Schistosomiasis and International Travel

Manuel Corachan
Tropical Diseases Unit, Institut d’Investigació Biomèdica Agustí Pi Sunyer, University Hospital, Barcelona, Spain

Infection with Schistosoma species is acquired by exposure to fresh water that harbors cercariae released by infected snails. Although the route of infection is clear, clinical presentation of the established infection in the nonimmune tourist typically differs from that in the local population of areas of endemicity. For the health care practitioner, the traveler’s syndrome presents distinctive management problems: water-transmitted bacterial and viral infections may coexist, and identification of the stage of disease at presentation, along with identification of the causative species, will maximize treatment options. Travel medicine clinics serve as epidemiological antennae, helping to identify the dynamics of species transmission in geographically distinct areas. Education of persons traveling to areas of endemicity and the development of mechanical protection against exposure are needed.

Infection with Schistosoma species is acquired by exposure to fresh water that contains cercariae (the parasitic form that is infective for humans) released by infected snails (the intermediate host). The infection affects up to 300 million people worldwide, and, in areas where Schistosoma infection is endemic, children aged 5–15 years have the highest prevalence and parasite loads [1]. The disease is present in most African countries and in limited areas of South America, the Caribbean, the Middle East, and Asia (figures 1 and 2).

The infection route for the local population in areas of endemicity is the same as that for the nonimmune tourist; however, the clinical presentation of the established infection differs greatly for these 2 groups of individuals. Several species of Schistosoma infect humans: S. haematobium, which is responsible for urinary schistosomiasis; S. mansoni, S. japonicum, S. mekongi, and S. malayi, which are responsible for gastrointestinal (GI) and hepatosplenic schistosomiasis; and S. intercalatum, which also affects the GI tract but which is associated with lower morbidity [3]. All species have been associated with Salmonella bacteremia.

The most common clinical presentation of S. haematobium infection includes hematuria, proteinuria, and leukocyturia accompanied by such symptoms as dysuria and nocturia. Long-standing chronic infections lead to obstructive uropathy, hydronephrosis, and calcified fibrotic bladder and/or ureter.

Patients with GI schistosomiasis produce bloody diarrhea during the early stages of this condition, which evolves to chronic colitis with the possibility of colonic polyps formation. Severe and long-standing infections will lead to the complication of presinusoidal portal hypertension due to schistosoma eggs retained in the portal spaces that will then undergo a fibrotic process. These symptoms occur in patients at an earlier age in cases of S. mekongi and S. malayi infection [4], although other liver flukes that are prevalent in Southeast Asia could also play a role. S. intercalatum infection does not produce these severe pathologic characteristics, and its association with blood in the stool is difficult to interpret, because the published studies include populations with multiparasitic intestinal infections [3].

CNS involvement, which is uncommon in travelers, is achieved through embolization of eggs from the portal mesenteric system to the brain and spinal cord via the paravertebral venous plexus. CNS involvement occurs more frequently in S. japonicum and S. mansoni infections [5] that, during the early stages of infection, affect the spinal cord (transverse myelitis) and, occasionally, the brain. This clinical situation requires treatment on an urgent basis, and the specific therapy for treatment of the parasite is given together with corticosteroids to avoid severe allergic reactions.

Diagnosis of schistosomiasis in areas where the disease is endemic usually depends on the demonstration of eggs in hu-
Figure 1. Global distribution of cases of schistosomiasis due to Schistosoma haematobium, Schistosoma japonicum, and Schistosoma mekongi. From [2].

man stool samples, and, occasionally, the diagnosis is made through examination of tissue biopsy specimens or ultrasonography, where available. Treatment involves the administration of praziquantel, which is effective against all Schistosoma species. Although it is generally agreed that a total dose of 40 mg/kg given in a single day is sufficient, treatment of infection with such species as S. japonicum requires higher doses (50 mg/kg). Other drugs, such as trichlorfon (for S. haematobium infection) and oxamniquine (for S. mansoni infection), are used in specific areas where a single species exists. Oxamniquine is administered in a single dose of 20 mg/kg in South America; in Africa, administration of 20 mg/kg per day for 3 days is necessary to achieve good results.

