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WEIL'S DISEASE (LEPTOSPIROSIS) A CLINICAL AND BACTERIOLOGICAL STUDY OF NINETEEN CASES OCCURRING CHIEFLY AMONG FISH WORKERS

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The occurrence in Minorca of an epidemic of jaundice was first described by Cleghorn in 1745. The publication by Weil in 1886 of an account of four cases of infectious jaundice led to the recognition of a symptom-complex of fever, jaundice, enlargement of the liver and spleen, the occurrence of haemorrhages, and, occasionally, febrile relapses under the designation of Weil's disease. Following the discovery of the *L. icterohaemorrhagiae* in the blood of a patient suffering from the Japanese form of the disease, and the proof of its specificity by Inada and Ido in 1915, the name "spirochaetosis icterohaemorrhagica" was suggested as a substitute for the many titles applied to this disease. Stokes and Ryle¹ in 1916 obtained bacteriological evidence of the existence of the disease among the British soldiers in Flanders; similar outbreaks were reported and confirmed among the German, French, and Italian troops on the Western Front.

The occurrence of spirochaetosis in the form of an acute febrile illness, without jaundice, was recognized.² In consequence it has been the practice of European workers to revert to the non-descriptive title of "Weil's disease," in preference to its synonyms laying emphasis on jaundice. Interest in the disease has increased in recent years in Holland, where in the past decade 452 cases have been observed, with a mortality of 10.2 per cent.³ Infection occurs by bathing and by accidental or suicidal immersion in the canals; a higher occupational incidence is reported among bargemen and workers in abattoirs and other rat-infested premises.

Leptospiral Infection in Britain

Potential sources of infection in Britain are known to exist, the carrier rate in rats varying from four out of 101 rats in London⁴ to thirty out of 100 in different parts of England.⁵ Buchanan⁶ found sixty-one infected rats out of a total of 166 from various parts of Scotland. In the light of these figures the reports of leptospiral infection in man are surprisingly few, and their authenticity is undoubted only in three outbreaks. Manson-Bahr⁷ in 1922 described a case in a seaman four days after immersion in the Thames, the *L. icterohaemorrhagiae* being isolated from the blood. An outbreak of epidemic jaundice in 1923, among miners in certain wet pits in East Lothian, was described by Gulland and Buchanan,⁸ the diagnosis in eighteen cases being based on the clinical features. Investigations by Buchanan resulted in proof

of the leptospiral origin of the East Lothian epidemic, a guinea-pig inoculated from the urine of a patient dying with typical post-mortem findings and showing the *L. icterohaemorrhagiae* in its tissues. A total of thirty-one cases in all was later reported on the combined clinical and bacteriological findings.⁶ The existence of the disease in Scotland among members of the community other than coal-miners, particularly those working in rat-infested areas—for example, near refuse dumps, piggeries, and breweries—was thus proved.

In May of this year the clinical diagnosis of a fatal case of Weil's disease, in a temporary sewer worker in London, was established by the recovery of the *L. icterohaemorrhagiae* from guinea-pigs inoculated with blood on the seventh day of the disease, and by the presence of a strongly positive sero-reaction with the typical "Weil" strain on the tenth day. Consequent inquiry by Hamilton Fairley,⁹ under whose charge the case had been, showed, on clinical and serological examination of ten persons, that a hitherto unrecognized and endemic focus of Weil's disease had existed for twelve and a half years among sewer workers in London. Other reports of isolated cases or localized outbreaks have been communicated on the clinical features. In some cases spirochaetes were stated to be present in the urine, but bacteriological proof of their identity with *L. icterohaemorrhagiae* was not produced. For a full discussion of the relevant literature the reader is referred to the papers by Hindle¹⁰ and by Taylor and Goyle.¹¹

Present Investigation

Workers in rat-infested premises, both in this country and in Holland, have been recognized as specially liable to the disease. The association of leptospiral infection with water workers in Holland and wetness of the mines in East Lothian is admitted. The object of the present paper, however, is to describe a current outbreak of Weil's disease among persons employed in the handling and cleaning of fish, and to indicate the circumstances rendering them liable to infection. So far as the present authors are aware, the peculiar incidence of the disease in this industrial group has not been reported previously.

