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Zur Information - Schistosomiasis Infektions-Cluster Südkorsika - Update

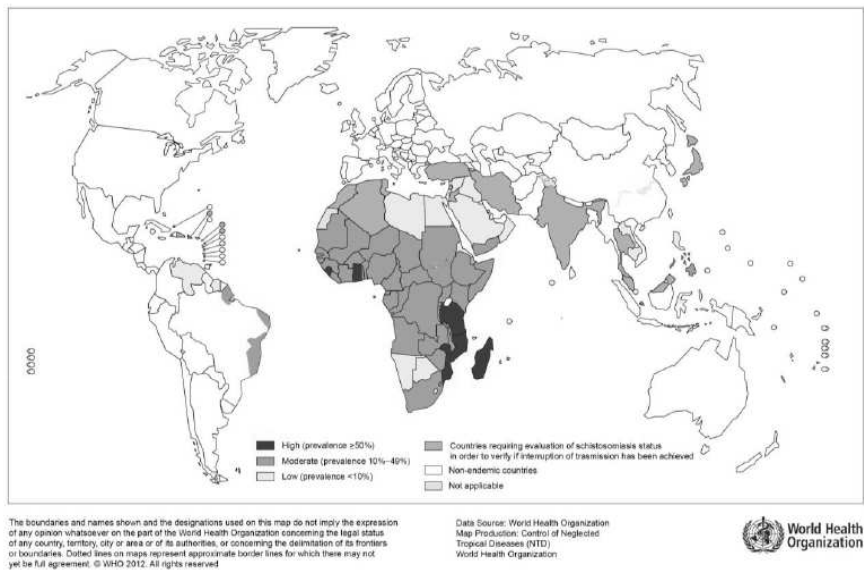
Sehr geehrte Damen und Herren!

Das ho Ressort übermittelt Ihnen aktuelle Informationen betreffend *Schistosoma haematobium* Infektionen ex Südkorsika. Am 7. Mai 2014 meldete das Französische Gesundheitsministerium Schistosomiasis-Fälle mit der wahrscheinlichen Infektionsquelle in Südkorsika.

Hintergrund:

Per 18.06.2014 wurden insgesamt 17 Fälle (12 in Frankreich und 5 in Deutschland) urogenitaler Schistosomiasis (Bilharziose) gemeldet, wobei alle Fälle zwischen 2011 und 2013 im Süden Korsikas eine Exposition im Fluss Cavu/Cavo hatten. Keine der Personen hatte eine Exposition in einem bekannten für *Schistosoma* spp. endemischen Gebiet (Figure 1).

Figure 1. Distribution of schistosomiasis in the world (2011)



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

Personen, die seit 2011 im Süden Korsikas Kontakt mit Wasser des Flusses Cavu/Cavo hatten, sollten vorsorglich Ihren Arzt/Ärztin zwecks Abklärung (*Schistosoma*-Screening) konsultieren, da die Erkrankung häufig eine lange Inkubationszeit hat und typischerweise oligosymptomatisch verläuft, das häufigste Frühsymptom ist eine (Mikro)hämaturie. Es gibt eine effektive Therapie mit Praziquantel (eine einmalige Dosis von 40mg/kg Körpergewicht, die nach einem Zeitraum von 4-6 Wochen wiederholt werden sollte), die in der Regel zu einer vollständigen Heilung führt. Unbehandelt zeigt die Erkrankung eine Tendenz zu einem chronischen Verlauf und ist auch als Präcancerose für Tumoren des Urogenitaltrakts einzustufen. Die Gewässer in denen die Transmission bestätigt wurde sind mittlerweile gesperrt. Die intermediären Wirte (Schnecken der Gattung *Bulinus*) wurden schon früher in der Gegend nachgewiesen, obwohl es bisher keinen Hinweis auf autochthone Übertragung gibt. Bei einer hohen Cercariendichte kann es zu einer Infektion nach mindestens 15 Minuten Kontakt mit kontaminiertem Wasser kommen. Goldstandard der Diagnose ist eine mikroskopische Harnuntersuchung (Nachweis der typischen Eier des zentrifugierten Urins), der am besten zwischen 10:00h bis 14:00h abgenommen werden sollte. Auch andere Nachweismethoden wie z.B. ELISA oder molekulare Tests können angewendet werden, jedoch mit unterschiedlicher Sensitivität.

Bei Hämaturie und Reiseanamnese mit entsprechender Exposition in Südkorsika (retrospektive bis 2011) sollte Bilharziose in die Differentialdiagnose miteinbezogen werden.