All of the aforementioned facts have been well established and subjected to minor variations according to clinical individual judgement. The great majority of the scientific contributions to the medical literature are from areas where schistosomiasis is endemic and have involved the local, semi-immune population of areas where infection-control programs have been in place for many years.

THE DISEASE IN TRAVELERS

Since the 1980s, the increase in ecotourism and adventure tourism has resulted in an increasing number of imported cases of schistosomiasis. This has contributed to a better understanding of the disease in the nonimmune population, for whom noteworthy differences in clinical presentation and management have been described [6]. Although no precise data exist on the incidence of infection in travelers, a European network of surveillance of imported diseases comprising 11 institutions reported 151 cases during a 3-year period [7].

Although the majority of infections go unnoticed and have an asymptomatic course [8], a number of tourists, when asked, will recall having certain self-limited signs and symptoms that could lead to the diagnosis. The earliest clinical manifestations of the disease are “swimmer’s itch”–like symptoms, a micropapular dermatitis that results from the contact with penetrating cercariae. This transient episode usually disappears within the first 48 h after contact with water; therefore, it is almost never seen at travel clinics [9].

Katayama fever (also called “Katayama syndrome”) is an acute, toxemic syndrome characterized by fever, malaise, and eosinophilia that occurs in persons who have been exposed to cercariae-infested water. The symptoms are usually accompanied by other, less common manifestations, such as hepatosplenomegaly, diarrhea, urticaria, and edema [10, 11]. Katayama fever occurs in a varying percentage of persons exposed to Schistosoma species, and it appears around the period of early oviposition. It has been shown that this syndrome rep-
represents an immunological reaction to a variety of circulating antigens to different stages of the parasite (cercariae, schistosomulae, adult Schistosoma organisms, and eggs), which usually appears 3–6 weeks after heavy exposure to cercariae [12]. However, a classic study of the disease, which included nonimmune patients, showed that it is very likely that, in some cases, the syndrome appears before any eggs have been laid [13].

The symptoms described are transient and disappear spontaneously while the infection progresses to the chronic phase. For the health care practitioner, this typical traveler’s syndrome presents several distinctive management problems.

**Diagnosis.** The diagnosis is usually made on the basis of clinical and epidemiological grounds, as stated above. Parasitological confirmation is not always possible during the acute stage of illness, because the parasite loads are mild or because oviposition has not yet occurred.

Serologic examination with more-sophisticated tests (e.g., antigen detection tests), which are only available in some research laboratories, is often the only tool for confirming the diagnosis, and such confirmation is only possible 5–6 weeks after infection [14]. The results of antibody detection tests (ELISA, indirect hemagglutination, and the circumoval precipitin test) become positive too late in the course of infection and are of poor value for early detection of infection in travelers. Most Schistosoma-infected tourists remain asymptomatic, and the diagnosis is often not made until years after the trip to an area of endemicity [6]. In such patients, the clinical and treatment-management schedules will not differ much from those for semi-immune patients.

However, because some patients visit the clinic (either for a checkup or because of Katayama fever) during the first weeks after swimming in cercariae-infested water, it is easily understandable that, because of the aforementioned diagnostic problems, the patient must believe that the physician is knowledgeable about this problem to allow the clinical process to develop to the point at which the decision to treat will be supported by sufficient clinical evidence.

**Treatment.** Administration of praziquantel is highly effective only against the adult worms and not against schistosomula [15]. The treatment regimens used during the initial stages of infection (weeks 5–6 of infection for *S. mansoni* and *S. japonicum* and weeks 10–12 of infection for *S. haematobium*), when there is clinical and epidemiological suspicion of infection and a positive serologic test result, is not the same as the regimen used for clinically established infection with positive parasitological evidence. The former situation means that not all worms will have reached the adult stage, which requires administration of a second treatment dose some weeks after administration of the initial dose. Moreover, in patients who present with Katayama fever, additional treatment with corticosteroid drugs is recommended to reduce the severity of the immunological reaction [16]. Because the addition of corti-
costeroids reduces the efficacy of praziquantel, Vazquez et al. [17] recommended increasing the standard dosage of praziquantel in such cases to 20 mg/kg given every 12 h for a 3-day period.

