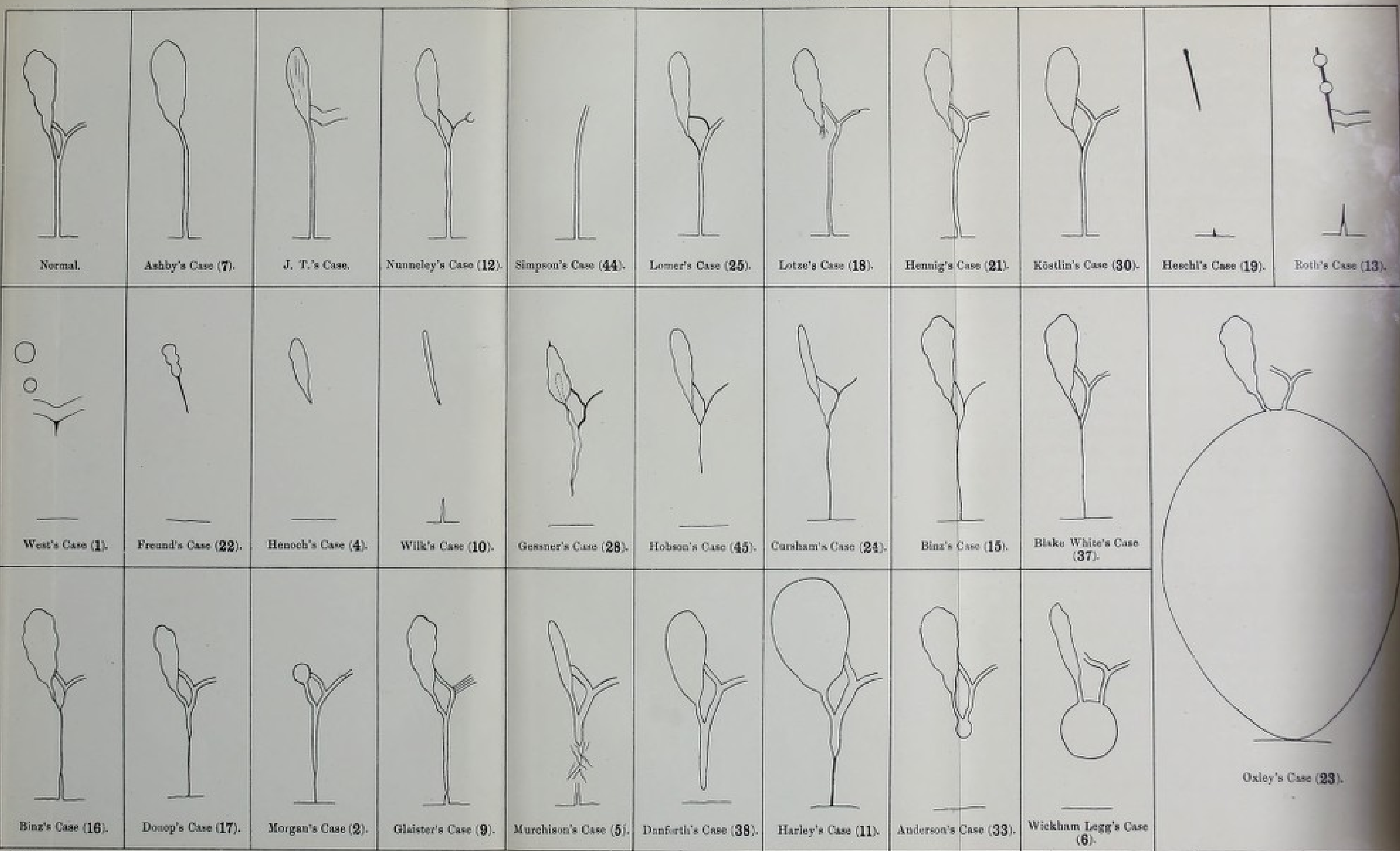
TABLE II.

No. of Case.	Reported by	Size of the Liver.	Its Weight.	Its Colour.	Its Surface and Capsule.	Perihepatitis.	Its Consistence.	On Section.	Gall-bladder.	Contents.	Cystic Duct.	Hepatic Ducts.	Common Duct.	Duodenum.	Hæd'rennels.
	J. T.	Much enlarged.	15 oz.	Dark olive-green.	Finely granular, not thickened.	None.	Very tough.	Creaks, dark-green; great excess of fibrous tissue.	Small, flaccid.	Brownish mucus.	Patent.	Impervious; greatly dilated, forming a long sinus.	Patent, small.	.....	Normal.
1	West.	Very large.	11½ oz.	.....	.....	.....	.....	.....	Replaced by two small blind sacs.	Greenish tenacious matter.	Absent.	Impervious, and greatly dilated.	.....	.....	.....
2	Morgan.	Slightly enlarged.	.....	Slightly congested.	.....	No thickening round the ducts.	Normal.	Tissue healthy.	Not larger than a pea.	Mucus, and no bile.	Patent, but empty.	Patent, but empty.	Represented by a fibrous cord for more than half an inch.	No opening into bowel.	Normal.
3	E. Smith.	.....	.....	Dark olive.	.....	.....	Increased.	.....	Rudimentary.	.....	.....	Absent.	Absent.	No opening.	.....
4	Henoch.	One-third smaller than usual.	.....	Olive-green.	.....	.....	.....	.....	Rudimentary.	.....	.....	Not a trace of bile-ducts.	.....	No opening.	.....
5	Murchison.	.....	.....	Jaundiced.	.....	A few fibrous adhesions.	.....	Ducts dilated.	Extremely small and collapsed.	A few drops of colourless fluid.	Dilated; otherwise normal.	Same.	Replaced by areolar tissue.	Opening of duct would not admit a probe.	.....
6	Wickham Legg.	Large.	.....	Deep olive-green.	Granular.	.....	.....	.....	Shrunken.	A small amount of yellow fluid.	Opens into a cyst the size of a largish marble.	Also open into this cyst.	.....	Papilla not perforated.	Normal.
7	Ashby.	Not large.	7 oz.	Dirty dark-green.	Finely granular, not thickened.	No adhesions.	Tough.	Creaks; excess of fibrous tissue.	Distended.	Non-biliary mucoid fluid.	Smaller than normal.	No trace of either.	Pervious.	Opening of duct normal.	Normal.
8	Ashby.	.....	9½ oz.	Olive-green.	Finely granular.	.....	Fibroid.	Dark-green.	Rudimentary.	.....	.....	No trace; lost in fibroid tissue.	No trace; lost in fibroid tissue.	.....	Normal.
9	Glaister.	.....	4½ oz.	.....	.....	None.	.....	.....	.....	.....	.....	Left duct split into threads.	All right down to a few lines from the bowel, where it is constricted.	Contained no bile.	Normal.
10	Wilks.	Usual size.	.....	Very dark green.	.....	.....	.....	.....	Lumen only large enough to hold a bristle.	.....	.....	Bile-ducts totally obliterated.	Only patent in part inside pancreas.	Opening of duct normal.	.....
11	Harley.	.....	.....	Green (not deep).	.....	.....	.....	.....	Distended to the size of a small hen's egg.	Full of fluid bile.	Enlarged.	Enlarged.	Impervious; the lower part a solid cord.	.....	.....
12	Nunneley.	.....	.....	Dark blackish-green.	.....	None.	Firm.	Ducts not obvious.	Very small.	A little colourless mucus.	Pervious.	Replaced by slender impervious fibrous cords; a dilatation on left.	Pervious.	No yellow colour.	Normal.
13	Roth.	Large.	.....	Olive-green.	Smooth, diffusely thickened.	.....	Tough as leather.	Ducts dilated; cirrhosis.	Replaced by a thick solid cord, containing two cysts like peas.	Filled with clear fluid.	Nothing to represent it.	A dilated duct about an inch long.	Nothing to represent it.	Papilla present, but only pervious for two lines.	Normal.
14	Binz.	Medium size.	.....	.....	Some thickened places on capsule.	.....	Soft.	.....	Full.	Tough, deeply greenish-yellow mucus.	Changed into an irregular mass of fibrous tissue.	Same.	.....	.....	Probably obliteration of portal vein and hepatic artery.
15	Binz.	Large.	.....	.....	Thickened and opaque.	.....	.....	.....	Filled.	Normal-looking bile.	.....	Bile-ducts were cords with no lumen.	.....	All the intestine coloured with bile.	As above.
16	Binz.	.....	.....	.....	Thickened.	.....	.....	.....	Very full.	Apparently normal bile.	Only patent for a few lines.	Only pervious at commencement.	Only pervious at end.	.....	.....
17	Dunop.	.....	.....	.....	Normal.	None.	.....	.....	Smaller than normal.	.....	Normal.	Normal.	Obliterated in most of its course.	.....	.....
18	Lotze.	Very large.	.....	Dark serpentine-green.	With prominent granulations.	Adhesions round gall-bladder.	Almost cartilaginous.	Dark green; cirrhosis.	Flaccid; whitish grey in colour; fixed by cicatricial tissue.	Clear, thin, slightly acid mucus.	Replaced by a few small solid cords.	Right pervious; left becomes a solid cord.	Pervious, but very narrow.	.....	Normal.
19	Heukl.	Somewhat enlarged.	.....	Brownish-green.	.....	.....	.....	.....	Replaced by solid cord half a line thick, with end enlarged.	.....	.....	Quite absent.	Quite absent.	Papilla present, but blind.	Normal.
20	Hennig.	.....	.....	Jaundiced.	.....	.....	.....	.....	.....	A little greyish-yellow mucus.	.....	.....	Quite closed.	.....	.....
21	Hennig.	.....	.....	Faintly jaundiced.	.....	.....	.....	.....	.....	Much dark greenish-brown bile.	Became obliterated near gall-bladder.	Normal.	Pervious.	Contained reddish-brown bile.	.....
22	Freund.	Somewhat enlarged.	.....	.....	.....	.....	Very hard.	Creaks.	Replaced by blind tube 1½ × ¼ ctm., with two hour-glass contractions.	Clear, watery, sticky fluid.	Solid white cord.	No trace.	No trace.	.....	.....
23	Onley.	.....	.....	.....	.....	None.	.....	.....	Of normal size.	No bile.	Opened into cyst the size of a cocoa-nut.	Same.	.....	Papilla present, but impervious.	Normal.
24	Cursham.	Enlarged.	.....	.....	.....	.....	Tough.	Peculiar striated appearance.	Atrophied; thickness of goose-quill.	.....	A fibrous cord.	Same.	Same.	Contents not tinged with bile.	.....

