FATAL CASE OF LEPTOSPIRAL JAUNDICE OF OBSCURE ORIGIN

BY

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AND

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LEEDS

It has seemed to us that the following brief account of a recent fatal case of leptospiral jaundice occurring in Leeds might be of interest for several reasons. First, the recorded cases in this country have, with rare exceptions, been shown to be related to certain occupations in which frequent contact of the skin with water soiled with rat excreta was undoubted and difficult to prevent. Secondly, the laboratory diagnosis of the case was complete, as the guinea-pig was successfully inoculated with the patient's blood, and this method of investigation, although recommended as the ideal one for diagnosis of the disease, has rarely been used successfully in this country—for example, the series of cases in workers in the fish industry recently published by Davidson *et al.* (1934) and the earlier series of Buchanan (1927). The only two cases of the disease successfully diagnosed in this way in the British Isles of which we have found records are those of Manson-Bahr (1922) and Fairley (1934). Lastly, the aetiological problem presented was unusually difficult.

Case Record

The patient, a healthy, active, and athletic man of 27, was taken ill on Thursday, September 7th, 1933, with severe headache and a temperature of 103.6° F. He vomited once, and the following day he had a slight rigor. When first seen by one of us (G. W. W.) on Saturday, September 9th, he was complaining of slight pain in the throat, which extended to the ears on swallowing; pain in the occipital region and back of the neck (not severe, but increased on flexing the head); and some discomfort in the back. Examination of the throat showed nothing very definite, and a swab failed to reveal the presence of any organisms of importance. On examination the conjunctivae were injected, but otherwise neither the eyes nor the nervous system generally showed anything abnormal. It is to be noted that the abdominal reflexes were brisk at this time.

The following day (Sunday, the 10th) there was little change in the general condition, and certainly no improvement. The pain in the back was, if anything, rather worse. The breathing was of a sighing character. By Monday, the 11th, the complexion had become faintly icteric, and there was pain and tenderness in the legs. The pain in the back was worse and the abdominal reflexes had disappeared. That evening there was retention of urine, requiring the use of the catheter. Spinal puncture yielded clear fluid under a little pressure, but cytological and bacteriological investigations were negative.

On Tuesday, the 12th, there was definite jaundice with bile in the urine. The retention of urine persisted, and there was some abdominal distension. There was much pain in the legs, and even slight manipulation caused great distress. On the following days the jaundice became much deeper, and the abdominal distension increased. Regurgitant bilious vomiting commenced and became increasingly troublesome. Increasing apathy and drowsiness without muscular twitching or tremor marked the end. Only during the last thirty-six hours had there been any haemorrhage into the skin. The spleen and liver had not been palpated at any time.

Death occurred early on the morning of Monday, September 18th, eleven days from the onset of symptoms.

NECROPSY

The body was intensely jaundiced, but muscular and well nourished. The *liver* (64 oz.) was pale, yellowish, and soft, showing much less bile-staining than the kidneys and no evidence of necrosis. All the main *bile-ducts* were patent

and contained mucus only. The *kidneys*, slightly enlarged, were notably bile-stained; their capsules stripped easily, leaving a smooth surface. The *stomach* contained a quantity of altered blood, the *oesophagus* adherent ante-mortem thrombus in its lowest three inches. There was an ancient calcified tuberculous gland in the mesentery. The *lungs* showed tiny patches of haemorrhage in their substance, and there were punctiform haemorrhages also in the *pleurae* and *pericardium*. The *heart muscle* was yellowish, soft, and flabby. The *appendix* had been removed three years before. None of the organs showed evidence of pathological change.

