Presentation and Diagnosis of Imported Schistosomiasis: Relevance of Eosinophilia, Microscopy for Ova, and Serology

Wouter F.W. Bierman, José C.F.M. Wetsteyn, and Tom van Gool

Background: In nonendemic countries a steady rise in cases of imported schistosomiasis has been observed. The objective of this study was to describe the presentation of patients diagnosed with schistosomiasis in the Outpatient Department (OPD) for Tropical Diseases in the Academic Medical Center, Amsterdam, the Netherlands.

Methods: In a retrospective study, patients with schistosomiasis from our OPD (1997–1999), including a subgroup of persons asking for screening for schistosomiasis and found positive, were analyzed. Diagnosis was based on freshwater exposure in an endemic area and positive serology for schistosomal antibodies. The following data were recorded: age, gender, country of birth, travel destination, symptoms, eosinophil count, and results of serology and stool and urine microscopy.

Results: Seventy-eight patients (42 travelers, 16 expatriates, and 20 immigrants) were diagnosed with schistosomiasis; 47% were infected in southern Africa. Twenty-four percent had specific symptoms, 57% had eosinophilia, and in 17 patients (22%) *Schistosoma* ova were found. Eleven travelers suffered from Katayama syndrome. Of the subgroup of 42 persons screened for schistosomiasis, 15 (36%) had schistosomal antibodies; the majority of these persons (10/15 [67%]) were infected in southern Africa.

Conclusion: In our OPD schistosomiasis was diagnosed in about 26 patients per year, 3% of all new presentations. Infections were almost exclusively acquired in Africa. In travelers high eosinophilia was due to acute schistosomiasis; in immigrants it was due to concomitant helminthic infections. One of three people asking to be screened for schistosomiasis had schistosomal antibodies. Eosinophilia was indicative but an insufficient screening tool, and stool and urine microscopy for ova were not sensitive. Screening by serology is easy and reliable and the method of choice in asymptomatic persons with a history of freshwater exposure in a high-risk area.

Schistosomiasis is a parasitic infection caused by trematodes (flukes) of the *Schistosoma* genus. According to an estimation of the World Health Organization, 200 million people are infected worldwide, the majority living in sub-Saharan Africa and South America. Infections occur by skin contact with cercaria-contaminated freshwater during swimming, fishing, and bathing. *Schistosoma mansoni* and *Schistosoma japonicum* cause intestinal schistosomiasis; *Schistosoma haematobium* causes urinary schistosomiasis. The trematodes have a long life span. It is not the adult worms but rather their eggs that are responsible for the most important clinical features. Among the endemic population, frequent exposure results in a large worm burden, which can lead to more severe clinical features such as hepatolienal schistosomiasis and carcinoma of the bladder. Nevertheless, a single infection with a low worm burden can still bring about unexpected morbidity, such as acute schistosomiasis (Katayama syndrome), neuroschistosomiasis, and transverse myelitis.[1,2] Except during the acute form and the late stages with complications, specific symptoms are usually absent.

In nonendemic countries the prevalence of imported schistosomiasis is steadily rising, partly owing to an increase in traveling to endemic areas, and partly to emigration from these areas. In the Hospital for Tropical Diseases in London, there has been a sharp increase in infection with *S. haematobium* since the end of the 1980s.[3,4] Recent publications from centers in Germany, Israel, and the Netherlands show the same trend.[5–7]

In the Netherlands, until 15 years ago, schistosomiasis was mainly found in immigrants from Surinam and in Dutch expatriates.[8] Since then a shift to infections in Dutch travelers was observed.[9] There is no recent data on the incidence of imported schistosomiasis in the

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Netherlands. At the Outpatient Department (OPD) for Tropical Diseases in the Academic Medical Center, Amsterdam, schistosomiasis was seventh on a list of the ten most frequently imported diseases.[10] During a study in healthy Dutch expatriates seen for post-tropical screening in our travel clinic during 1997 and 1998, (asymptomatic) schistosomiasis was one of the most common diagnoses, with a seroprevalence of 18% (unpublished data, 1997–1998). Several cases of neuroschistosomiasis in travelers further emphasized the importance of this disease.[1,2]