TABLE II.—*Continued.*

No. of Case.	Reported by	Size of the Liver.	Its Weight	Its Colour.	Its Surface and Capsule.	Perihepatitis.	Its Consistence.	On Section.	Gall-bladder.	Contents.	Cystic Duct.	Hepatic Ducts.	Common Duct.	Duodenum.	Bloodvessels.
25	Lomer.	Left lobe large; right lobe small.	60 grms.	.....	Uneven; brain-like.	.....	.....	Left lobe normal; right lobe composed of fibrous tissue, and hollowed into cysts.	Collapsed, but patent.	.....	A fibrous cord.	Left normal; right, a fibrous cord.	Normal.	.....	Normal.
26	Schüppel.	At least a third larger than normal	.....	Dark brownish-green.	Smooth.	Thickened connective tissue round portal vein.	Soft and flabby.	Increase of fibrous tissue.	.....	Only watery mucus.	A hard cord.	A hard cord.	A hard cord.	.....	Portal vein obliterated by fibrous tissue.
27	Schüppel.	Somewhat enlarged.	.....	Dark green.	.....	Same.	Soft and flabby.	.....	.....	As above.	As above.	As above.	As above.	.....	As above.
28	Gosmer.	Very large.	.....	Greenish-grey, partly yellowish.	Granular; nowhere markedly changed.	None.	Leathery; extremely tough.	Yellowish colour; no dilatation of bile-ducts.	Conical in shape; very thick walls; no outlet.	A brownish pulpy mass.	Impervious near gall-bladder.	Have no lumen.	Wider than normal; obliterated towards duodenum.	.....	Normal.
29	Kostlin.	.....	.....	Jaundiced.	.....	.....	.....	.....	Quite full.	Thin, colourless fluid.	Completely closed.	.....	.....	.....	.....
30	Kostlin.	.....	.....	.....	.....	.....	.....	.....	Distended.	Clear yellow fluid.	Closed.	.....	.....	.....	.....
31	Campbell.	Normal size.	.....	Colour of burnt umber.	.....	.....	Softer than usual.	.....	Very small and collapsed; no outlet.	A little mucus, like gelatine.	Absent.	.....	Absent.	.....	.....
32	Campbell.	Very large.	.....	.....	.....	.....	.....	.....	Not to be found.	.....	.....	No bile-ducts found.	.....	.....	Perfectly normal.
33	Anderson.	Large.	.....	Reddish-brown.	.....	.....	.....	.....	Distended.	Greenish-yellow bile.	Patent.	Patent to beyond junction with cystic duct; ended in *cul de sac*.	.....	.....	.....
34	Gould.	.....	.....	Dark coloured, engorged with blood.	.....	.....	Friable.	.....	Flaccid.	A drachm of serous fluid.	Impervious.	Same.	Same.	.....	All umbilical vessels pervious.
35	Gould.	.....	.....	Bronze-green.	.....	.....	.....	.....	Partially filled.	A little gelatinous fluid.	Apparently closed.	Apparently closed.	Dilated.	.....	As above.
36	Dean.	Appeared normal.	.....	Appeared normal.	.....	.....	.....	.....	.....	.....	.....	Bile-ducts impervious.	.....	.....	.....
37	White.	Greatly enlarged.	.....	Engorged.	.....	Peritonitis.	.....	.....	Filled.	Blackish syrupy bile.	Evidently constricted.	Normal.	A fibrous cord-like band.	.....	.....
38	Danforth.	Enlarged.	.....	Congested.	.....	.....	.....	.....	Very much distended.	Syrupy bile.	Slightly enlarged.	Slightly enlarged.	Distended, and terminated abruptly before reaching intestine.	.....	.....
39	Home.	.....	.....	.....	.....	.....	.....	.....	None.	.....	.....	No duct leading from liver into duodenum.	.....	.....	.....
40	Blundell.	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Terminated blindly.	.....	No bile entered intestine.	.....
41	Blundell.	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	As above.	.....	As above.	.....
42	L'hommeau.	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Duct imperforate.	.....	.....
43	Jenkins.	Apparently normal.	.....	.....	.....	.....	.....	.....	.....	.....	Impervious.	Impervious.	.....	.....	.....
44	Simpson.	Spigelian and quadrate lobes absent.	.....	.....	Covered with yellow lymph.	Recent.	.....	.....	No trace of one.	.....	.....	.....	Normal; entered liver without dividing.	Normal.	Normal.
45	Hobson.	Much enlarged.	.....	Dark purple.	Not thickened.	.....	Firm.	Looked cirrhosed.	Shrunken.	Empty.	A mere cord.	.....	A mere cord, coming to an end below.	.....	.....
46	Meyer.	Much enlarged.	.....	Deep green.	Uneven.	.....	Remarkably hard.	Cirrhosed.	Absent; replaced by dense cicatricial tissue.	.....	.....	.....	Ends blindly in cicatricial tissue.	Intestine normal.	.....
47	Thomas.	.....	.....	.....	.....	.....	.....	.....	.....	A small quantity of bile.	An impervious cord.	.....	As impervious cord.	.....	.....
48	Caspf.	Enlarged.	.....	.....	Smooth.	.....	.....	Brownish-green.	Not found.	.....	Replaced by a little loose connective tissue.	Same.	Same.	Its contents colourless.	.....
49	Caspf.	Normal.	.....	Serpentine-green.	Smooth, thickened.	.....	.....	Cirrhosed.	Quite absent.	.....	As above.	As above.	As above.	As above.	.....

TABLE III.—Diagrammatic representation of the local conditions described in 29 of the reported Cases of Obliteration of the Bile-ducts, showing the great variety which exists in the position and extent of the Lesions.



Wm Cathie Lith.

they were normal, and in 4 there was obliteration of the portal vein. It is significant that all these 4 cases (Nos. 13, 14, 26, and 27) were probably syphilitic.

(C.) *Gall-bladder and Ducts.*—As these are apparently the seat of the primary lesion in our cases, we shall examine their condition somewhat minutely.

(*a.*) Firstly, then, as to the *precise lesion* described in the various cases. Space will not allow of the exact descriptions being quoted, but an abridged account of them will be found in Table II., and a selection of them are sketched on Table III.

In the latter I have arranged, in a sort of order of sequence, diagrammatic representations on a small scale of the exact conditions of the gall-bladder, cystic, hepatic, and common ducts, and the duodenum, as described by the writers in a majority of the published cases. The others are not represented, either because they seem to have been exactly like one of those figured, or, in some cases, because so few particulars were given that it was not possible to say whether they differed or not. Where a part of the apparatus (*e.g.*, gall-bladder, cystic duct, etc.) is not mentioned in the description, I have represented it as normal. Of course, in many of the descriptions, much that one would have liked to know is left out, and what is given is not always very intelligible; but I think that the main points will be found to be fairly and accurately represented in the Table, so far as they can be ascertained.

In studying this diagram, we may look first at the

(*b.*) *Situation of the Obliteration.* We find that this varies almost indefinitely.

