



RAPID RISK ASSESSMENT

Local transmission of *Schistosoma haematobium* in Corsica, France

16 May 2014

Main conclusions and options for mitigation

As of 16 May 2014, eleven cases (six from France and five from Germany) of uro-genital schistosomiasis have been reported. All cases were exposed to freshwater in a natural swimming area in southern Corsica (Cavu River). None of the cases reported contact with freshwater in an area known as endemic for contracting schistosomiasis.

This is the first locally acquired infection of *Schistosoma haematobium* in France. The disease is known to be highly focal in its geographic distribution. Therefore, the risk of acquiring the infection exists only for residents and people who visit the affected area and engage in occupational or recreational activities in the river.

- Epidemiological investigations – including the identification of cases and patterns of exposure – should eventually identify the likely place(s) of infection; molecular identification of the parasite should determine the origin of the introduction(s) and its population dynamics, as well as the parasite's presence in the intermediate host. These factors define the focality and seasonality of transmission and are required to assess the receptivity of the area.
- Malacological studies are required to identify the species involved as intermediate host, the snail distribution and its population dynamics, as well as the parasite's presence in the intermediate host. These factors define the focality and seasonality of transmission and are required to assess the receptivity of the area.
- As the infection may result in mild symptoms over a long period, informing people who were exposed to freshwater from the Cavu River in the summer of 2011 and 2013 of their possible exposure may decrease their risk of developing complications.
- Informing physicians in the EU could increase the detection of possible uro-genital *Schistosoma* infections among travellers who visited the affected area in Corsica (in 2011 and 2013) or other areas in the EU which potentially pose a risk of transmission due to the introduction of the parasite in the environment.
- Coordinated communication at EU and country level might enhance the awareness of travellers and residents and could be instrumental in the prevention of the infection and its complications.

Source and date of request

Directorate-General for Health and Consumers (DG SANCO), C3, 8 May 2014

Public health issue

To assess public health significance for the EU of autochthonous transmission of *Schistosoma haematobium* in the Cava river area, southern Corsica, France.

Consulted experts

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Disease background information

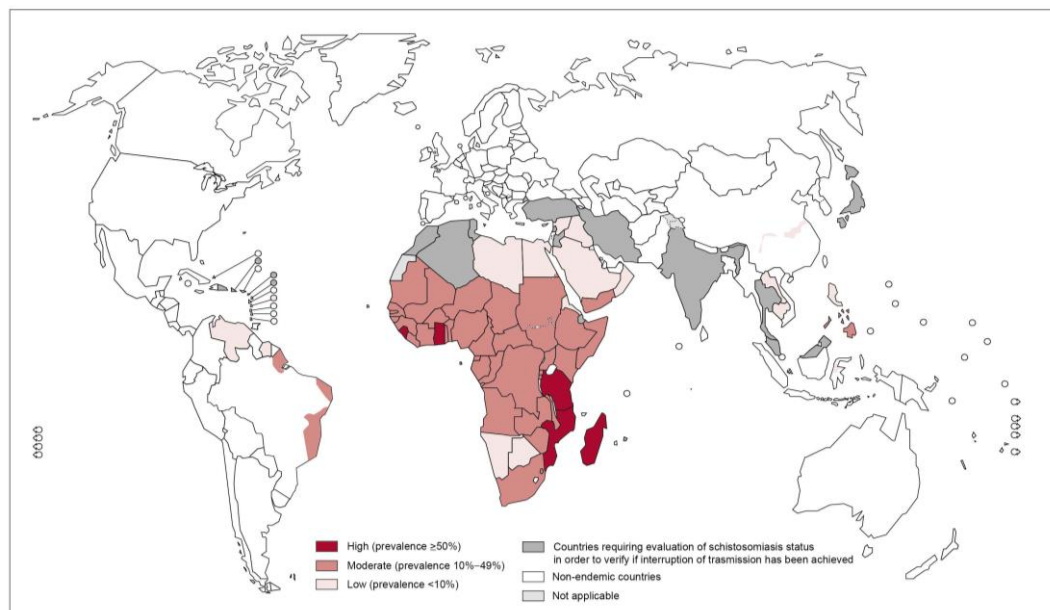
Schistosomiasis, or bilharzia, is a parasitic disease caused by trematode flatworms of the genus *Schistosoma*. The major species of schistosomes which infect humans are:

- *Schistosoma haematobium*, causing uro-genital schistosomiasis in Africa and the Arabian peninsula;
- *Schistosoma mansoni*, causing intestinal and hepatic schistosomiasis in Africa, the Arabian peninsula, and South America;
- *Schistosoma japonicum*, causing intestinal and hepatosplenic schistosomiasis in China, the Philippines, and Indonesia; and
- *Schistosoma intercalatum* and *Schistosoma mekongi*, which are only of local importance.

According to WHO, at least 249 million people received preventive treatment for schistosomiasis in 2012. Preventive treatment reduces morbidity in endemic countries with moderate to high transmission (Figure 1) [1].

This rapid risk assessment focuses on *Schistosoma haematobium*, which was identified as the pathogen involved in the reported cases.

Figure 1. Global distribution of schistosomiasis (2011)



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2012. All rights reserved

Data Source: World Health Organization
Map Production: Control of Neglected
Tropical Diseases (NTD)
World Health Organization



Source: http://qamapservr.who.int/mapLibrary/Files/Maps/Schistosomiasis_2012.png

Schistosoma haematobium infection

Distribution

Uro-genital schistosomiasis due to *S. haematobium* is a disease which was already known in ancient Mesopotamia and the southern part of the Mediterranean basin, where it was detected in Egyptian mummies with calcified bladders, a characteristic of the uro-genital form of the disease. It was described in the Sahel, where, in the Middle Ages and later during the 17th century, Arabic doctors reported blood in the urine of caravaneers.

The current geographic distribution of *S. haematobium* covers sub-Saharan Africa, the Middle East and the Arabic peninsula, with a total of 54 affected countries [2]. According to WHO, the interruption of transmission in three Maghreb countries (Morocco, Algeria and Tunisia) needs to be confirmed [3].

Uro-genital schistosomiasis is based on a parasitological cycle involving a human reservoir and an intermediate host. Determinants of the geographical distribution of the disease are: freshwater snails of the genus *Bulinus*, environmental conditions, and social behaviours.

Schistosomiasis is not established in the EU. However, cases are repeatedly identified among migrants and travellers returning from endemic areas. In 2010, EuroTravNet reported 152 cases among 7 408 persons seen in the EuroTravNet clinics (number of clinics >600). Most *Schistosoma* infections (40%) occurred in missionaries, volunteers and aid workers, followed by tourists (19%), visiting friends and families (16%), and immigrants (13%) [4]. In 2011, 131 cases were reported by EuroTravNet, corresponding to 2.2% of 5 965 patient seen in the EuroTravNet clinics [5]. Schistosomiasis is not notifiable at the EU level. In the early 1900s, a focus of *S. haematobium* was present in in the Algarve region of Portugal [6].