In June, 1934, two patients (Cases 3 and 5 in Table I), suffering from an acute febrile disease associated with jaundice and nephritis, were admitted to the wards in the Aberdeen Royal Infirmary under the charge of the professor of medicine. A diagnosis of Weil's disease was made on the clinical features. Inoculation of the blood and urine into guinea-pigs gave negative results. (An

* Since this paper was submitted to the *British Medical Journal* four more cases of proved Weil's disease in fish workers have been investigated, making a total of twenty-three.

explanation of these failures is discussed later.) Sera collected on the twenty-first and thirty-second days of the disease, respectively, were dispatched to Amsterdam, and Professor Schüffner, who generously agreed to test sera in these and other suspected cases, reported positive agglutination reactions in titres of 1 in 30,000 with the classical "Weil" strain. As both these patients were fish workers inquiries were instituted; these showed clearly that several additional cases had occurred in this occupational group over a period beginning in April of this year. Infective jaundice being a notifiable disease in Scotland since February, 1924, it was decided to request the medical officer of health to circularize the medical practitioners of Aberdeen and its regional area for information as to "any cases of infectious jaundice which they may at present have, or in the past have had, under their care," and to investigate the working conditions of the fish trade.

As a result of the better recognition of the clinical manifestations of Weil's disease, other than icterus, during the past decade in Holland the proportion of mild cases unassociated with jaundice has risen from 13 to 60 per cent. of the total.³ Since information was requested from the Aberdeen practitioners about cases of infectious jaundice, we claim that a reliable index of the prevalence of leptospiral infection was not produced as a result of this inquiry.

We propose to divide the cases reported in this paper into two groups. Group I consists of a series of fifteen cases investigated between June and October, 1934, in which the diagnosis has been confirmed by bacteriological or serological methods. Points of particular interest in Group I are given in Table I. Group II comprises a series of four cases of great severity, diagnosed as Weil's disease from their clinical manifestations, but lacking bacteriological or serological confirmation. The value of serological tests is of recent establishment, and accordingly had not been undertaken in these cases.

Group I

In order to save space individual case histories are omitted, and the general picture of the disease as seen in these cases is presented and compared with the clinical features reported elsewhere. Of the fifteen cases in Table I, Cases 14 and 15 occurred in Edinburgh, the remaining thirteen in Aberdeen, and all have occurred during the present year. Twelve of the thirteen patients

were connected with the fish trade. Eleven were employed in cleaning, filleting, curing, or packing fish, and one in the transport of fish from the yards to the railway station. Of the remaining cases one was a farm labourer working in fields and ditches, another was a labourer at the zoological gardens, while a third was a labourer engaged in laying water-mains. Seven out of the twelve cases in fish workers occurred in April, May, and June, and the remaining five in September and October. Males were affected in eight, females in seven instances. The ages varied from 14 to 67 years, ten being under 25. Juvenile and adolescent labour, however, is preponderant in the fishyards. The incubation period is stated to range between the limits of four and nineteen days, with an average of 10.3 days.³ In view of the continuous exposure to sources of infection it was not possible to determine the incubation period in any of our cases.

Onset and Early Symptoms

The onset can be described as sudden in fourteen out of the fifteen cases, the illness developing acutely within twenty-four hours or less. All of these patients were confined to bed from the onset. Thirteen were admitted to hospital at periods varying from the second to the fourteenth day of the disease. Several of the following symptoms were present in the first four days of the illness: severe headache; weakness and marked prostration; muscular pains; shivering; anorexia, nausea, vomiting, and constipation; sore throat; abdominal pain; epistaxis and insomnia. Diarrhoea occurred at the onset in one case, and was followed by marked constipation. Meningeal symptoms with acute pain on moving the neck led in one case to suspicions of a cerebral condition. Abdominal tenderness was generalized or localized to the epigastrium, right hypochondrium, or right iliac region. The tongue was coated, moist in the early stages, and dry later. Muscular pains and a feeling of prostration were present in practically every case. Cases 9 and 10 were exceptional in this respect, although they had been diagnosed as influenza until the sero-reactions revealed their true nature. In the severe cases muscular pain was a very prominent symptom, affecting the back, loins, shoulder-girdle, neck, thighs, or calves, and lasting as long as seven days; acute tenderness of the muscles on pressure was associated. Joint pains were present in the most severe surviving case.