Among our 50 cases there are examples of almost every conceivable variety. We may divide them roughly into four groups:—

(1.) Those in which there is no passage whatever leading from the liver to the duodenum, although the gall-bladder and cystic ducts remain more or less normal.

(2.) Those in which there is at least one permeable canal leading from the liver into the gut, but no exit from the gall-bladder, or even nothing to represent that organ.

(3.) Those in which both cystic and hepatic ducts are obliterated.

(4.) Those in which the obliteration has occurred at a variable point below the junction of the cystic and hepatic ducts.

Now this great diversity in the precise situation of the lesion is

a point of considerable interest, and of itself throws some light on certain aspects of the etiology. Were the obliteration due simply to an arrest of the normal process of development of the parts, as has often been suggested, we should certainly expect that in most, if not in all, of the cases the obliteration would be found in or about the same situation. Again, were the local cause of the blocking an inflammatory process set up inside the lumen of the tube by a concretion or other local source of irritation, as others have thought, we should in the same way have expected a tendency for the obliteration to be situated about the same place in different cases.

We get, therefore, at the outset an impression that the cause is one which is not localized at any "seat of election," and therefore most probably either acts on the tubes from outside, or results in a process affecting their walls for a considerable extent before actual obstruction occurs.

(*c.*) If we next look at the diagram again to see what can be learned from it as to *other secondary changes in the external excretory apparatus*, we are again struck with the great variety met with. The significance of these differences, however, are difficult to determine; and, indeed, the anatomical descriptions are scarcely sufficiently full to allow us to attach much weight to the figures in this connexion.

I shall therefore only refer to a few points of interest.

(1.) When the cases are grouped together according to whether jaundice is said to have been present at birth, or only came on later, no special difference is found in the nature of the malformation in the two groups.

(2.) We find, as might have been expected, that the most severe malformations are almost all met with in cases which had lived several months. Inflammatory action evidently goes on spreading after the obliteration is complete, and affects the rest of the ducts and the gall-bladder—at least in many cases it does so. In Dr West's case (No. 1) this was so to a marked extent. For when the child was 3 weeks old, the gall-bladder could be felt through the abdominal wall, "the size of an egg;" and, when the post-mortem took place nine or ten weeks later, there was nothing of it left but two blind sacs—one the size of a pea, and the other twice as large (see Table III.) The inflammation set up in the bile-ducts of adults by an impacted stone spreads in a similar way.[1]

[1] Courvoisier, *loc. cit.*

(3.) Dilatation of the canal above the point of obliteration is by no means invariably present (*e.g.*, Nos. 2 and 17), although it may occur to an enormous extent (No. 23). When present, it may either take the form of a mere dilatation of the ordinary passages (Nos. 11 and 38), or there may be a more or less abrupt and saccular enlargement of the end of the tube (Nos. 33, 6, and 23.)

(4.) An obliterated duct or portion of a duct may remain as a fibrous cord or may entirely disappear.

(5.) The obliteration of the upper end of a duct does not necessarily cause the same of the lower end (Nos. 13, 16) even after the lapse of four and a half months (No. 16). This is probably due to the continuous passage of the pancreatic secretion.

(*d.*) *The Contents of the Gall-bladder* vary very much, from "thick syrupy bile" to clear watery fluid; but we notice that they are almost always described as colourless if the child lived more than a month. In all the cases where it is definitely stated that the motions were colourless from the first (with one exception, No. 11) there was no bile found in the gall-bladder.

(D.) *Microscopic Appearances of the Liver.*—The facts given under this head are very few.

Forty of the cases seem not to have been examined microscopically; in one case examined (Nunneley's) cirrhosis is not mentioned; in the remaining 9 cases, cirrhosis was present. It seems probable that biliary cirrhosis always occurs if the child lives long enough. The only apparent exception is Nunneley's case (No. 12), in which the description is not full, and no mention is made of cirrhosis, but it is not said that it was not present.

Several of the writers describe the masses of inspissated bile in the small bile-ducts, and some mention having seen fragments of the same substance inside the cells.

(E.) *The Spleen.*—In 12 of the cases the spleen is mentioned. In one of these it was small, and in one not enlarged; in all the others it was large—generally very large.

The spleen usually, though not invariably, enlarges in animals after ligature of the common duct.[1] The cause of this does not seem to be settled; possibly it may be explained in the same way as the occurrence of the hæmorrhages (see p. 23). In 7 of the cases with enlarged spleen hæmorrhages are noted.

[1] J. C. H. Mackay, *loc. cit.*

(F.) *Other Morbid Conditions.*—These are very various, and do not appear to have any direct connexion with the liver-affection. In many of the cases, pulmonary complications seem to have been the immediate cause of death.

III. Cases of Infantile Jaundice with symptoms similar to those of Obliteration of the Bile-ducts, but with Pervious Ducts.

A considerable number of instances have been reported in which children with symptoms exactly the same as those of our cases were found, post-mortem, to have diseased livers, but in which no mention is made of the state of the bile-ducts. These cases are, of course, of no use in our present inquiry.

In a few, however, a more or less careful account of the appearances of ducts which were pervious is given. I have tabulated (Table IV.) a few of the more satisfactory of these, and it is very interesting to compare their details with those of our other cases. In doing this one is struck with the close resemblance of the two sets of cases. In fact, the resemblance is such that we cannot avoid the conclusion that they are just examples of different stages or degrees of the same disease.

The most striking point of difference is the shorter duration of life in the cases with pervious ducts (17 days average, as against more than 2½ months); and this goes to confirm the idea that these are merely earlier cases of the same morbid condition—before the blocking has been completed.

In the only one of the cases where the condition of the ducts is exactly described (Cheyne's), their walls are said to have been thickened and white and contracted "like those of arteries." Possibly this may have been so in the other cases also, for nothing is said about the walls or calibre of the ducts in any of them, and they are not stated to have been normal. The fact of the ducts in any case being permeable at the post-mortem does not, of course, prove that they were practically so during life, for it is well known that the pressure of tumours, etc., on the ducts causes complete stoppage of the passage of bile long before absolute obliteration is produced, so that, at the post-mortem, probes or a stream of water can pass through a duct that was impervious to bile during life.

TABLE IV.

No.	Reported by	Where.	Health of Parents.	Other Children.	Age at Death.	Sex.	State at Birth.	Signs of Syphilis.	When Jaundice began after Birth.	Meconium.	Motions.	Progress of Jaundice.	State of Nutrition.	Position of Hæmorrhages, if Present.	Ascites.	Spleen.
1	Underwood.	"Diseases of Children," 3th edit., vol. i. p. 29.	.....	First 9 died, under a month old, from jaundice; the 10th, aged 4 years, from jaundice also.	8 days.	..	.....	.....	3rd day.	.....	.....	Varied from day to day.	.....	.....	.....	.....
2	Cheyne.	"Diseases of Children," vol. ii. p. 8.	.....	.....	17 days.	F.	Remarkably stout and healthy.	.....	3rd day.	.....	White, like putty.	Did not change.	Emaciated.	Umbilical (fatal).	.....	.....
3	Bednar.	"Die Krankheiten der Neugeborenen und Säuglingen."	.....	.. ..	18 days.	M.	Delicate.	.....	.....	.....	Reddish brown.	.....	.....	.....	.....	.....
4	Campbell.	Northern Journal of Medicine, Aug. 1844.	.....	Three other children, one of whom died with exactly the same symptoms.	11 days.	M.	Healthy.	Healthy.	3rd day.	Present.	.....	Became deeper.	.....	Umbilical (fatal).	.....	.....
5	E. Ray.	London Med. Gazette, vol. xiv., 1849.	.....	Three girls alive and healthy; two boys died with jaundice and umbilical hæmorrhages.	12 days.	M.	Remarkably strong and healthy.	.....	3rd day.	.....	White.	.. ...	.....	Umbilical (fatal).	.....	.....
6	Hatfield.	Trans. American Pediatric Society, 1889, p. 147.	No syphilis.	Six other children, one of whom died jaundiced with similar symptoms.	13 days.	M.	Well-nourished, weighed 7¼ lbs.	.....	At first, little or none; soon began, and maximum on 4th day.	Ordinary amount.	Yellow, more or less mixed with green.	Gradually increased till the 6th day.	Emaciated.	Umbilical, subcutaneous, and into right pleura.	.....	.....
7	D'Espine.	Gaz. Méd. de Paris, 1880, Nos. 43 and 48.	No trace of syphilis.	One dead; two alive, one of whom suffered from jaundice for some days after birth.	33 days.	M.	Healthy.	None.	Present at birth.	Natural.	Well coloured.	Became deeper after.	Failed rapidly.	Umbilical, subcutaneous, and into bowel, and into heart-muscle.	None.	Large.

