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Abstract. Among ill returned travelers to Schistosoma-endemic areas reported to the GeoSentinel Surveillance Network over a decade 410 schistosomiasis diagnoses were identified: 102 Schistosoma mansoni, 88 S. haematobium, 7 S. japonicum, and 213 Schistosoma unknown human species. A total of 83% were acquired in Africa. Unlike previous large case series, individuals born in endemic areas were excluded. Controlling for age and sex, those traveling for missionary or volunteer work, or as expatriates were more likely to be diagnosed with schistosomiasis. Sixty-three percent of those with schistosomiasis presented within six months of travel. Those seen early more often presented with fever and respiratory symptoms compared with those who presented later. One-third of patients with schistosomiasis were asymptomatic at diagnosis. Half of those examined for schistosomiasis were diagnosed with infection. Screening for schistosomiasis should be encouraged for all potentially exposed travelers and especially for missionaries, volunteers, and expatriates.

INTRODUCTION

Schistosomiasis is a parasitic disease caused by infection with the trematode genus Schistosoma. According to the World Health Organization (WHO), ~200 million people are infected with Schistosoma species in at least 76 countries, and ~85% of those infected are believed to live in Africa.1–3 Most infections worldwide are attributable to three species: Schistosoma mansoni, S. haematobium, and S. japonicum.4

Many Schistosoma infections diagnosed in nonendemic areas are chronic infections identified in immigrants; however, disease in returning travelers has received increasing attention. Most reports are descriptions of outbreaks from a single source or observational studies from individual institutions.5–19 A recent cross-sectional study reviewed schistosomiasis in 333 travelers and immigrants treated at several medical centers in Europe.20 Although the clinical and epidemiologic features of schistosomiasis in European and non-European travelers were compared, it does not compare these features to those observed in ill travelers without schistosomiasis and about half the patients were born in Schistosoma-endemic areas. In a prospective study of fever in ill returned travelers, the clinical and laboratory features of acute schistosomiasis were compared with those of other causes of febrile illness to identify diagnostic predictors of tropical diseases in ill travelers.21 To date, however, no study has compared returned travelers with schistosomiasis to travelers with other illnesses to identify factors associated with Schistosoma acquisition during travel. We report on the clinical and epidemiologic features of 401 cases of travel-associated schistosomiasis collected over a decade at 27 GeoSentinel sites in 12 countries.

MATERIALS AND METHODS

Study design. This is a cross-sectional study of ill returned travelers who reported to a GeoSentinel clinic and had completed travel to a Schistosoma-endemic area.

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GeoSentinel Surveillance Network. GeoSentinel sites are specialized travel and tropical medicine clinics on six continents staffed by clinicians who are recruited on the basis of demonstrated training, experience, and publication in travel and tropical medicine. They contribute clinician-based information on all ill returned travelers seen, including travel history. Additional detail has been previously published or is available at www.geosentinel.org.22,23 The sites accounting for the majority of patient intake are within academic centers; several smaller volume sites (almost all with current academic affiliation) are in freestanding locations. The intake at sites reflects a mixed population of tertiary care and self-referred patients. Some sites are restricted to outpatients. No site has its entire practice limited to ill travelers.

To be eligible for inclusion in the GeoSentinel database, patients must have crossed an international border within 10 years and be seeking medical advice at a GeoSentinel clinic for a presumed travel-related illness, referred to as “ill returned travelers.” This terminology is used to emphasize that travelers seen at GeoSentinel clinics do not necessarily represent all returned-travelers, only those seeking medical advice regardless of symptoms. Anonymous surveillance data are entered into a structured query language (SQL) database at a central data center. Final diagnoses reported by physicians are used to assign diagnostic codes from a standardized list of over 500 etiologic or syndromic diagnoses.22

Study groups. All ill returning travelers who reported to a GeoSentinel site from March 1997 through February 2008, and who had completed travel to a Schistosoma-endemic area were eligible for analysis. Persons born in Schistosoma-endemic countries and those traveling for the sole purpose of immigration were excluded.2,24 A case of travel-associated schistosomiasis was defined as a confirmed or probable Schistosoma infection diagnosed by parasitologic or serologic methods.

A sub-analysis exploring the reasons for presenting to a GeoSentinel clinic was also performed using all patients who had completed travel to a Schistosoma-endemic area and were examined for schistosomiasis. Patients with schistosomiasis were compared with patients who were suspected of having schistosomiasis, based on exposure history with or
without clinical findings, but were ultimately found not to be infected (referred to as ruled-out for schistosomiasis). Symptomatic patients were excluded from this part of the analysis if the reporting site documented that it was screening the patient for schistosomiasis and believed the patient was symptomatic with another illness (e.g., soft tissue infection).