Cycle

Human

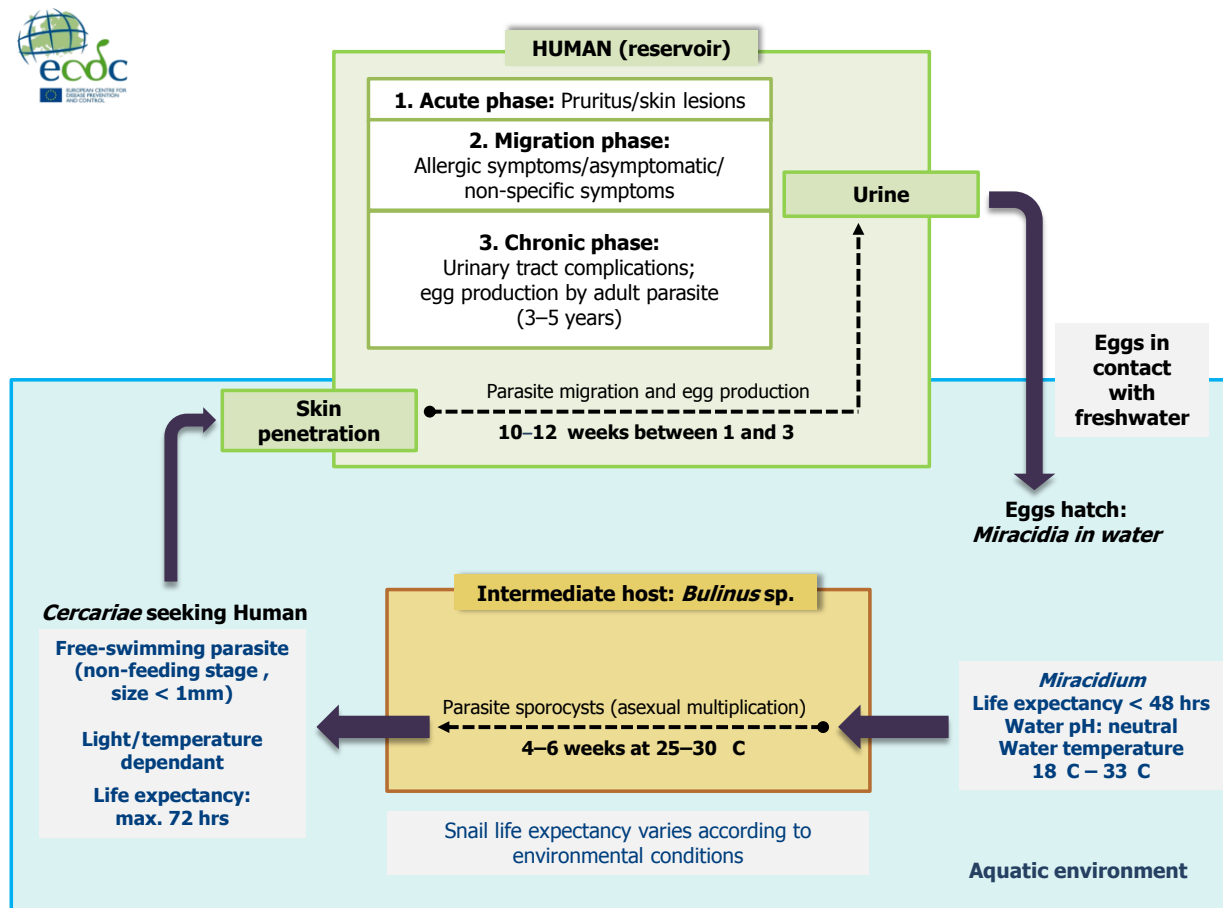
Humans are considered to be the only reservoir of *S. haematobium*. The infection in humans can be divided in successive phases: penetration, invasion and chronic phases. A human can be infected after recreational or occupational contact with freshwater hosting the immature forms (*cercariae*) of the free-swimming parasite [2,7]. The main types of exposure to infested water are connected to agricultural, domestic and recreational activities. The cutaneous penetration of the parasite is limited to skin exposed to the water. If there is high concentration of *cercariae* in water, transmission can occur in less than 15 minutes of exposure to infested water [8].

The invasion phase corresponds to the parasite reaching maturity; in infected humans, this is accompanied with generalised allergic reactions. *Schistosoma haematobium* adult parasites reach the venous plexuses of the bladder at worm maturity. Adult females deposit eggs in the small venules of the portal and perivesical systems. Then, eggs are moved progressively toward the bladder and ureters, and are discharged into the environment with urine. The time between exposure and excretion of eggs is estimated at between 10 and 12 weeks [9]. The excretion of eggs of an established infection without medical treatment can persist for 3 to 5 years, the average lifespan of an adult schistosome (Figure 2).

Aquatic environment

Excreted eggs hatch in freshwater, releasing *miracidia* that will search actively for suitable freshwater snails as their obligatory intermediate hosts. For *S. haematobium*, the intermediate host is a snail of the genus *Bulinus*. After an asexual multiplication stage in the snail, *cercariae* are shed by the snail. A period of four to six weeks, depending on the temperature (>20–25 °C), is required from penetration by the *miracidium* to the shedding of *cercariae*. The optimum temperature for the infection of the snail ranges from 20–30°C, which explains the tropical and subtropical distribution of the disease. Cercarial shedding occurs mainly during the warmest hours of the day. A large number of *cercariae* are released when the local environment is favourable. Search for humans by chemotaxis can occur up to 72 hours after shedding (Figure 2).

