AN OUTBREAK OF LEPTOSPIROSIS AMONG ISRAELI TROOPS NEAR THE JORDAN RIVER


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Abstract. An outbreak of leptospirosis that involved 7 of a team of 27 Israeli troops occurred following a military exercise in northern Israel near the Jordan River. The organism implicated in the outbreak was Leptospira interrogans serovar Hardjo. The clinical course was uncomplicated and all patients fully recovered. There were no cases of asymptomatic infection. Military personnel should be recognized as having an occupational risk for contracting leptospirosis, especially when military activity takes place near natural water sources inhabited by cattle, taking into account the local epidemiology of this disease. Moreover, outbreaks among military personnel may serve as a sentinel for leptospiral infection in the context of both pilgrimage and civilian recreational activities.

"Bathe and you will become clean. So he went down and immersed himself seven times in the Jordan, as Elisha had told him to do. And his flesh became clean once more like the flesh of a small child."

II Kings 5:14

INTRODUCTION

Leptospirosis is one of the most common zoonoses worldwide and is caused by serovars of the spirochete Leptospira interrogans. The spectrum of human disease ranges from subclinical infection to severe clinical disease with multi-organ failure (Weil's disease) and high mortality rate, and depends both on the host and the infecting serovar.† Leptospirosis may occur either sporadically or in the context of an outbreak and is commonly related to occupational or recreational activities that involve direct or indirect contact with the urine of animal species that are reservoirs of the disease.2,3

Whereas outbreaks of leptospirosis are not uncommon worldwide, there are only a few accounts of outbreaks of leptospirosis in the military setting. We report an outbreak of human leptospirosis that occurred in northern Israel near the Jordan River, involving troops of the Israeli Defense Forces (IDF) after a military exercise. The Jordan River is an important site for recreational and religious activities but there are no previously reported associations with human leptospiiral infection.

MATERIALS AND METHODS

During July 2002, we investigated an outbreak of anicteric leptospirosis that involved IDF troops who participated in a military exercise near the Jordan River in northern Israel. Suspected cases were patients with symptoms and signs compatible with acute leptospirosis observed following the exercise. All trainees underwent confirmatory serologic testing and were followed-up for three months in a military clinic.

Convalescent-phase sera were subjected to the microscopic agglutination test (MAT) with 23 reference and control serovars of live leptospires at the National Reference Laboratory for Leptospirosis.7 Acute-phase sera (if obtained) were subjected to the MAT at least three weeks prior to convalescent-phase samples. A single titer ≥ 1:200 or a four-fold increase in agglutinating titer for Leptospira spp. in individuals with symptoms and signs suggestive of leptospirosis was considered diagnostic and fulfilled the case definition. Samples that tested positive for serovars that belong to serogroups other than that of the serovar implicated in the outbreak were subject to flow cytometry light scatter analysis (FCM) as described elsewhere.5

To identify epidemiologic risk factors for acquisition of leptospirosis, all symptomatic and asymptomatic trainees who had participated in the exercise were interviewed soon after the recognition of the outbreak, as well as one month later. The following data were obtained: age, sex, full or partial participation in the exercise, degree and duration of immersion (if any) in the Jordan River and nearby stagnant water, ingestion of river water, presence of skin cuts or abrasion during immersion, immersion while barefooted, passage by cowsheds, and exposure to cattle or rodents during the exercise. In addition, participants were questioned regarding possible symptoms and signs that may be associated with acute leptospiiral infection.

Statistical analysis was performed using the Epi-Info statistical software version 2002 (Centers for Disease Control and Prevention, Atlanta, GA). Frequencies and means were compared between seropositive and seronegative soldiers using the two-tailed Fisher's exact test and analysis of variance. A P value < 0.05 was considered statistically significant.

