

THE INCIDENCE OF WEIL'S DISEASE IN FISH WORKERS IN ABERDEEN

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IN previous papers (Davidson *et al.* 1934; Davidson & Smith, 1936), attention has been called to the occurrence of Weil's disease in fish workers in Aberdeen. In the first paper some thirteen cases were described, while in our more recent one the clinical and bacteriological findings in forty-six cases have been analysed and presented in detail. In this latter series three of the cases terminated fatally. Furthermore, a report of a fatal case occurring in a fish worker in the United States of America has recently been published by Jeghers *et al.* (1935). Evidence has also been obtained by us that an individual contracted the disease in the Isle of Man while following this particular occupation. After careful consideration of the conditions under which the trade is carried on, we have come to the conclusion that in this occupation the risk of contracting the disease is definitely greater than in any other in Great Britain. It seemed probable that if an intensive examination was undertaken of workers engaged in the fish trade in the various ports of this and other countries, many further cases would be brought to light. We determined, therefore, to make a survey of the fish workers engaged in the industry in this city, with a view to obtaining information as to the true incidence of the disease, the criterion of previous infections being the presence of immune bodies—agglutinins and lysins—in the sera.

METHODS

By the helpful collaboration of the employers and of the health visitor working under the auspices of the trade, it was possible to obtain the consent of the workers to allow blood specimens to be taken. Accordingly, at a convenient time the premises were visited, and blood samples were collected in Behring venules.

The blood was then centrifuged, and various dilutions of the serum were tested against a living culture of *Leptospira icterohaemorrhagiae* by the technique elaborated by Prof. Schüffner of Amsterdam. A non-virulent strain of *L. icterohaemorrhagiae*—Wijnberg—originally obtained from Prof. Schüffner, has been utilized in the test. This organism was grown in tubes containing culture medium (as used by the Dutch workers) which is prepared as follows: To 1500 c.c. tap water add 1½ g. Witte peptone; boil; add 300 c.c. Ringer's solution and 150 c.c. Sorensen buffer mixture pH 7·2; boil until phosphates

have precipitated; place in ice-chest to cool; filter; check pH. For use, 3 c.c. of the medium are placed in small tubes and sterilised in the autoclave. Then 0.3 c.c. of fresh, sterile rabbit serum is added, the tubes are heated to 56° C. for 30 min., placed in the incubator at 37° C. overnight to test for sterility, and subsequently inoculated as required with a pipette instead of a platinum loop. Occasionally rabbits have been encountered which have provided unsuitable sera for culturing the leptospirae. The leptospirae are grown at 30° C. for 4 days, and then used in the sero-reaction. The essential test was prepared by setting up a series of dilutions of the patient's serum in small, sterile tubes instead of in the cells of a porcelain plate.

The method by which Schüffner obtains the various dilutions has already been described in detail (Davidson *et al.* 1934), and it will be sufficient to say that small test-tubes containing three drops of the varying dilutions of serum and three drops of the leptospiral culture are incubated in a water bath at 37° C. for 3 hours. The results are then determined by placing a drop of each mixture on a slide with a platinum loop, and examining it under the microscope by the dark-ground illumination method. For this purpose the most suitable optical equipment has been found to be the Leitz "dry" dark-ground condenser DO 80 in conjunction with the achromatic objective 3 ($\frac{3}{8}$ in.) and oculars $\times 8$ or $\times 10$, the source of light being the 100 c.p. pointolite lamp.

When drops of the various dilutions of a normal serum and leptospirae are examined, the leptospirae are uniformly distributed. When, however, a serum contains immune bodies, the drops from the 1/10 and 1/30 dilutions show agglutination of the leptospirae, and, in higher dilutions, marked lysis, the end-titre of the reaction being determined by the dilution of the serum which shows fewer leptospirae than the control. In practice there is little difficulty in determining the end-point. For example, the leptospirae may have practically disappeared from the tubes containing 1/100 and 1/300 dilutions of the serum, becoming progressively more numerous in the tubes containing 1/1000 and 1/3000, and eventually showing no diminution in numbers in the drops from the 1/10,000 or 1/30,000 dilutions. In the present series the sera from the various individuals were tested, in the first instance, in only four dilutions—1/10, 1/30, 1/100 and 1/300. If the test was positive, and the end-titre of the immune bodies in the serum was not reached, it was repeated with additional dilutions of 1/1000, 1/3000, 1/10,000 and 1/30,000.