Figure 2: Schematic representation of the *Schistosoma haematobium* cycle



Eco-epidemiology

The distribution of the different *Schistosoma* species depends largely on the ecology of the snail hosts. Natural streams, marshes, swamps, small ponds, rivers and lakes are typical sources of infection. Man-made dams and irrigation systems have contributed to the spread of schistosomiasis. The disease is largely a rural problem, but urban foci can be found in endemic areas. Snail populations, cercarial density, and type of human water contact show strong temporal and spatial variations, resulting in a focal distribution of the infection within countries, regions, and villages [10].

The main intermediate host species are:

- *B. africanus* in Africa and the Sahara [11];
- *B. reticulatus* in Ethiopia and the Arabian Peninsula [12];
- *B. truncatus* complex, widely distributed Africa and the Middle East. The main areas of distribution in Africa are Lower Egypt, Sudan, and westwards into Mauritania. The species has been found in all oases in northern Africa and is widespread in western and eastern Africa. The northern distribution limits of this species are Portugal, Spain, Sardinia and Corsica [13,14].

It should be noted that more than 30 nominal species can transmit *S. haematobium* [8].

Temperature influences the development of the *Bulinus* aquatic snails: temperatures between 22 °C and 26 °C are usually optimal, but the snails can tolerate a wider temperature range depending on the species [15]. Snails can survive out of the water for weeks or months, depending of the species (aestivation capability). In tropical and subtropical settings, parasites can be carried by the snails during the aestivation period, thus prolonging the release of the parasite in the infected foci. Comprehensive studies are required to describe snail survival, their population distribution and possible infection – as these factors are known to vary with the type of habitats and climate – in order to define patterns of transmission (focality, seasonality). Human behaviour (frequency and patterns of human-water contact, including recreational, domestic or occupational activities) will define the exposure to infected water.

Pathogenesis of *Schistosoma haematobium*

In endemic settings, the most affected age group is between 5–15 years old. The skin penetration of *cercariae* can be associated with skin eruption and pruritus. After the *cercariae* penetrate the skin, the parasite transforms into young worms, or *schistosomulae*, which migrate through the blood to reach the venous plexuses and mature to

the adult stage (Figure 2). During the first month of infection, a non-immune individual can present with general immune-allergic reactions during the migration phase and early egg deposition.

Only a small proportion of cases will progressively develop chronic symptoms, which is more likely in people with heavy infections and recurrent exposure as seen in endemic settings. The infection can remain pauci-symptomatic for a long period but still cause progressive damage to the uro-genital tract.

The chronic stage of the infection of *S. haematobium* corresponds to uro-genital complications as the female worm releases eggs which migrate through the wall of the bladder and the uro-genital system. These retained eggs provoke a granulomatous inflammatory response, which is the main cause of pathology in the human host. While medical complications are progressive, microscopic haematuria is an early sign that should be investigated for individuals with known exposure to the parasite. Haematuria and dysuria are the main symptoms of uro-genital schistosomiasis, and early complications are infections of the upper and lower uro-genital tract and lithiasis. Chronic infections are characterised by long-term complications such as obstructive and fibrous lesions of the uro-genital tract, chronic cystitis, calcification in the bladder and renal impairment. *Schistosoma haematobium* is considered a risk factor for cancer of the urinary bladder in endemic settings.

Diagnosis

Egg detection in urine is a standard method for the identification of *S. haematobium* infection. It is particularly helpful in high-prevalence settings, and eggs are identified by their size and shape [10,16]. The urine should be collected between 10.00 and 14.00 because of the circadian pattern of egg excretion, and samples should be processed with filtration and centrifugation methods. In low transmission settings, the number of examined slides should be increased to ensure the technique's sensitivity. Tests will return negative results during the migration phase preceding egg excretion.