TABLE I

No.	Sex and Age	Occupation	Onset	Muscular Pains	Haemorrhages	Jaundice	Nephritis	Duration (Days)
1	Male, 17	Fish worker	Sudden	++	Haemoptysis; occult blood in stools	++	Albumin, casts	58
2	Female, 18	"	"	++	Epistaxis	+++ 70	Albumin, pus cells	77
3	Female, 16	"	"	++	Epistaxis. ? Haematemesis	++ 33	Albumin, casts, pus cells. 58	87
4	Male, 18	"	"	+	None	++ 50	Albumin, casts, pus cells	(16)
5	Male, 40	"	"	+++	Epistaxis; occult blood in stools	+++ 60	Albumin, casts, pus cells. 152	(57)
6	Female, 16	"	"	++	Epistaxis	None	Albumin, casts, pus cells, red blood cells. 52	(36)
7	Male, 22	"	"	++	Occult blood in stools	++ 35	Albumin, casts, pus cells, red blood cells. 143	(42)
8	Female, 14	"	"	++	? Haematemesis	++ 35	Albumin, casts, pus cells, red cells. 43	(43)
9	Female, 18	"	"	None	None	None	None	14
10	Female, 21	"	"	+	None	None	None	(25)
11	Female, 16	"	"	+	[None]	+++ 60	Albumin	20+
12	Male, 63	Fish carter	"	Not noted	Epistaxis; petechiae	+++	Anuria	9
13	Male, 39	Labourer: pipe layer	Gradual	Not noted	Not noted	None	Albumin, casts, pus cells, red cells. 38	(56)
14	Male, 39	"Zoo" labourer	Sudden	Not noted	Not noted	+ 28	Albumin, casts, blood. 94	112
15	Male, 67	Farm labourer	"	++	Petechiae; haematemesis; melaena	+++ 52	Albumin, casts, blood	14

+ = Slight. ++ = Moderate. +++ = Severe. Figures in Columns 7 and 8 apply to icterus index in Murphy units and blood urea in mg. per 100 c.cm. respectively. Figures in Column 9 indicate total days of incapacity from work; where convalescent period is not included, figures are enclosed in parentheses. Death occurred in Cases 12 and 15; the remainder recovered.

Stress is laid by authors in the East Indies and Holland on the flushed conjunctivae ("red eyes") due to dilatation of the episcleral capillaries. "Red eyes" was not noted in any of our cases, but its absence may be explained on the grounds that the patients were admitted to hospital on the average five days after the onset of acute symptoms. Herpes labialis was seen only in one case, and was not haemorrhagic. Haemorrhage from some situation was present in nine out of thirteen cases. Epistaxes were the most frequent, occurring in five instances. Nose-bleeding was slight in degree, occurred in the first four days, and was revealed only on direct inquiry. Severe haemorrhages of multiple origin are recorded in the two fatal cases of this group.

Fever was present in ten of the patients. Case 12 was collapsed, with a subnormal temperature, while Case 13 was admitted late in the disease. The temperature varied in its maximum height from 99° to 104° F., according as admission was late or early. The highest figures were recorded on the third, fourth, and fifth days. The duration of the primary fever was six to nine days. A secondary rise in temperature in six cases followed from four to eleven days after the termination of the primary fever, and lasted from five to twenty days; a maximum figure exceeding 100° was reached in four of these. Splenic and glandular enlargement was absent in all cases, but there was liver enlargement in one. A red, measly rash was seen on the legs of one patient on the tenth day of the disease, and disappeared within two days. Jaundice was detected in eleven out of the fifteen cases, being first seen on the fourth to the tenth day; in six of the cases it was present by the sixth day. Fluctuations in the jaundice were not observed. Save in two cases where jaundice persisted until the seventh week, icterus had disappeared by the third week.