The objective of this study was to describe the presentation and diagnosis of schistosomiasis at an OPD for Tropical Diseases, where travelers, expatriates, and immigrants are seen, and the relevance of eosinophilia, microscopy for ova, and serology in diagnosis. Special attention was given to patients with acute schistosomiasis and asymptomatic persons who wanted to be screened for schistosomiasis.

Patients and Methods

Patient Selection and Characteristics

From the database of our OPD (1997–1999), all patients diagnosed with schistosomiasis (based on exposure in an endemic area, microscopy, and serology) were selected; this included a subgroup of Dutch travelers who had had freshwater exposure in a high-risk area in Africa and had wished to be screened and who were proved to have schistosomal antibodies. Acute schistosomiasis (Katayama syndrome) was defined as the combination of fever and allergic symptoms after ≥ 6 weeks postexposure to freshwater in a high-risk area and (hyper-)eosinophilia, confirmed by the presence of schistosomal worm antibodies only.

Excluded were patients diagnosed and/or treated previously. Travelers were defined as those who spent ≤ 6 months in the tropics, and expatriates as those who spent > 6 months abroad. Immigrants were patients born and bred in endemic areas. They were not routinely checked upon arrival, and most were settled immigrants. They were referred by their general practitioner or referred themselves because of symptoms.

The following data were recorded: age, gender, country of birth, travel destination, symptoms, eosinophil count, and the results of schistosomal antibodies and stool and urine microscopy.

Methods

Eosinophilia is defined as a total eosinophil count ≥ 440×10^6/L. Microscopy consisted of examination of fecal material for *S. mansoni* ova and/or examination of 24-hour urine for *S. haematobium* ova. For serologic testing a combination was used of an indirect hemagglutination (IHA) assay and an enzyme-linked immunosorbent assay (ELISA) with cutoff points: IHA ≥ 80 and/or ELISA ≥ 0.222.[11]

Full examination is defined as serology and stool and 24-hour urine microscopy.

Results

Of all 2,556 consecutive patients presenting at the OPD from 1997 to 1999, 78 (3%) were diagnosed with schistosomiasis; 49 of 78 (63%) were male. The median age was 33 years (range 17–69 yr). Among these 78 cases were 15 (36%) who were of the subgroup of 42 travelers who had wished to be screened and who appeared to have schistosomal antibodies. Table 1 shows the data of the three patient categories: travelers, expatriates, and immigrants.

Eosinophilia

In 39 of 68 patients (57%) in whom an eosinophil count was performed, eosinophilia was found (see Table 1). Among the 42 screened persons, in 38 the eosinophil count was known: 7 of 38 (18%) had eosinophilia (range 490–2,290 × 10^6/L); 4 of these (58%) turned out to have schistosomal antibodies, which results in an odds ratio (OR) of 3.26 (Table 2).

Stool and Urine Microscopy

Schistosoma ova were found in 17 of 78 (22%) patients—9 of 78 (12%) had *S. haematobium* ova, and 8 of 78 (10%) had *S. mansoni* ova (Figure 1). Full examination for *Schistosoma* ova was only carried out in 31 patients; 7 of 31 (23%) excreted *S. haematobium* ova and 3 of 31 (10%) excreted *S. mansoni* ova.

In 2 of 15 (13%) with schistosomal antibodies, *S. haematobium* ova were found; 1 in the 9 who underwent full examination, and 1 in the 6 with incomplete microscopy.

Country of Exposure

See Table 1 for details of country of exposure for the whole group. Table 3 shows the country of exposure in patients with *Schistosoma* ova; 6 of 9 (67%) patients with *S. haematobium* ova had stayed in Malawi. In the subgroup, 25 of 42 patients (60%) had visited Malawi; 9 of the 25 (36%) had schistosomal antibodies and all 9 gave Lake Malawi as their only freshwater exposure (Table 4).

