Imported Schistosomiasis in Europe: Sentinel Surveillance Data from TropNetEurop

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Background: Schistosomiasis is a major parasitic disease, increasingly imported into temperate climates by immigrants from and travelers to endemic areas.

Method: To generate valid data on imported infectious diseases to Europe and to recognize trends over time, the European Network on Imported Infectious Diseases Surveillance (TropNetEurop) was founded in 1999. Three hundred and thirty-three reports of schistosomiasis were analyzed for epidemiologic and clinical features.

Results: Male patients accounted for 64% of all cases. The average age of all patients was 29.5 years. The majority of patients were of European origin (53%). Europeans traveled predominantly for tourism (52%). Main reasons for travel for people from endemic areas were immigration and refuge (51%) and visits to relatives and friends (28%). The majority of infections were acquired in Africa; 92 infections were clearly attributable to *Schistosoma haematobium*, 130 to *Schistosoma mansoni*, and 4 to *Schistosoma intercalatum*. Praziquantel was the only treatment used. No deaths were recorded.

Conclusion: TropNetEurop sentinel provides valuable epidemiologic and clinical data on imported schistosomiasis to Europe.

Schistosomiasis is a major helminthic disease of widespread endemicity in the tropics and subtropics. With approximately 200 million people in 74 countries infected, its prevalence as a human parasitic disease ranks second behind malaria.[1,2] Due to an increasing number of travelers and changing patterns of travel activities while abroad, schistosomiasis imported to nonendemic areas is no longer almost exclusively seen as chronic infection in immigrants from endemic areas but also in increasing figures as acute[1,3–9] and chronic condition[1,7,10–12] in returning travelers who exposed themselves to contaminated freshwater.

Because of lack of surveillance data on imported cases of infectious diseases in Europe, the European Network

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on Imported Infectious Diseases Surveillance (Trop NetEurop) was founded in 1999 as an electronic network of clinical sites related to imported infectious diseases. Objectives and structure of the network have been described in detail elsewhere.[13,14] The capacity of the network to detect outbreaks has been demonstrated before.[15] This report summarizes data from the first 3 years of sentinel surveillance for imported schistosomiasis.

Patients, Materials, and Methods

Member sites of the TropNetEurop network covered approximately 51,000 patients per year in the study period in 1999 to 2001, during which 22 sites within the network reported 412 patients with a diagnosis of schistosomiasis. For every patient, the final diagnosis was qualified by the reporting center as either probable, suspected, or confirmed. For a diagnosis of confirmed schistosomiasis, pathogen detection (i.e., egg detection in urine, semen,stool,or biopsy material) was required. For a probable diagnosis, immunoglobulin G (IgG) detection by indirect hemagglutination (IHA), fluorescence antibody test (FAT),or enzyme-linked immunosorbent assay (ELISA) was used. Suspected cases were those with unambiguous clinical/imaging evidence but lack of confirmatory laboratory results at the time of reporting. This applies particularly to the high number of patients presenting with signs and symptoms suggestive of acute schistosomiasis. In this early phase of disease, egg detection is frequently not possible.

A standardized and anonymous questionnaire was used for data submission. Reported individuals were classified according to patient characteristics (immigrants, refugees, and foreign visitors from endemic areas to Europe; and students, tourists, business travelers,expatriates, military, and missionaries from Europe);and for reason for travel (e.g.,tourism, business,immigration, research/ education, missionary/volunteer/humanitarian aid, or visiting relatives/friends). Travel and case histories were analyzed for clinical and epidemiologic features of the infection. Presenting symptoms were analyzed, taking multiple entries by patients into account. Individual data points were stored in a computerized database (*Access*, Microsoft, Redmond, WA) and were analyzed by *SAS* 8.01 (SAS Institute Inc., Cary, NC, USA). For categorical data, Wald chi-square tests and for continuous data, Mann-Whitney U tests were performed.

