WEIL'S DISEASE IN COAL-MINERS

BY

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In 1886 Weil described four cases of infectious jaundice characterized by the presence of fever, enlargement of the liver and spleen, nephritis, and a liability to febrile relapses. He considered that these cases differed from any other previously described forms of jaundice and presented them as a new clinical entity. Subsequently other cases were reported, but it was not until 1915 that Inada and Ido showed the causal organism to be a spirochaete, which was later named *Leptospira icterohaemorrhagiae*. In this country isolated cases have since been recorded, and a comprehensive and excellent report of a large outbreak among coal-miners in Scotland was made by Buchanan (1927). More recently a valuable account of the epidemiology has been given by Alston and Brown (1935), who also comment on the increasing frequency of the disease in this country. It seems quite clear that the incidence is confined to certain occupations, those mainly affected being sewer workers, field workers, coal-miners, and fish workers. The largest single outbreak in coal-miners in the British Isles is referred to above. The occurrence of six cases in the South Wales coal-field, apparently the first recorded in this area, prompted the present contribution.

Case Records

Of the six men whose cases are here reported three worked in the same part of the same pit and two others were employed in a colliery some considerable distance away. In each instance it was found that they worked in very wet places, and it was known that the pits concerned were infested with rats. In all six cases the clinical diagnosis was confirmed by positive serological results. The details of one further fatal case were reported by the local practitioner. The history strongly suggested the possible diagnosis of Weil's disease, but as this case was not under my direct observation it is not included. In this series of cases very full and detailed investigations were carried out in each instance by Dr. A. F. Sladden (p. 605). Brief mention only will be made of these findings, as they form the subject of a separate paper.

CASE I

M. W., a man aged 48, was admitted to hospital on November 20, 1936. He was suddenly taken ill six weeks previously with an attack of shivering, sweating, weakness, generalized muscular pains, and vomiting, followed a week later by the appearance of jaundice. There was frequency of micturition accompanied by haematuria. On admission the temperature was 101° F., there was definite jaundice, and the liver was palpably enlarged. A few days later he complained of severe occipital headache and was somewhat delirious. A lumbar puncture was performed. The cerebrospinal fluid showed a slight increase of cells, increased protein content, and a Lange curve of parietic type. The Wassermann reaction was strongly positive in the fluid and weakly positive in the blood. Examination of the urine revealed blood, bile, albumin, and many granular and hyaline casts, and the blood contained 171 mg. of urea per 100 c.cm. The van den Bergh reaction showed a jaundice of obstructive type. A blood count revealed an anaemia in which a characteristic feature was the high monocyte count. The blood pressure was 108/72. The possibility of spirochaetal jaundice was considered, as the serum agglutination reaction for leptospira was strongly positive. The patient made steady progress; at the end of ten days the jaundice had faded and the renal function showed marked

improvement. The blood Wassermann reaction became negative, and on January 21, 1937, the patient was discharged cured.

CASE II

J. D., a man aged 47, was admitted to hospital on September 8, 1937. He was convalescent, and was referred to hospital as he had been working in the same site as Case I. He was slightly jaundiced and gave a history that eight weeks previously he had had a sudden attack of vomiting associated with generalized muscular pains. This was followed by epistaxis, and about two weeks after the onset of the illness jaundice was first noticed. The faeces were dark in colour, but no urinary symptoms were noted. On examination there was very slight jaundice but the liver was not palpable; the urine showed no gross abnormality. The blood pressure was 124/72. The agglutination reaction for leptospira was positive. He made an uninterrupted recovery.

CASE III

D. H. J., a man aged 39, was admitted to hospital on August 1, 1937. He was very ill, and in fact died a few days after admission. I am indebted to Dr. Alfred Davies, his own practitioner, for the notes of his previous history. Six weeks before admission he complained of sudden severe generalized pains in the head, back, and limbs, accompanied by shivering. The temperature was 104° F. In a few days he became deeply jaundiced and vomited a great deal. The jaundice began to fade, but there was frequent epistaxis. On admission to hospital the temperature was 99.4° F.; he was very drowsy and jaundiced, and complained of epigastric pain. The urine passed was scanty and contained blood and albumin. The blood urea was 537 mg. per 100 c.cm. and the blood Wassermann reaction proved negative. Clinical examination showed no hepatic enlargement, but there were a few small subcutaneous haemorrhages. Agglutination tests for leptospira were strongly positive. As indicated, he became progressively worse and died.

