WEIL'S DISEASE IN CAPE TOWN

A CASE REPORT

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This following case history is, to the best of our knowledge, the first record of the isolation of *Leptospira icterohaemorrhagiae* from a patient in South Africa.

CASE REPORT

The patient, a Coloured male aged 25 years, was employed in the Cape Town docks. His illness commenced quite suddenly with a bout of diarrhoea and vomiting followed within 6 hours by dizziness, upper abdominal cramp, and a rigor. On his way to the doctor he experienced severe frontal headache, and that same night he could not sleep at all on account of headache, sweats, and abdominal pain. In addition to the above symptoms he suffered, on the following day, from severe aching pains in the arms, calves and thighs, and he noticed that his urine had become dark-brown in colour. The pains in his limbs were so intense that he could walk to the doctor only with the aid of a walking stick. Over the following 2 days his symptoms mounted in intensity, with a high fever and severe headache and pains in the limbs. Neither vomiting nor diarrhoea recurred; indeed no bowel action occurred after the initial brief diarrhoea. By the 5th day of the illness he was extremely weak and had to be carried into a van and taken to the Woodstock Hospital, where he was admitted on 12 December 1961.

On examination he was thin, apathetic and drowsy. His skin was icteric and he was sweating slightly. His temperature was 100·8°F. and his pulse 100 per minute. His sclerae were jaundiced and his conjunctiva congested — a striking and unusual combination which gave his eyes a dirty-orange colour. Herpes was present at the angle of his mouth. Generalized tenderness of the whole abdomen was present, with particular tenderness over the liver, which was palpable to 2 finger-breadths below the subcostal margin. There was no splenomegaly, and free fluid was absent. His calves were exquisitely tender, and to a lesser degree he resented palpation of the thigh and arm muscles. Cranial nerves were intact, tendon reflexes were present, and the cutaneous reflexes were normal. The cardiovascular system was normal, with the blood pressure 120/75 mm.Hg.

A blood count showed a haemoglobin of 14 G. per 100 ml., red cells 4,930,000 per c.mm., a leucocytosis of 14,600 per c.mm., and a differential count of 81% polymorphs, 8% monocytes and 11% lymphocytes.

The urine was dark and contained albumin and bilirubin. Dark-ground examination of the urine and of specially stained preparations of the urine failed to reveal any spirochaetes. Microscopically the urine contained hyaline casts and 5 leucocytes per high-power field.

Course of the Disease

The patient's condition worsened during the first 2 days in hospital. He vomited incessantly and coughed up mucoid sputum containing occasional blood clots the size of a 5-cent piece. His temperature reached 101·4°F. with a pulse rate of 85 per minute. Clinical examination of the chest showed no abnormalities, but X-ray examination showed a small patch of consolidation in the posterior basal segment of the right lower lobe.

The serum bilirubin was 9·4 mg. per 100 ml. (67% directly reacting). Blood proteins totalled 7·0 G. per 100 ml. with albumin 5·3 G. per 100 ml. and globulin 1·7 G. per 100 ml. The van den Bergh reaction was direct positive. Thymol turbidity was 1·1 units and zinc sulphate 2·8 units.

An intravenous infusion of 5% dextrose in water was set up as the vomiting continued. A lumbar puncture was performed; the cerebrospinal fluid was xanthochromic but clear and contained 6 polymorphs and 4 lymphocytes per c.mm. No red-blood cells were present. The CSF protein was 60 mg. per 100 ml. and globulin not in excess. Bilirubin was present in the fluid.

On the 3rd day in hospital, the 8th day of the illness, the patient's condition remained *unchanged*. Blood was inoculated intraperitoneally into a guinea-pig, and treatment with penicillin was commenced, in doses of 2 mega-units every 6 hours. His condition improved gradually over the following 3 days. The vomiting stopped, muscle tenderness decreased, and the temperature fell gradually from 100° or 101°F. to 99° and 98°F. Jaundice was still marked and the liver still enlarged and tender.