TABLE IV.—*Continued.*

No.	Size of Liver.	Colour.	Perihepatitis.	Consistence.	Gall-Bladder.	Contents.	Cystic Duct.	Hepatic Duct.	Common Duct.	Duodenum.	Bloodvessels.
1	Almost twice usual size.	Natural on the whole.	Slight adhesion of lower part of right lobe to the peritoneum.	Of natural firmness.	Nearly full.	Bile of deep yellow colour.	Permeable.	Same.	Same.	.....	.....
2	Full.	Dark-green, earthy.	.....	Firm.	Quite empty and contracted.	A small soft dark mass.	Contracted, firm, white, pervious.	Same.	Same.	No bile in intestine.	.....
3	.....	Stained with bile.	.....	.....	Markedly enlarged; very full.	Thick bile.	.....	.....	Permeable.	Contents reddish-brown.	.....
4	.....	.....	.....	.....	.....	A quantity of bile.	.....	.....	Blocked by an indurated cord-like plug of inspissated bile.	.....	.....
5	Natural size.	Olive-green.	.....	.....	.....	.....	Permeable.	Same.	Same.	.....	Umbilical vessels permeable.
6	5 × 3½ × 1½ in.	Dark blackish-brown.	Capsule unchanged.	Normal.	.....	.....	It is implied that they were permeable.	Same.	Same.	.....	.....
7	Large.	Olive-green.	.....	.....	.....	Dark sticky bile.	Perfectly permeable.	Same.	Same.	.....	Normal.

Also, catarrhal conditions of the mucous membrane may give rise to utter blocking during life, and yet after death there may be no actual obstruction.[1]

IV. Pathology of the Lesion of the Ducts.

The lesion has been ascribed to three different morbid processes, either acting separately or in combination, namely—

1. *Peritonitis and its results*, acting on the ducts from outside, and either compressing them or being a source of inflammatory action, which spreads afterwards to their walls.
2. *An inflammatory or other lesion of the ducts themselves.*
3. *An arrest or defect of development.*

And, further, various predisposing causes have been described as accounting for these morbid processes, namely—

4. *Congenital syphilis.*
5. *Digestive disturbance on the part of the parents.*
6. *Injuries or exposure to cold*, either of the mother or child.
7. *Erysipelas* of the child.

Let us consider in order these possible factors in the etiology.

1. *Peritonitis.*—In 1838, Sir J. Y. Simpson collected together in a most interesting paper[2] a series of cases "to prove that peritonitis forms a common variety of fœtal disease, and probably constitutes one of the most frequent causes of death of the fœtus during the later months of pregnancy;" and a good deal has been written since to the same effect.

The following facts regarding it may be mentioned:—It may begin early in intra-uterine life (Sir James had found it in the third month), or during the later months of pregnancy, or it may arise within the first few days after birth. The exact time of onset must often be impossible to discover, owing to lack of symptoms. Its distribution may be general, or it may occur in patches.

It is certainly often due to syphilis; but it may also be caused, quite apart from that disease, by chill or over-exertion on the part of the mother, or, in new-born children, by erysipelas. It may be set up by many local causes in the child, such as

[1] See Wickham Legg, *Bile, Jaundice, and Bilious Diseases*, p. 252.

[2] Simpson, *Edinburgh Med. and Surg. Journ.*, v., 15, 1838, pp. 390–414.

rupture of the bladder or strangulation of the intestine, or arteritis umbilicalis.[1]

We not uncommonly meet with cases in which it has existed to a considerable extent without there having been any symptom noticed during life.[2] It may be, and often is, fatal either before or after birth. If recovered from, it often leaves adhesions, and these are a not very uncommon cause of malformations of the intestine and other viscera.[3]

There are several considerations apparently in favour of a localized form of this disease (peripylephlebitis) being the cause of obliteration of the duct in some of our cases. As we have already seen, adhesions are mentioned as having occurred in four of the cases, and some fluid was found in the peritoneal cavity in a few of the others. The fact of the neighbouring bloodvessels being obliterated by fibrous tissue in several of the cases (Nos. 14, 15, 26, and 27) suggests, of course, the previous occurrence of peritonitis in them.

Although, however, we have facts which *seem* to point pretty strongly to peritonitis having been the cause in a small number of the cases, we have stronger grounds for thinking that the large majority could not have been so produced. Of these I may mention a few—namely, the absence of any traces of past peritonitis in them; the fact of the lesion being limited to the gall-ducts or gall-bladder, and not affecting the bloodvessels and other neighbouring structures; and, lastly, the consideration that this theory of the etiology of these cases affords no explanation of the recurrence of the disease in families.

We must also remember that, even if peritonitis is shown to have existed, this does not prove it to have been the cause; in two of our cases (Nos. 37 and 44) there was peritonitis present which was certainly secondary to the malformation of the ducts. It seems very probable that the affection of the peritoneum is always secondary to that of the ducts, and very likely it is a result of it.

2. *Inflammatory or other affections of the ducts themselves* have been suggested as the cause by several writers. Unfortunately,

[1] Max Runge, *Die Krankheiten der ersten Lebenstage*, Stuttgart, 1885, p. 84.

[2] Billard, *Traité des Maladies des Enfans*, 1837, pp. 479–483.

[3] Ahlfeld, *Archiv f. Gynæc.*, v. p. 236; and Küttner, Virchow's *Archiv*, Bd. 54, p. 37.

microscopic examination of them does not seem to have been made in any of the cases. A few instances have been published in which a real or imaginary cause of obstruction of the bile-ducts in an infant was found, but these do not help us very much in determining the usual causation of our cases.

The lesions of the ducts which have been described as possible causes of obstruction are as follows:—

(*a.*) *Catarrh of the mucous membrane,* followed by erosion and adhesion of the bared surfaces, is naturally the morbid condition first thought of. This is a recognised cause of blocking, and even of entire obliteration of the ducts in adults.[1] In them the commonest cause of it is, of course, the irritation of a calculus; but it is also set up by syphilis, and it is said that other impurities in the blood may give rise to it. The position in which obliteration from this cause usually occurs is the pars intestinalis of the common duct.[2]

(*b.*) *Gall-stones* must be extremely rare in infants, but one case has been put on record;[3] and another case, in which calcareous concretions were met with in a young child's liver, has been described by Wronka.[4]

(*c.*) *A plug of inspissated bile* was found in the bile-duct in one carefully described case,[5] and was supposed to be the cause of the obstruction which had ended in death.

(*d.*) One case of fatal obstructive jaundice in a young infant[6] has been described as due to "*spasmodic stricture of the duct;*" but the writer gives no facts in support of his hypothesis, and it is difficult to see how it can be entertained.

(*e.*) *Gummatous inflammation of the walls of the ducts* has been described by Beck[7] in one case, in which there was exudation confined to the immediate neighbourhood of this region along with syphilitic cirrhosis of the liver.

[1] Cornil and Ranvier, *Manual of Pathological Histology* (Transl.), vol. ii. p. 409.

[2] Von Schüppel, Ziemssen's *Cyclopædia* (Transl.), ix., p. 583.

[3] Lieutaud, *Mém. de l'Acad. Roy. de Méd.*, 1847, xiii., p. 264.

[4] Wronka, *Beiträge z. Kenntniss der angeb. Leberkrankheiten*, Inaug. Diss., Breslau, 1872.

[5] A. D. Campbell, *Northern Journal of Medicine*, Aug. 1844, p. 237.

[6] Waring Curran, *Medical Press and Circular*, Sept. 9th, 1868.

[7] H. Beck, *Prager medicin. Wochenschrift*, 1884; quoted in Schmidt's *Jahrbuch*, 1884, p. 204.

In considering these morbid conditions as to their influence in causing obliteration, the second, third, and fourth may be put aside on account of their extreme rarity or dubiousness. *Gummatous inflammation* may also be dismissed, because, although it seems a likely enough lesion to occur under favourable conditions, yet we could not expect to meet with it so often entirely apart from any signs of syphilis elsewhere, and without there being gummatous or interstitial syphilitic hepatitis at the same time.

A catarrhal condition of the ducts seems, *à priori*, quite a possible cause of the malformations met with. We do not, indeed, know of any general influence (except syphilis) capable of setting up catarrh at that period of life; but then we are familiar with the fact that ulcers for which no cause can be assigned sometimes occur in the stomach and duodenum in very young infants,[1] although they are very rare. The cicatrization of a duodenal ulcer might possibly explain the malformation in such a case as Oxley's, No. 23 (see Table III.)

A more likely way in which catarrhal inflammation of the ducts might lead to obliteration of their lumen is that a thickening of their walls might be produced by the inflammatory action spreading to the fibrous tissue there.

It seems quite possible that a congenital malformation might exist which, although not entirely obliterating the lumen of the duct, might occasion so much irritation from interference with the free outflow of bile as to cause a chronic and progressive catarrh.