Urinary Features

These seem to be worthy of emphasis. Albumin and casts were found in nine cases, albumin alone in three, and red blood cells in six. The urinary output was not markedly diminished, except in one fatal case with anuria. There was no associated puffiness of the face or other oedema. The association of jaundice and nephritis was found of great diagnostic value. Whether the azotaemia of Weil's disease is wholly dependent on impairment of renal function or in part at least on increased urea production is an undetermined problem.¹² Figures for blood urea values are available only in four cases before the tenth day of the disease (Cases 3, 5, 7, and 8). Raised values are present in these instances. Case 7 is of interest in that a urea content of 66 mg. per 100 c.cm. was recorded on the third day of the illness, later rising to the high level of 143 mg. per 100 c.cm. on the tenth day. These high degrees of nitrogen retention suggest that the association of a sudden onset, high fever, muscular pains, nephritis, and raised blood urea values in the absence of oedema or hypertension might be of considerable diagnostic service in the early stages of severe cases. A secondary rise in the blood urea content occurred during the period of secondary fever in two cases.

Course of the Disease

While the distressing subjective features of the onset, such as headache and muscular pains, disappeared within a week, and jaundice resolved on the average by the twenty-first day, the urinary findings took considerably longer to return to normal. Even in mild cases a trace of albumin was present six weeks after the onset, while in the severe cases albumin and casts in the centrifuged deposit were detected in the eighth week of the disease. In Cases 3 and 5 blood urea values fell to normal upper limits after six weeks. In six cases loss of hair, beginning

in the third week of the disease, was marked, and led to a state of partial baldness. It has been impossible to estimate the total period of disability except by the duration of stay in hospital. Convalescence thereafter was prolonged, since many of the patients felt unable to work owing to general weakness and tiredness, and complained of vague muscular pains for several weeks after discharge from hospital. There were two fatal cases in this group, death occurring on the ninth and fourteenth days.

Group II

Group II consists of the series of four fatal cases reported on clinical grounds. They extend over a period from 1929 to 1934. The several occupations of the patients were restaurateur, farm worker, market gardener, and fish carter. Three were males and one a female, and their ages were 64, 34, 34, and 24 respectively. A typical history of one of these cases is as follows. The patient was suddenly taken ill with severe muscular pains followed by sickness, vomiting, and haemoptysis, succeeded by jaundice on the fourth day. On the sixth day he was admitted to hospital moribund, when the findings and subsequent course were: severe jaundice, albuminuria slight, hyaline granular and epithelial casts in urine, blood urea 349 mg. per 100 c.cm., gradually increasing jaundice, repeated haemorrhages; finally, anuria, coma, and death on the ninth day. It is to be noted that one of the patients in these fatal cases was a fish carter. In another a history was obtained of fatal jaundice in two younger members of the family, aged 7 and 17 years respectively. Since the premises were rat-infested it was suspected that all three deaths had a common origin.

Bacteriological Investigations

It has been the experience of Dutch and other workers that *L. icterohaemorrhagiae* can best be recovered from human cases of infection by intraperitoneal inoculation of blood, urine, and tissue emulsions into young guinea-pigs rather than by direct cultural methods. In the present series blood samples from five cases and ten specimens of urine from six cases were inoculated into guinea-pigs, 1/2 to 1 c.cm. of blood and 5 c.cm. of urine being used. The results of these tests have, however, been vitiated by the fact that for the most part the cases were recognized a considerable period after the onset of the illness. To recover the organism from the blood it is necessary to obtain a specimen in the early stage of the disease—one to six days after the onset, while the patient is yet febrile. So with the urine the most favourable time for the demonstration of the organism is the period fourteen to twenty-one days after the onset. A most important point in connexion with the examination of urinary specimens is that guinea-pigs must be inoculated within one hour, otherwise the leptospira will have died off.