On the 7th day in hospital there was definite improvement in his appetite, muscle tenderness and liver tenderness. He complained of a generalized itch, which was most annoying, on the soles of the feet. The jaundice persisted, with the serum bilirubin 13·6 mg. per 100 ml., of which 66% was direct reacting. The blood urea was 44 mg. per 100 ml., thymol turbidity 3·6 units, and zinc-sulphate turbidity 6·6 units. The alkaline phosphatase was 3·6 Bodansky units. The urine still contained albumin and bilirubin.

The jaundice cleared gradually from the 14th day in hospital and he maintained a steady improvement until his discharge after 42 days.

Bacteriology

The clinical diagnosis was confirmed by the following laboratory investigations undertaken by the pathologist, Dr. M. Finlayson:

1. Positive result from intraperitoneal inoculation of the patient's blood into a guinea-pig: On the 5th day after inoculation numerous spirochaetes, morphologically resembling short forms of *Leptospira icterohaemorrhagiae*, were seen in the peritoneal exudate.

2. Positive serology:

Day of illness	*Leptospiral agglutination test*	*Titre*
7	+	1/2,000
13	+	1/8,000
22	+	1/4,000

A serum sample on the 7th day of illness was also submitted to Prof. H. D. Brede, of the Department of Microbiology, Karl Bremer Hospital, Bellville, who reported as follows:

	1/20	*1/200*	*1/400*	*1/800*	*1/1,600*	*1/3,200*	*1/6,400*	*Control*
L. pomona	±	—	—	—	—	—	—	—
L. canicola	±	—	—	—	—	—	—	—
L. icterohaemorrhagiae (Type A) ..	+	+	+	+	+	±	—	—
L. sejroe	±	—	—	—	—	—	—	—

DISCUSSION

From a clinical standpoint the principal problem in this patient was the differentiation of Weil's disease from infective hepatitis. The presence of severe muscle pain (which so impressed the casualty officer that he was disposed to diagnose arsenical intoxication), together with the conjunctival suffusion, herpes febrilis, leucocytosis, and the abnormalities of the cerebrospinal fluid were typical of leptospirosis. Indeed xanthochromia owing to

bilirubin is very suggestive, although bile-staining of cerebrospinal fluid can occur in severe jaundice from other causes.

Weil's disease is most frequently due to *L. icterohaemorrhagiae*, but occasionally a similar clinical picture is produced by other leptospirae. The disease has been encountered in all 5 continents, but to the best of our knowledge *L. icterohaemorrhagiae* infection of humans is very rare in South Africa.[1,2] Epidemics have occurred in Japan, Indonesia and Malaya, particularly, and in Europe it is prevalent in Holland and Germany. It is endemic in the Congo near Lake Kivu, French Equatorial Africa, and Abyssinia.

Weil, of Heidelberg, gave an accurate description of the illness in 4 patients in 1886 and claimed a separate identity for it though he was unable to isolate its cause. In 1915 Inada identified the offending spirochaete in Japan. Shortly thereafter the disease was recognized in outbreaks affecting Allied and German armies during World War I, especially in Flanders and Gallipoli.

The disease was epizootic in rats, but these animals have become immunologically tolerant so that the organism is found as a harmless commensal in the kidneys of wild rats and mice. It is excreted in their urine, thus allowing human infection. The leptospirae survive for an unknown period in the favourable circumstances provided by water, mud, and the slime of sewers. Workers exposed to a special hazard of infection include sewer-workers, miners, fish-gutters and rat-catchers. The organism enters through abraded skin or through the intact mucous membrane of the conjunctival sac, nose, mouth, or throat. Acid media are inimical to the survival of leptospira, therefore the stomach is not likely to allow infection.

