ON PYELITIS COMPLICATED BY JAUNDICE.

BY

PROFESSOR E. GÖRTER and DR. G. O. E. LIGNAC

(From the University Clinic for Diseases of Children, and the University Laboratory for Pathology at Leyden.)

Some time ago I was interested by a suggestion in a paper in the *Monatschrift für Kinderheilkunde*,¹ that the peculiar yellowish tint shown by children suffering from pyelitis might be due to an hyperbilirubinæmia. In relation to this suggestion the following observations are of special interest.

CASE 1. L. N., 3½ months old, fell ill with symptoms of an acute infectious complaint: he was restless, cried day and night, had fever, with a little cough, and vomited immediately after taking food, or refused to take his bottle. Moreover he was tender when touched.

During the first five days there was nothing to be found that could be considered as the cause of the fever; but then new symptoms appeared. The colour of the child became yellow, urine was dark brown, and at the same time the stools were completely decolourized after having been fluid and dyspeptic some days before. At the same time the patient became somewhat somnolent.

The child, although prematurely born at 8 months with a birth weight of 2.5 kgrm., had developed satisfactorily and had never been ill before. Nevertheless the mother had the impression that his colour had always been yellowish, though her assertion seems doubtful and is not confirmed by her doctor. The parents were healthy, have had no other children, and no other case of jaundice could be traced in the neighbourhood. The child had been breast fed during the first month of his life, afterwards he had been fed on mixtures of cow's milk to which rather large amounts of meal and sugar had been added. He took more than one litre every day.

On examination the child appeared to be normally developed, presented a thick layer of subcutaneous fat, weighed 5.4 kgrm., but his skin was somewhat flabby on palpation. The colour of the skin was a pronounced dark yellow, like saffron; the conjunctivæ had a greenish tint. He was slightly somnolent and although his temperature was continually high, he did not give the impression of being seriously ill.

Nothing abnormal could be detected in lungs and heart. The abdomen was somewhat distended, the spleen was enlarged, palpable and rather hard. The liver was enlarged and hard on palpation. No enlargement of lymph-glands. No rickets. Urine was dark-brown, containing much bilirubin. Moreover we found albumin, many leucocytes, some red blood cells, and epithelial cells and large numbers of short Gram-negative bacilli. The stools were grayish-white, and did not contain any biliary pigment.

On bacteriological examination a pure culture of para-colon bacilli was obtained.

The blood was not examined, because we feared a serious bleeding from even a small wound, an experience we had previously encountered in a new-born infant suffering from fatal jaundice.

The condition of the child remained practically identical during the first week of its stay in the hospital. No improvement whatever was obtained by the use of urotropin or saliformin; and he lost weight, although he took fair amounts of food (buttermilk) and had no vomiting or diarrhœa. But after a few weeks his condition grew worse and worse and he died suddenly from exhaustion. There were no other symptoms observed besides those already mentioned, and we found that even during the last days no bile had passed to the intestine.

The results of the autopsy are given later in this paper.

It seems to me [E. G.], that this case ought to be considered as a coli septicæmia, in which bacilli have been excreted in the pelves and in the bileducts, and have been able to settle there, although proof is lacking of the presence of colon bacilli in the bloodstream. It is certainly a striking fact that the child had not, at the beginning, the appearance of being dangerously ill, and did not show any symptoms besides those with which we are familiar in an uncomplicated case of pyelitis. Perhaps it would be more correct to make the diagnosis of pyelitis complicated by an infectious jaundice, as we were obliged to do in two other cases which we have since observed.

CASE 2. W. O., a girl, 9 months old, was sent to the hospital by her physician because she had had fever for a week.

The actual disease began ten days before admission with a chill, followed by a fever which lasted till we saw her. The child vomited several times, had no diarrhoea, but lost weight because it refused food. It cried on being touched. There were no symptoms capable of interpretation as the cause of the fever. She had suffered from measles at the age of 3 months. No other people suffering from illness could be traced in her surroundings. Although she had never been breast fed, she had developed fairly well, while under the supervision of the infant welfare centre, on ordinary 2/3 milk mixtures. She weighed 7.2 kgrm. on admission.