So far the organism has not been recovered from any blood specimens, but has been recovered from the urine of Case 8 and from emulsions of the tissues of one fatal case (12). The urine which contained the leptospira was obtained on the sixteenth day of the patient's illness, and a further specimen, obtained on the twenty-ninth day, failed to kill the guinea-pigs. It should also be pointed out that it is not necessary to wait for the death of the animals in order to obtain positive results. Two days after inoculation the febrile reaction in the infected guinea-pig begins, and if a small quantity of fluid is withdrawn from the peritoneum from day to day by puncturing the abdominal wall with a sharp-pointed glass pipette, sufficient material will be obtained for examination by dark-ground illumination methods. If the peritoneal fluid shows a positive result blood may be obtained by heart puncture and cultured, several drops being added to four or five tubes of medium.

Cultural Methods

The culture medium used by the Dutch workers consists of the following: tap-water, 1,500 c.cm.; Witte's peptone, 0.15 gram; Ringer's solution, 300 c.cm.; and Sorensen's solution pH 7.2. The final reaction of this peptone medium should be between pH 6.8 and pH 7.2. Three c.cm. of the medium is placed in a small tube and sterilized. For use 0.3 c.cm. of fresh rabbit serum is added; the tubes are then heated at 56° C. for thirty minutes and incubated at 37° C. overnight. Certain rabbit sera seem to be somewhat inimical to the growth of leptospira, and, furthermore, guinea-pig serum filtered through an L5 Chamberland candle can be employed with success. Samples of horse serum have given less favourable results than rabbit or guinea-pig sera. The patient's blood can be cultured in this medium, and so also the urine if obtained free from other organisms. A point of practical interest is that since the leptospira may remain alive for days in clotted blood from human cases, the blood clot can be broken up and inoculated into guinea-pigs. To culture the leptospira the tubes are placed in an incubator at 32° C. and examined after three or four to seven days.

Sero-reactions

It is obvious that since only some 40 per cent. of cases show signs of jaundice, and since many cases recover after a febrile illness lasting four to seven days, it would be difficult to diagnose the disease on a clinical basis. If, however, the occupation of the patient is kept in mind, some indication of the possibility of a leptospiral infection should present itself. Schüffner and Mochtar¹³ showed that when the serum from human infections obtained after the seventh day of the illness was tested in various dilutions against an emulsion of living *L. icterohaemor-*

Peptone = culture medium without addition of serum.

rhagiae, agglutination was obtained in the lower and lysis in the higher dilutions of the serum. This essential test is performed by setting up a series of dilutions of the serum in the cells of a sterile porcelain plate (painter's palette), or in small sterile test tubes 1 inch by half an inch. Figure 1 gives the details of Schüffner's method by which dilutions of the serum ranging from 1 in 5 to 1 in 15,000 can be obtained rapidly, and when three drops of the leptospiral emulsion (four days' growth at 32° C., and up to three days' growth at room temperature) are added to each the final serum dilutions range from 1 in 10 to 1 in 30,000. The serum dilutions are made with a sterile pipette. The tests are then incubated at 32° C. for three hours. The results are determined by examining a drop (obtained with a platinum loop from each dilution of the

serum) under the microscope by the dark-ground illumination method. For this purpose a most suitable optical equipment has been found to be the Leitz "dry" dark-ground condenser D 0.80 in conjunction with the achromatic objectives 3 (2/3 inch) and 6L (1/6 inch), the source of illumination being a 100 c.p. pointolite lamp. A $\times 20$ ocular can be used in conjunction with the 2/3 inch objective, and an $\times 8$ to $\times 10$ ocular with the 1/6 inch objective. A drop of the serum and living leptospiral emulsion is placed on a clean slide (0.9 mm. to 1.1 mm. in thickness, and examined first with the 2/3 inch objective and later with the 1/6 inch objective, no counterslip being interposed between the preparation and the objective.

