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## SPIROCHAETOSIS ICTERHAEMORRHAGICA IN EAST LOTHIAN.

BY

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### CLINICAL OBSERVATIONS.

By PROFESSOR GULLAND.

CONSIDERABLE interest has been excited by communications in the daily press with regard to an epidemic of spirochaetal jaundice occurring in East Lothian. The sufferers have been almost entirely young coal miners employed in the different pits, the earlier cases coming from one pit, the later from another. One farm labourer, however, has also suffered. The first cases occurred in April or May, 1923, so far as is known; two cases were in my ward at the time of the meeting of the Association of Physicians in Edinburgh last May, and one of them was demonstrated to the meeting. Probably about a dozen and a half cases in all have occurred. Some of the milder cases were treated at home; the severer ones have generally been sent to the Royal Infirmary, and six of them have been in my ward. Of these, two died. On the whole, the earlier cases have been more severe than the later. I have one case in my ward at present in which the duration of the jaundice and temperature was very short, and the haemorrhage was confined to a slight epistaxis, so that the diagnosis might easily have been missed had the man's doctor not already become familiar with the disease.

The pits affected were "wet," and rats were numerous. I endeavoured in vain to get rats from the first pit affected, though, on my representation to the manager, the rats were destroyed. It is only within the last three weeks that, by the kindness of the owner of the other pit, I received rats. Though there was no doubt about the diagnosis of the earlier cases—spirochaetes were found in the blood of one of the first cases—I delayed publication of any of the cases till the chain of evidence could be completed from both the human and the rat side. It happens that the case which I am about to describe shortly is the first in which we have been able to find the typical spirochaetes in the urine both microscopically and by animal inoculation. The symptoms of the other cases, which I shall publish later, followed the course described in Lord Dawson's classical account of the epidemic in

France, and the pathological findings in the fatal cases were of the usual type. The following case is typical of the milder form.

T. W., aged 18, a miner, was perfectly well till November 23rd, 1923. On his way home he had a rigor, with headache and pain in the abdomen. That afternoon he vomited a small quantity of brownish fluid—probably a haematemesis. He was markedly prostrated—this is a feature of all the cases—the headache continued, and he suffered from dull aching pains in all his muscles. There was apparently melaena from the first, with diarrhoea followed by constipation. He had slight epistaxis. Jaundice appeared gradually, but on his admission to the ward on November 29th was already well marked. The conjunctivae were injected and the eyes watery. He was dull, listless, and stupid. Temperature 101° F., pulse 84, respirations 32. The lips were dry, and the tongue furred and fairly moist. The lungs were normal, the heart not dilated, blood pressure 128/80. The abdomen showed no abnormality except that the liver region was tender; the liver was easily palpable at first, later it extended to 1½ in. below the rib margin. The spleen was not enlarged. The urine contained bile, albumin in small quantity, and microscopically red corpuscles, a few pus and "kidney" cells, and a few epithelial and granular casts. The blood count was: red cells 5,400,000, haemoglobin 70 per cent., and white cells 10,800. No spirochaetes were seen. The muscles were tender all over the body, and there was great muscular weakness; knee-jerks were absent. Bile was present in the faeces, which gave a definite blood reaction.

The temperature fell by lysis, being only 99° F. on the evening of December 2nd—a duration of nine days; soon after admission the pulse fell to about 70 and the respirations to about 25. Jaundice was at its height about December 5th, the twelfth day; thereafter it gradually diminished, but did not disappear till about the beginning of January. No further haemorrhage occurred.

As in some of my other cases, there was a rise of temperature of very remittent type—reaching 103° F. on one evening—from December 18th to 26th.

This was not associated with any symptoms or change in the results of physical examination; the pulse remained slow throughout, seldom over 70. Thereafter his convalescence was uneventful, the urine gradually cleared up, the slight leucocytosis disappeared, but about the end of December his hair began to fall out, and is only now coming again as a soft and fluffy growth.

Spirochaetes were first found in the urine on December 24th, about a month from the beginning of his illness. In the second part of this note Dr. Buchanan reports on their nature, and on those found in the rats we received.