**Diagnoses.** Final diagnoses included *S. mansoni*, *S. haematobium*, *S. japonicum*, and Schistosoma-unknown human species. The diagnosis of schistosomiasis was made by microscopy or serologic testing. The exact method of diagnosis was not reported, but all sites used the best serologic technique available in their country, including the Falcon assay screening test–enzyme-linked immunosorbent assay (FAST-ELISA) followed by confirmation and speciation with an enzyme-linked immunoelectrotransfer blot, conventional ELISA, indirect fluorescent antibody (IFA), and indirect hemagglutination (IHA) tests. Because serologic testing is unable to distinguish between active and past infections, including those that have been successfully treated, only infections believed by the reporting site to be active on the basis of clinical or epidemiologic information were reported. Also, many of the commercially available serologic tests are genus-specific, not species-specific, thus in many cases the *Schistosoma* species was not known. Furthermore, no distinction was made between acute schistosomiasis (e.g., Katayama fever) and chronic forms of schistosomiasis.

**Definition and groupings.** Traveler type. Patients were assigned to one of four groups (traveler type) based on their reason for travel: tourists, business travelers, travel for missionary, volunteer, research or humanitarian aid work (referred to as missionaries and other volunteers), and all others. The other category includes students, military travelers, travelers visiting friends and family, and those whose reason for travel was unknown. It was also reported whether the patient had lived as an expatriate, which was defined as living in an independent residence with the infrastructure used by local residents of the same economic class.

**Clinical symptoms and diagnoses.** Presenting symptoms in 14 general categories were reported. More than one presenting symptom could be reported for each traveler.

Travelers sometimes were diagnosed with other illnesses in addition to schistosomiasis; therefore, all additional confirmed or presumptive final diagnoses were examined and were sorted into six categories: gastrointestinal, genitourinary, respiratory, malaria, and two helminth diagnoses groups. All reported *Strongyloides stercoralis, Ascaris lumbricoides*, and hookworm (*Ancylostoma duodenale* and *Necator americanus*) infections, which are known to cause respiratory symptoms during their migration through the lung, were classified into one helminth group. All other reported helminth infections were classified into the second helminth group.

**Timing and duration of travel.** For travel completed within six months before the clinic visit, the duration of travel for the entire most recent trip with likely exposure and time-to-presentation from that trip was calculated in weeks.

For travel completed more than six months before the clinic visit, duration of travel was reported as “30 or more consecutive days” or “fewer than 30 days”; time-to-presentation was recorded as years before the clinic visit (6 months–2 years, 3–4 years, or ≥ 5 years).

**Region of exposure.** Regions were defined as the United Nations Statistics Branch macrogeneographic regions and sub-regions, with the exception of Sudan, which was included in East Africa. When a single region of exposure could not be identified, the likely region of exposure was reported as the continent of exposure or as “multiple regions.” When country of exposure was not stated by the reporting site, the likely region of exposure was determined by reviewing individual travel itineraries and the geographic distribution of schistosomiasis.

**Statistical analysis.** Data analysis was performed with Microsoft Access (Seattle, WA, 2000) and SPSS version 16 (Chicago, IL). Statistical significance was determined by χ² tests. Fisher’s exact test was used if one or more of the expected values were less than five. Age was examined as both a continuous variable and a dichotomous variable (less than 45 years of age, the 75th percentile). We used logistic regression with backwards elimination to evaluate factors potentially associated with a diagnosis of schistosomiasis after travel to *Schistosoma*-endemic areas, compared with a different diagnosis after travel to the same areas. *P* values reported from logistic regressions were based on Wald χ² statistics. A two-sided *P* value of < 0.05 was considered to indicate statistical significance.

**RESULTS**

**Demographics and travel type.** From March 1997 through February 2008, 25,240 ill returned travelers had completed travel to a *Schistosoma*-endemic area within 10 years and were reported to the GeoSentinel Surveillance Network. A total of 410 (16 diagnoses per 1,000 ill returned travelers) schistosomiasis diagnoses were identified among 401 travelers. A total of 102 cases were the result of *S. mansoni*, 88 to *S. haematobium*, 7 to *S. japonicum*, and 213 to an unidentified human *Schistosoma* species. Nine travelers were co-infected with *S. haematobium* and *S. mansoni*. Cases were reported from 27 of 40 active GeoSentinel sites: 37% from Europe, 24% from North America, 15% from Oceania; and 24% from Western Asia (including the Middle East).