Several widely used immunological methods are available for schistosomiasis antibody detection. The most important ones are the indirect immunofluorescence test (IFT), the indirect hemagglutination test (IHAT), and the enzyme-linked immunosorbent assay (ELISA). ELISA is the most commonly used test for the serological detection of schistosoma infection, particularly in the diagnosis of egg-negative cases. A rapid dipstick antigen capture assay based on antigen detection is also used, but shows low performance for *S. haematobium*. In general, serological assays cannot differentiate between recent and old infection, only direct parasitological diagnosis can confirm an active infection.

Molecular assays offer high sensitivity which is particularly important in the context of low parasitic loads as observed in low transmission settings. These assays can be useful to identify species (species-specific DNA amplification), determine the origin of the parasite by comparing results with international gene sequence databases, and assess unique or multiple introduction in a transmission focus.

Real-time polymerase chain reaction (PCR) is an alternative method for quantifying parasitic load. In addition, a 28S rRNA gene-based nested PCR assay was used to define *Schistosoma* species in migrants and international travellers [17].

As haematuria (macro- or microscopic) is the main symptom of *S. haematobium*, confirmation by reagent strips for micro-haematuria in urine is a criterion to direct further laboratory investigation in population-based studies. Heme dipstick diagnosis of *S. haematobium* infection is available and was reviewed in recent publications. However, the sensitivity of this test decreases in population subgroups with lower parasitic loads [18]. According to the authors, this test is more suitable for monitoring community prevalence following the implementation of population-based control of uro-genital schistosomiasis.

Disease complications due to uro-genital tract lesions can be investigated with ad hoc methods (e.g. echography or cystoscopy) based on the patient's symptomatology.

Treatment

Praziquantel, an acylated quinoline-pyrazine, is the most widely used treatment against all *Schistosoma* species. It directly affects adult worms, acts within one hour, but has little or no effect on eggs and immature worms. The preferred timing of follow-up is therefore 4–6 weeks after treatment. After a single dose of 40 mg/kg, 70–100% of patients cease to excrete eggs.

Control

Control of schistosomiasis is based on drug treatment, snail control, improved sanitation and health education.

Control of disease transmission is mainly based on population-based chemotherapy with Praziquantel. Population-based chemotherapy allows quick gains, but needs careful long-term planning to ensure sustainability and progression to the more demanding stages of infection and transmission control [10].

Targeting the intermediate host (i.e. the snail) has largely ceased. Snail control with molluscicides is expensive and logistically complex. The use of molluscicides has a number of disadvantages: the cost of the chemicals; the need for repeated applications; the need for rigorous supervision of the application; and the adverse effects on non-target organisms, particularly fish.

In general, schistosomiasis can be eliminated through behavioural changes, improved sanitation, safe water supplies, and population-based chemotherapy.

Event background information

On 23 April 2014, the parasitology unit of the university hospital of Toulouse notified the InVS (institut de veille sanitaire, France) about a cluster of three cases of *Schistosoma haematobium* infections in a family (two children and their father). The family visited southern Corsica during the second part of August 2013. During their stay, family members were exposed to freshwater from the Cavu River near Porto Vecchio, Corsica. None of the cases reported contact with freshwater in an area known as endemic for contracting schistosomiasis.

The family had visited the area two years before (2011), where they visited the same freshwater site (Cavu River). The infection of the father might have been evolving for a few years as he had unexplained macroscopic haematuria since early 2012. One of his children presented with chronic bladder lesions related to *Schistosoma* infection. Therefore, the initial infection for these two family members may have occurred in 2011.

Additional cases were detected in two other French families. One family had accompanied the family mentioned above in 2011 and 2013, and accounted for two cases. A third family had joined the family mentioned above in 2013; one case was detected. All three families stayed at the same campground near the Cavu River during the second half of August 2013. All cases shared the same exposure to the Cavu River freshwater swimming area. In total, six cases were confirmed in a total of 12 persons (three families) through the detection of *S. haematobium* eggs in urine; also, two probable cases were identified. Four of the six persons with a confirmed infection were children. Overall, none of them had a history of swimming in freshwater in an endemic area.

The WHO Collaborating Centre for Snail/Schistosome relationships, Perpignan, France, reported five additional cases of uro-genital schistosomiasis diagnosed in Germany in a family of six tourists to InVS. The travel history of the German and French families showed that they all had stayed at the same campground; they also reported recreational water activities in the Cavu River in the second half of August 2013.

