THE PREVALENCE OF WEIL'S DISEASE IN CERTAIN OCCUPATIONS

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It is rapidly becoming recognized that infection by *Leptospira icterohaemorrhagiae*, causing haemorrhagic jaundice, is more frequent in this country than was previously known. The new cases have been found chiefly among sewer men (Fairley,¹ Alston and others,² Halstead³) and fish workers (Davidson and others⁴). The occurrence of this infection among British coal miners has been well known since Buchanan and others^{5, 6, 7} provided a full clinical and bacteriological survey of cases arising in East Lothian mines. Other instances of the infection have been met with in various circumstances, and in most of these contact with material contaminated by rats' urine has been a likely occurrence. Since, however, certain occupations, such as the three mentioned, appear to provide more readily than others the circumstances necessary for infection, the work reported here has been undertaken to determine the degree of exposure to risk of sewer workers and to explore the possibility of prevention by vaccination and other methods.

Possibilities of Prophylactic Vaccination

The prophylactic vaccination of dogs with the killed cultures of leptospira has proved successful in the hands of Dalling and Okell,⁸ but the literature on the subject of the prophylactic vaccination of men is somewhat conflicting. The most recent work on this subject appears to be that of Wani,⁹ who has inoculated 10,000 Japanese miners in a heavily infected coal-mining district with apparently good results. Immune bodies were found as long as nineteen months after inoculation. He assumes that this was due to inoculation and not to a previous infection. As regards the reactions produced, about half the patients continued to work without interruption; of the rest, 1,365 took time off after the first injection (varying from one day in the case of 21.3 per cent. to more than one week in the case of 1.6 per cent.) and 795 (varying from one day to more than a week) after the second injection. The vaccine used was a phenolized culture, grown in a medium consisting of horse serum and guinea-pigs' blood.

It seemed desirable, however, to approach prophylactic vaccination from the beginning, and certain information has therefore been sought. The first object aimed at was the discovery of what evidences there are that immune bodies are produced in the blood of men who have been exposed to risk of leptospiral infection, and particularly whether an antibody capable of protecting susceptible animals against living leptospira can be demonstrated in these individuals. On the hypothesis that immunization produced by vaccination will give results similar to the immunity of natural subinfections, information of this sort might give reason for hoping that active prophylactic vaccination is a possibility. Secondly, evidence has been sought and reviewed as to how long such antibodies may remain in the blood stream, since this may give an indication of how lasting any successful vaccination might be. Thirdly, means have been sought of producing massive cultures of *L. icterohaemorrhagiae* in a medium which would contain little or no protein foreign to the human

body, in order to reduce to a minimum non-specific reactions to the vaccine.

Some evidence as regards anti-leptospiral immune bodies in London sewer workers was given by N. H. Fairley.¹ He reported that eight such workmen who had suffered from jaundice while engaged at sewer work showed a significant degree of serum agglutination against *L. icterohaemorrhagiae* at periods varying from seven months to eight years and two months after the illness characterized by jaundice. In the present work we have examined the serum of one sewer worker who had suffered from jaundice and of forty-five who declared that they had never had that symptom in connexion with any illness since they began sewer work. The antigen in the agglutination test was a formalized culture of a London human strain of *L. icterohaemorrhagiae*. Interaction took place for eighteen hours at room temperature. The dilutions were put up according to the technique of Professor Schüffner.¹⁰ A certain number of sera were also tested with the adhesion test elaborated by Brown and Davis,^{11, 12} and when both tests were used they gave results approximately to the same titre.

The man who gave a history of jaundice stated that the illness occurred twenty-three years ago, eighteen months after he had begun sewer work, and the end titre of his serum in the agglutination test was 1 in 300. Among the forty-five who had no recollection of jaundice nine (20 per cent.) showed by one test, or when both methods were applied by each of them, a reaction with an end titre of 1 in 30 in five instances and 1 in 100 in four instances. The period of sewer work of the nine reactors varied from eight to thirty-seven years, and those who showed no reaction had a similar range of service. As a control to these results sera submitted for Wassermann reaction from 107 men, women, and children were examined, and none of these gave a reaction when tested by the agglutination method in a dilution of 1 in 20: positive control sera were also put up at this dilution. These results gave some hope that anti-leptospiral immune bodies may be produced by vaccination, for the nine men whose serum gave positive reactions not only denied any history of jaundice, but most of them said that they had had no illnesses at all "to remember" since commencing sewer work.

Agglutinins as an Indication of Protective Antibodies

An endeavour was next made to determine whether the presence of agglutinins is necessarily an indication of protective antibodies in the serum of sewer men, and it was shown that four sera which were positive in the agglutination test showed the power of protecting guinea-pigs from the effect of injection of virulent *L. icterohaemorrhagiae*: the sera of two adult men chosen from the general population and showing no agglutinins were used as controls in this experiment. The experiment was carried out with twelve pairs of young guinea-pigs of the same breed and matched by weight as between the pairs as well as possible. Each pair of animals were given intraperitoneal injections of 0.5 or 1.5 c.cm. of one of the six sera used, and after an interval of one hour each animal was injected intraperitoneally with 0.2 c.cm. of a seven-days-old culture diluted in physiological saline of a virulent strain (McVady) of *L. icterohaemorrhagiae* in a rabbit-serum broth medium. The diluted culture contained one or two leptospira in each darkground field when examined with a 1/12-inch objective and 10x eyepiece. The result of the experiment was that seven out of eight of the guinea-pigs treated with one or the other of the control sera died within six to seven days after infection—all seven showed typical lesions of haemorrhage and jaundice, and in one of each pair of animals leptospira