TABLE II

Case No.	Day after Onset of Illness on which Blood was Taken	Titre of Sero-reactions (aggn. and lysis) against:		
		<i>L. icterohaemorrhagiae</i> Weil	<i>L. canicola</i>	<i>L. icterohaemorrhagiae</i> Indian Strain
1	116th	1,000	300	30
2	65th	1,000	300	0
3	50th	30,000	1,000	300
4	64th	3,000	300	100
5	25th	30,000	300	100
6	29th	30,000	300	100
7	21st	10,000	300	100
8	9th	300	100	0
9	28th	3,000	100	30
10	8th	1,000	100	0
11	8th	1,000	0	0
12	8th	1,000	100	30
13	42nd	1,000	100	0
14	327th	300	0	0
15	10th	1,000	100	0

By these methods agglutination and lysis are observable with ease and rapidity. The results of the sero-reactions are given in Table II, the sera being tested against the three living strains as used by the Dutch workers. It will be observed that the end titres of the reactions against *L. icterohaemorrhagiae* Weil are extremely high, the agglutination of the leptospira occurring in dilutions ranging from 1 in 10 to 1 in 300 or 1 in 1,000, and lysis occurring from 1 in 300 to 1 in 30,000, a typical result being:

	Serum Dilutions :							
	1 in 10	1 in 30	1 in 100	1 in 300	1 in 1,000	1 in 3,000	1 in 10,000	1 in 30,000
Agglutination...	++++	++++	++++	++	—	—	—	—
Lysis ...				++	++++	++++	++	—

The reactions against *L. canicola* and *L. icterohaemorrhagiae* (Indian strain) are believed to be of the group type, *L. canicola* and *L. icterohaemorrhagiae* (Indian strain) being different serologically.¹⁴ If, however, formalized killed cultures are employed, then agglutination only is observable, the lytic action being inhibited. In one case, a fatal one, the serum failed to give any reaction on the sixth day of the illness, but when obtained two days later reacted to a titre of 1 in 1,000. The agglutinating and lytic action of the serum can be employed for the diagnosis of a recent infection, or an infection which has occurred many years previously.

Source of Infections

The industry which has grown up around the preparation of fish for human consumption cannot be said to be conducted entirely on up-to-date, hygienic principles. The patients in the present series have been employed, for the most part, in the handling of white fish. The girls are engaged as filleters and cleaners, and the men in the general handling and distribution of the raw material and offal. In this city some 250 different establishments, each employing perhaps five to six girls and two to three men, are constantly at work. These small businesses account for about 60 per cent. of the total, the remaining 40 per cent. being in the hands of larger firms, employing forty to 100 or more workers.

At the outset it may be said that for economic reasons the smaller businesses are less able to employ hygienic methods than the larger concerns, though this does not always follow. A visit to many of these establishments shows that the premises and equipment are often unsatisfactory. The fish are taken from the market in boxes; they are dumped in a corrugated iron shed in which at a wooden table five or six girls proceed to fillet and prepare the fish for sale to the retailer. The water for washing is obtained from the municipal supply, which is entirely satisfactory, but often, instead of being withdrawn from the tap, it is drawn from a tub placed underneath the tap. The latter source, the table, and the floor all rapidly become covered with slime and offal. In the evening the bulk of the dirt and offal is collected into barrels, which are not removed until the following morning. As the premises are often rudely constructed there is little protection against rats, which infest the whole area in which the business is conducted.

Some years ago one of us showed¹⁵ that 24 per cent. of rats, young and old, in the city harboured *L. icterohaemorrhagiae*. Recently, in July, 1934, when the disease was recognized, a visit was paid to some of the premises where the patients had been working. Six samples of water were obtained—four from floor washings and two from the tubs. To demonstrate the leptospira the technique of Applemann¹⁶ was employed. Young guinea-pigs were chosen, and the hair was depilated from the abdominal skin. The water samples to be examined were placed in buckets to a depth of two inches or so, and brought to a temperature of 32° C. The abdominal skin of the guinea-pig was then scarified, and two animals were placed in each bucket and allowed to remain there for one hour. The animals were then removed and replaced in their cages. In two instances guinea-pigs died on the tenth and eleventh day respectively after immersion in the water. Both animals showed the typical features of infection due to *L. icterohaemorrhagiae*, the organism being easily demonstrable by microscopical examination in preparations from the liver, and the disease was repeatedly reproduced in other animals by inoculation with liver emulsions.