Schistosomiasis ist zwar nicht meldepflichtig gemäß österr. Epidemiegesetz, es wäre dennoch nützlich, wenn die zuständigen Bezirksverwaltungsbehörden von den ÄrztInnen über diagnostizierte Fälle informiert - und diese dem Bundesministerium für Gesundheit und der AGES (Dr. Daniela Schmid) weitergeleitet - werden würden.

Detaillierte Informationen entnehmen Sie dem beiliegenden Rapid Risk Assessment des ECDC.

Mit freundlichen Grüßen

Für den Bundesminister:
Dr. Peter Kreidl

Beilage/n: ECDC_RRA_Schistosoma haematobium_France_Germany_16-05-2014

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RAPID RISK ASSESSMENT

Local transmission of *Schistosoma haematobium* in Corsica, France

16 May 2014

Main conclusions and options for prevention and control

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 the same natural swimming area in southern Corsica without known exposure to fresh water in an endemic area of *Schistosoma*. This is the first locally acquired infections of *Schistosoma haematobium* in France. The disease is known to be very focal in its geographical distribution. Therefore, the risk of acquiring the infection exists only for residents and people visiting the affected place and having occupational or recreational activities in the river.

- Epidemiological investigations including the identification of cases and patterns of exposure will delineate the likely place(s) of infection, and molecular identification of the parasite will enable to assess the origin of the introduction(s);
- Malacological studies are required in the focus to identify the species involved as intermediate host, the snail distribution and population dynamics, and parasite presence in 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 for a long period, informing people who were exposed to the Cavu River during 2011 and 2013 summer months of their possible exposure may decrease their risk of developing complications;
- Informing physicians in the EU would increase the detection of possible uro-genital *Schistosoma* infections among travellers who visited the affected area in Corsica since 2011 and 2013, or other areas in the EU where a potential risk of transmission in case of introduction of the parasite in the environment exists;
- Co-ordinated 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

EU 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 Cavu river, Southern Corsica, France.

Consulted experts

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External: InVS: Harold Noel, Henriette de Valk

RKI: Christina Frank, Hendrik Wilking, Mirko Faber

André Théron: Head, WHO Collaborating Centre for Snail/Schistosome relationships, Perpignan, France

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Dr Jean-Luc Termignon: French Directorate for Public Health, France

Dr Richter: University of Düsseldorf, Germany

Disease background information

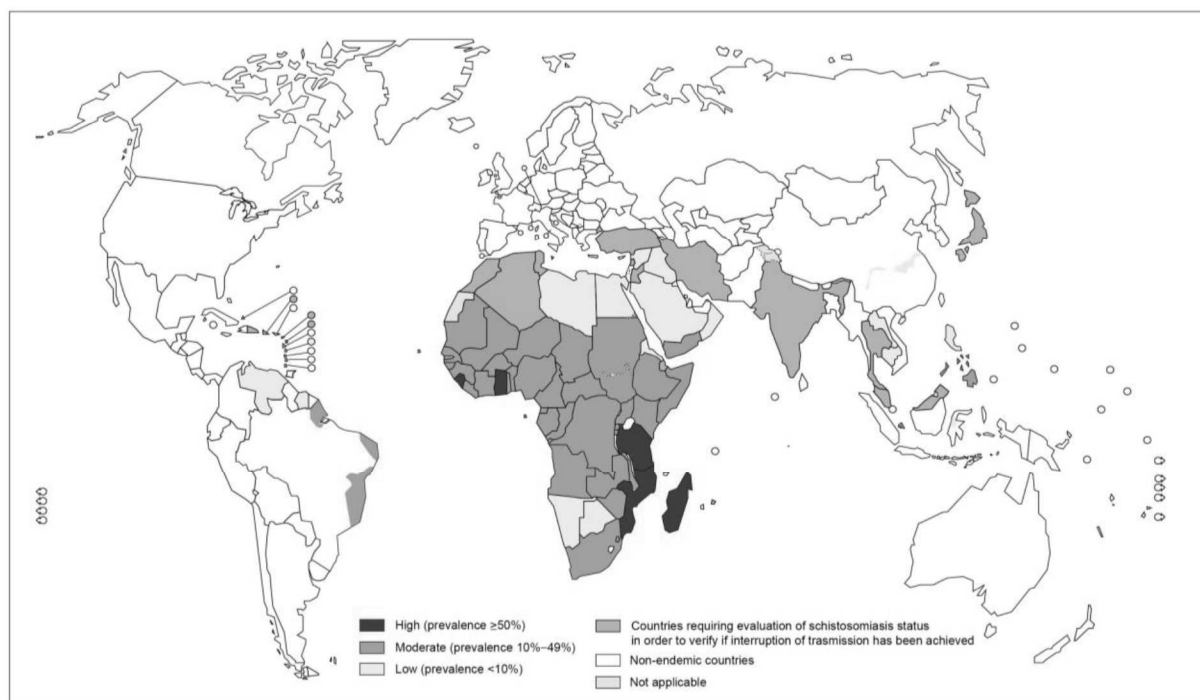
Schistosomiasis, or bilharzia, is a parasitic disease caused by trematode flatworms of the genus *Schistosoma*. The main schistosomes infecting humans are:

- *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;
- *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 which will reduce and prevent morbidity in the endemic countries with moderate to high transmission (Figure 1) [1].

The current rapid risk assessment focuses on *Schistosoma haematobium* identified as the pathogen involved in the reported cases.

Figure 1. Distribution of schistosomiasis in the world (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://qamapserver.who.int/mapLibrary/Files/Maps/Schistosomiasis_2012.png

Schistosoma haematobium infection

Distribution

Uro-genital schistosomiasis due to *S. haematobium* is an historical disease of Mesopotamia and the southern part of Mediterranean basin and was described in Egyptian mummies with calcified bladders, a characteristic of the uro-genital form of the disease. It was described in Sahelian region as Arabic doctors reported blood in the urine from caravaneers during the middle age and later during the 17th century.

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

As uro-genital schistosomiasis is based on parasitological cycle involving a human reservoir and an intermediate host, fresh water snails of the *Bulinus* genus, environmental conditions and social behaviours are determinants of geographical distribution of the disease. Schistosomiasis is not established in EU. However, cases are repeatedly identified among migrants and travellers returning from endemic areas. In 2010, 152 cases were reported by EuroTravNet 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 EU level. In the beginning of the 20th century a focus of *S. haematobium* was present in Algarve, Portugal [6].

Cycle

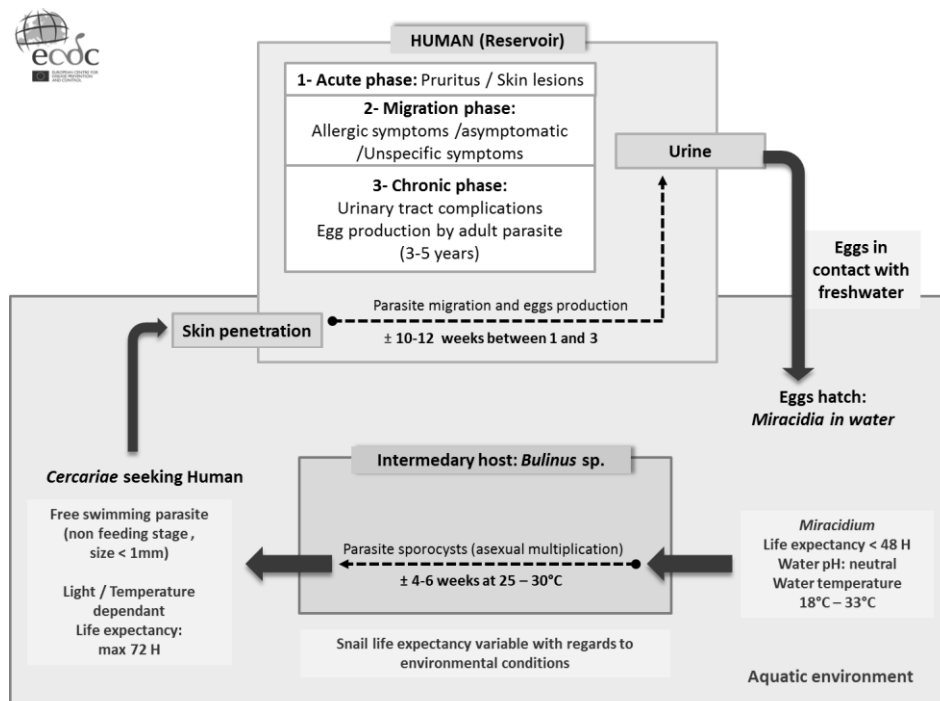
Human

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

The next phase is the invasion that corresponds to the maturation to adult parasite that might be accompanied with general allergic reactions. *Schistosoma haematobium* adult parasites are reaching 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 eliminated into the environment with urine. The time between exposure and excretion of eggs is estimated 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 fresh water releasing *miracidia* that will search actively for suitable freshwater snail as obligatory intermediate host. For *S. haematobium*, the intermediate host is a snail from the genus *Bulinus*. After an asexual multiplication stage in the snail, *cercariae* are shed by the snail. Four to six weeks, depending on the temperature (>20-25°C), are required from penetration by the *miracidium* to the shedding of *cercariae*. It cannot be achieved below a water temperature of 20°C, explaining the tropical and sub-tropical distribution of the disease. Cercarial shedding occurs mainly during the hot hours of daytime. A large number of *cercariae* are released when the local environment is favourable and search for humans by chemotaxis 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, river 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 widespread in western and eastern Africa. The northern limit of this species is known to be Portugal, Spain, Sardinia and Corsica, and the Near East [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 they can tolerate a wider temperature range depending on the species [15]. Snails have the capacity of surviving 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 prolonging the release of the parasite in the infected foci. Comprehensive studies are required to describe the 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 setting, the most affected age group is between 5–15-year-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 general immune-allergic reactions during the migration phase and early eggs deposition.

Only a small proportion of cases will progressively develop chronic symptoms more likely in people with heavy infections and recurrent exposure as seen in endemic setting. The infection can remain pauci-symptomatic for a long period but still causing 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 is releasing eggs, which migrate through the wall of the bladder and 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 individual 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 complication such as obstructive and fibrous lesions of uro-genital tract, chronic cystitis, calcification in bladder and renal impairment. *Schistosoma haematobium* is considered as risk factor of 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 valuable 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 due to the circadian pattern of egg excretion and samples proceeded with filtration and centrifugation methods. In low transmission settings, the number of examined slides should be increased to ensure technique's sensitivity. The test will be as well negative during the migration phase preceding eggs excretion.