She was rather a fat child, having the characteristic pale and puffy face of a patient with pyelitis. No other symptoms of any importance could be found beyond the typical urinary findings: albumin, an enormous number of pus cells and colon bacilli, and from time to time some casts. The colon bacilli were atypical in so far as they did not produce indol, and did not split saccharose.

The pyelitis was treated first of all by the alkaline treatment introduced by John Thomson. This produced a rapid fall of temperature after 5-6 days. Later we tried to get rid of the persisting pyuria by auto-vaccine treatment without success in this case. It took three months before the urine was free from pus.

It is clear that this was a typical, and not very serious, pyelitis. Nevertheless we noticed on admission that the child had a slight degree of jaundice; not only the skin was yellowish, but the conjunctivæ and the scleræ were yellowish green. The blood contained more than 20 mgrm. of bilirubin per litre, being four times the normal amount. The direct reaction was negative.

CASE 3. The other patient, E. G., was a girl of 6 months, who on admission on 17.4.1926 was seriously ill. Seventeen days before the child had started a fever, which had persisted. During the first few days there were no gastro-intestinal disturbances, but for the 2 or 3 days previous to admission there had been some vomiting and diarrhoea. The patient had lost considerable weight and had refused food.

The chief symptoms noticed were that she was coughing and had some dyspepsia, that she was tender to the touch, without showing any stiffness of the neck. She was quiet and somnolent. A few days ago the yellow discoloration of the skin had attracted the attention of the parents. The child was very fat, had been overfed with milk (1½ litre every day) and considerable amounts of farina. Since her illness her weight had fallen from 8 to 7.340 kgrm.

The fat pasty faced child seemed slightly toxic, and had a distinct jaundice. She had rickets. The liver was somewhat enlarged and firm in consistency. In the lungs there were signs of bronchitis, but none of consolidation. Under the left costal margin we could feel a tumour, which gave the impression that it was an enlarged kidney.

In the urine we found albumin and pus, with a great many colon bacilli—slightly atypical in character on bacteriological examination—and rare chromocytes and casts, and at the same time some bile-pigments, bilirubin as well as urobilin. The blood serum was yellow: the direct reaction of H. v. d. Bergh was positive.

It took a long time to establish a complete cure. The temperature remained high for almost a month, with only a few days of normal temperature. As was indicated by the weight curve, the child was very hydrolabile, for an injection of saline produced a quick rise in the curve.

At the end of the first month, the tumor had disappeared and there was no trace of jaundice left.

CASES PREVIOUSLY REPORTED.

Among the authors who have mentioned the occurrence of jaundice in cases of pyuria, we must cite Finkelstein², who writes in his book: "Eine ziemlich seltene aber um so auffälliger Komplikation bildet die Vereinigung der Pyelitis und Ikterus."

Several authors^{3,4,5} have given descriptions of cases that were remarkable owing to some special feature, but so far as I know no autopsies have been made which throw any light on the condition of the liver. As to the clinical study of the form of the disorder of the liver, in one case reported, the bilirubin reaction of Hymans van den Bergh was found to be a *direct* one.

In the ten cases observed by Finkelstein, only one could be considered as a septicæmia, whereas in all the other cases complete cure was obtained, even sometimes in a strikingly short time, although serious symptoms were present.

Mazzeo⁴ has given an account of a child of ten years old who had a pyelocystitis complicated by jaundice with great enlargement of the liver and spleen. In the urine a staphylococcus was discovered. Complete cure was obtained by auto-vaccine treatment.

Greenthal³ saw a premature child of 7 weeks ill with a mucous and hæmorrhagic diarrhœa, who suffered afterwards from a grippe followed by pyuria.

In the case reported by W. Bayer,⁶ the jaundice was probably due to the transfusion and not to the pyuria. This child after a temporary improvement died, having presented œdema and oliguria and jaundice. No autopsy was held.

On the other hand Lasch, Fischer and Silber¹ saw a series of twelve severe cases of pyelitis, of which five were fatal. All but one of the fatal group had an increase of the bilirubin in the serum, whereas none of the surviving patients showed this. They cite another group of nine infants suffering from different infectious diseases (6 pneumonia, 1 meningitis, 1 retropharyngeal abscess and pemphigus), among whom they found one only who presented a high level of bilirubin in the blood. The increase of bilirubin was pronounced; in this patient it reached 4.6 mgrm. per 100 c.cm., whereas in the others it was not above 1.3 mgrm. per cent.