CASE IV

R. L., a man aged 42, was admitted to hospital on October 20, 1937. A week before admission he had had a sudden attack of vomiting, muscular pains, and extreme weakness. Two days later he was jaundiced and labial herpes was present, the eruption afterwards becoming haemorrhagic. On admission the pulse was rapid and the temperature 99°. During the next four weeks there were periodic rises up to 100° or 101°. He was deeply jaundiced and lethargic. The liver and spleen were not palpable. A few purpuric spots were seen on the body. The urine contained a trace of albumin, bile, and a few red blood cells. The blood Wassermann reaction was negative. The blood pressure was 102/65. The van den Bergh reaction showed an obstructive type of jaundice. Serological tests were negative on the seventh day but strongly positive on the sixteenth day of the illness. Urine was injected into a guinea-pig and *L. icterohaemorrhagiae* was identified in the spleen and adrenal medulla of the killed animal. The patient made satisfactory progress and was discharged cured on November 29, 1937.

CASE V

G. J., a man aged 39, was admitted to hospital on January 1, 1938. A week previously there was sudden onset of shivering, generalized muscular pains, and extreme weakness. Two days later jaundice was noted. On admission the temperature was normal, but ten days later it rose to 100.6° and remained at this level for a further ten days. He was deeply jaundiced, and scattered petechiae were present on the skin. The liver and spleen were not palpable. Blood examination showed the typical monocytosis, the blood urea was 117 mg. per 100 c.cm., and the van den Bergh reaction disclosed jaundice of an obstructive type. The blood Wassermann reaction was negative. The blood pressure was 125/75. A direct examination of the blood by Schüffner's method revealed the presence of a few leptospirae. The cerebrospinal fluid showed a pleocytosis with a "pseudo-positive" Wassermann reaction. Serological tests showed the existence of leptospirae. This patient was gravely ill on admission, but he progressed satisfactorily and was ultimately discharged. He was again seen in October, 1938.

All serological tests were then negative. He complained of defective vision of the left eye, and examination showed the presence of a corneal opacity. The ophthalmological report suggested this was probably a healed ulcer attributable to a herpetic lesion of the cornea.

CASE VI

O. G., a man aged 25, was admitted to hospital in a very ill condition. Fourteen days before admission, while at work, he had a shivery attack associated with aching pains in the back and limbs and marked weakness. Jaundice appeared four or five days later, followed by labial herpes and very troublesome epistaxis which was not controlled by plugging. He was admitted to hospital on December 31, 1937. The temperature was 100°, he was deeply jaundiced, haemorrhagic herpes was present, and there was a purpuric rash on the chest and upper abdomen. The liver was palpably enlarged, and small shotty glands were palpable in the neck, axillae, and groins. It was noted that the diastolic blood pressure (118/36) was unusually low. At first he was extremely ill, and epigastric pain and vomiting soon became prominent features. A blood-urea estimation gave a reading of 414 mg. per 100 c.cm.; a trace of albumin was present in the urine, and microscopy showed the presence of many granular casts. A blood count revealed an anaemia with an increased polymorphonuclear and monocyte count. The cerebrospinal fluid was completely negative and the blood Wassermann reaction doubtfully positive. Serological tests for leptospira were positive. He was given calcium gluconate intramuscularly daily and, in view of his very grave condition, one injection of antileptospiral serum. He gradually improved and was discharged cured.

Diagnosis

The feature in Case I which first led to a suspicion of the real nature of the disease was the association of jaundice and nephritis. This association has been noted by other writers, and is a diagnostic point of great importance. The sudden onset, with generalized muscular pains and extreme weakness, was almost constant in each case of this series. Among haemorrhagic manifestations epistaxis and herpes were most commonly seen, and in Case V the involvement of the cornea has left some degree of permanent impairment of vision. An interesting feature in Cases I and V was the finding of a positive Wassermann reaction in the cerebrospinal fluid. After recovery the reaction became negative. Case III was extremely ill on admission, and at first the patient was thought to be suffering from uraemia. The associated jaundice, his occupation, and our previous experience rapidly suggested the true diagnosis. One particularly interesting observation, of which no mention seems to have been recorded in other outbreaks, is the finding of a monocytosis in the blood picture. In all cases, as already indicated, the clinical diagnosis was verified by serological investigation and the finding of a positive agglutination reaction for leptospira.