3. *Arrest or defect of development of the ducts* (Vitium primæ formationis).

When cases of the condition we are considering are referred to in general works on medicine and pathology they are usually put down to this origin, and many of the writers who have reported cases have regarded the lesion as of this nature.

There are certain facts which constitute strong arguments in favour of this etiology. Of these, the following two are the most worthy of note:—

Firstly. There can be no doubt that various malformations of the liver and bile-ducts do occur which are certainly of this nature. For example, congenital absence of the gall-bladder has been fre-

[1] Henoch, *loc. cit.*, vol. i. p. 66.

quently described,[1] and some of the cases were due to arrest of development, although many were probably of inflammatory origin. Again, Wenzel Gruber[2] has published a case in which a forked cystic duct was found; and Konitzky[3] has described another, in which the common duct had an unusually long and curved course, and opened into the middle of the horizontal portion of the duodenum, its lumen being narrowed. O. Witzel,[4] also, has published notes of an infant born with a large number of congenital abnormalities, in whom, in addition to hemicephalus, situs viscerum inversus, six fingers on each hand, etc., there was a cystic condition of the liver and complete impermeability of both the cystic and common ducts. Finally, in two of our own tabulated cases there were other developmental defects observed—namely, in Heschl's, absence of the bile-ducts in the liver-tissue; and in Professor Simpson's, want of the Spigelian and quadrate lobes.[5]

Secondly, The frequency with which this exceedingly rare condition affects several members of the same family is very strongly in favour of this view, and indeed it seems difficult to explain it otherwise. It has been suggested[6] that this reappearance of the disease in the same family might be explained by supposing a common syphilitic taint. This suggestion, however, cannot be accepted, for we never find a tendency for an extremely rare manifestation of syphilis to recur four or five times in a family without any of the common symptoms of that disease being present at the same time.

The developmental defect may be supposed to be of various kinds. For example—(*a.*) It may be regarded as the sole cause of the obstruction—"an incomplete hollowing out of the originally solid bile-ducts" occurring, as Lotze supposes possible. (*b.*) Again, Cheyne regards the narrowing of the bile-ducts in his case to be secondary to an impermeable thickening of the beginnings of the

[1] For references see Courvoisier, *loc. cit.*, p. 139; Meckel, *Pathologische Anatomie*, i., p. 606; Förster, *Die Missbildungen des Menschen*, Jena, 1861; and Cnopf, *Münchener med. Wochenschrift*, 28th April 1891, p. 307.

[2] Wenzel Gruber, Virchow's *Archiv*, lxiii.

[3] G. Konitzky, Inaug. Diss., quoted in Virchow and Hirsch's *Jahresber.* 1888, ii., p. 290.

[4] O. Witzel, *Centralblatt für Gynæcologie*, 1880, p. 561.

[5] See also Appendix ii.

[6] Goodhart, *Atlas of Pathology*, New Sydenham Society, fasciculus v.

hepatic duct. (*c.*) Lastly, we may imagine the defect to consist in a congenital narrowness or irregularity of the lumen of the ducts of such a nature as to render them unnaturally liable to disease from its interference with the proper performance of their function.

Now, against the first of these hypotheses there are two important arguments. *Firstly*, such a developmental defect would necessarily occur at a very early period of intra-uterine life, and it is, therefore, excluded in all the cases where any coloured meconium was passed; and, *secondly*, as already pointed out, the great variety in the situation at which the obliteration occurs seems strongly against this etiology.

The last hypothesis, however, is not open to these objections, and seems to me, indeed, to afford a very necessary help in explaining the causation of a large proportion, if not all of the cases.

4. *Congenital Syphilis.*—The majority of those who have written on the pathology of this condition have ascribed it to syphilis. A few have had good reasons for so doing, but most seem to have given this explanation merely for lack of a better, or, at least, without any adequate proofs of the presence of the taint. The mere fact of the presence of cirrhosis of the liver has been erroneously regarded by several writers as a proof of syphilis.

A priori, we should certainly regard it as a very probable factor in the etiology, but when we study the details of the published cases we find very little in support of the idea. The facts in favour of syphilis as a cause are as follows:—*Firstly*, Five of the parents of the affected children were certainly syphilitic. *Secondly*, Six, possibly nine, of the children themselves showed signs of syphilis.

On the other hand, the case against syphilis is certainly a strong one. The main points are—*Firstly*, Several of those who have reported cases (notably Mr Morgan) seem *quite* sure that the parents were not syphilitic. *Secondly*, Out of the 96 parents of the 50 children whose cases are tabulated, syphilis was discovered only in 5. Of course we do not forget the difficulty of ascertaining the presence of the taint; but still, when we take into consideration the great probability that in these cases syphilis would almost always be inquired about, such a small proportion seems strongly against the idea that the lesion is a manifestation of syphilis

Thirdly, Although many facts are given about the other children in the same families as the patients, in no single case is it mentioned that any of them suffered from any recognised symptom of congenital syphilis. *Fourthly*, 23 of the patients lived three months or over, and yet only two of these are said to have had any symptoms which could be put down to syphilis.

Fifthly, and lastly, It is interesting to note that when we group together these six certainly, and three possibly, syphilitic cases (namely, Nos. 14, 15, 25, 26, 27, and 46, and Nos. 6, 13, and 18), and compare them with the other 41 cases, we find certain interesting points of difference. This small group contains three of the five children who were prematurely born, all but one of the cases in which there were peritoneal adhesions, and all those in which the bloodvessels were obliterated.

These considerations justify us, I think, in believing that congenital syphilis is not an element of essential importance in the etiology of these cases.

Is it not possible that the presence of inherited syphilis may cause an unusual liability to peritonitis, so that an irritation which in a healthy infant or fœtus would set up inflammation confined to the ducts, may, in a syphilitic one, involve the peritoneum also more or less extensively ?

5. *Digestive Disturbance on the part of the Parents.*—As already mentioned (p. 13), this has been seriously suggested as a possible cause by two writers, but it scarcely needs further discussion.

6. *Injuries or Exposure to Cold*, either of the mother when pregnant or of the child, are recognised causes of peritonitis in the latter. And as the circumstances attending birth are sometimes such as to occasion both, they seem worthy of consideration here. On looking over the cases, however, we find that there are no facts at all to suggest the probability that these causes of disease were in operation in any number of the cases.

7. *Erysipelas* also deserves only a short notice. In one case (No. 31) it is mentioned as having occurred and been followed by peritonitis; in another (No. 44) it may possibly have been the cause of death. There seems, however, no reason to suppose that it ever bears a causal relation to the local lesion of the bile-ducts.

Conclusions.

Let us see, then, what material we have gathered in the course of our investigation towards answering the two questions which we put at the outset.

I. *What is the etiology and pathology of these cases?*

The main conclusions we have arrived at with regard to these points may be summarized as follows:—

1. In the great majority (if not all) of the cases there is, to begin with, a congenital malformation of the bile-ducts due in some way to defective development.

2. This malformation probably affects a considerable extent of the walls of the ducts, and may consist in narrowness of their lumen.

3. The interference with the outflow of bile thus caused, gives rise to catarrh, and finally to blocking and obliteration of the ducts, owing to the inflammatory process spreading to the walls of the ducts and gall-bladder.

4. This progressive inflammation goes on slowly spreading, the local condition getting gradually worse during many months, if the patient lives.

5. The obliterated ducts or gall-bladder, or portions of them, may entirely disappear, not even leaving a distinct band of fibrous tissue to indicate their original position.

6. The obliteration generally becomes complete at an early, but variable period of intra-uterine life, but occasionally it does not occur till after birth.

7. In a few cases the inflammatory process spreads to the peritoneum, and possibly the presence of inherited syphilis may favour this extension. The occurrence of peritonitis is probably always secondary to the blocking of the ducts; and syphilis has nothing to do with the original lesion in them.

8. When the lumen of the duct is so far encroached upon as to obstruct the free passage of bile into the intestine, "biliary" cirrhosis of the liver begins, which as it goes on causes increasing interference with the most important functions of that important organ. The result of this is the setting up of a sort of chronic

blood-poisoning which causes vomiting, spontaneous hæmorrhage, and convulsions, and gradually leads to emaciation, diminished vitality, and death.

II. *How are the various symptoms to be explained?*

A few suggestions as to the causation of some of the more interesting of the clinical phenomena may be recapitulated as follows :—

1. The reappearance of the disease in several members of the same family can only be explained by the theory that a congenital defect of development is at the root of the mischief.

2. The fact that the onset of the jaundice is not at all contemporaneous with the blocking of the bile-ducts, and usually only begins several days after birth, is best explained by taking into account the effect on the liver-cells exerted by the enormous changes in the hepatic circulation which occur at birth in new-born children.