AUTOPSY ON AUTHORS' CASE.

CASE 1. L. N., aged 4 months, boy, length 58 cm., and weight 5 kgrm. The skin was saffron coloured, the scleræ were also intensely yellow from jaundice. Rigor mortis was strongly developed; the hair was thin, the anterior fontanelle was almost entirely closed. Irides were grey-blue, the diameter of both pupils was 3 mm. Post-mortem staining of the tissues of the back was well developed, and could not be displaced by pressure. Both testicles were present in the scrotum; there were no signs of rickets; the external lymphatic glands were not swollen.

On internal examination it was observed that the blood-vessels in the ligamentum teres were obliterated. The subcutaneous fat was a few millimetres thick and of an intense yellow colour. The muscles were well developed, in good condition and of a red-brown colour. The liver looked dark green, the lower edge being 3 cm. below the right costal margin. The spleen was not visible. The position of the diaphragm was on both sides at the level of the 5th intercostal space. The sternum contained 5 centres of ossification.

The lungs were collapsed slightly. The pleural cavities contained no free liquid; there were 5 c.cm. of clear, yellow liquid present in the pericardium. All the serous membranes were smooth, glossy and transparent.

Heart. Weight, 40 gm. The yellow colour of the endocardium (jaundice) was remarkable. The blood in the cavities was liquid and dark violet.

Lungs. The anæmic portions of the lungs were conspicuous by their yellow colour, the bronchial mucous membrane was also of a yellowish tint and covered with mucus. The sternal and parasternal portions were emphysematous, and some patches of lung tissue in the para-vertebral areas were atelectatic (on the right side more pronounced than on the left). Microscopic examination showed a catarrh of the bronchioli (mucous and leucocytic inflammation) and focal inflammations in the lung (sero-fibrinous degenerative inflammation), probably broncho pneumonia.

Glands. All the internal lymphatic glands were somewhat swollen, and of a distinct red violet colour. Microscopic examination indicated that there existed a pronounced erythrophagia. The lymph sinuses were filled with erythrocytes, which lay partly free, partly enclosed in swollen reticular cells. Morsels of erythrocytes were present here and there.

Spleen. Through the capsule the contents appeared to be of a light violet colour. Dimensions: 3 by $6\frac{1}{2}$ by $\frac{1}{2}$ cm., and weight 25 gm. The capsule could be slightly wrinkled. The lower pole of the spleen was of a dirty green colour (necrotic). On section a trace of blood appeared on the surface, the Malpighian bodies could just be seen; the trabeculae were well developed. The pulp was of a light violet colour, and under pressure slightly resistant. Under the microscope it was observed that the pulp and reticular cells were swollen, and phagocytosis of erythrocytes was clearly present in the reticular cells. Some hæmorrhages were also to be seen. Groups of polymorphonuclear leucocytes were to be found in the pulp. In some places the connective tissue was increased (slightly local fibrosis). Stains for bacteria had no results. The presence of splenitis was diagnosed.

Liver, gall-bladder and large bile-ducts. The gall-bladder was not swollen; on exerting a light pressure on the gall-bladder, light brown bile appeared at the papilla of Vater, though the contents of the intestine were not coloured by bile. The bile in the gall-bladder was viscous, and light brown in colour. The wall of the gall-bladder was normal.

On section but little blood appeared on the surface of the liver, which was of a diffuse green colour, showing patches of a dark green colour. The cut surface did not extrude the capsule. Weight of the liver, 250 gm. Microscopically the portal connective tissue was infiltrated throughout by polymorphonuclear leucocytes (cf. Fig. 1, showing a lobule of the liver slightly magnified, and Fig. 2, an area of portal connective tissue highly magnified); further it contained distended capillaries, filled with blood. The small bile-ducts were often difficult to see in the connective tissue. Further, there were also inflammatory connective tissue cells present.

Staining for bacteria in the liver was without result. Bile pigment in the liver cells was to be found especially in the central portions of the liver lobule (cf. Figs. 1 and 3), and here there could be also seen large liver cells with many nuclei, clustered together (compare Fig. 3 particularly), so-called multinucleated giant liver cells (irritated liver cells). Liver cells, containing fatty vacuoles, were to be seen here and there. *Diagnosis:* Cholangiolitis and pericholangiolitis. What sort of jaundice was present here, is difficult to determine.