Treatment

In the first two cases no special line of treatment was employed, but in Cases IV, V, and VI a series of calcium gluconate injections were given intramuscularly; the impression gained was that this treatment was of some value. In Case III the patient was so seriously ill on admission that it is doubtful if any treatment would have been of avail.

Anti-leptospiral serum was given in Case VI only, and it cannot be said that any definite conclusion was reached as to its value. Certain writers (Murgatroyd, 1937; Fairley, 1934; Davidson *et al.*, 1934) are of the opinion that serum treatment is of undoubted value and that it should be administered as early as possible in the course

of the disease. A recent paper by Robertson (1938) appears to confirm this view. The use of prophylactic vaccines in the presence of a widespread outbreak or in workers known to be exposed to infection has also been suggested (Alston and Brown, 1935).

Discussion

It is obvious that Weil's disease is far more common in this country than was once thought. The disease is essentially associated with certain occupations. The common factor is the presence of the infected rat, whose excreta are disseminated by water or wet conditions; the individual is infected through accidental abrasions or through the mucous membranes of the eye or nose. It is important to note that the organism flourishes only in fresh water. If the disease is becoming more common it seems possible that transmission by fresh-water bathing, in these days so popular a form of recreation, may well become a matter for serious consideration. Robertson (1938) has recently reported four cases where the infection appears to have originated from this source. This seems all the more important, since, as pointed out by Murgatroyd (1937), the organism has been found in the urine of a recovered case thirty-three weeks after the onset of the disease, and long after all its manifestations had disappeared. The possibility of spread of infection here is obvious. Again, as pointed out by Alston and Brown, workers exposed to infection may harbour what may be termed a "subclinical" form of the disease. In a series of apparently healthy sewer workers investigated it was found that 20 per cent. showed positive serum agglutination reactions for *L. icterohaemorrhagiae*. As a result of this investigation these writers suggest that prophylactic inoculation of workers exposed to the risk of infection would seem to be indicated. A further point of importance is that the disease does not always exhibit itself in its well-recognized characteristic form. Meningitis may be the presenting picture, as in the case described by Murgatroyd, who draws attention to the fact that it would be wise to consider a possible diagnosis of Weil's disease in many cases of so-called "aseptic meningitis." Again, it is recognized that in 50 per cent. of cases there may be no jaundice. This being so, in all cases of pyrexia of unknown origin the possibility of spirochaetal infection should be considered.

In this present series of cases the symptoms were fairly typical. The association of jaundice and nephritis, and the sudden onset of generalized muscular pains and weakness, were features which soon indicated the correct diagnosis. One observation of interest was that in three cases the blood pressure was definitely low. This seemed significant in view of the general complaint of weakness, and particularly so since necropsies of infected guinea-pigs have shown the presence of leptospira, especially in the adrenal bodies. With regard to treatment, no definite inference can be drawn from this short series. All but one patient recovered, no serum, in effective dose, having been administered to any case. Four of these patients were extremely ill, and it seems possible, from the experience of other workers, that the use of serum might have shortened the duration of illness. It is recognized, however, that to be effective serum must be given early, and in this series it was not our good fortune to attend the patients before jaundice had appeared and the disease was well established.

Certain final conclusions present themselves: (1) The incidence of Weil's disease is definitely on the increase. (2) The possibility of atypical forms should be borne in

mind. (3) Known infected communities should be investigated in view of the possibility of carriers. (4) Active prophylactic measures, both by inoculation and by extermination of rats, should be considered.

Summary

Six cases of Weil's disease occurring in coal-miners are described and certain points of particular interest in these cases are discussed.

Attention is drawn to the increasing incidence of the disease in its various forms, and the need for preventive measures is stressed.