HISTOLOGY

1. The *liver* shows a moderate grade of subacute hepatitis in the form of cellular infiltration of the portal tracts, some being notably affected, especially the medium and smaller, others very slightly. The infiltrate is largely polymorphic, with varying numbers of lymphocytes and plasma cells, and a few eosinophil cells. There is no liquefaction of tissue, however, and the term "suppuration" cannot be applied to it. The hepatic parenchyma shows definite changes: (a) intracellular bile stasis in the central zones of the lobules; (b) a general loosening and detachment of the epithelial cells with slight early necrotic changes in a few only; and (c) mitotic figures in small numbers. It is to be noted that there is no biliary obstruction in even the smallest intercellular canaliculi—only within the cells themselves.

2. The *kidney* shows a very notable accumulation of bile pigment both in the convoluted tubular epithelium and in the lumina of the tubules throughout both cortex and medulla. There is some evidence of toxic change, otherwise the kidneys show nothing of note. Small foci of plasma cells and polymorphs are present here and there.

3. In the *spleen* the pulp is congested and very cellular. The Malpighian bodies show a definite focus of hyaline degeneration at the centre, which does not take the amyloid stain.

4. The *heart muscle* shows fragmentation of muscle cells, otherwise nothing of note.

5. The *lung* contains a number of small vessels filled with purulent plugs, while others show polymorphic infiltration of the perivascular lymphatics. There is much patchy haemorrhage and oedema. Some of the bronchi contain a trace of pus, but the condition is essentially an acute interstitial inflammation, probably spreading by the blood vessels or lymphatics, or both.

Summary.—The principal lesions present are therefore subacute hepatitis with intracellular bile stasis, and acute interstitial pneumonia.

BACTERIOLOGICAL FINDINGS

The case was first seen by the bacteriologist on the fifth day of the disease. On account of the existence of definite jaundice combined with a febrile condition and very marked prostration, it was thought desirable to inject some citrated blood from the patient into the peritoneum of the guinea-pig, as well as to do a blood culture. No attempt was made to cultivate the blood under conditions suitable for the growth of leptospira, and a negative result was recorded on cultivating in the medium used for routine work. When the patient died a few days later with pronounced icterus, preparations of liver juice were examined for leptospira under dark background, but without success.

Eleven days after its inoculation with the patient's blood a guinea-pig, one of two injected, developed icterus and died the following day, its fellow having died prematurely. Leptospira were not detected in preparations of its viscera observed under dark background, but two guinea-pigs injected from it died in eight days. Again we failed to detect spirochaetes in the liver juice of these animals. The third pair of guinea-pigs injected in series died in six days, and in their viscera typical leptospira were readily demonstrated under dark background, and were also recovered in culture on the usual semi-fluid Locke serum-agar media incubated at 30° C. for a week. For the successful cultivation of the leptospira we owe much to Mr. G. N. Boxhall, B.Sc.

The difficulty encountered in demonstrating the leptospira in the experimental animal at the outset may have been partly due to lack of experience in observing these

organisms in the living state, since sections prepared by Levaditi's method revealed their presence in the viscera of the first guinea-pig in the series. There is in any case a great contrast between the sharpness with which these micro-organisms are defined in culture and their relative elusiveness in the tissue juices, and it may be useful to laboratory workers unfamiliar with these forms at the outset of their investigations, as we were, to draw attention to it. When you have once seen them, the extremely characteristic movements of the leptospira are very helpful in their recognition. We found it notably difficult to get a convincing preparation by staining smears from tissues or cultures.

Discussion

The most interesting problem in connexion with this case was the source of infection, since it was entirely isolated, no case having been recorded in Leeds or its vicinity for many months. The most plausible suggestion, and the only one which seems to have any claim to attention, is that this was a bathing infection.

The patient was in the habit of bathing in the Yorkshire streams as and when he had the opportunity, and especially in the River Wharfe and some of its tributaries. In the second week of July, 1933, he went for a fishing holiday to Upper Wharfedale, and bathed frequently in one of the becks. He complained of being unduly tired at this time, and he had a long-standing abrasion on one heel. The last occasion on which he bathed—in the Wharfe at Ilkley—was on September 3rd, four days before he was taken ill. The river was unusually low at the time.