Results

Of the 412 patients with a reported diagnosis of schistosomiasis, 299 (72.6%) were reported as confirmed cases,according to the definitions used by the network. Further, 34 (8.3%) were classified as probable and 27 (6.6%) as suspected cases.Sixteen (3.9%) were classified as status post (i.e., clinical and laboratory results were suggestive of a past episode of schistosomiasis that was successfully cured). For 36 individuals (8.7%), information on the final diagnosis was not obtainable. In the following analysis, only the 333 cases classified as confirmed and probable have been included. Basic demographic data are given in Table 1. Patient group (European versus Non-European origin) characteristics differed statistically significantly except for sex. Table 2 shows the frequency of schistosomiasis diagnoses by TropNetEurop member country and patient origin. Table 3 displays the region of infection by patient origin. Not surprisingly, the overwhelming majority of infections were contracted in Africa,with West Africa as the single region with most infections.The five largest contributors at country level were Malawi (48 patients; 14.4%), Ghana (45; 13.5%),Mali (27;8.1%), Burkina Faso (19; 5.7%), and Egypt (15; 4.5%).

Ninety-two cases were clearly attributable to *Schistosoma haematobium*, 130 cases were clearly attributable to *Schistosoma mansoni*, and 4 to *Schistosoma intercalatum*. Infections with *Schistosoma japonicum* or *Schistosoma mekongi* were not explicitly stated.No mixed infections were recorded.Given the spatial distribution of acquisition of infections, only a minority of cases was probably due to these species, that remained unrevealed among the 107 cases for which the diagnosis was not broken down to species level.Thirty-six schistosomiasis patients were coinfected with malaria. These were excluded from symptom analysis. In the two subgroups of patients with specified symptoms, or absence of symptoms, respectively (179 symptomatic individuals in total;90 of European, 89 of non-European origin), the most common problems were fever and diarrhea.Genitourinary symptoms were exclusively attributable to *S. haematobium*. Fatigue, skin involvement, and headache were among the next frequently encountered signs and symptoms. Abdominal pain was the predominant symptom among those 65 miscellaneous events named in both groups (24 of 39 specified episodes). A synopsis of signs and symptoms of these patients and a calculation of the statistical significance of differences between both patient groups is given in Table 4. Clinical complications of schistosomiasis were explicitly stated for 6 patients, for example, ectopic granulomas in spinal cord with neurologic complications (n=2), hydronephrosis of left kidney (n=1), liver cirrhosis (n=1),prolonged bloody diarrhea (n=1), and reactive arthritis (n=1).Of those 297 patients with schistosomiasis only (36 patients with *Plasmodium* spp coinfection excluded),240 (80.8%) were treated as outpatients,whereas 53 (17.8%) individuals required hospital admission (no data: n=4,1.3%).There were no deaths attributable to schistosomiasis reported in our patient collective. All patients were treated with praziquantel, of

Table 1 Basic Demographic Data*

Observation	*European*	*Non-European*	*Total*	*p-Value*†
Age‡ (Years)				
Mean	31.5	27.3	29.5	
Median	30.0	28.0	29.0	
Range	0–76	0–65	0–76	.0097
Sex§				
No data	0	1 (0.6)	1 (0.3)	
Male	115 (65.3)	96 (61.5)	212 (63.7)	
Female	61 (34.7)	59 (37.8)	120 (36.0)	.52000
Pretravel Advice§				
No data	99 (56.3)	86 (55.1)	186 (55.9)‖	
Yes	53 (30.1)	6 (3.8)	59 (17.7)	
No	24 (13.6)	64 (41.0)	88 (26.4)	.0001
Malaria Prophylaxis§				
No data	26 (14.8)	40 (25.6)	66 (19.8)	
None	80 (45.5)	96 (61.5)	177 (53.2)‖	
Yes	70 (39.8)	20 (12.8)	90 (27.0)	.0003
Travel Purpose§				
No data	7 (4.0)	5 (3.2)	13 (3.9)‖	
Tourism	91 (51.7)	20 (12.8)	111 (33.3)	
Visiting relatives and friends	9 (5.1)	44 (28.2)	53 (15.9)	
Business	26 (14.8)	2 (1.3)	28 (8.4)	
Immigration/refuge	0	79 (50.6)	79 (23.7)	
Research/education	6 (3.4)	2 (1.3)	8 (2.4)	
Missionary/humanitarian‖	37 (21.0)	4 (2.6)	41 (12.3)	p<0.0001

*n total=333.
†Wald chi-square test for categorical data, Mann-Whitney U test for continuous data.
‡No data available for 1 patient.
§Data are number (%) of patients. No data for origin of 1 patient.
‖Missionary/humanitarian.

which only 2 were explicitly reported as having drug-related side effects (1 generalized skin rash following treatment;1 with nausea following medication).Again, underreporting is likely to have occurred,as there is no established standard in use with our concise reporting tool, which would allow for comparing severity of adverse events.No patient received oxamniquine for S. *mansoni* or metrifonate for *S. haematobium*. Reporting of follow-ups to the network was not done routinely.