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WEIL'S DISEASE IN SOUTH WALES CLINICAL PATHOLOGY

BY

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Rather elaborate investigations were made in this series of cases, seven of which were under the care of Dr. Esmond Rees at Swansea General Hospital and the others seen with Dr. J. Lloyd Davies of Swansea. Seven of these men were coal-miners and two were farmers: A. W. lived on a rat-infested farm in a village within the coal-field where several coal-miners dwelt, and T. W. R., the last case, was a dairy-farmer on whose farm rats were intermittently a pest. A detailed clinical account of the first six coal-miner cases is given in this issue by Dr. Rees (p. 603). Of the other three it is sufficient here to say that the farmer (A. W.) when first seen was acutely ill with fever, jaundice, herpes, pneumonia, uraemia, and meningitis, and died a few hours later. W. T., a coal-miner, was not very acutely ill, but had short-lived fever, herpes, pains in the chest, and later jaundice, nephritis, mild meningitis, and low blood pressure (105/60). This man reported that during the past year three of his mates had jaundice and illness which he believed had been similar to his own. T. W. R., a dairy-farmer aged 52, originally came to hospital on account of dysuria, which had followed a period of some ten days' general malaise. Enlarged prostate was found and cystotomy done, but a few days later jaundice was noticed and the possibility of a leptospiral infection came up for consideration in the fourth week of the illness.

Diagnosis was verified in each case by the specific agglutination test with leptospira, carried out very kindly by Major Brown at the Wellcome Bureau of Research; his ready help and advice are cordially acknowledged. There are certain technical difficulties in the performance of the agglutination test which, in Major Brown's opinion, make it desirable for the present to centralize the carrying out of these tests, and therefore no antigen is available for general laboratory use.

Laboratory Investigations

The various laboratory investigations made in this series are set forth below in tabulated form. The main points noteworthy are:

1. The reliability of the agglutination test when carried out by expert hands. Our "control" cases, with jaundice but with history and clinical manifestations not compatible with Weil's disease, all gave negative tests.

2. If the patient comes under observation very early in the course of the infection agglutinative power may not have developed; in such circumstances the direct demonstration of leptospira in the blood by the use of Schüffner's technique is valuable and satisfying, and this technique was applied successfully in some of the later cases of this series. The persistence of blood infection after six months in the patient G. J. is remarkable.

3. A full blood count, with differential and estimation of absolute values of the white-cell categories, is most valuable as an aid to diagnosis and far more reliable than a mere percentage differential from a film of blood. The characteristic changes are: Polymorph increase and monocyte increase but no alteration in absolute lymphocyte figures; as a result the lymphocyte:monocyte ratio is greatly altered, and instead of the normal (about 85:15) it may become 60:40, or even as low as 50:50. This applies only to the earlier stages of the illness. In catarrhal or other forms of jaundice any alterations in the lymphocyte:monocyte ratio are of an entirely different order.

4. Among these cases was occasionally found a *temporary* positive Wassermann reaction, especially in the cerebrospinal fluid.

5. The few gastric analyses made suggest the possibility of hypochlorhydria and achlorhydria as factors favouring the establishment of infection if leptospira be swallowed.

6. Animal inoculation methods, though conclusive when positive, are not uniformly successful—witness the case of G. J. As they are tedious and rather expensive it is convenient if for routine diagnosis one can dispense with their use.

7. Blood and urine analyses revealed the frequency of severe uraemia in this disease and the possibility of recovery in very acute cases.

8. Van den Bergh tests show very high degrees of bilirubinemia in the early stages of infections, and as the jaundice is of the obstructive type there is correspondingly high saturation of the urine with bilirubin.

9. Urobilinogen was not increased in the urines of any of the cases tested, nor was there excess of urobilin; the existence of severe nephritis may explain the failure of urobilinogen to pass through the kidneys.

Guinea-pig Inoculations

Some guinea-pigs appear to be relatively immune to leptospira, so that a negative experiment does not necessarily exclude. Several of the animals (Table VI) failed to develop illness or jaundice, but after a period of some weeks agglutinins in significant amount were found in their sera, and in silver-stained sections of the organs leptospira could occasionally be observed, particularly in the adrenals. In view of the low blood pressures recorded in human cases of Weil's disease this observation is clearly of considerable clinical interest.

Preventive Methods

Since the appearance and recognition of this series of cases in one locality active measures have been taken by the colliery owners to rid the mines of rats, and it is encouraging to note that no further cases of Weil's disease have appeared in the mines concerned.