were looked for by darkground illumination and were demonstrated. The single survivor among the eight control animals was one of the pair treated with 1.5 c.cm. of one of the sera. In contrast, only two of the sixteen animals treated with the sewer men's serum died, and the remainder survived and were perfectly healthy five weeks after the time of infection. The two animals which succumbed died at nine days and fifteen days after the commencement of the experiment, in the second case the death being markedly delayed compared with the deaths of the control animals. The guinea-pig which died after nine days had received 0.5 c.cm. of one of the specimens of serum, and that which died after fifteen days received 1.5 c.cm. of another serum. The protocol of the experiment is given for the sake of clarity.

Protocol of Protection Experiment

Source of Serum	Agglutination Titre	Fate of two Guinea-pigs treated with Serum 1 hour before Injection of <i>L. icterohaemorrhagiae</i>	
		0.5 c.cm. Serum	1.5 c.cm. Serum
K. (Sewerman)	1 in 100	1 survived, 1 died* after 9 days	2 survived
Pe. (Sewerman)	1 in 100	2 survived	2 survived
Pr. (Sewerman)	1 in 100	2 survived	2 survived
E. (Sewerman)	1 in 100	2 survived	1 survived, 1 died* after 15 days
Al. (Control)...	Negative	2 died* after 6-7 days	2 died* after 6-7 days
Au. (Control)...	Negative	2 died* after 6-7 days	1 survived, 1 died* after 6-7 days

* All animals which died were examined thoroughly post mortem and the typical signs of haemorrhagic jaundice were discovered. Leptospira were sought in one animal of each pair and found.

It is considered that this experiment demonstrates that protective antibodies accompany agglutinins in the serum of certain sewer men.

Persistence of Immune Bodies

Circumstantial evidence that anti-leptospiroal immune bodies remain in the blood for a considerable time after infection is provided by Fairley's¹ report (corroborated by one case in our series) of agglutination titres (up to 1 in 1,000) higher than those which we found in men who, although exposed to risk of infection, had never had jaundice. The length of time that immune bodies persist after infection is not accurately determined by this review, because the men concerned have been exposed to risk continually after the infection which caused illness. Wani,⁹ referred to above, states that immune bodies were demonstrable nineteen months after vaccination of coal miners with leptospiral vaccine, but again no estimate can be made of the effect of possible subinfections. However, it seems clear from the evidence of recovered cases that a high agglutinin titre or the ability to respond to subsequent subinfections by a high titre may persist for a long time. This also may be taken as an encouragement to efforts at vaccination.

In order to obviate as much as possible reactions due to foreign proteins, such as rabbit and horse serum, attempts are now being made to grow massive cultures of leptospira in media containing only digests of human placenta, to which small quantities of human sera have been added. Experiments on these lines have been successful with small amounts of medium, and it remains to be tested whether massive cultures can be maintained thus in successive subcultures.

Summary

1. Nine out of forty-five sewer workers who were not aware of having had any form of jaundice showed significant serum agglutinins for *L. icterohaemorrhagiae*.

2. Evidence is given that protective antibodies are present in those specimens of human serum which show agglutinins.

3. Prophylactic inoculation of those exposed to risk appears to offer a means of prevention of this disease, and work on the preparation of a suitable vaccine in a medium containing no foreign protein is in progress.

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Clinical Memoranda

A Case of *B. suipestifer* Septicaemia

The following case is recorded on account of the rarity of *B. suipestifer* of the European type as a cause of septicaemia, and of the fact that the patient was suffering from an entirely unconnected surgical condition at the same time.

Cases of septicaemia due to the American type of this organism have frequently been recorded,¹ and were associated with pneumonia, cystitis, and arthritis. On the other hand, those reported as due to the European variety have usually shown symptoms of gastro-intestinal disturbance. Scott² reports four outbreaks of food poisoning due to the European type (Subgroup II) with over 100 cases. The incubation period was from sixteen to thirty-six hours, and all showed gastro-intestinal irritation—abdominal pain, vomiting, and diarrhoea. Clayton and Milne³ report a mass infection of seven out of eight persons who had consumed an infected pork pie, and two of these died. J. T. Duncan⁴ published a very comprehensive report of an Indian removed from a boat in the London Docks whence he had come from Bombay. He showed mild typhoidal symptoms and recovered. The organism found was a Type "G" *Salmonella* closely related to the Reading type, and it was designated Type "Alphonso."

The case here described was that of a married woman aged 40, who was admitted with acute abdominal pain, which had started three weeks earlier. After the onset symptoms had subsided somewhat, but had increased shortly before admission. Associated with the pain was vomiting and diarrhoea with dark-coloured motions, but there was no evidence that this was due to blood. Menstruation had been regular.

On admission the patient was pale, restless, and anxious. Her tongue was furred, and there was slight abdominal distension on the left side, but no local tenderness or rigidity could be detected. After a preliminary transfusion, a laparotomy was done, and a quantity of blood-stained fluid and blood clot was removed, together with a ruptured right Fallopian tube. Her condition improved after the operation, but five days later the wound broke down and the temperature rose. Rigors followed, and the temperature