Several widely used immunological methods are available for schistosomiasis antibody detection. The most important are the indirect immunofluorescence test (IFT), the indirect hemagglutination test (IHAT), and enzyme-linked immunosorbent assays (ELISA). The latter is the most commonly used test for the serological detection of schistosoma infection in particular to support the diagnosis in egg-negative cases. Rapid dipstick based on antigen detection is also used but with 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 are well developed for the diagnosis and offer a high sensitivity in the context of low parasitic load that can be observed in low transmission settings. These assays can be useful to identify species (species-specific DNA amplification), the origin of the parasite by comparison with international public gene sequence database, and to assess unique or multiple introduction in a transmission foci. The real-time polymerase chain reaction (PCR) is an alternative method for quantifying parasitic load. In addition, 28S ribosomal RNA gene PCR assay was used to define *Schistosoma* species among migrants and international travellers [17].

As haematuria (macro- or microscopic) is the main symptoms of *S. haematobium*, confirmation by reagent strips for micro-haematuria in urine is a criterion to orient further laboratory investigation in population-based studies. Heme dipstick diagnosis of *S. haematobium* infection has been developed and reviewed in recent publications. However the sensitivity decreases in population subgroups having lower parasitic load [18]. According to the authors, this test will be better adapted for monitoring community prevalence following implementation of population-based control of uro-genital schistosomiasis.

Diseases complication of uro-genital tract lesions can be investigated with ad hoc methods in function of patient symptomatology (such as echography, or cystoscopy).

Treatment

Praziquantel, an acylated quinoline-pyrazine, is the most widely used treatment active against all *Schistosoma* species. It has an effect on adult worm, acts within 1 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.

Transmission control is mainly done through population-based chemotherapy using Praziquantel. The 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].

The control targeting the intermediate host has been largely ceased. Snail control with molluscicides is expensive and logistically complex. The use of molluscicides in general has a number of disadvantages related to the need for repeated applications to ensure a long-term impact, the cost of the chemicals, the need for good supervision of the application and their adverse effects on non-target organisms, particularly fish.

Schistosomiasis can in principle be eliminated by behavioural changes, sanitation, and safe water supply, and population-based chemotherapy.

Event background information

On 23 April 2014, the parasitology unit of the university hospital of Toulouse notified to the InVS (Institut de Veille Sanitaire, France) a cluster of three cases of *Schistosoma haematobium* infection in one family, two children and their father. The family visited southern Corsica in second part of August 2013 where they were swimming in the fresh water river Cavu near Porto Vecchio. None of the cases reported an exposure to fresh water (swimming) in an area endemic for *Schistosoma haematobium*. The family visited the same area in 2011 and had contact with same fresh water site in the Cavu River. The infection of the father might have been evolving for a few years as he had unexplained macroscopic haematuria evolving since early 2012. One of his children presented with chronic bladder lesions related to *Schistosoma* infection. Therefore, initial infection for these two family members may have occurred in 2011.