OUTBREAK DESCRIPTION

During June 2002, 27 male troops of the IDF participated in an exercise in the Jordan River in northern Israel. The Jordan River area is rural but has a developed agricultural infrastructure including extensive dairy-farming. The river serves as a favorable site for recreation, especially rafting, and is also a focus of attraction for religious individuals who immerse in its waters due to its historical and biblical tradition. This area of northern Israel is known to be endemic for leptospirosis among cattle infected with L. interrogans serovar Hardjo.6

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Nevertheless, there have been no previous accounts of leptospirosis in humans associated with the Jordan River.

The soldiers exercised in the area for a period of a few weeks, during which the weather was typical of the spring season in Israel. The exercise involved intense combat skill training performed over long time periods. Most of the training involved contact with river water (both freshwater in the main river stream and stagnant water nearby the river’s edge) and included immersion in the water, occasionally for long time periods, and at times, near-complete submersion but no diving.

The index case was a 20-year-old otherwise healthy soldier who was admitted to the hospital with a four-day history of fever up to 40.4°C that had begun 17 days after the exposure in the Jordan River area. The patient complained of headache, anorexia, vomiting, abdominal pain, and myalgia. Physical examination showed conjunctivitis and mild splenomegaly. Laboratory values were normal, except for mild elevation of liver enzyme levels. The erythrocyte sedimentation rate, results of urinalysis, and chest radiograph were normal. Empirical therapy with doxycycline (100 mg twice a day for seven days) was administered and marked clinical improvement was noted after two days of therapy. The patient was discharged while serologic tests were still pending.

Six additional team members sought medical attention for similar symptoms and signs that had begun 11–19 days following the exercise. The clinical presentation of all seven patients is shown in Table 1. Notably, all six had significant patchy palmar skin desquamation that appeared after defervescence and disappeared after 7–10 days, a finding not previously described in acute leptospirosis. These individuals denied any mechanical factors that may damage the skin. No other dermatologic signs were observed. One patient received empirical amoxicillin (500 mg three times a day for seven days) therapy. Clinical resolution took place after a few days in all patients, and there were no significant differences in the clinical course of individuals who received antibiotic therapy compared with those who did not.

Blood test results were available for six patients (Table 2). The mean leukocyte count was 7,500 cells/mm³ and mean serum aspartate and alanine aminotransferase levels were 69 U/L and 143 U/L, respectively. Abnormal liver function test results invariably resolved during the course of illness. Bilirubin levels and results of renal function tests were normal in all patients.

Six patients were positive for L. interrogans serovar Hardjo. These samples represented convalescent-phase sera because they were drawn 3–4 weeks after the onset of disease. One additional patient tested positive for both the Hardjo and Ballum serovars during the acute phase, but a four-fold increase was detected only for the Ballum serovar during convalescence. Analysis of serum from this patient by FCM also demonstrated leptospiral agglutillation of the Ballum serovar. All asymptomatic individuals (20 troops) were also subjected to testing with the MAT and all were seronegative. Thus, there were no cases of asymptomatic leptospirosis infection.

The seven seropositive patients and 20 seronegative asymptomatic individuals comprised the case and control groups, respectively (Table 3). The mean age was 20 years and all 27 troops were male. Full participation in all exercises was reported by 93%. All reported immersion in river water. However, being exposed for a longer period (> 20 hours) was reported in all cases and in only 70% of the controls (relative risk [RR] = 1.43, 95% confidence interval [CI] = 1.1–1.9). Ingestion of river water was also more often reported by cases than controls (100% versus 70%, RR = 1.43, 95% CI = 1.1–1.9). Immersion while barefooted was reported in 89% and presence of skin cuts or abrasion during immersion was reported in 52%. One-third (33%) reported exposure to cattles, and exposure to cattle or rodents was reported in 56% and 15%, respectively. The latter were more common among cases although the results of the analysis did not reach statistical significance (possibly due to the small sample size).

**DISCUSSION**

Leptospirosis is thought to be the most widespread zoonosis throughout the world, and is especially common in tropical climates.