RESULT OF THE INVESTIGATION

Blood samples were obtained from 210 workers employed by sixteen firms (Table I), fifty being males and 160 females. Of the fifty male workers, twelve gave positive sero-reactions in dilutions of the serum ranging from 1/10 upwards, while thirty-nine of the 160 females gave positive results. Thus, out of a total of 210, 24.2 per cent. showed immune bodies in the serum, the percentage for the male workers being 24 and for the female workers 24.3. The highest number of employees tested in any one firm was thirty-six, and the

Table I. *Incidence of positive sero-reactions in employees of various firms*

No. of firm	No. of samples	No. +	Males		Females	
			Total No.	No. +	Total No.	No. +
1	36	1	0	0	36	1
2	35	12	7	1	28	11
3	24	8	1	0	23	8
4	7	0	3	0	4	0
5	6	2	2	1	4	1
6	10	1	3	0	7	1
7	5	5	5	5	0	0
8	12	5	1	0	11	5
9	4	2	4	2	0	0
10	10	1	0	0	10	1
11	24	3	11	3	13	0
12	18	3	7	0	11	3
13	8	5	2	0	6	5
14	5	0	4	0	1	0
15	2	1	0	0	2	1
16	4	2	0	0	4	2
	210	51	50	12	160	39
Percentage positive		24.2	24		24.3	

smallest number two. Cases of Weil's disease were known to have occurred amongst the employees in eight of the firms, but in the other eight no such information was available. There was considerable variation in the number of positive results in different firms. For instance, firm No. 7 employed five men and all showed evidence of previous infection. In firm No. 2, thirty-five employees were tested, and the sera from no less than twelve gave positive reactions; whereas in the case of firm No. 1, where thirty-five individuals were tested, only one gave a positive agglutination test.

As regards the strength of the fifty-one positive sero-reactions, thirteen reacted to a titre of 1/30, twenty-two to 1/100, twelve to 1/300, four to 1/1000, and none to a titre of 1/3000. Amongst those tested, nine individuals were known to have had a previous attack of Weil's disease, and the details of this group are given in Table II, from which it is seen that in three instances the

Table II

Case	Date of attack of Weil's disease	Highest titre then recorded	Titre of serum on March 1936
1. W. F.	23. vi. 34	1/30,000	1/1000
2. J. G.	28. ix. 34	1/ 3,000	1/ 300
3. H. E.	13. x. 34	1/ 1,000	1/ 100
4. F. McB.	30. xi. 34	1/10,000	1/1000
5. E. H.	1. xii. 34	1/ 1,000	1/ 300
6. E. K.	14. i. 35	1/30,000	1/ 100
7. A. T.	25. i. 35	1/ 1,000	1/ 30
8. E. B.	14. v. 35	1/30,000	1/ 300
9. C. F.	17. ix. 35	1/10,000	1/1000

titre was still 1/1000, in three 1/300, in two 1/100, and in one 1/30. In individual 77, who had an attack of the disease some 15 months previously, the titre of the serum had already fallen to 1/30, so that there is no reason to suppose that reactions in a 1/30 dilution could be accounted for by non-specific effects. This point will be considered in more detail later.

The main features of the clinical histories of the workers were noted, and when these were correlated with the sero-reactions the following was found:

	Sero-reaction		Total
	No. +	No. -	
Individuals with history of jaundice	15	2	17
Individuals with history of "P.U.O."	18	30	48
Individuals with no definite illness	18	127	145

It is obvious, therefore, that in this trade where a person has an attack of jaundice, in association with a febrile illness, the possibility of the disease being leptospiral in origin is very great. One individual gave a history of having had the illness 20 years previously, and his serum still reacted to a titre of 1/30; in others the attack was 14, 15 and 16 years ago, and the serum titres were 1/100, 1/300 and 1/100 respectively. Of thirty individuals who gave a history of some febrile illness such as influenza or sore throat with general malaise, eighteen gave positive sero-reactions. It is impossible to state whether the clinical manifestations complained of were due to a leptospiral infection, to the virus of influenza, or to other organisms. Lastly, no less than 18 persons with positive sero-reactions gave no history whatsoever of any illness since being employed in handling and cleaning fish. Presumably, therefore, a subclinical or latent infection with *L. icterohaemorrhagiae* can occur, and, as a result of this, immune bodies are produced which will protect the individual from any further attack. The results are summarized in Table III, where it is seen that, on the whole, higher titres were obtained in

Table III

	Titres of sera					Total
	1/10	1/30	1/100	1/300	1/1000	
Group 1: individuals with history of jaundice	0	2	6	4	3	15
Group 2: individuals with history of "P.U.O."	0	4	9	5	0	18
Group 3: individuals with no clinical history	0	7	6	4	1	18

the group of cases with a history of jaundice. In group 2, where there was a history of a febrile disturbance, there was no reaction above 1/300, whereas in group 3, which gave no history of illness, the serum from one individual had a titre of 1/1000, while the remainder had titres comparable with those in group 2.