Demographic characteristics and type of travel for patients with a diagnosis of schistosomiasis were compared with those without schistosomiasis (Table 1). Male travelers and travelers < 45 years of age were more likely to be diagnosed with schistosomiasis relative to another illness. When the data were controlled for age and sex, those traveling for missionary or other volunteer work were twice as likely to be diagnosed with schistosomiasis as were tourist and other types of travelers. Business travelers were less likely to be diagnosed with schistosomiasis than were tourists and other types of travelers. Individuals traveling as expatriates, regardless of the type of travel, were twice as likely to be diagnosed with schistosomiasis as those staying for shorter times and staying in hotels. Having a pre-travel consultation was also associated with being diagnosed with schistosomiasis.

**Region of exposure.** More than 80% of infections were acquired in Africa, the majority of these in sub-Saharan Africa (Table 2). All seven cases of *S. japonicum* were acquired in Southeast Asia. Frequently mentioned locations for *Schistosoma* exposure included Lake Malawi, the Nile and Omo Rivers, and a hotel swimming pond in Tanzania, where 23 patients were exposed.

**Timing and duration of travel.** Sixty-three percent of the 401 ill returned travelers with schistosomiasis presented to a
GeoSentinel clinic within six months after travel with a median time-to-presentation of six weeks (IQR 2–12 weeks; Table 3). The median duration of travel for this group was 13 weeks (IQR 4–33 weeks). One hundred ten (27%) travelers presented to a GeoSentinel clinic more than 6 months after travel. Time-to-presentation was between 6 months and two years for 73 (18%), three to four years for 16 (4%), and five or more years for 18 (4%). Of those presenting more than 6 months after travel, 23 (21%) stayed 30 or more consecutive days in at least one Schistosoma-endemic country. Altogether 210 (52%) ill returned travelers with schistosomiasis stayed at least 30 days in a Schistosoma-endemic country. The duration of travel could not be determined for 32 (8%) travelers and time-to-presentation for 40 (10%) travelers who had limited travel information or multiple opportunities for exposure.

Clinical symptoms and diagnoses. A total of 828 people were evaluated for schistosomiasis and 49% were eventually diagnosed with schistosomiasis. Gastrointestinal symptoms, fever, genitourinary symptoms, and fatigue were the most commonly reported symptoms. Returned travelers with schistosomiasis were more likely to present with fever than those who were ruled-out for schistosomiasis. Those with S. haematobium and S. mansoni infections presented with more respiratory symptoms than did those ruled-out for schistosomiasis. Moreover, returned travelers with schistosomiasis who were seen within six months of travel more often presented with fever and respiratory symptoms compared with those who presented later (Table 3).

No difference was observed in the frequencies of additional diagnoses (i.e., gastrointestinal, genitourinary, malaria, or helminth diagnoses) between those with schistosomiasis and those ruled-out for schistosomiasis. A total of 106 (26%) patients with schistosomiasis had an additional diagnosis. No difference was observed in the frequencies of additional diagnoses among those infected with different Schistosoma species.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Regions of travel exposure for patients with schistosomiasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td>N = 401 (%)*</td>
</tr>
<tr>
<td>AFRICA</td>
<td>N = 102 (%)</td>
</tr>
<tr>
<td>East</td>
<td>233 (83)</td>
</tr>
<tr>
<td>West</td>
<td>214 (53)</td>
</tr>
<tr>
<td>Central</td>
<td>48 (12)</td>
</tr>
<tr>
<td>North</td>
<td>16 (4)</td>
</tr>
<tr>
<td>South</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Multiple regions</td>
<td>8 (2)</td>
</tr>
<tr>
<td>ASIA</td>
<td>42 (10)</td>
</tr>
<tr>
<td>Southeast</td>
<td>34 (8)</td>
</tr>
<tr>
<td>Western</td>
<td>19 (5)</td>
</tr>
<tr>
<td>Southern</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Eastern Asia</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Multiple regions</td>
<td>2 (0)</td>
</tr>
<tr>
<td>SOUTH AMERICA</td>
<td>7 (2)</td>
</tr>
<tr>
<td>CARIBBEAN</td>
<td>2 (0)</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>25 (6)</td>
</tr>
</tbody>
</table>

* Percentage of travelers with schistosomiasis.
DISCUSSION

This is the largest cohort to date examining schistosomiasis exclusively in returned travelers, i.e., those born in non-endemic countries and traveling to Schistosoma-endemic countries. Sixteen per 1,000 ill returned travelers reported to the GeoSentinel Surveillance Network after travel to a Schistosoma-endemic region were diagnosed with active schistosomiasis. More than half had trips that lasted 30 or more days; and 27% presented to a clinic more than six months after the completion of travel.