THE SPECIFIC CONTRIBUTION OF TRAVEL MEDICINE

Epidemiological contribution. Some tourist destinations, such as the Dogon tribe’s region of Mali [18, 19], Banfora in Burkina Faso [20], the Omo National Park in Ethiopia [12], and the southern shores of Lake Malawi [21], to mention just a few, have been signaled in medical publications as areas of high risk.

The field of travel medicine has also contributed to the understanding of the dynamics of transmission of S. intercalatum. Two years after Dutch [19] and Spanish [18] authors pointed out the presence of S. intercalatum in tourists who visited the Dogon tribe’s region of Mali, a team of researchers screened the zone to verify the finding. Although parasitological investigations did not find the parasite, a hybrid of S. haematobium and S. intercalatum was noted [22]. The disappearance of S. intercalatum was later explained by other authors as a competitive phenomenon among species [23]. These facts show that the importance of travel medicine clinics as epidemiological antennae is not to be neglected.

Clinical contribution. Advances in knowledge about acute schistosomiasis are likely to come from the travel-clinic physician’s observations.

In infected travelers, during the early stages of the disease, hematospermia has been shown to be an important symptom [24]. Lesions on the prostate and seminal vesicles of Schistosoma-infected male patients (age, <35 years) were shown by means of transrectal ultrasound techniques [25], which introduced many questions about potential male infertility problems related to Schistosoma infection. This has led to the use of parasitological studies of semen specimens when the results of urine and stool studies were negative, but clinical suspicion remained high because of suggestive ultrasound findings, the results of serologic tests, or the presence of such clinical symptoms as hematospermia [24, 26].

Recently, acute pulmonary schistosomiasis with abnormal radiological findings and that was associated with S. haematobium infection has been described in tourists who returned from Lake Malawi [27]. If, as the authors suggest, this represents a new parasite variant present in the lake, researchers in the field of travel medicine will again confirm its important role in epidemiological surveillance. Moreover, researchers in the field of travel medicine could further contribute to an explanation of some of the pending questions about schistosomiasis research: what is the pathogenesis of Katayama fever, and what is the exact relationship between exposure to infectious agents and the acquisition of infection?

In the field of chemotherapy, artemether, a derivative of the antimalarial drug artemisine, has recently been introduced for the control of schistosomiasis; this is good news on one hand and bad news on the other. The good news is that artemether is active against young S. japonicum schistosomula [28] and that it shows prophylactic effect against S. mansoni [29]; therefore, the drug could play a role in the treatment of acute schistosomiasis, especially in association with Katayama fever, in which there are circulating young schistosomula that praziquantel treatment will not kill (praziquantel eliminates only the adult flukes). The bad news is that, if artemether is widely used (i.e., in control activities), it could rapidly select for resistant plasmodia [29]. At this stage, we do not have sufficient experience with management with this drug before there is clinical evidence of infection; therefore, it cannot be widely recommended.

ADVICE FOR TRAVELERS

At the present time, many vacations involve unavoidable contact with infected water. Adventure travel in tropical regions involves rafting, snorkeling, windsurfing, canoeing, and other water-based activities that are becoming increasingly popular. Persons who partake in these activities risk not only the acquisition of schistosomiasis (if the activities take place in known areas of endemicity), they also risk acquiring viral hepatitis and leptospirosis [30]; these conditions, together with other water-transmitted bacterial or viral infections, should be kept in mind by the treating physician.

In these circumstances, I highly recommend that travel clinics (1) provide good information about areas where Schistosoma is endemic and the potential dangers, and (2) if contact with water in areas of endemicity is unavoidable, recommend that the person undergo a checkup at a specialized clinic that has adequate experience in tropical medicine and sufficient diagnostic capacity. The traveler must know the areas in which schistosomiasis is endemic, and the potential short- and long-term problems associated with infection need to be explained. Then, the final decision about contact with water would be left in the hands of an instructed traveler.

Possible ways of avoiding the infection have not been thoroughly analyzed and include different protective measures. Some protective measures are purely mechanical, such as energetic rubbing of the body with a towel immediately after swimming; others involve the use of a body soap that serves as a barrier against the infecting cercariae. The use of artemether as chemoprophylactic is not recommended for the reasons discussed above.