Katayama Syndrome

Acute schistosomiasis was diagnosed in 11 travelers; 7 were infected in southern Africa (4 in Malawi), 2 in East Africa, and 2 in West Africa. In 9 of 11 patients (81%), an eosinophil count was performed: all had eosinophilia (median 2,649 × 10^6/L; range 650–4,407).

Table 1 Region of Infection, Symptoms, and Eosinophilia in Patients*

	Travelers (n = *42*)	*Expatriates* (n = *16*)	*Immigrants* (n = *20*)	*Total* (n = *78*)
Region of infection				
West Africa	7 (17%)	2 (13%)	10 (50%)	19 (24%)
North Africa (Egypt)	—	—	3 (15%)	3 (4%)
East Africa	8 (19%)	2 (13%)	2 (10%)	12 (15%)
Southern Africa	27 (64%)	10 (63%)	—	37 (47%)
Surinam	—	—	5 (25%)	5 (6%)
Several regions	—	2 (13%)	—	2 (3%)
Symptoms				
Asymptomatic	15 (36%)	6 (38%)	3 (15%)	24 (31%)
Nonspecific	13 (31%)	6 (38%)	12 (60%)	31 (40%)
Specific	14 (33%)	1 (6%)	4 (20%)	19 (24%)
Hematuria	2	1	1	4
Blood in stool	—	—	2	2
Fever	12	—	1	13
Unknown	—	3 (19%)	1 (5%)	4 (5%)
Eosinophil count†				
Eosinophilia	23 (61 %)	5 (45%)	11 (55%)	39 (57%)
Median ($\times 10^6$/L) (range)	1,480 (470–4,407)	520 (460–1,010)	670 (450–2,060)	1,090 (450–4,407)

*78 patients with positive serology for schistosomal antibodies in the Outpatient Department for Tropical Diseases of the Academic Medical Center in Amsterdam, the Netherlands, 1997–1999.

†Travelers, $n = 37$; expatriates, $n = 11$; immigrants, $n = 20$; total $n = 68$.

Discussion

Schistosomiasis is among the world's six most important tropical diseases, endemic in 74 countries. Partially owing to human action, such as building reservoirs and irrigation projects, prevalence is rising rather than falling, despite many national and international attempts to control the disease.[12] With the increase in travel to these areas, schistosomiasis has made its entry as an imported disease. Even a single exposure (eg, from swimming, rafting, or kayaking) can cause infection.[7,13] Recently several studies have investigated the presentation of schistosomiasis in nonendemic countries.[3–7,14] Our study is comparable to a large-scale retrospective study in London.[4] In our clinic schistosomiasis was diagnosed in 26 patients per year—3% of all new presentations. The species of the *Schistosoma* was not always detected, owing both to a lack of sensitivity of stool and urine microscopy in light infections, and to the omission of microscopy for the same reason.

Eosinophilia was found in 57% of all patients, similar to results in other studies (40–65%).[8,9,15,16] In travelers the percentage (61%) was the highest, largely owing to the patients with acute schistosomiasis (Katayama syndrome), in whom the eosinophilia is part of the clinical diagnosis.[17,18] In expatriates eosinophilia was found in 45%. Although in chronic schistosomiasis eosinophilia is rare, a high percentage of the immigrants had eosinophilia (55%). This was mostly caused by concomitant helminthic infections: in 5 of 11 immigrants with eosinophilia an additional worm infection was found—strongyloidiasis in 3 of 5 and filariasis in 2 of 5.

S. mansoni was acquired in all regions, but *S. haematobium* was mainly from southern Africa. These differences reflect the geographic distribution of the *Schistosoma* species and the favorite travel or working destination, or the country of birth. In the Netherlands, until the 1980s, mostly *S. mansoni* infections were seen, among Surinam immigrants.[8] In our study, 15 years later, a clear shift to travelers and to tropical Africa is shown.