More recently (October) six more samples have been similarly examined, with one positive result. The sample of water that produced this was obtained from the floor of the premises in which two cases of Weil's disease had occurred during the past summer. Probably the incidence and prevalence of *L. icterohaemorrhagiae* may be to some extent seasonal. Obviously, therefore, the opportunities for infection and the conditions for the survival and perhaps multiplication of *L. icterohaemorrhagiae* after being deposited by the rats are present. Persons employed in the trade have the skin on their hands frequently broken by their knives, and presumably infection occurs through the exposed flesh surfaces, or it may occur, as in Holland, by infection through the nasal mucosa and upper respiratory tract.

Discussion

In a subsequent paper it is proposed to deal with certain aspects concerning the aetiology, prevention, and treatment of Weil's disease. A short discussion regarding the importance of early diagnosis appears, however, to be desirable. Favourable results have been reported following the administration of specific antiserum in the early stages of the disease, and also in cases with commencing icterus. The best results, however, are obtained when serum is given within the first three days of the onset. Since jaundice does not appear regularly before the fifth day the clinical diagnosis depends on the recognition of such symptoms as abrupt febrile onset, muscular pain, "red eyes," and marked prostration. None of these symptoms, however, can be held to be specific for Weil's disease, since they may occur in many acute infections. This is particularly true of influenza and acute tonsillitis. A mistaken diagnosis of influenza had been made in several of our cases, and in none of the patients in Group I was Weil's disease suspected prior to our investigation. While it is true that the occurrence of a sudden acute fever in a sewer worker might suggest the possibility of leptospirosis, even in the pre-icteric stage, the problem is entirely different in workers connected with fish-curing and cleaning. For every case of Weil's disease occurring among the thousands of fish workers in Aberdeen there must be hundreds of cases of acute febrile illness of other origin with symptoms similar to those mentioned above. Weil's disease in the early stages might be suspected on the following additional grounds: a leucocytosis with a shift to the left in the polymorph series, latent icterus with a direct or biphasic van den Bergh reaction, acute nephritis unassociated with oedema or hypertension but indicated by slight albuminuria, the presence of granular and cell casts in the urine, and a raised urea or non-protein-nitrogen content in the blood. The tests required to obtain the above data, as well as guinea-pig inoculation with blood, would be impossible in view of the numbers concerned; hence it appears to us that the clinical diagnosis in the early stage, before jaundice occurs, presents almost insuperable difficulties to the practitioner in Aberdeen. Accordingly the full benefits of specific serum treatment are unlikely to be realized.

In view of the practical difficulties connected with guinea-pig inoculation of blood and urine, the sero-reaction will remain the chief method by which the diagnosis will finally be confirmed. Since a positive sero-reaction does not occur before the seventh day of the disease the information obtained is of little value in regard to treatment. It is reassuring to know that Professor Schüffner's investigations indicate that this reaction in Weil's disease is as specific as the Widal reaction in enteric fever. Our own experience is in keeping with this, since sera from 180 cases other than those of Weil's disease have been examined, and in no instance has the reaction been obtained even in a dilution of 1 in 10.

Conclusions

1. Nineteen cases of Weil's disease are reported, in fifteen of which the clinical diagnosis was confirmed by bacteriological or serological tests.
2. Thirteen of the patients were employed in the handling and cleaning of fish.
3. These findings show for the first time that workers among fish must be included in the occupational groups especially liable to Weil's disease.

It is necessary for us to express our indebtedness to Professor W. Schüffner, director of the Tropical Disease Department of the Royal Dutch Colonial Institute at Amsterdam, for assistance in the serological diagnosis of the first cases, and for his

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AN ACCOUNT OF WEIL'S DISEASE IN QUEENSLAND

BY

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On July 7th, 1934, reference was made in the *Journal* (pp. 10 and 14) to the occurrence of Weil's disease in England. The arrival of that issue of the *Journal* in Brisbane coincided with an outbreak of the disease in Queensland. It is considered that a short review of the occurrence might be of value.