Table 2 Frequency of Schistosomiasis Diagnosis by TropNetEurop Member Country and Patient Origin*

Country	*European*	*Non-European*	*Total*
Belgium	3 (1.7)	0	3 (0.9)
Czech Republic	0	2 (1.3)	2 (0.6)
Denmark	9 (5.1)	8 (5.1)	17 (5.1)
Germany	69 (39.2)	32 (20.5)	101 (30.3)
Ireland	15 (8.5)	2 (1.3)	17 (5.1)
Italy	2 (12.5)	81 (51.9)	104† (31.2)
Portugal	1 (0.6)	0	1 (0.3)
Spain	39 (22.2)	17 (10.9)	56 (16.8)
Sweden	2 (1.1)	5 (3.2)	7 (2.1)
Switzerland	7 (4.0)	6 (3.8)	13 (3.9)
United Kingdom	9 (5.1)	3 (1.9)	12 (3.6)
All countries	176 (100)	156 (100)	333 (100)

*Data are number (%) of patients.
†No data for origin of 1 patient.

Table 3 Region of Infection by Patient Origin

Region of infection	*European*	*Non-European*	*Total*
Africa, Central	10 (5.7)	17 (10.9)	27 (8.1)
Africa, East	26 (14.8)	15 (9.6)	41 (12.3)
Africa, North	7 (4.0)	11 (7.1)	18 (5.4)
Africa, South	57 (32.4)	11 (7.1)	68 (20.4)
Africa, West	56 (31.8)	90 (57.7)	147† (44.1)
America, Central	2 (1.1)	0	2 (0.6)
America, South	2 (1.1)	2 (1.3)	4 (1.2)
Asia, East	1 (0.6)	0	1 (0.3)
Asia, Southeast	4 (2.3)	2 (1.3)	6 (1.8)
Asia, West	2 (1.1)	0	2 (0.6)
Caribbean	1 (0.6)	0	1 (0.3)
Indian Subcontinent	1 (0.6)	1 (0.6)	2 (0.6)
Madagascar‡	5 (2.8)	6 (3.8)	11 (3.3)
Oceania	1 (0.6)	0	1 (0.3)
No data	1 (0.6)	1 (0.6)	2 (0.6)
Total	176 (100)	156 (100)	333 (100)

*Data are number (%) of patients.
†No data for origin of one patient.
‡And surrounding islands

Table 4 Signs and Symptoms by Patient Origin

	*% with Sign or Symptom**		
Sign/Symptom	*Europeans (n=90)*	*Non-Europeans (n=89)*	*p-Value†*
Fever	33	9	p<.00009
Fatigue	26	12	p=.04
Skin	9	6	p=.6
Respiratory	12	2	p=.04
Headache	10	9	p=1.0
Lymphadenopathy	2	1	p=1.0
Musculoskeletal	9	1	p=.03
Diarrhea	36	16	p=.003
Vomiting	1	5	p=.2
ENT	1	5	p=.2
Genitourinary	13	32	p=.004
Neurologic	4	1	p=.4
Others	27	46	p=.008

ENT=ear, nose, and throat.
*Multiple entries possible.
†Wald chi-square test.

Discussion

A detailed update of the current global epidemiologic schistosomiasis situation has been recently given,[16] and the current concepts of schistosomiasis control have been reviewed.[17] The pattern of countries, or regions where immigrants and tourists contracted schistosomiasis differs significantly from the spatial distribution of schistosomiasis foci in endemic areas. For example, the size of the major focus in Egypt along the Nile River is not reflected in our cohort in terms of figures of imported disease. Overestimates within a sentinel system striving for detection of epidemiologic trends of a condition that is frequently encountered in endemic countries but infrequently diagnosed as imported disease may arise from a single group of travelers or immigrants. Steady figures of high infection rates from particular areas,such as Dogon country in Mali and Lake Tanganyika in Malawi, reflect the elevated risk for the specific type of adventure traveler who is either uninformed, or, more frequently, deliberately takes risks,[6] such as freshwater exposure. In turn,underestimates appear to arise mainly from the lack of touristic attractiveness of some highly endemic regions,or political instabilities,thus defraying tourist activities. The absolute figures of imported schistosomiasis show large differences between sentinel countries.This is due to the absolute population figures and the number of contributing centers. With regard to immigrants, political conditions and terms of immigration from endemic areas into various European countries are the factors mainly responsible for the distribution pattern of schistosomiasis imported into Europe. Whereas up-to-date epidemiologic data are available for many endemic areas,true estimates of risks of infection are difficult to obtain. This is partially due to the fact that reliable denominators are difficult to define. Although this has been tried with various approaches,[7,18] reliable figures on travelers exposed are lacking. However, the data obtained with the TropNetEurop sentinel surveillance system offer a unique tool to monitor changes of the absolute number of cases imported from every endemic country and therefore might function as a warning system.They are of use to aid accurate and timely diagnosis and treatment of both returning tourists and immigrants as well.