Suprarenal bodies consisted of violet medulla and grey cortex. Microscopically, hæmorrhages appeared to be present in the medulla.

Kidneys were large (weight, 125 gm.). On section the tissue bulged above the capsule and was anæmic. Mucous, yellow matter was present in the pelvis; thin, yellow membrane covered the pyramids and the mucous membrane of the calyces. Microscopically these membranes consisted of fibrin and desquamated surface-epithelium (cf. Fig. 4, portion of a calyx slightly

magnified). The vessels in the mucous membrane of the pelvis were distended and therefore better seen. The colour of the cortex of the kidney was greyish yellow, yellow patches being present here and there, while fan-shaped yellow lines stretched from the tips of the pyramids to the edge of the medulla.

Microscopic examination showed that fibrin was present on the epithelium of the pelvis, even extending here and there between the epithelium cells. The hæmoglobin gave the fibrin a glittering light brown colour (*cf.* Fig 4). Polymorphonuclear leucocytes were also found in patches between the epithelial cells, while the sub-epithelial connective tissue was cedematous and contained here and there infiltrations of lymphocytes and polymorphonuclear leucocytes. The capillaries were also distended and filled with blood. The tubuli recti in the medulla were in some places wider than normal and filled with a homogeneous or granulated matter, coloured pink by eosin and full of polymorphonuclear leucocytes (*cf.* Fig 5, portion of medulla highly magnified). Colonies of bacteria were present, some between, and some in, the tubuli recti. These colonies consisted of bacilli which were Gram-negative (*cf.* Fig. 5.) The capillaries between the tubuli recti were distended and filled with blood, there were also red blood corpuscles scattered outside the blood-vessels.

The yellow patches in the cortex near the edge of the medulla consisted of polymorphonuclear leucocytes with pycnotic nuclei, while the kidney tissue at that place was scarcely recognizable as such (commencement of pus-formation). No particular changes were to be seen on the Malpighian bodies; the protoplasm of the tubuli contorti in general showed granular degeneration, the nuclei were badly coloured.

Bladder. The mucous membrane was of a yellow colour (jaundice). Microscopically there was hardly any trace of inflammation.

Aorta. The intima was of a yellow colour (jaundice).

Intestine. Pathologically nothing special was noted.

Pathologically a diagnosis of fibrinous pyelitis and cellular pyelo-nephritis was reached.

CONCLUSION.

The post-mortem investigation permits us to formulate the following conception of the disease in this four month's old boy :—

Both kidneys, infected by Gram-negative bacilli (in connection with the clinical-bacteriological investigation, they belong to the bacillus coli communis group), and showing signs of pyelo-nephritis, are the centre of the disease. The infection has been of a serious nature, not only by reason of the nature of the tissue changes in the pelvis (fibrinous pyelitis) and in medulla and cortex of the kidney (cellular to suppurative nephritis), but also because of the presence of cholang(iol)itis and pericholang(iol)itis with icterus and splenitis.

It is difficult, from this post-mortem investigation alone, to be dogmatic about the pathogenesis of this disease. We can only ponder on certain possibilities :

1. Has it been a coli septicæmia with particular localizations in the pelves of the kidneys and in the liver and spleen ?
2. Have the pyelitis and pyelo-nephritis first arisen by infection by way of the blood-vessels, and subsequent coli infection localized in the liver and spleen ?
3. Has the pelvis been infected with colon bacilli by the lymphatics from the intestine^{7, 8}, so that a pyelitis has developed with all its consequences ?

It may be recalled that on section the lower urinary organs were almost entirely free from inflammation.

Fig. 1.—Slight magnification of a liver lobule showing cellular cholangiolitis, pericholangiolitis. Bile pigment in the central portions of the liver lobule.

Fig. 2 —High magnification of an area of the portal connective tissue showing cellular inflammation.

Fig. 3.—Giant liver cell with many nuclei and bile pigment.

Fig. 4.—Fibrinous pyelitis (slight magnification).

Fig. 5.—Cellular inflammation of the medulla (tubuli recti) and two colonies of bacteria (finely granulated, blue stained patches).

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