3. The presence of coloured meconium in some cases, and of only white discharge in others, is due to the blocking of the ducts having occurred at different periods of intra-uterine life in the two groups.

4. When green matter is passed along with the colourless motions during the progress of the case, this is probably due to the chemical action of the contents of the bowel on mercury which has been administered to the child.

5. The tendency to spontaneous hæmorrhages is probably due to the occurrence of a state of chronic blood-poisoning; the arrest of the outflow of bile damaging the liver so that its functions are interfered with, and it lets past into the circulation organic products of digestion of a poisonous nature.

6. The enlargement of the spleen, the convulsions, and the vomiting, are probably more or less connected with this same condition of blood-poisoning.

7. The fact that the children live as long as they do, and do not usually become emaciated early, is to be explained by the theory that the presence of bile in the bowel is not very necessary for digestion. When the nutrition and general health do begin to suffer, it is probably due to the interference which the secondary changes in the liver-tissue are causing with the more important functions of the organ.

APPENDIX I.

CASE OF CONGENITAL OBLITERATION OF THE SMALL INTESTINE.

Mrs G.'s infant (male), two and a half days old, seen on 12th Nov. 1890, on account of complete obstruction and constant vomiting, along with my friend Dr Home Ross, to whose kindness I am indebted for permission to publish the case.

Family History.—Father and mother healthy; no syphilis. The mother has had four pregnancies. The first child is alive, but is strumous; the second was still-born (full-time, cross-birth); the third pregnancy ended in a miscarriage at the fifth month, owing to the presence of an ovarian tumour. The patient is the fourth child.

Pregnancy.—When the mother was about two months pregnant [1] she had a left ovarian cyst removed by laparotomy. The operation was not a complicated one. Shortly after it, she had a threatening of miscarriage which was successfully treated by large doses of morphia. After that, everything went well till the full term.

Birth (*10th November*, 3 A.M.) easy and natural. There was an extremely large quantity of liquor amnii, and an unusually thick layer of vernix caseosa, both said to be of perfectly normal colour. The child's extremities were noticed to be very blue, and his body of a brighter red colour than usual.

Since birth he has vomited everything given to him (milk and water, and four doses of castor-oil). No motion of any kind has

[1] The last menstruation began on 4th March; the operation took place on 23rd May.

come from the bowel. The skin has gradually assumed a distinctly yellow tinge.

Present Condition.—The child is well developed and of natural size. The skin is bright red, with a strong orange tint. The conjunctivæ are only slightly yellow. The lips, the vertex of the scalp, the palms and soles, and the neighbourhood of the anus, are all markedly cyanosed, and there is a bluish tinge over some other parts of the body. The tongue and gums, however, are quite free from this. The child cries constantly, as if from hunger. No external malformation. The thorax is well shaped, but there is considerable indrawing of the episternal and epigastric regions with each inspiration. The percussion-note over the bases of the lungs is not very clear. The examination of the heart reveals no abnormality.

Abdomen not distended, but its walls are very tense. On percussion a tympanitic note is got over the region of the stomach, but over all the lower part of the belly the note is absolutely dull. The liver and spleen cannot be felt. The anus seems small, but admits the little finger without much difficulty, and is felt to contain a few soft rounded masses. These, when removed by an enema, are found to amount to rather more than a teaspoonful in bulk. The matter is absolutely without odour and of a whitish colour, with no tinge of green or yellow. It consists of rounded agglomerations of little many-sided bodies, from the size of a lentil to that of a split pea; these have an ivory-white colour on section, and the consistence of lightly-boiled white of egg, and they are held together by thick white mucus. There is also a little pasty amorphous matter. (The contents of the rectum were put into spirit and afterwards examined microscopically. They seemed to be composed of epithelial débris.) When the rectum is cleared, the little finger can with some difficulty be passed up nearly $2\frac{1}{2}$ inches, and there is no obstruction. The vomited matter is greenish-yellow in colour. The urine passes freely. At first it is said to have been clear and not to have stained the clothes; now it is thick and dark, and stains them yellow. On the prepuce and on the napkin there is a large quantity of "brick-dust" deposit.

Treatment.—In addition to the enema, several injections of glycerine were given.

Progress (*November* 15*th*).—Child more deeply jaundiced. Con-

tinues to vomit everything. Has passed nothing by the bowel but a few drops of colourless fluid.

November 19th.—Has not vomited at all for two days, although taking a little sugar and water. One very small colourless motion. Urine dark, staining the napkins yellow. Child becoming extremely emaciated. Cyanotic tinge almost gone. On removing the napkin the child is found to have passed about half a tea-spoonful of dark-green matter, homogeneous and slimy. The shade of colour is not so dark as that of ordinary meconium, and is a good deal yellower.

This was submitted to Dr Noël Paton, who kindly examined it, and reports :—

"Specimen consisted of several very small, irregular masses with a greenish-yellow colour, some parts distinctly green, other parts yellow. The pigment is insoluble in alcohol, chloroform, or ether. On treatment with alcohol and sulphuric acid, the yellow pigment goes into solution; the green pigment does not. The solid masses of green pigment, when treated with nitroso-nitric acid, give a faint but distinct play of colours.

"In their solubility these pigments differ from the bile-pigments, but they give Gmelin's test. Possibly they may consist of bile-pigments which have been for a long period in the bowel and have undergone some change. But it is also possible that they may be pigments produced in some other way. The specimens were so small that it was not possible to make an extended investigation."

Under the microscope, the specimen was found full of micrococci.

Nov. 20th.—The child died at 7 A.M., aged ten days and four hours.

Post-mortem Examination.—Body extremely emaciated; skin slightly but distinctly jaundiced; no obvious cyanosis. Rigor mortis considerable. Dark-green discoloration over the left side of the abdomen.

On opening the abdomen, a large tumour of a purplish-red colour is found to occupy the greater part of the left half of its cavity. This is found to be the distended portion of gut just above the seat of the obliteration. The rest of the bowel is found to be contracted to its fullest extent, and is of a pale yellowish colour. The surface of the peritoneum is smooth and glistening, and, with the exception of the narrow band to be afterwards described, no sign of peritonitis, either old or recent, can be found.

The liver is somewhat large, and very dark and congested, but otherwise normal to the naked eye.

The gall-bladder is normal in appearance, and is filled with dark bile. The cystic duct seems normal and permeable, but is unusually long. The hepatic and common ducts are also pervious and apparently normal.

The pancreas, spleen, and mesenteric glands seem normal.

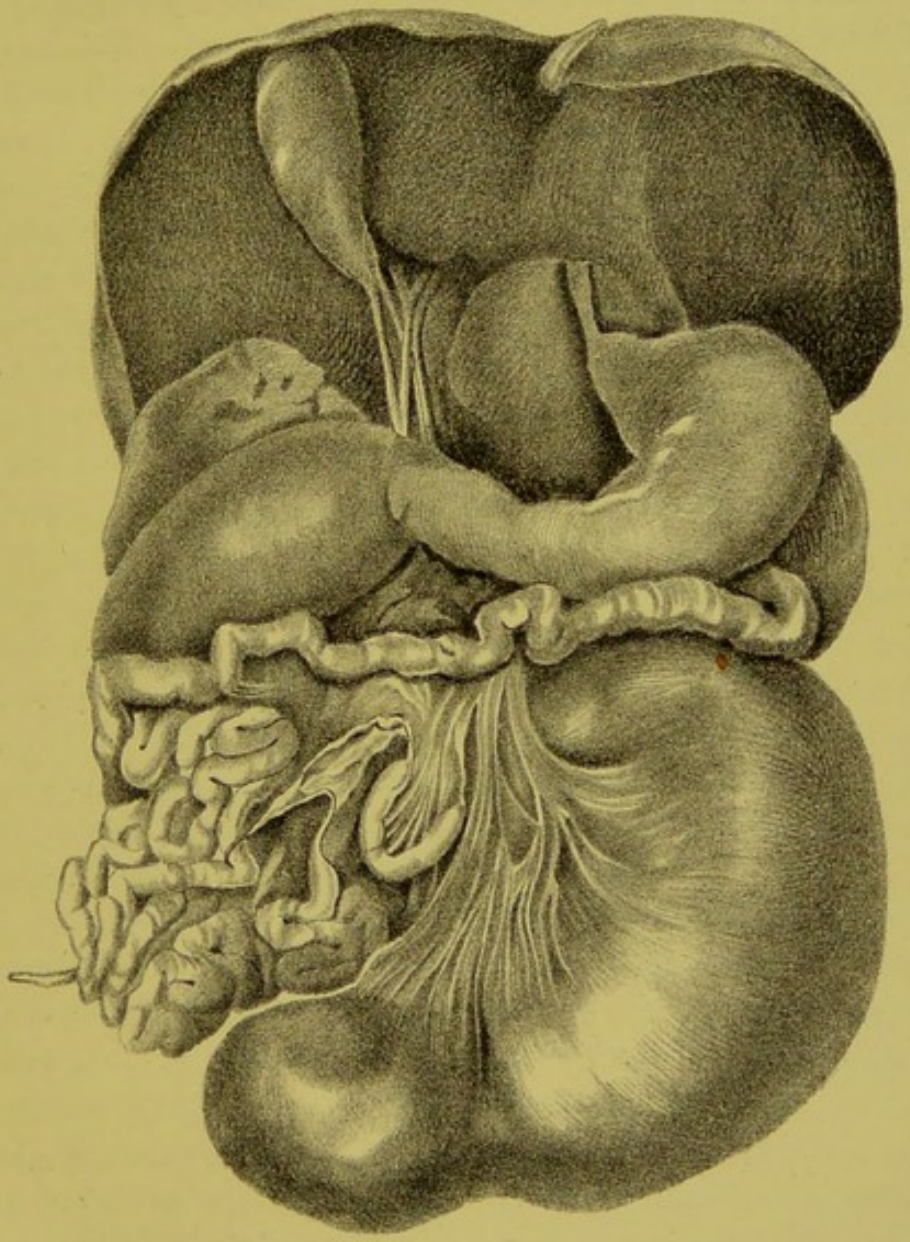
The kidneys are congested, showing extremely copious uric acid infarcts in the pyramids.