**Table 1**

Clinical features of soldiers infected with leptospirosis

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Duration of illness (days)</th>
<th>Fever peak (°C)</th>
<th>Symptoms and signs</th>
<th>MAT titer*</th>
<th>Antibiotic therapy</th>
<th>Highest MAT titer*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Constitutional</td>
<td>Gastrointestinal</td>
<td>Respiratory</td>
<td>Dermatologic/ ophthalmologic</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>40.4</td>
<td>Weakness, weight loss, headache</td>
<td>Abdominal pain, nausea, vomiting</td>
<td>–</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>39.5</td>
<td>Weakness, weight loss, headache</td>
<td>Abdominal pain, nausea</td>
<td>–</td>
<td>Palmar skin desquamation</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>39.6</td>
<td>Weakness, headache</td>
<td>Abdominal pain, nausea, vomiting</td>
<td>Sore throat</td>
<td>Palmar skin desquamation</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>39.5</td>
<td>Weakness, weight loss, headache</td>
<td>Nausea, vomiting</td>
<td>–</td>
<td>Palmar skin desquamation</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>39.2</td>
<td>Weakness, weight loss, headache</td>
<td>Abdominal pain, nausea, vomiting</td>
<td>Sore throat</td>
<td>Palmar skin desquamation</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>40.3</td>
<td>Weakness, weight loss, headache</td>
<td>Abdominal pain, vomiting, diarrhea</td>
<td>Sore throat</td>
<td>Palmar skin desquamation</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>39.2</td>
<td>Weakness, weight loss, headache</td>
<td>Abdominal pain, nausea, vomiting</td>
<td>Cough</td>
<td>Palmar skin desquamation</td>
</tr>
</tbody>
</table>

*Numbers in parentheses represent highest agglutinating titers by a microscopic agglutination test (MAT).*
and sub-tropical countries. Rodents, such as rats and mice, are the most important reservoir of leptospires, although cattle, fish, birds, dogs, swine, and domestic farm animals may also harbor these spirochetes. Humans are infected through direct or indirect contact of damaged skin or mucous membranes with the urine, blood, or tissue of an infected animal. Infection through intact skin may occur after prolonged immersion in water. Contact with soil, mud, sewage, and especially water contaminated with infected animal urine are of particular importance regarding disease transmission because leptospires can survive in these media for several weeks or months.

Although leptospirosis may occur sporadically, recreational exposure to water is considered a major risk factor for contracting the disease in recent years, especially in relation to water sports such as swimming, running, canoeing, rafting, waterskiing, and other endurance or extreme sports. During the last 50 years, at least 17 outbreaks of leptospirosis associated with water exposure have been documented, affecting more than 500 individuals. Of note are recent outbreaks that involved triathlon participants in Illinois and Wisconsin, participants of the Eco-Challenge in Malaysia, white-water rafters in Costa Rica, and swimmers in Brazil. Other significant outbreaks with relation to water occurred in India, Argentina, Cuba, Brazil, and Nicaragua after floods and other natural disasters.

Occupational exposure is a classic risk factor for leptospirosis and involves those in direct contact with animals such as farmers, veterinarians, abattoir workers, and meat inspectors, or indirect contact such as sewer workers, miners, farmers, and fish handlers. Livestock farming had previously constituted a major occupational risk factor worldwide, with the highest risk associated with dairy farming and involving the serovar Hardjo. Although such classic exposure is now less common in Western countries due to improvements in work sanitation, substantial rates of leptospiral infection may still be found in cattle, as is evident from a survey performed in Texas in which more than one-third of cattle sera tested positive for leptospirosis, with 15% being infected with the Hardjo serovar.