In this spirochaetal infection the lytic titre of a serum seems to be a true index of its immune body content. It has been shown that when formalin-killed leptospirae are substituted in the sero-reaction for living leptospirae, the agglutinin titre is practically identical with the lytic titre. It is, however, well recognized that agglutinin titres are no real guide to the immune properties of a serum, and it seems preferable to regard the lysins as the true immune bodies. Various animal protection experiments carried out from time to time have shown that the lytic titre of any serum is a satisfactory indication of its protective and curative properties.

The incidence of positive sero-reactions in relation to age, and to the period during which the individuals have been employed in this particular trade, has also been considered. The findings are presented in Table IV. It

Table IV

Incidence of positive sero-reactions in relation to age groups

Age group ...	15-20		21-25		26-30		31-40		41+	
	+	-	+	-	+	-	+	-	+	-
Sero-reaction										
Males	1	5	3	4	1	5	3	12	4	12
Females	13	48	12	28	6	21	4	15	4	9
Totals	14	53	15	32	7	26	7	27	8	21

Incidence of positive sero-reactions in relation to length of employment

Length of employment ...	1-5		6-10		11-15		16-20		21-30		31+	
	+	-	+	-	+	-	+	-	+	-	+	-
Sero-reaction												
Males	1	5	4	6	1	11	3	7	3	5	0	4
Females	16	63	11	28	6	15	2	9	3	6	1	0
Totals	17	68	15	34	7	26	5	16	6	11	1	4

will be seen that there is some evidence that age and length of employment may play a part in the liability to infection, since approximately one in four persons below the age of 25 years who have been working 5 years or less have become infected, while one out of two or three persons older than 25 years and with periods of service ranging from 5 to 30 years gave positive tests. Since no less than 154, or 73 per cent., of the workers were in the age group 15-25 years, the figures for the higher age groups are insufficient for satisfactory statistical analysis. The fish trade is one in which the main labour element consists of young females who, in the majority of instances, after a comparatively short period of work, migrate to domestic duties.

CONTROL SERIES OF TESTS

With a view to controlling the serological results presented above, and in order to obtain some idea of the prevalence of leptospiral infections in the general population, sera as sent for the Wassermann reaction and for various agglutination tests were utilised. The specimens were tested by the Schüffner technique in dilutions ranging from 1/10 to 1/300 against both *L. icterohaemorrhagiae* and *L. canicola*. The sera submitted for the Wassermann reaction from 265 individuals gave entirely negative results. In a similar manner the sera from 138 individuals suffering from various febrile disturbances—typhoid and paratyphoid fevers, undulant fever, septicaemia, and pyrexias of unknown origin—also gave entirely negative findings. It may be concluded, therefore, that Weil's disease has a very special distribution amongst the population, and, furthermore, that the Schüffner sero-reaction is an entirely specific one, the agglutinins and lysins being formed as a result of leptospiral infection only.

DISCUSSION

The main feature of the investigation is the evidence produced of a high incidence of previous infection with *L. icterohaemorrhagiae* in those engaged as fish workers. The incidence is far greater than we anticipated, and leads one to the conclusions that the disease hazard in this particular trade is very high indeed. In the minority of cases, infection has produced the characteristic symptom complex associated with intense jaundice. In more numerous instances the disease has been "influenzal" in type, with no apparent jaundice. Finally, in a third group the infection appears to have been latent or sub-clinical, but nevertheless those infected have acquired immunity. In a recent review, Meyer (1936) states that the symptomatology of an infection oscillates between the frank, clinically typical disease and the unrecognizable reaction. It is a well-established fact that apparently latent infections with *L. icterohaemorrhagiae* occur in wild rodents and guinea-pigs. It must be concluded that a similar state occurs in man.

If the 210 volunteers represent a true sampling of the workers exposed to infection, then it may be calculated that there are in Aberdeen at least 300 individuals who have been infected, this figure representing 25 per cent. of those actually engaged in the cleaning and gutting of fish at the present time. Workers engaged in transporting fish from the market are not included in this figure. Over and above these there must be many other female workers now in other occupations, or married, who may have been infected while previously employed as fish workers. The high incidence of this disease must be a matter for the most serious thought for the medical profession, but the black side of the problem is partly relieved when it is considered from another aspect. Of the forty-six cases of Weil's disease which have been diagnosed by us during the past 18 months, three died, giving a mortality rate of 6.5 per cent. A figure of 10 per cent. has usually been accepted on the Continent. The mortality rate among fish workers in Aberdeen, as estimated from positive sero-reactions, must, in reality, be a fraction of 1 per cent. Furthermore, the three deaths occurred in males of middle age or older, and several cases who were extremely ill belonged to the same age group. We suggest, therefore, that the low mortality and morbidity rate in fish workers may be closely connected with the age and sex of the workers, since three-quarters of them are healthy girls between the ages of 15 and 25 years. The social habits of individuals prone to infection may be as important in this infection as in another spirochaetal disease, syphilis. Thus, two of the three cases which terminated fatally were males who had alcoholic tendencies. Moreover, both had had a previous attack of jaundice, suggesting that a damaged liver is peculiarly susceptible to the toxins of *L. icterohaemorrhagiae*.