The *Leptospira icterohaemorrhagiae* organism is a spiral filament; the largest is 20 μ in length, but the average length is 6 - 12 μ. It has tapering ends set at an angle, and when in motion is often C- or S-shaped. The incubation period of 8 - 12 days is followed by an abrupt onset of fever, often with rigors. Headaches and photophobia are prominent, and severe muscular pains occur. The conjunctivae are conspicuously injected. Fever may terminate by lysis after 4 - 7 days, or hepatitis and nephritis may dominate the clinical picture. 60% - 70% of cases show hepatitis with jaundice and an enlarged liver. Nephritis is less frequent and rarely occurs without hepatitis. In 10% there is clinical evidence of meningitis. Haemorrhagic pneumonia may occur. Relapse or 'after-fever' occurs in 20% during the 3rd or 4th weeks of the illness.

The laboratory diagnosis in the 1st week of the disease depends upon the initial leptospiraemia. Dark-field microscopy may reveal the organism to an expert observer, but the preferred method is inoculation of patients' blood intraperitoneally in guinea-pigs. The animals are readily infected, and after 3 - 15 days of incubation they become pyrexial and jaundiced, and organisms can be recovered from the tissues. Inoculation of patients' urine into guinea-pigs gives diagnostic recovery of leptospirae in 20% of cases. Antibodies appear in the 2nd week of the illness, with peak levels in the 3rd and 4th weeks. Agglutinin titres of 1 in 300 or above are diagnostic, especially if a rising titre is demonstrable. Titres of 1 in 10,000 to 1 in 100,000 are not uncommon.

Leucocytosis is the rule and is a considerable aid in differential diagnosis. The cerebrospinal fluid almost always shows a pleocytosis with lymphocyte preponderance regardless of the presence or absence of clinical meningitis. In icteric patients the fluid is yellow. Muscle biopsy can provide an early presumptive diagnosis by showing acute localized necrosis of muscle fibres with virtually no inflammatory cells or vascular change.

The mortality is approximately 5% in recognized cases, but in some series the mortality has been 40%.[3] The prognosis is grave in a severe hepato-renal syndrome of deep jaundice, azotaemia, and oliguria.

The value of specific therapy is still in dispute. Good results have been claimed for antiserum, but its use is not widely accepted. Organic arsenicals are ineffective. Penicillin is lethal for leptospirae in cultures and protects guinea-pigs if given within 48 hours of infection. It has been used in most cases reported since 1944, but some authorities still question its value.

The Present Case

Our patient was a dock-worker whose main occupation was unloading cargo from crane nets. He stated that the cargoes were 'often' soiled with rats' excreta, and he recalled a recent episode when some stagnant 'water' in a canvas sail spilled over him.

We have not been able to trace any reports of Weil's disease in South Africa. It would be of interest to know whether the rodent population of Cape Town Docks are infected with leptospira to any degree.

SUMMARY

The case history of a patient suffering from Weil's disease is presented and the course of the illness is described. The patient recovered. A brief account of the disease is given. This is believed to be the first reported case of Weil's disease from *L. icterohaemorrhagiae* in South Africa.

ADDENDUM

A second patient with Weil's disease was admitted to Woodstock Hospital on 11 September 1962. The patient was brought to the hospital by casual acquaintances who thought that he behaved strangely when they found him scratching the ground in the open veld. The patient was a Coloured male dockworker, approximately 60 years of age. He was deeply jaundiced with the characteristic appearance of the eyes. The liver was not enlarged. Muscle tenderness and marked dehydration were present. The serum bilirubin was 36 mg. per 100 ml. (72% conjugated); blood urea 209 mg. per 100 ml.; thymol turbidity 2 units; zinc sulphate 3·6 units; and the white-cell count 29,500 (90% polymorphs). Guinea-pig inoculation with the patient's blood grew leptospirae in the peritoneal exudate after 3 days. Agglutinations to *L. icterohaemorrhagiae* were positive in a titre of 1/100, and to *L. Sejrφe* 1/200, which suggested a short-term illness. In the ward the patient was delirious, and severe diarrhoea occurred. Lumbar puncture was not done. Death occurred 24 hours after admission and permission for a postmortem examination was not obtained.

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