In February of this year the medical officer of health for the shire of Hinchinbrook (Dr. G. C. Morrissey) reported to the Department that during the past six months about thirty patients came under his notice displaying symptoms of a disease new to the district. The centre of this district is Ingham, a small town in one of the sugar-cane areas, situated in lat. 18° 8' S., a few miles from the coast, with an annual average rainfall of over sixty inches. The population is predominantly Italian.

Symptoms

The symptoms noted were as follows. The illness began as in influenza, with "shivers," frontal or temporal headache, generalized pains, and prostration, which was marked during the acute period and for a considerable time during convalescence. An early sign was the deep congestion of the conjunctivae. The symptoms varied in intensity. Some patients developed herpes of the lips, frequently haemorrhagic in character. Over 50 per cent. complained of upper abdominal pain of variable severity; the pulse was slow, but quickened as heart failure supervened. The temperature, initially of the febrile type, fell in a few days (six days) to normal, and in severe cases jaundice then appeared, with epistaxis and petechial haemorrhages.

The prostration became very pronounced, the spleen was enlarged and tender, and the urine was scanty and con-

tained blood. The tongue became brown, almost black, and dry. Vomiting of black vomitus tended to be persistent. In two cases there were terminal convulsions of moderate severity, preceded by delirium. One interesting feature of aetiological value was that most of the patients had enlarged axillary glands, and the hands showed evidence of old cuts and septic abrasions caused by the patient's occupation. The inguinal glands were enlarged also, but not so markedly as the former. During the occurrence of these cases the district had been experiencing exceptionally heavy and continuous rain.

Shortly after receiving this report the disease waned, but the shire council was instructed to set in motion an intensive campaign of rat destruction, as the district was heavily infested with these rodents. The Commonwealth Health Laboratory at Townsville was asked to assist by the examination of rats with the object of isolating the causative organism. The disease continued to be non-evident until the beginning of July, when it broke out again with renewed intensity. Up to the period of writing, when a further lull is in evidence, there have been 136 cases with seven deaths, and of the former a very large percentage of the patients were so seriously ill that recovery appeared doubtful. The treatment in all cases was purely symptomatic.

With the recrudescence of the disease Dr. T. J. Cotter of the Townsville Commonwealth Health Laboratory proceeded to Ingham, where he inoculated guinea-pigs direct with blood and urine taken from two patients, in accordance with the methods used by Fletcher of Malaya. Urine and emulsions of faeces from rats were also directly inoculated, but in all the results were negative.

Post-mortem Findings

Post-mortem findings reported by Dr. Cotter in one case were as follows:

"Well-developed muscular male, with marked icterus and generalized scattered skin petechiae. The liver was moderately enlarged, smooth, and congested, and finely streaked with bile. The gall-bladder was distended, with thickened walls, and contained thick dark green bile. The mucous membrane of the cystic duct appeared to be swollen. The spleen was enlarged, being about two and a half times the normal size. It was deep red in colour and very friable, tearing on removal; there was haemorrhage into the pulp. Renal system: a horse-shoe kidney was found with lower ends united across the vertebral column, the union consisting of kidney tissue, with ureters passing anteriorly. The kidney was swollen, soft, and engorged, with scattered subcapsular haemorrhages. The surface was smooth, and the capsule peeled off easily. The cortex was congested, and occasional haemorrhages were present. The pelvis and calices showed petechial haemorrhages on the mucous membrane. The heart was not dilated, and showed nothing abnormal macroscopically. There was hypostatic congestion of the bases of the lung. The bowel appeared normal."

Later, a post-mortem examination of an infected guinea-pig showed multiple small haemorrhages in all the viscera, with "butterfly" patches in the lungs.

At this time, further north, a large number of cases of "coastal fever" were occurring. This is an indeterminate fever, the cause of which is unknown, but which is probably due to a virus of the Rickettsia type conveyed in the bite of an insect. As the *L. ictero-haemorrhagiae* had not been isolated in the cases at Ingham the occurrence of these cases of "coastal fever" tended to complicate the position, which became more pronounced as all the laboratory tests proved to be negative (Widal against Rawlings and Cairns strains, Weil-Felix reaction, blood examination for malarial parasites, and agglutination tests for *Br. abortus*). In addition, influenza was also present, further complicating the outbreak.