Historically, leptospirosis has been considered a significant disease among military personnel deployed in the tropics, especially during the 1960s in the Canal Zone and Vietnam. However, only a few outbreaks of leptospirosis have been reported to occur in the military setting. A water-borne outbreak occurred on the island of Oahu in the State of Hawaii in 1992 that involved two U.S. male service personnel with culture-confirmed leptospirosis. Another water-borne outbreak of leptospirosis occurred among U.S. military personnel in 1987 on the island of Okinawa, Japan. Epidemiologic findings showed two case-clusters with attack rates of 46.6% (7 of 15) among recreational swimmers and 18.3% (15 of 82) among combat skills training participants. Swallowing of water (but not immersion itself) was identified as a risk factor for leptospirosis in this outbreak. All of our seven patients reported ingestion of river water; this variable did not reach a statistically significant P value but appears to have significance based on the 95% CI.

Leptospiral illness has been documented in the military setting in several other instances. A two-year study performed among servicemen in Vietnam showed that leptospirosis accounted for 20% of the cases of febrile illness.

### Table 2

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Leukocytes (cells/mm³)</th>
<th>Granulocytes (%)</th>
<th>Hemoglobin (g/dL)</th>
<th>Platelets (cells/mm³)</th>
<th>Alkaline phosphatase (U/L)</th>
<th>Aspartate aminotransferase (U/L)</th>
<th>Alanine aminotransferase (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9,000</td>
<td>85</td>
<td>16.4</td>
<td>171,000</td>
<td>&lt;100</td>
<td>59</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>6,900</td>
<td>79</td>
<td>13.1</td>
<td>181,000</td>
<td>133</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>5,500</td>
<td>54</td>
<td>14.2</td>
<td>194,000</td>
<td>NA</td>
<td>42</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>10,200</td>
<td>82</td>
<td>15</td>
<td>201,000</td>
<td>60</td>
<td>139</td>
<td>303</td>
</tr>
<tr>
<td>5</td>
<td>3,700</td>
<td>43</td>
<td>14.1</td>
<td>150,000</td>
<td>192</td>
<td>101</td>
<td>160</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>9,700</td>
<td>59</td>
<td>13.5</td>
<td>408,000</td>
<td>144</td>
<td>51</td>
<td>134</td>
</tr>
</tbody>
</table>

*NA = not available.
† Normal range = 0.35 U/L.

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n = 7)</th>
<th>Controls (n = 20)</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± age, years</td>
<td>20.1 ± 0.4</td>
<td>20 ± 0.9</td>
<td>NA</td>
<td>NA</td>
<td>0.41</td>
</tr>
<tr>
<td>Immersion in Jordan River</td>
<td>7 (100%)</td>
<td>20 (100%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Full participation in exercise</td>
<td>7 (100%)</td>
<td>18 (90%)</td>
<td>1.1</td>
<td>0.96–1.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Duration of immersion &gt; 20 hours</td>
<td>7 (100%)</td>
<td>14 (70%)</td>
<td>1.43</td>
<td>1.1–1.9</td>
<td>0.15</td>
</tr>
<tr>
<td>Ingestion of river water</td>
<td>7 (100%)</td>
<td>14 (70%)</td>
<td>1.43</td>
<td>1.1–1.9</td>
<td>0.15</td>
</tr>
<tr>
<td>Skin abrasions while immersing</td>
<td>4 (57%)</td>
<td>10 (50%)</td>
<td>1.14</td>
<td>0.5–2.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Immersion while barefooted</td>
<td>6 (86%)</td>
<td>18 (90%)</td>
<td>0.95</td>
<td>0.7–1.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Immersion in nearby stagnant water</td>
<td>3 (43%)</td>
<td>15 (75%)</td>
<td>0.57</td>
<td>0.2–1.4</td>
<td>0.17</td>
</tr>
<tr>
<td>Passage by cowsheds</td>
<td>4 (57%)</td>
<td>5 (25%)</td>
<td>2.3</td>
<td>0.85–6.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Exposure to cattle</td>
<td>5 (71%)</td>
<td>10 (50%)</td>
<td>1.43</td>
<td>0.75–2.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Exposure to rodents</td>
<td>2 (29%)</td>
<td>2 (10%)</td>
<td>2.9</td>
<td>0.5–16.6</td>
<td>0.27</td>
</tr>
</tbody>
</table>