Only a small percentage of the patients had symptoms specific for schistosomiasis. The highest percentage of symptomatic infections was found in travelers (33%), almost fully attributable to the cases of Katayama syndrome. The specific symptoms in immigrants (20%) were mainly signs of chronic infection, caused by a higher worm burden related to sustained exposure in the past.

Table 2 Eosinophilia and Schistosomal Antibodies in a Subgroup of Asymptomatic Travelers*

	Eosinophilia			
	Positive	*Negative*	*Unknown*	*Total*
Negative serology	22	3	2	27
Positive serology	9	4	2	15
Total	31	7	4	42

*42 patients screened for schistosomiasis in the Outpatient Department of Tropical Diseases, the Academic Medical Center in Amsterdam, the Netherlands, 1997–1999.

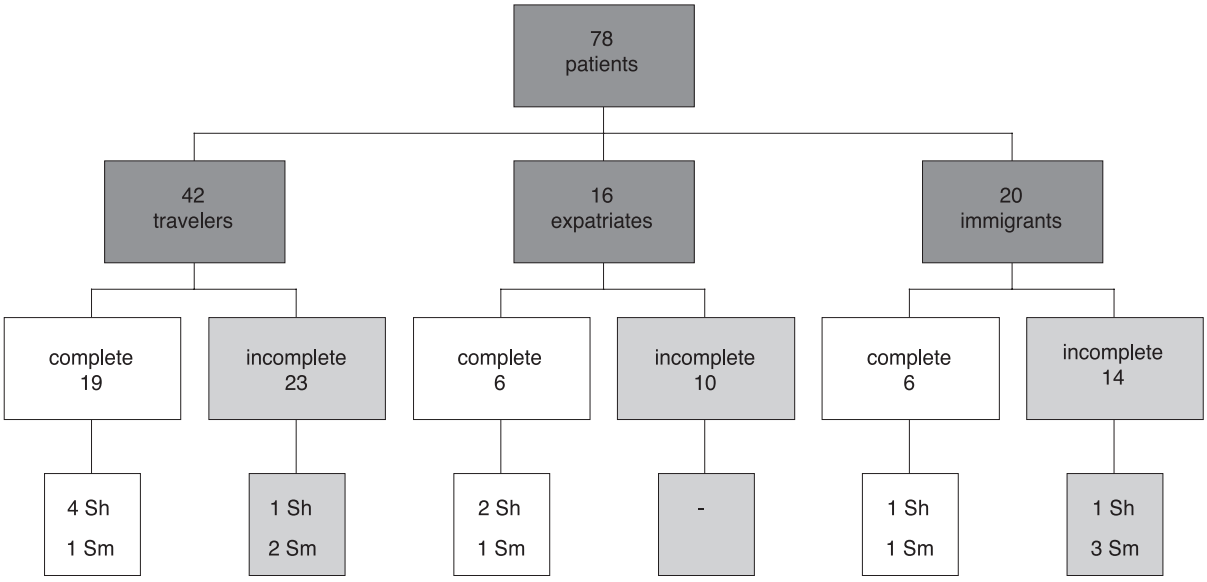

Figure 1 Results of complete (stool and urine) or incomplete (stool or urine or neither) microscopy for *Schistosoma haematobium* (Sh) and *Schistosoma mansoni* (Sm) ova in 78 patients (42 travelers, 16 expatriates, and 20 immigrants) with positive serology for schistosomal antibodies.