In studies of imported schistosomiasis, a bias in favor of symptomatic individuals is to be expected.[19] The high number of nonsymptomatic patients in our records is consistent with previous findings.[1,7] In general, symptom analysis pointed neither toward a sensitive nor a specific sign indicative of schistosomiasis.

Symptoms possibly associated with Katayama fever (fever, diarrhea, fatigue, pulmonary and musculoskeletal symptoms,headache, abdominal pain, and vomiting) were reported more frequently among Europeans compared with non-Europeans. The high proportion of Europeans presenting with acute disease is not unexpected,as most short-term travelers tend to present early in the course of disease, whereas chronic stages are predominantly found in patients from endemic areas.However, some of these features, such as fatigue, (bloody) diarrhea, and abdominal discomfort, might also occur in patients with chronic disease. Nevertheless, our data suggest that a considerable proportion of patients originating from endemic areas also presented with acute disease. Apart from patients with

S. japonicum infections, acute disease is not frequently observed in endemic areas, thus suggesting that these patients were nonimmune.

Uncommon manifestations of schistosomiasis are neurologic manifestations predominantly in the spinal cord tissue. Although only anecdotally described in returning travelers,[20–22] 50% of the few reported complications in our cohort were attributable to neuroschistosomiasis.

Among the centers contributing to TropNetEurop, a wide range of diagnostic means for acute, chronic, and past schistosomiasis,including various parasitologic methods for egg demonstration, antibody, and antigen detection[23] is in use both for routine diagnostic and research purposes. To harmonize diagnostic criteria,the above given definitions were strictly applied to all reported cases, resulting in 61 (14.8%) cases of both suspected (diagnosis based solely on clinical evidence) and probable (diagnosis based on both clinical and serologic evidence) cases at the time of reporting.Whereas this standard was chosen to maintain a high level of certainty on the correct diagnosis, it has been shown before in imported schistosomiasis that serology alone can reach up to 96% sensitivity and high specificity compared with the gold standard of direct egg detection,[24] thus, being an acceptable screening test in nonendemic areas for active and past infection.

Praziquantel is the drug of choice for the treatment of schistosomiasis.[25–28] This finds its reflection in our network data,with all patients having been treated with praziquantel. Jelinek and colleagues found 6 of 62 travelers who contracted schistosomiasis relapsing within 12 months after administration of praziquantel therapy.[7] Whitty and colleagues found a definite failure rate of 1.3% and a possible praziquantel failure rate of 2.9% in 550 schistosomiasis patients in London who were followed up for between 3 months to 2 years after treatment.[1] For the schistosomiasis patients reported to our network between 1999 and 2001, only few treatment failures have been reported until April 2002; namely, 3 patients of a series of 5 patients with Katayama fever who relapsed after praziquantel treatment.Definite or suspected treatment failures of later stages of schistosomiasis have not been reported until April 2002. We understand that this might reflect the difficulty in long-term follow-up of patients within the framework of this sentinel surveillance network rather than a 100% long-term treatment efficacy.

Schistosomiasis is a nonnotifiable disease in our European partner countries. TropNetEurop as a sentinel surveillance system has the capacity to facilitate better understanding of epidemiology and clinical characteristics of imported schistosomiasis and provides valuable information to improve both pretravel advice and clinical practice. Since membership is self-selected,it is evident that the network cannot provide a representative data collection throughout Europe. However, in most European countries medical services for immigrants and returning travelers are offered primarily at specialized centers.It is the only clinical network that collects data on imported infectious diseases on a European level that adds much-needed information on epidemiologic changes in afflicted areas in times of increasing travel activity and migration.

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A dream of a beach. Foiata Island. Vava'u, Tonga. Submitted by Danielle Gyurech MD and Julian Schilling MD.