* CI = confidence interval; NA = not applicable.
An attack rate of 37% was recently found among Peruvian military recruits training in a jungle rain forest.\textsuperscript{26} Chemoprophylaxis with doxycycline has been shown to be effective in reducing the attack rate of leptospirosis among American soldiers deployed for jungle training in Panama from 4.2% to 0.2%.\textsuperscript{29}

Leptospirosis is endemic in some parts of Israel, but to the best of our knowledge, similar human outbreaks of leptospiral illness have not been reported to date. A recent review of leptospirosis cases has shown that the incidence of the disease in Israel has decreased overall during the last three decades. This decrease was due mainly to diminished infection with serovars associated with agriculture (such as the serovar Hardjo), and reduced exposure due to improved sanitation and mechanics and other changes in agricultural practice, and probably did not reflect reduced zoonotic infection.\textsuperscript{2} \textit{Leptospira interrogans} serovar Hardjo, the main serovar causing this outbreak, was reported in Israel on 1977 for the first time (in dairy workers),\textsuperscript{30} and accounted for 12 human cases (20% of all leptospirosis cases) between 1985 and 1999.\textsuperscript{2} Infection with \textit{L. interrogans} serovar Hardjo in this outbreak may suggest contamination of river water by cattle, especially given that this serovar is known to be endemic among cattle in the area.\textsuperscript{6}

We did not detect any cases of asymptomatic infection among exposed individuals. Most outbreak studies to date have focused on symptomatic patients rather than merely exposed individuals; thus, the literature on asymptomatic infection is sparse. It is has been recently shown in Nicaragua that only 30% of seropositive individuals were symptomatic during an outbreak of leptospirosis.\textsuperscript{31} However, establishing the diagnosis of asymptomatic infection in hyperendemic areas may be complicated by the limitation of serologic testing because seropositivity may be largely attributed to past exposure. Given that the development of clinical leptospirosis illness depends on both the host and infecting pathogen, this variability in the incidence of asymptomatic infection deserves further study.

The finding of patchy palmar skin desquamation among six of seven cases is intriguing and to the best of our knowledge has not been previously reported in leptospirosis. The fact that all six patients were not aware of any mechanical factors that may have caused skin damage and that skin desquamation appeared only during defervesence (over a two-week period after the conclusion of the exercise) suggest that this finding is not related to physical activities performed during training. Skin desquamation should be looked for in future case-series to assess its role in the manifestation of leptospirosis infection, especially that involving the Hardjo serovar.

In our series, six cases involved the Hardjo serovar and one case the Ballum serovar. It can be speculated that this outbreak involved exposure to water sources contaminated with more than one serovar of leptospirosis. Although the Hardjo serovar is usually acquired from dairy cattle, Ballum is almost exclusively associated with exposure to infected mice\textsuperscript{32} and indeed, potential exposure to rodents was reported by 15% of the soldiers. Conversely, the MAT has been known to be at best serogroup specific and is by no means serovar specific. Levett has recently stressed that conclusions regarding infecting serovars cannot be drawn in the absence of bacteria isolation, and that the ability of convalescent-phase MAT titers to predict even the infecting serogroup is as low as 40%.\textsuperscript{3}

Although the concordant result produced by the FCM method raises the odds for co-existence of two different serovars, laboratory test limitations cannot be ruled out with certainty.

In conclusion, outbreaks of acute leptospirosis occur less commonly after classic occupational exposure, but are increasingly encountered in recreational settings that involve exposure to materials infected by animal secretions, especially water. Contamination of the Jordan River may be attributed to cattle and further investigation is thus required.

Soldiers should be recognized as a unique occupational risk group for contracting leptospirosis, especially in the context of military activity that is performed near natural water sources. Moreover, outbreaks among military personnel may serve as a sentinel for leptospiral illness, such as in the area of the Jordan River in which civilian recreational exposure and religious rituals take place.

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