The French observers draw attention especially to the importance of contact with mud rather than water (Vincent, 1933), but Troisier, Bariéty, Erber, and Gabriel (1934) mention the possibility that swimmers habitually passing through dirty water may acquire immunity from latent or mild infections, and show abnormal agglutinating powers in their sera for suspensions of leptospira.

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According to L. Fischer (*Zentralbl. f. Gynäk.*, February 2nd, 1935, p. 249) in the pre-insulin era the comparatively rare cases of gestation in diabetic women almost invariably gave issue to over-weight children, of whom two in five were "giant children"—that is, weighed over 5 kilograms. In a series of thirty-one recent collected cases of childbirth in diabetics who had been treated with insulin there was, however, no "giant child": that some of the children were over-weight is explained by the fact that not all the mothers had received sufficient insulin treatment. In pre-insulin days an improvement of the maternal sugar metabolism was not infrequently noted towards the end of pregnancy, and this has been attributed to the activity of the foetal pancreas in making up the deficient insulin production of that of the mother. Anatomical and biological evidence has been adduced, from many sides, of the insular activity of the foetal pancreas in the second half of pregnancy. A more probable explanation, according to Fischer, is that the foetus abstracts from the maternal circulation considerable amounts of sugar, which are converted in the foetal circulation to glycogen and indirectly to deposited fat. Probably the insulin molecule is too large to pass through the placenta, and certainly "giant children" show insular hyperplasia and hypoglycaemia.

RADIOLOGY OF THE APPENDIX (APPENDICULOGRAPHY)

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There are many cases of obscure abdominal pain in which an accurate x-ray representation of the appendix may be of considerable aid in the diagnosis. It is not generally realized that this can now be obtained in all cases in which the lumen of the appendix is not obliterated by disease or obstructed. The method of filling the organ is relatively simple, and consists in giving a preparation of barium with milk or cornflour at night, following this after an interval of three hours by a dose of magnesium sulphate varied according to the requirements of the individual patient.¹ Radiograms are obtained on the following morning, and are continued at such intervals as may appear necessary during the following days, until the caecum is entirely empty.

What are the normal appearances of the appendix in a radiogram? Rönberg² states that the appendix may be considered as normal if it lies in its usual position, is freely movable, has a smooth outline, fills rapidly, and empties at the same rate as the large bowel. Not every normal appendix fulfils these requirements.

Position.—There is no definite position for the appendix, but it is most frequently identified medial to the caecum. It may point upwards, downwards, or transversely, and may even lie lateral to the caecum; in the latter case it is probably abnormal.

Contour.—When completely filled, the walls are smooth in outline until emptying commences. The presence of peristalsis then gives it a segmented appearance rather like a string of small sausages.³ Incomplete filling can impart an irregular appearance to a perfectly normal appendix.

Emptying Rate.—The appendix normally empties at the same rate as the caecum. Any delay in emptying after forty-eight hours is suggestive of an appendicular lesion.

Mobility.—If the appendix is identified on screen examination it can be moved by palpating with the hand, and it will be seen that it moves freely in conjunction with the caecum. However, if it is of sufficient length it will also have an independent mobility of its own. In the serial radiograms it will be seen changing its position under the influences of peristalsis rather like a pendulum. This, however, never occurs if the meso-appendix is short.

Filling Defects.—The barium-filled normal appendix frequently shows partial filling defects apparently due to the presence of faecal material. Filling defects may, however, be due to the presence of faecaliths, when they will be more sharply defined and constant in position.

In a series of one hundred patients examined during the last two years, the appendix was successfully filled in ninety-three and failed to fill in seven. Thirty of the patients were operated upon, and the x-ray appearances correlated with the operation findings and the pathological reports. In twenty-eight cases gross and obvious changes in the appendix were noted at operation, whilst the remaining two showed no evidence of abnormality.

Case Records

The following seven cases are selected from the series in order to demonstrate the changes seen in the radiograms in disease.