The fatal cases differ from the milder ones mainly in the much greater amount of haemorrhage, weakness, and toxæmia. Bleeding may occur from the nose, lungs, stomach, bowel, kidneys, and into the skin. One of our fatal cases died with a temperature which had been subnormal for several days previously.

The original source of the rat infection and the reason for the occurrence of the epidemic at this time are difficult to explain. One can imagine a miner returned from the war starting a rat infection, as the men often micturate in the pits, but it is not easy to see why in that case the infection should have remained latent so long. The method of transmission from rat to man can be surmised. Some of my patients were careless in leaving their food on the ground where it might have been infected; others admit drinking water in the pit. It remains to be seen

whether the energetic campaign of destruction of the rats will stop the epidemic. It is evident that the rats, both above and below ground in that neighbourhood, are widely infected, as two out of three captured by chance were found to contain spirochaetes.

LEPTOSPIRA ICTERHAEMORRHAGIAE.



FIG. 1.—In urine of patient. Fontuna's stain. The characteristic hooks at the ends are seen, but not the elementary spirals.



FIG. 2.—In liver of guinea-pig inoculated with urine of patient. Stained by Levaditi's method.

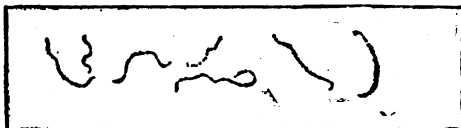


FIG. 3.—In smear made from kidney of wild rat. Unfixated and stained by Giemsa's method.



FIG. 4.—Dark-field view of leptospira in culture six days old. Note the characteristic small elementary spirals and hooked ends.

The figures have been drawn approximately 1,000 diameters.

## MICROSCOPICAL AND EXPERIMENTAL OBSERVATIONS.

By Dr. BUCHANAN.

Non-motile spirochaetal forms were found in the urine of the patient on examination by dark-ground illumination. The closely set, elementary spirals typical of the genus *Leptospira* were not evident. This may have been due to the fact that the forms seen were lying on or under epithelial cells which obscured their delicate structure. In stained films of urine a few spirochaetes were found, some of which showed one end or both with small hooks, which are a feature of *Leptospira icterohaemorrhagiae*.

Intraperitoneal inoculation of the urine into a guinea-pig proved fatal in fourteen days. The ears, nose, conjunctivae, and feet were visibly jaundiced. The subcutaneous tissue showed deep jaundice along with innumerable petechial haemorrhages. There were large subpleural haemorrhages in both lungs, presenting a typical "butterfly" appearance. The liver and spleen were enlarged, but the marked congestion masked any evidence of jaundice in the liver. The kidneys showed intense congestion, and numerous subcapsular haemorrhages were prominent. The suprarenals were enlarged and congested. The intestines showed adhesions and haemorrhages. Organisms identical with *Leptospira icterohaemorrhagiae* were found on dark-ground examination to be very numerous in the liver, but fewer in the other organs. They were also present, but less numerous, in the blood and urine. In sections of the liver stained by Levaditi's method leptospiral forms were abundant.

Another guinea-pig, inoculated with an emulsion made from the liver of the infected animal, died in five days with lesions similar to, but not so marked as, those described above.

*Occurrence of Leptospira in the Rats of the Neighbourhood.*

Three live wild rats were obtained by the courtesy of the pit owner, two from one of the coal mines and one from the surface at about a quarter of a mile from the pits. Motile and characteristic leptospiral forms were found by dark-ground examination in emulsions made from the kidneys of the surface rat and one of the pit rats. No spirochaetes were found in the other organs, the urine, or the blood. The blood was infected with *Trypanosoma lewisi*. The rats were well nourished and showed no signs of disease.

Guinea-pigs were inoculated intraperitoneally with kidney emulsion from each of the three rats. The one inoculated from the surface rat was found dead on the seventh day. It showed definite jaundice, haemorrhages, and lesions similar to those found in the animal inoculated with the patient's urine. Leptospiral forms were found as before. Noguchi's medium was inoculated from the liver and blood of this guinea-pig. After six days' incubation at 37° C., actively motile and obviously multiplying forms of leptospira were still demonstrable at that period.