ECDC threat assessment for the EU

The available information is consistent with locally acquired infections of *Schistosoma haematobium* in the Cavu River in Corsica. So far, eleven cases (six from France and five from Germany) of uro-genital schistosomiasis have been confirmed.

The epidemiological data point to an autochthonous transmission of *S. haematobium* in 2011 and 2013:

- The timing and the clinical presentation of two French cases suggest that the infection has been present for more than one year and is therefore most likely due to an exposure to freshwater from the Cavu River in 2011.
- One French case and the German cases were exposed during the second half of August 2013.

The notification of locally acquired *Schistosoma haematobium* infections implies the presence of an efficient intermediate host in a suitable environment. Historical accounts of the presence of *Bulinus* spp. snails in southern Corsica date back to the mid-1960s [19]. The northern distribution limits of *Bulinus truncatus* species are known to be Portugal, Spain, Sardinia and Corsica [13,14,20]. Climatic conditions in Corsica are likely to be favourable from June through September for the development of *S. haematobium* in the freshwater snail. The same time period is favourable to transmission if people have contact with water that has been contaminated by the parasite. Moreover, previous foci of *S. haematobium* in the Mediterranean region (i.e. north of the Maghreb) share a similar climatic profile [10].

Humans are the only reservoir of *S. haematobium*, and people who contracted schistosomiasis can contaminate freshwater sources with their urine because it contains parasite eggs. Consequently, the parasite must have been introduced by an infected person who lives in the area, or who has visited the area.

Several scenarios can be considered:

1. Scenario 1: Unique introduction from an infected human shedding *S. haematobium* eggs in the Cavu River in 2011, with subsequent establishment of the aquatic part of the cycle and persistence of the parasite in the snails. This would imply the survival of infected *Bulinus* in the Cavu River over the winter, which is not very likely because infected snails are less viable. This is considered an unlikely scenario. A study of the current population of *Bulinus* in the river could provide data to evaluate this scenario.
2. Scenario 2: Multiple introductions from infected humans shedding *S. haematobium* eggs in the Cavu River in 2011 and 2013, with subsequent establishment of the aquatic part of the cycle and the contamination of French and German families.
 - Scenario 2a: Different infected visitors introduced the parasite to the Cavu River in the early summer (June) of 2011 and 2013. The transmissions in 2013 cannot be explained as a result of a cycle initiated in 2013 by the French family who was first infected in 2011 because the development of the parasite in the snail takes

several weeks.

- Scenario 2b: infected local residents re-established the aquatic part of the cycle in the early summer of 2011 and 2013. This scenario assumes that infected locals shed *S. haematobium* eggs in the Cavu River, which lead to the contamination.

Epidemiological investigations, including a molecular analysis of the parasite, population-based studies and malacological investigations are ongoing or are planned in the affected focus and surroundings in order to acquire the necessary information to assess the source of introduction and the pattern of transmission. The results of these investigations will assess the risk for exposure in time and space and guide further preventive measures.

Risk for the EU

This disease is based on a parasitological cycle involving a human reservoir and an intermediary host. Environmental conditions and social behaviours are determinants of the geographical distribution of schistosomiasis and result in a highly focal occurrence. Consequently, the autochthonous transmission of *Schistosoma haematobium* in Corsica is a local public health event but with potential implications for the EU:

- The area is a popular tourist destination for recreational water activities during the summer months. Persons who were exposed to the water of the Cavu River in 2011 and 2013 are at risk to have been infected.
- Given the existence of asymptomatic infections and the delay between infection and symptoms, it is possible that additional cases of infections in people exposed to the infested water of the Cavu River swimming area between 2011 and 2013 could be identified in the EU.
- This event confirms that the transmission of *Schistosoma haematobium* in Europe is possible when the parasite is introduced to areas where the intermediate host is present and climatic conditions are suitable. Receptive areas are likely to be present in other EU countries around the Mediterranean, in particular in areas where *Bulinus truncatus* is known to be present, e.g. Portugal, Spain, Sardinia and Corsica [20].

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