Additional cases were detected among two other French families. One of the families, among which two cases were diagnosed, accompanied the first family on vacation in 2011 and 2013. The other family, among which one case was detected, accompanied the first family only in 2013. All families were staying at the same campground near the Cavu River in the second half of August 2013. All cases shared the same exposure to the natural swimming area (fresh water) in the Cavu. In total, among the three families (12 persons) six cases were confirmed through detection of *S. haematobium* eggs in urine and 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 fresh water in an endemic area.

The WHO Collaborating Centre for schistosomiasis of Perpignan, France, reported to InVS five additional cases of uro-genital schistosomiasis diagnosed in Germany in a family of six tourists. The travel history of the German and French families showed that they all had stayed in the same campground and 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. Eleven cases (six from France and five from Germany) of uro-genital schistosomiasis have been confirmed.

The epidemiological data points to 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 therefore, likely due to an exposure to Cavu river in 2011;
- one French case and the German cases were only exposed in during the second half of August 2013.

The notification of locally acquired *Schistosoma haematobium* infections implies the presence of the efficient intermediate host in a suitable environment. Historical accounts of the presence of *Bulinus* sp. snails in Southern Corsica date back to mid-1960's [19]. The northern distribution limit of *Bulinus truncatus* species is known to be Portugal, Spain, Sardinia and Corsica, and Near East [13,14,20]. Climatic conditions are likely to be favourable during the period June through September in Corsica for the development of *S. haematobium* in the fresh water snail and for the transmission to occur when people come in contact with infected water, should the parasite be introduced. Moreover, foci of *S. haematobium* existed in the Mediterranean region namely north of the Maghreb, sharing a closely related climatic profile [10].

Humans are the only reservoir of *S. haematobium* and people suffering from schistosomiasis can contaminate freshwater sources with their urine containing parasite eggs. Consequently, the parasite must have been introduced by an infected person living in or visiting the area.

With regard to this introduction 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, while it is known that infected snails are less viable. This is considered as an unlikely scenario, but a study of the current population of *Bulinus* in the river searching for infected snails could provide evidence to evaluate this scenario.
2. Scenario 2: multiple introductions from infected humans of *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 affected French and German family.
 - a. Scenario 2.a: different infected visitors introduced the parasite in the Cavu River early in the summer season (June) of 2011 and 2013. The transmission in 2013 cannot result from cycles initiated in 2013 by the first family infected in 2011, as the development of the parasite in the snail requires several weeks.

- b. Scenario 2.b: local infected residents have re-established the aquatic part of the cycle early in the summer season in 2011 and 2013. This scenario requires close contact between locally infected people and water leading to noticeable contamination of the environment.

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

Risk for the EU

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

- The area is a popular touristic destination during the summer months for recreational water activities. Persons who were exposed to the Cavu river in 2011 and 2013 are presenting a risk to have been infected.
- Given the existence of asymptomatic infections and the delay between infection and symptoms, additional cases of infections can be identified across the EU in the coming months among people exposed to the infested water between 2011 and 2013.
- This event confirms that the transmission of *Schistosoma haematobium* in Europe is possible upon introduction of the parasite in 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].

Conclusions

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 the same natural swimming area in southern Corsica without known exposure to fresh water in an endemic area of *Schistosoma*. This is the first locally acquired infections of *Schistosoma haematobium* in France. The disease is known to be very focal in its geographical distribution. Therefore, the risk of acquiring the infection exists only for residents and people visiting the affected place and having occupational or recreational activities in the river.

- Epidemiological investigations including the identification of cases and patterns of exposure will delineate the likely place(s) of infection, and molecular identification of the parasite will enable to assess the origin of the introduction(s);
- Malacological studies are required in the focus to identify the species involved as intermediate host, the snail distribution and population dynamics, and parasite presence in intermediate host. These factors define the focality and seasonality of transmission and are required to assess the receptivity of the area;
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- Informing physicians in the EU would increase the detection of possible uro-genital schistosomiasis infections among travellers who visited the affected area in Corsica since 2011 and 2013, or other areas in the EU where a potential risk of transmission in case of introduction of the parasite in the environment exists;
- Co-ordinated 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.

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