A guinea-pig inoculated from one of the pit rats died thirteen days after the injection. Leptospiral forms were again found in the blood, urine, and organs generally. Jaundice and haemorrhages were a feature of the *post-mortem* examination. The remaining guinea-pig, inoculated from the second pit rat, in which no organisms were found, is still alive and apparently well up to date—that is, sixteen days after inoculation.

## CONCLUSIONS.

It has been definitely established that the leptospiral organisms found in man and rats in the infected area produce lesions typical of infectious jaundice when inoculated into guinea-pigs. The result of the inoculations proved fatal in from seven to fourteen days. Subinoculation into the same species, with either human or rat strains from dead infected guinea-pigs, proved more rapidly fatal in both cases, the period being five to six days.

The two organisms isolated in this instance from man and wild rats are morphologically identical. The organism has been cultivated. Its characteristics in dark-ground illumination consist of very minute regular spirals throughout its entire length, and a hook at one or both ends. The

hooked end rotates in the manner of a propeller, and progress occurs in the direction of the unhooked end. If both ends rotate it remains practically in the one place.

The pathogenic action, morphology, and behaviour in culture of the leptospira show it to be, so far as the work has proceeded, identical with the Japanese, European, and American strains described and compared by Noguchi.

Further investigation is in progress, the results of which will be published in detail at a later date.

The microscopic and bacteriological part of the work has been carried out in the Pathological Department of the Royal Infirmary, and the experimental part in the Royal College of Physicians Laboratory, Edinburgh.

Press communications by the Scottish Board of Health have already appeared in the *Scotsman*. The information given resulted from the above bacteriological investigation.

## METASTASIS OF MELANOTIC CANCER EIGHTEEN YEARS AFTER REMOVAL OF THE EYEBALL.

BY

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The following case is of some interest, and we feel should be put on record.

A lady, aged 57, came under our care in August, 1922, complaining of a swelling below the left scapula, which she had noticed for two weeks. She also complained of gradual loss of strength during the past few months. She had no pain at the site of the swelling, but some dull aching round the chest. An elastic swelling, oval in outline and about the size of an ordinary lemon, could be felt protruding from beneath the inferior angle of the scapula on the left side.

The patient gave a history of having had the left eyeball removed in June, 1904, by the late Mr. Juler. Mr. Frank Juler has kindly given us an extract from his father's notes on the case. The eyeball was removed for suspected sarcoma of the ciliary body. There was a large dark brown mass in the vitreous, just behind the lens, with haemorrhage upon it. There was some bulging of the periphery of the iris. Though there is no note of the histological appearance of the tumour, there can be little doubt that it was an intraocular melanotic cancer.

The swelling on the back was explored, and was found to be a dark pigmented growth involving the sixth and seventh ribs, near their angles. A mass, including about five inches of the length of each of these ribs, was removed. The growth was adherent to the underlying pleura, which could be felt to be adherent to the lung. There were some small dark nodules, forming prominences on the surface of the pleura. The patient recovered rapidly from the operation, and returned to her usual domestic activities.

The growth removed proved to be a melanotic cancer. An examination of the urine at the time of operation, and one month later, showed that there was no melanin or melanogen present. Three months afterwards the patient began to fail. In the middle of December, 1922, she complained of numbness and tingling in her right foot. This was followed in a few weeks by complete loss of power, with rigidity. Shortly afterwards the left hand and arm were affected in the same way, followed by the same condition in the left leg, and then in the right hand and arm. By the beginning of April, 1923, both arms and legs were paralysed and rigid. There was loss of control over the bladder, and obstinate constipation. The patient died on April 16th, 1923.

No general discussion of the delayed appearance of metastases from melanotic cancer of the eyeball is called for, as the whole subject has been dealt with recently by Mr. W. G. Spencer in his Bradshaw Lecture.<sup>1</sup> It is, however, worthy of note that so late as eighteen years after removal of the primary tumour there was still no evidence of metastasis in the liver, if, as stated by Garrod,<sup>2</sup> melanuria can be taken as an indication of that having occurred. In melanotic cancer of the eyeball death usually occurs within three years of operation, but numerous instances of delayed recurrence or metastasis have been reported. Cairns<sup>3</sup> reported a case of metastasis in the scapula eighteen years after removal of the eyeball, and metastasis has been delayed as long as twenty-four years,