Expatriates and those traveling as missionaries, volunteers, researchers, and aid workers were more than twice as likely to be diagnosed with schistosomiasis compared with other travelers. Missionaries and other volunteers tend to remain at their destinations for longer periods of time, which may place them at greater risk for acquiring schistosomiasis. They also may be more likely to engage in behaviors that are similar to those of the local populations. Assigning travelers to categories based on purpose of travel and type of traveler allows identification of persons who would benefit from specific preventive education and post travel follow-up. Our findings should encourage sponsoring organizations to more uniformly screen returning missionaries, volunteers, and expatriates.

Having a pre-travel consultation was associated with being diagnosed with schistosomiasis. One possible explanation for this finding is that sponsoring organizations require their employees or volunteers to have a pre-travel consultation, particularly in preparation for prolonged travel, and that people who receive pre-travel health advice are more likely to seek care when they return. Those who presented within six months were more likely to have had a pre-travel encounter, regardless of type of travel.

The effectiveness of the pre-travel consultation may wane over time, as travelers interact with other travelers who may have received different pre-travel health advice or who have never encountered other foreigners seriously ill with schistosomiasis. In a study on the utility of history, examination, and laboratory testing in screening returned travelers for parasitic infections, written and verbal pre-travel briefing did not influence the rate of Schistosoma seropositivity in travelers who stayed three months or longer.\(^\text{27}\) In 1998, 26% of U.S. Peace Corps Volunteers serving in Tanzania, who had received stan-

### Table 3

<table>
<thead>
<tr>
<th>Type of traveler</th>
<th>Time to presentation ≤ 6 months</th>
<th>Time to presentation &gt; 6 months</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 251 (63%)</td>
<td>N = 110 (27%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tourist traveler</td>
<td>147 (59)</td>
<td>64 (58)</td>
<td>0.68</td>
</tr>
<tr>
<td>Missionary/volunteer/researcher/aid worker</td>
<td>80 (32)</td>
<td>36 (33)</td>
<td></td>
</tr>
<tr>
<td>Business traveler</td>
<td>21 (8)</td>
<td>7 (6)</td>
<td></td>
</tr>
<tr>
<td>Other types of travelers</td>
<td>3 (1)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Duration of travel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 days</td>
<td>64 (25)</td>
<td>87 (79)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 30 days</td>
<td>187 (75)</td>
<td>23 (21)</td>
<td></td>
</tr>
<tr>
<td>Had pre-travel encounter (%)</td>
<td>185 (74)</td>
<td>65 (59)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Top 6 presenting symptoms‡

- Asymptomatic screening
- Fatigue
- Gastrointestinal
- Genitourinary
- Respiratory
- Consultation type (%) 0.68

Consultation type (%)

- Outpatient consultation 222 (88)
- Inpatient consultation 23 (9)
- Missing 6 (2)
- Expatriate (%) 51 (20)

### Table 4

Comparing the most common presenting symptoms for travelers examined for schistosomiasis

<table>
<thead>
<tr>
<th>Presenting symptoms</th>
<th>Examined for Schistosoma</th>
<th>Ruled out*</th>
<th>S. mansoni</th>
<th>S. haematobium</th>
<th>Unknown human species</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic screening</td>
<td>319 (39)</td>
<td>187 (44)</td>
<td>30 (29)</td>
<td>19 (21)</td>
<td>83 (39)</td>
<td>0.006</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>206 (25)</td>
<td>119 (28)</td>
<td>20 (19)</td>
<td>16 (18)</td>
<td>51 (24)</td>
<td>0.21</td>
</tr>
<tr>
<td>Fatigue</td>
<td>101 (12)</td>
<td>54 (13)</td>
<td>11 (11)</td>
<td>6 (7)</td>
<td>30 (14)</td>
<td>0.38</td>
</tr>
<tr>
<td>Fever</td>
<td>133 (16)</td>
<td>53 (12)</td>
<td>28 (27)</td>
<td>17 (19)</td>
<td>37 (17)</td>
<td>0.007</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>104 (13)</td>
<td>47 (11)</td>
<td>4 (4)</td>
<td>33 (37)</td>
<td>17 (8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory</td>
<td>53 (6)</td>
<td>19 (4)</td>
<td>12 (12)</td>
<td>15 (17)</td>
<td>10 (5)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Time-to-presentation could not be determined for 40 travelers with schistosomiasis.
† χ² test.
‡ Columns do not add to 100% because patients can have more than one presenting symptom and only the six most common presenting symptoms are given.