In other studies the percentage of asymptomatic *Schistosoma* infections has varied between 25 and 90%, but the populations are not comparable.[5,19,20] Whitty and colleagues considered tiredness a specific symptom of schistosomiasis because of its disappearance after treatment.[4] We regard it as nonspecific. Moreover, in a study of expatriates, Harries and colleagues found no difference in prevalence of tiredness in persons with and without schistosomiasis.[14]

Little is known about the risk of infection in travelers and expatriates. Cetron and colleagues found in Malawi in a cross-sectional study of expatriates and tourists (defined as a stay < 1 mo) a seroprevalence of 33% and 11%, respectively.[13] Seroprevalence increased with the length of stay and the number of visits to Lake Malawi. Whitty and colleagues did not find this relationship, but they tested after 3 to 12 months, 1 to 3 years, and > 3 years of stay.[19] When screening asymptomatic expatriates (1993–1997), they found a seroprevalence of 16%.[19] During post-tropical screening of expatriates in our travel clinic (1997–1998), 18% had positive serology for schistosomal antibodies (unpublished data, 1997–1998).

Screening of American expatriates (1981–1987) revealed schistosomiasis in only 1.3%, but it is unclear whether all screened expatriates had actually stayed in an endemic area.[15]

In the subgroup of persons wishing to be screened, we tried to make a rough estimate of the risk of infection for travelers with freshwater exposure: 36% of the

Table 3 Region of Infection of Microscopically Proven *Schistosoma haematobium* and *Schistosoma mansoni* Infections*

Region of Infection	S. mansoni *(n = 8)*	S. haematobium *(n = 9)*
West Africa	3	2
North Africa (Egypt)	1	0
East Africa	2	1
Southern Africa	1	6
Surinam	1	—

*Of the 78 patients with positive serology for schistosomal antibodies in the Outpatient Department of Tropical Diseases of the Academic Medical Center in Amsterdam, the Netherlands, 1997–1999; (*n* = 17).

Table 4 Travel Destination of a Subgroup of Asymptomatic Travelers Screened for Schistosomiasis and of Those Diagnosed with Schistosomiasis*

Travel Destination	*Total Screened (n = 42)*	*Travelers with Schistosomiasis (n = 15)*
West Africa	6	1
North Africa (Egypt)	1	0
East Africa	4	4
Southern Africa	30	10
Several African countries	1	0

*In the Outpatient Department of Tropical Diseases of the Academic Medical Center in Amsterdam, the Netherlands, 1997–1999.

"worried" travelers were infected, a high percentage in comparison with the above-mentioned percentages. Certainly, it is an overestimation, owing to our definition of travelers as those who spent < 6 months abroad; Cetron and colleagues used 1 month as a cutoff and recorded a growing seroprevalence with increasing length of stay.[13] Also, selection biases have occurred: the persons presented in a specialized OPD of a university hospital; it is a retrospective study—patients have been selected through data recorded in a database; and, finally, the subjects often sought medical attention themselves. The significance of this factor is hard to determine: did they want to be checked because of an awareness of greater risk or because of greater concern? Remarkably, most of the people who wanted to be screened gave Lake Malawi as their only freshwater exposure. Ten years ago Lake Malawi was considered the only *Schistosoma*-free great African lake. Although travelers are forewarned nowadays, it does not keep them away from contaminated freshwater. Our data show that the warnings for Lake Malawi are not exaggerated.

In this subgroup blood eosinophilia enhanced the chance of actually diagnosing schistosomiasis (OR 3.26), but the large number of seropositive results without eosinophilia demonstrates that eosinophilia should not be the guiding principle to perform serology. Screening for schistosomiasis in persons at risk is best performed by serologic testing, preferably > 6 weeks after freshwater exposure. Absence of antibodies virtually excludes infection.[11] When serology for schistosomal antibodies is positive, ideally stool and urine microscopy should be performed; however, owing to the fact that most infections are light, *Schistosoma* ova are not always found. A more pragmatic approach is treatment with praziquantel. If the eosinophil count was elevated, it should drop after about 6 weeks. If not, concomitant helminthic infection may be present. Whether the decline in antibody titers is useful for monitoring effectiveness of treatment needs to be investigated.

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