The *œsophagus* and *stomach* are normal.

Intestines (see Plate).—At the very commencement of the duodenum, the gut becomes enormously dilated. The dilated portion measures 10 inches in length, and from 1 to 1½ inches in diameter, and is of a dark purplish-brown colour. It comprises the whole of the duodenum, and probably also a few inches of the jejunum. Its lower extremity is an abruptly rounded end; it is perfectly closed, and there is a gap between it and the next portion of bowel. The mesentery belonging to it also comes to an abrupt end, there being a deep fissure between it and that of the succeeding piece of intestine. The bloodvessels in the mesentery are very unusually large. When the distended duodenum is opened, it is found to be full of turbid yellowish-brown fluid—evidently the food swallowed mixed with bile and other secretions.

A short distance from this dilated portion of bowel is a small bit of gut, 1¼ inch in length and ⅛ inch in diameter. It is blind at both ends (which are rounded), and is fixed in the shape of a horse-shoe by a little tongue-like flap of mesentery.

When the mesentery is followed to the right, its free margin is found to be thickened in places by what appear to be fragmentary remains of obliterated bowel, and it is prolonged into a peaked flap lying horizontally (see Plate). From the point of this flap a small, rounded, fibrous band passes in among the neighbouring coils of intestine; and, after encircling the mesenteric attachment of a large portion of the bowel, is fixed by a fan-shaped end into the middle of the upper surface of the mesentery of a coil of jejunum, about 7 or 8 inches below the lowest point of obliteration. This fibrous band is 1 inch in length, it is very dense in texture, and resembles fine silkworm gut in size and appearance.



Congenital Obliteration of the Small Intestine ·

The small intestine becomes pervious again about 2½ inches below the horse-shoe shaped fragment. During the rest of its course it varies in diameter from ⅛ to ⅙ inch. In one or two situations the lumen is seen to be occupied by small masses of green matter; elsewhere it seems quite empty.

The large intestine is similarly contracted, measuring only about ¼ inch in diameter, and is in a similarly empty state.

Thorax.—The lungs show a little collapse at both bases, but are otherwise normal. Thymus of medium size; pleuræ and pericardium normal; heart normal, all the valves healthy and the septa complete, with the exception of a small valvular opening in the fossa ovalis (posteriorly); ductus arteriosus patent, admitting a probe the size of a No. 1 catheter.

Remarks.—The main points of interest in this case seem to be—(1) the nature of the green fæcal matter passed on the tenth day, and (2) the pathology and etiology of the obliteration of the bowel.

1. *The Nature of the Green Fœcal Matter.*—As we see from Dr Noël Paton's report, the analysis which was possible of the small quantity submitted to him did not settle this question. The fact of a faint play of colours with nitroso-nitric acid being observed is the only point in favour of the green colour being due to bile-pigment. On the other hand, the other reactions were quite different from those of ordinary meconium.[1] Dr Paton suggests that possibly the length of time the matter had been in the bowel might account for these differences, but it cannot have been any longer there than ordinary meconium usually is.

We get more light, however, from the clinical facts. The main *bulk* of normal meconium is made up of matters derived from the vernix caseosa which the infant has swallowed *in utero* along with liquor amnii. In this case these matters would be arrested by the obliteration. This accounts for there being, at birth, not more than 2½ drachms of fæcal matter in the lower stretches of this child's bowel, instead of about 2½ oz., as is normally the case.

In a normal new-born child's bowel, the nearer the anus the darker is the colour of the contents. Consequently the first motions are the darkest of all, and those passed later become gradually paler, until about the third day they have acquired the characteristics of ordinary fæces.

[1] Zweifel, *Arch. f. Gynæcol.*, vii. p. 474, 1875.

In this child, the first two motions were absolutely devoid of any green or yellow tinge; indeed, no coloured motion was passed till the tenth day, after numerous enemata. Were the green colour of the last motion due to bile-pigment which had passed through the intestine before its lumen was interfered with, how could the motions passed during the first ten days possibly have escaped colouring?

The above facts seem sufficient to prove that the green colour was not caused by bile-pigment; and we are therefore forced to the conclusion that the micro-organisms contained in the discharge must be held responsible for it.

2. *Pathology and Etiology of the Lesion of the Bowel.*—There can be little doubt that the obliteration of the lumen of the bowel in this case was secondary to, and caused by the action of the narrow fibrous band described above.

It seems a recognised fact that such bands are the remains of peritonitic adhesions, the shape of which has been altered by prolonged traction.[1] We must therefore suppose that at some (probably early) period of intra-uterine life there had existed a patch of peritonitis, which caused adhesion of a coil of jejunum to a neighbouring piece of mesentery, and that, as the intervening gut elongated in the process of development, these parts were pulled asunder. In this way elongation of the adhesion occurred and kinking, followed by eventual obliteration and partial disappearance of the implicated bowel. As to the isolated horse-shoe-shaped fragment, its form and that of its mesentery suggest the probability that it is the remains of a volvulus or of a loop of gut which had at one time been caught and constricted by the fibrous band.

The question naturally arises—Had the ovariotomy anything to do with causing this peritonitis? On *à priori* grounds, and looking at the probable date of the occurrence of the latter, it would seem quite possible that it may have had. On the other hand, however, ovariotomy is frequently performed during pregnancy, and yet after considerable search I have not been able to find a single case recorded in which any malformation of or injury to the child resulted. I have also asked a number of experienced ovario-

[1] Treves, *Intestinal Obstruction*, 1884, p. 5.

tomists, and find that none of them have had any experience of a child born soon after an ovariotomy having suffered at all from the operation. It is therefore quite probable that the occurrence of the peritonitis about the same time as the operation is merely a matter of coincidence.

APPENDIX II.

Case of Partial Obliteration of the Gall-Bladder in a New-born Infant, associated with numerous other Congenital Malformations.

For the opportunity of examining and reporting the following case, I am indebted to my friend Dr T. J. Thyne, by whom I was asked to see the child. The infant was born on the evening of January 13, 1892.

Family History.—The mother (Mrs R.) is a strong, healthy-looking woman, and this is her fifteenth child. Nine of her former children are alive and healthy, and five have died from various ordinary complaints. None of the family have, so far as can be ascertained, suffered from any congenital malformation or disease, and there is no history of syphilis and no reason to suspect it.

Pregnancy.—The mother says that when she was about one month pregnant she got a very great fright from a cat, with a kitten in its mouth, suddenly jumping through the glass of the window into her room. The fright made her feel ill at the time and for some days after.

The birth was normal, but was thought to be about a month premature. There was an unusually large amount of liquor amnii.

After birth, the infant was noticed to be deeply cyanosed, and its extremities were swollen (œdematous). On auscultation, a loud, harsh, systolic murmur was heard by Dr Thyne all over the front of the chest. A quantity of normal meconium was passed. There was no jaundice. The child got rapidly weaker, and he died at 2 P.M. on January 14, shortly before I saw him.

Post-mortem Examination, 15th January :—

External Inspection.—The child is small, and, from his general appearance and the state of his nails, would seem to be more than one month premature. The body presents the following abnormalities :—

1. The whole of the right external ear, with the exception of the lower part of the lobule, is adherent to the adjacent scalp. The left ear, though poorly formed, is not specially abnormal.