The prevention of Weil's disease

We have already shown that, by exposing susceptible guinea-pigs to the chance of infection, virulent leptospirae can be recovered from the washings obtained from tables and floors of premises in which cases have occurred. The attainment of such results can only occur if the premises are contaminated regularly and frequently with the urine of infected rodents. Since there can be no Weil's disease without rats, a campaign for the extermination or reduction of the rodent population would appear to be of paramount importance. Sporadic efforts are made at present by individual firms and by inspectors of the Local Authority towards that end. We suggest, however, that individual and sporadic efforts at cleanliness and rat extermination are of little value, since they merely drive the rat population to neighbouring premises for food and shelter. A joint organized campaign appears to be an essential factor if success is to be obtained. The second preventive measure to be considered is connected with the premises in which the trade is carried on. In many of the smaller businesses in particular, the buildings are rudely constructed, and present no obstacle to the entrance of rats. It must be admitted that to render these premises rat-proof would entail much additional expense to the industry, and while it is probably out of the question to bring these buildings up to a proper state of efficiency, we believe that a considerable improvement in this respect could be effected with little expense if careful thought were given to the problem.

A further point we wish to consider is the cleanliness of the premises, since it is fish remnants which attract the rats and since the spirochaetes live in the slimy water. More care and time should be spent in the removal of all offal at the end of each day's work. All such materials should be placed in receptacles inaccessible to rats, and a thorough hosing of benches, floors and boxes should be carried out by an individual or individuals detailed for the purpose, and the duty not left to the discretion of employees who are desirous of leaving the workplace at the earliest possible moment.

It has already been pointed out that during the night the premises are infected by urinating rats. We suggest, therefore, that half an hour before work commences in the morning the floors, benches, etc., should be vigorously hosed with water, and thereafter treated with suitable disinfectant, e.g. the hypochlorite solution known as "Chloros", which we found to have a lethal effect on leptospirae in a dilution of 1/4000. The manufacturers indicate that 2 fluid ounces of "Chloros" should be added to each gallon of water, i.e. the disinfectant is diluted 1/64. There is therefore a great excess of chlorine available to act effectively even in the presence of large amounts of protein material. Furthermore, this substance, when applied, leaves no odour or taste, nor has it any deleterious effects which would interfere with marketing arrangements.

In the course of the investigation, three cases of Weil's disease were en-

countered in individuals who were fish porters. These men did not gut and clean fish, so that they must have contracted their infection while handling fish boxes. Fish boxes should therefore never be dumped on contaminated floors, but after being washed and cleaned should be placed on wooden platforms. Again, water used for washing the premises, the hands of the workers, and the fish should be drawn from the tap and not from large wooden tubs which are often contaminated with fish offal and slime, and which may become infected by the rats. We feel that, with little expense but with increased effort and time spent on organizing the preventive methods detailed above, the production of cleanliness and consequently a reduction in the incidence of the disease might be expected.

We have produced adequate evidence that leptospirosis is an occupational disease, and it is felt that it cannot be considered to be a special problem confined to this City only, but that it must be occurring in various fishing ports in this and other countries. In our opinion, therefore, the disease should be scheduled under the Workmen's Compensation Act so that workers suffering from this infection may become rightly entitled to financial recompense.

SUMMARY

1. Two hundred and ten blood samples were obtained from workers in the fish trade. Of these, fifty-one, or 24·2 per cent., gave positive sero-reactions in dilutions of the serum ranging from 1/30 to 1/1000.

2. There was no significant difference in the number of positive sero-reactions occurring in male or female workers.

3. In a control series of 406 blood specimens from individuals not engaged in the fish trade, no positive sero-reactions were obtained.

4. Evidence is adduced that leptospiral infections occur in three grades: (a) severe infections associated with jaundice; (b) mild infections with pyrexia and no jaundice; and (c) latent or inapparent infections with no clinical manifestations.

5. Preventive methods have been detailed which, if put into practice, would, it is believed, reduce the incidence of this disease.

6. Sufficient evidence has been produced to show that this disease is occupational in nature, and as such should be scheduled under the Workmen's Compensation Act.

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