These findings encourage sponsoring organizations to more uniformly screen returning missionaries, volunteers, and expatriates.
dard in-country training, were found to be infected with schistosomiasis at the end of their 27 months tour.28 After introduction of an intensive schistosomiasis education campaign, which consisted of additional emphasis on schistosomiasis in pre- and mid-service training sessions and in twice-yearly newsletters and increased one-on-one counseling during routine contact for other reasons, the seroprevalence of schistosomiasis dropped to 5–7% in 1999–2001. In general, avoidance of freshwater in endemic areas, or only using water that has been chlorinated, heated, or left to sit for 48–72 hours, is critical to preventing infection.24

As seen in our study and others, a large proportion of travelers with schistosomiasis are asymptomatic at diagnosis (33% in our study), and when symptoms are present, gastrointestinal symptoms, fever, genitourinary symptoms, and fatigue are most commonly reported11,16,17,20,27 Because we only used cases that were confirmed by microscopy or serology, we were unable to distinguish between acute schistosomiasis and more chronic forms of schistosomiasis; microscopy and serologic testing are often negative during acute schistosomiasis and may take several weeks to become positive.4–9,17,18 In our study, however, fever and respiratory symptoms, which are common during acute schistosomiasis,10,15,17,18,29 were more often reported in travelers who presented within six months; whereas genitourinary symptoms were more often reported in those who presented later. Respiratory complaints are increasingly recognized as an important part of acute schistosomiasis.17,18,29–31 Although first described after infection with S. japonicum, acute schistosomiasis can be seen also after infection with S. mansoni and S. haematobium.4–8,17,29–31 We show that symptoms consistent with acute schistosomiasis are seen in a high proportion of those with S. haematobium and S. mansoni infections, supporting the notion that acute schistosomiasis can occur in all nonimmune travelers, regardless of infecting Schistosoma species. Furthermore, in a recent study of returned Israeli travelers with schistosomiasis, ~25% of asymptomatic travelers went on to develop symptoms of chronic schistosomiasis; therefore, screening for and treating schistosomiasis in all travelers with potential exposure, even if asymptomatic, should be encouraged.17

The limitations of this analysis include those applicable to other published studies that used the GeoSentinel database. The findings can only be generalized to travelers seen in tropical or travel medicine clinics after travel. GeoSentinel sites are specialized travel and tropical medicine clinics recruited on the basis of demonstrated training, experience, and publication in travel and tropical medicine. They contribute clinician-based surveillance data recorded as part of normal patient care. There are no standard protocols dictating the work-up of patients; however, GeoSentinel clinicians would be expected to have tested methodically for schistosomiasis when indicated by exposure history. Some cases may have been missed, as some Schistosoma infections that were ruled out may not have been reported and patients with other illnesses were not necessarily tested for schistosomiasis if the patient or payor declined testing. Although the GeoSentinel database is a comprehensive sample of illnesses acquired by ill returned travelers presenting in 19 countries with exposure in over 230 countries, biases for certain behavior-related diagnoses likely exist because of the geographic distribution and proportionate contribution of the individual sites.

Because GeoSentinel sites do not report the method used for diagnosis, it is unknown what proportion of schistosomiasis cases were diagnosed by direct egg detection or by serology. Only those with suspicion of current infection and/or disease would have been tested in the GeoSentinel setting. Previously treated patients can still have disease. Previously treated infections still provide the information needed for the present analysis in terms of place of exposure, duration of travel, and type of travel.

More information is needed about the effectiveness of pre-travel education on disease prevention in long-term travelers, particularly those traveling for missionary or other volunteer service. Even after the introduction of an intensive schistosomiasis education program, emphasizing the importance of freshwater avoidance, only 26% of Peace Corps Volunteers did not swim in freshwater for their entire tour.28 Even a history of no freshwater exposure, however, is not sensitive enough to rule out infection in potentially exposed travelers; 4.8% of returning travelers were found to be infected with Schistosoma species despite reporting no freshwater contact.27 Prevention messages, especially for those traveling for an extended period of time, should include the possibility of asymptomatic infection and the need for screening on return home, regardless of symptoms.

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