2. There is harelip on the right side, extending into the nostril and communicating with

3. A complete cleft of the hard and soft palates.

4. There is a curious abnormality of both hands. The bones of the hands and fingers are normal in number and size; but the index finger stands apart from the medius—parallel with the thumb—as if opposing the other fingers along with the thumb. As far as can be made out without dissection of the hand, the articular surface of the metacarpal bone of the index finger must be abnormal in direction. Both the index and medius seem incapable of complete extension. There is no corresponding abnormality of the feet.

The scrotum is empty, but otherwise the external genitals are normal.

Thorax well formed. Thymus large; pleuræ and pericardium normal, containing no fluid; lungs normal and well expanded.

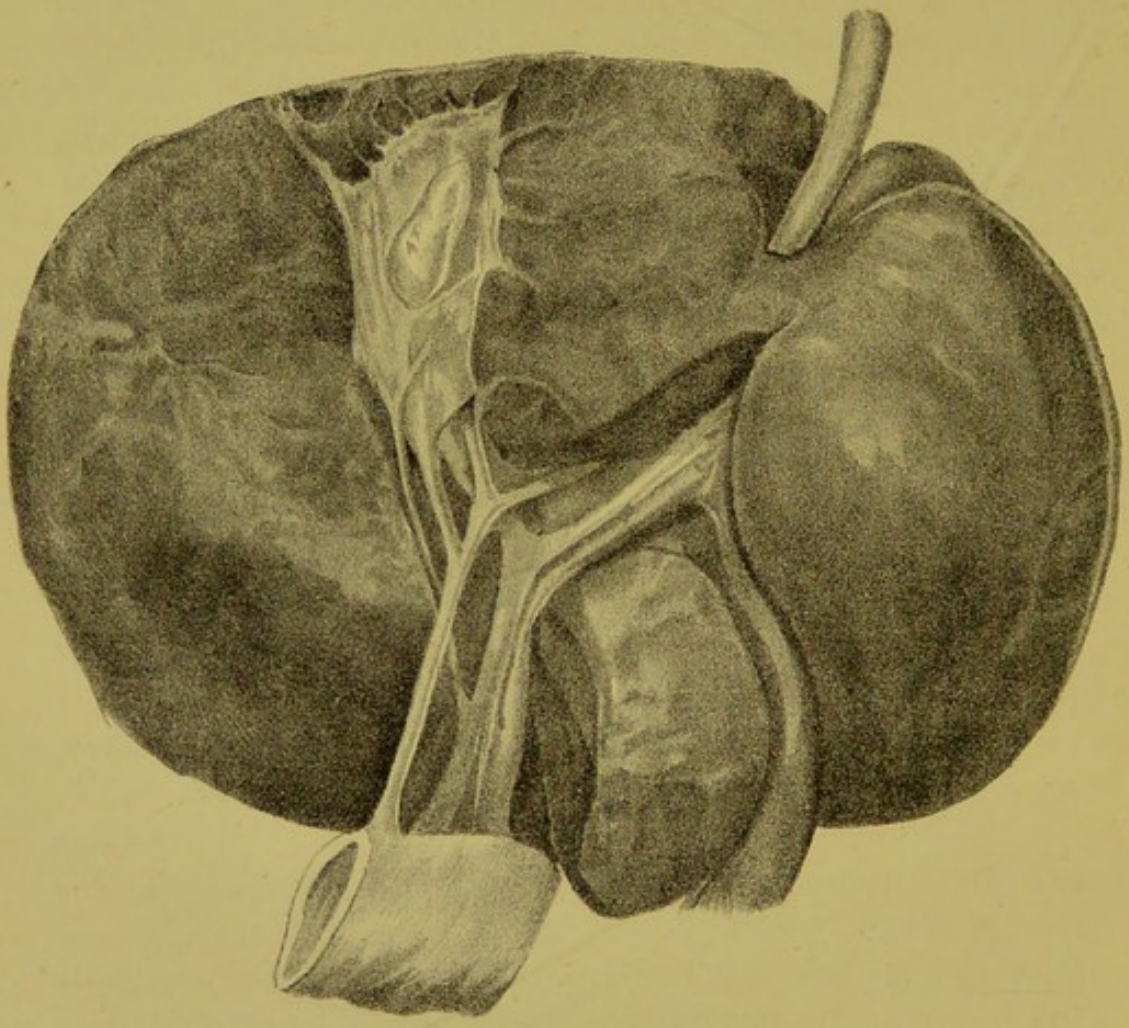
The heart and great vessels present the following abnormalities :—

1. The latter have a completely fœtal conformation. The ductus arteriosus is very wide (about $\frac{1}{7}$ inch internal diameter). The aorta is very slightly narrowed before the ductus joins it; there is no narrowing of the pulmonary artery.

2. The pulmonary and aortic orifices are each provided with only two semilunar valves. These are normal in texture, and seem to close the orifices satisfactorily.

3. There is an oval opening in the upper part of the interventricular septum, measuring $\frac{2}{3} \times \frac{1}{3}$ inch.

The auriculo-ventricular valves appear normal, and the foramen ovale is closed by a loose membrane which, besides showing the usual opening at its upper part, has numerous small apertures in



Congenital Obliteration of the Gall Bladder.

Wm CATHIE LITH.

it. The thickness of the wall of the right ventricle is to that of the left as 2 to 3.

Abdomen.—No trace of peritonitis visible.

Liver (see Plate[1]) appears normal in size (weight 2 oz.), and is very dark in colour and congested.

The gall-bladder is very small—about half-an-inch in length. It is embedded in a mass of white cicatricial tissue. On further dissection, it is found that its walls are very much thickened, and its lumen very small and somewhat stellate in shape. It contains a few drops of thin yellow fluid. Its posterior end and the anterior third or so of the cystic duct are entirely obliterated.

The posterior two-thirds of the cystic duct, and the hepatic and common ducts seem to have thickened walls and small lumina, but they are pervious. The bloodvessels supplying the gall-bladder are unusually large. The peritoneum covering the gall-bladder and adjacent parts is perfectly smooth and normal.

On microscopical examination, the thickened wall of the gall-bladder is found to have a fibro-cellular structure resembling that of granulation-tissue. It is lined by normal-looking columnar epithelium, and, in its substance, there are some small cysts, lined by similar epithelium, which look like dilated mucous glands. The obliterated part of the gall-bladder shows the same fibro-cellular structure, with cysts like dilated acini, but has no trace of a lumen. The connective tissue in which the gall-bladder is embedded seems to consist of a great hypertrophy of that usually surrounding the organ. It contains some very large blood-vessels.

The liver-tissue shows a slight increase of leucocytes in the portal spaces.[2]

Nothing abnormal is noticed about the intestines. The papilla of the ductus communis is normal and patent. The large bowel is filled with normal-looking meconium. There are some enlarged mesenteric glands.

The spleen is a little larger than natural and is dark in colour, but otherwise normal.

[1] The drawing is one and a half times the natural size.

[2] A further examination of the minute anatomy of the liver and ducts in this case has been undertaken by Dr R. Muir, and will be published on another occasion.

The kidneys are irregular in shape, and are united to one another below for about ¾ of an inch, forming a "horse-shoe kidney." The ureters come off from the anterior surface of the kidneys. The adrenals are normal in size and shape.

The bladder is normal, as are also the testicles, which are situated at the brim of the pelvis.

Remarks.—This case is of considerable interest, because the condition of the gall-bladder found in it is evidently due to the disease which produces "congenital obliteration of the bile-ducts;"[1] and some of the other facts of the case may help to throw light on the somewhat obscure subject of the etiology of that condition.

The present writer has already (p. 34 *et seq.*) attempted to prove that the inflammatory process which is the immediate cause of the malformation in these cases has nothing whatever to do with syphilis (as is usually taken for granted), but is, probably always, secondary in some unexplained way to a developmental abnormality.

This case affords strong confirmation of that view. For, on the one hand, we find that there is no history of syphilis in the parents; that they have had fourteen previous children without a sign of it; and that the child itself presents no appearance in any other organ that could be held to be due to syphilis. While, on the other, the numerous developmental abnormalities, both internal and external, certainly afford strong presumptive evidence in favour of the malformation of the gall-bladder being of the same nature.

The fact of the epithelium lining the gall-bladder being normal and healthy-looking (and that of the bile-ducts also, so far as they were examined), seems to prove that the cause of the inflammation cannot have consisted, as might have been suggested, in abnormal composition and consequently irritating properties of the bile.

[1] In several of the cases of congenital obliteration of the bile-ducts which have been recorded, the gall-bladder is described as being in very much the same condition as in this case. See, for example, Lotze, *Berliner klin. Wochenschrift*, 1876, No. 30, p. 438; Freund, *Jahrb. f. Kinderheilk.*, ix., 1876, p. 406; E. Gessner, *Ueber congen. Verschluss der grossen Gallengänge*, Inaug. Diss., Halle, 1886.