RAPID RISK ASSESSMENT

Local transmission of *Schistosoma haematobium* in Corsica, France

First update, 23 July 2015

Main conclusions and options for prevention and control

The autochthonous transmission of *Schistosoma haematobium* in Corsica in 2013 is a local public health event that highlights a potential risk for other parts of the EU. Therefore, there is a need to consider enhancing public and professional awareness and epidemiological surveillance for schistosomiasis.

This would entail the following:

- Identifying receptive areas through the conduct of malacological surveys in southern Europe, defining the optimal period of transmission and evaluating factors linked to the introduction of the parasite.
- Raising public awareness in receptive areas and providing information about the symptoms of schistosomiasis symptoms, its prevention and treatment.
- Reminding travellers to schistosomiasis-endemic areas about the risks of acquiring the disease and the means of avoiding it.
- Raising awareness among clinicians of the possibility of schistosomiasis among travellers presenting with unexplained chronic urinary symptoms that have engaged in previous years in recreational water activities in endemic countries or in receptive areas of southern Europe and particularly in the Cavu River.
- Developing an algorithm for testing patients in the EU, criteria for considering presumptive treatment of patients, and a case definition for public health surveillance in the EU.
- Thoroughly investigating cases to confirm the diagnosis by sending samples to reference laboratories and documenting time and location of bathing exposure.
- Informing the country of suspected exposure about the findings of the investigation of the cases for timely implementation of public health prevention and control measures.

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Internal decision to do an update, 29 June 2015.

Public health issue

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

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Disease background information

Schistosomiasis, or bilharziasis, is a parasitic disease caused by trematodes of the genus *Schistosoma*. Urinary schistosomiasis is a disease caused by *Schistosoma haematobium* of tropical and inter-tropical zones. The disease is endemic in several areas in Africa, Madagascar and the Middle East. The route of infection for humans is skin exposure to parasite-infested fresh water during routine occupational, recreational or domestic activities [1].

The parasitological transmission cycle starts when people with urinary schistosomiasis contaminate freshwater sources with urine that contains parasite eggs which hatch in the water under specific environmental conditions. The parasite penetrates specific snail intermediate hosts (*Bulinus* spp.) in order to pursue its life cycle. After maturation in the intermediate host, the parasite leaves the snail as an infective form (cercariae) that can penetrate the skin of a human host. Following penetration, cercariae migrate from the skin into the portal vein, where they reach adult stage, then mate and migrate to the venous plexus of the bladder and genitals and start producing eggs. The parasite eggs move gradually toward the lumen of the bladder and ureters where they are excreted into the environment with the urine. In their human hosts, adult *Schistosoma* live three to ten years, but in some cases can reach 40 years.

The disease caused by *S. haematobium* is characterised by chronic urogenital complications due to the presence of eggs in tissues [2]. In endemic areas, the infection in people can remain subclinical for a long period, but still causes progressive damage to the urogenital tract. The diagnostic standard for active urinary schistosomiasis is the detection of viable eggs in urine [1,4]. In 1999 WHO published surveillance standards defining a confirmed case from a non-endemic or low prevalence area as a person with eggs of *S. haematobium* in their urine [3]. Schistosomiasis infection is predominantly asymptomatic with a low parasite burden in most returning travellers who have acquired the infection abroad [5]. Therefore, the sensitivity of diagnosis of schistosomiasis due to *S. haematobium* among travellers by the detection of eggs in urine is known to be reduced compared to its use in endemic regions [5,6]. Serology is a useful method in this context to indicate an exposure to the parasite and to initiate presumptive treatment for travellers returning from endemic settings [7]. The performance of serological assays can vary (ELISA, indirect haemagglutination test, immunofluorescence) and results should be interpreted in the context of the clinical presentation and differential diagnoses, especially in the absence of a confirmatory test. New diagnostic tools such as antigen detection in urine and DNA detection are being developed, mainly in reference laboratories [4,7].

Urinary schistosomiasis, as for other forms of schistosomiasis, can be treated with praziquantel [1]. More detailed information about urinary schistosomiasis is available in the previous rapid risk assessment [8].

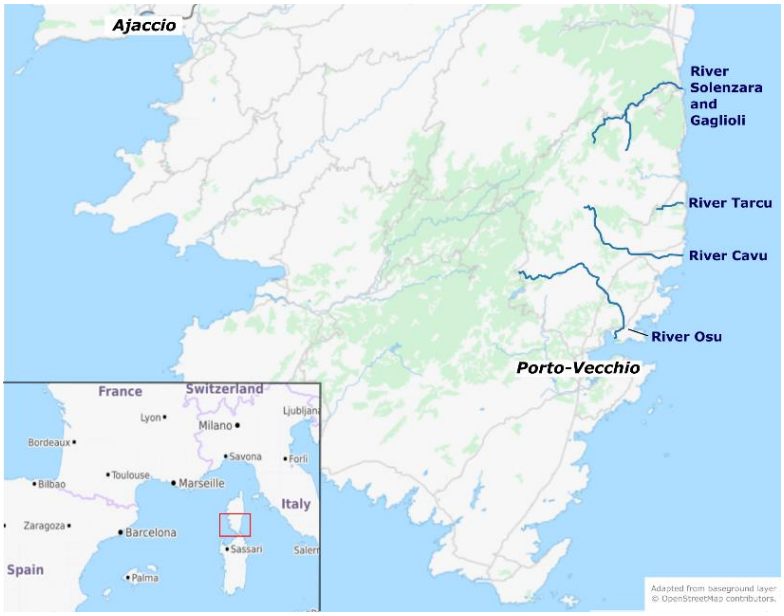
Event background information

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 *S. haematobium* infection affecting two siblings and their father. The French family visited southern Corsica during August 2013 and were bathing in fresh water from the Cavu River near Porto Vecchio, Corsica. No prior travel to endemic areas for schistosomiasis was reported [9]. The family was exposed to the same site of the Cavu River in 2011. The father presented with unexplained macroscopic haematuria in 2012, raising concerns about a possible exposure in 2011 (unconfirmed to date). Cases were detected among members of two additional French families having been exposed to the Cavu River while residing at the same campsite in 2013, and not having had exposure in endemic areas. In total, six cases were confirmed among the eleven members of the three families through the detection of *S. haematobium* eggs in urine and two were considered probable as presenting with positive serology only [9-11]. Five Germans from a family of six residents at the same campsite in 2013 were also diagnosed with urogenital schistosomiasis [12].

On 16 June 2014, the prefecture of South Corsica banned swimming in the river. The French Health Authorities initiated national screening using serology (haemagglutination, ELISA and western blot assay) and direct urine examination [13,14] for people exposed to the Cavu River in the summers of 2011 to 2013. Individuals with multiple exposures to river water in the area through recreational or professional activities were invited to visit their medical practitioners and to be part of the screening investigation. As a result, around 37 000 individuals were investigated for urogenital schistosomiasis through screening, compared to around 6 000 tests per year during previous years. As of 25 March 2015, 110 individuals presented with at least one positive serological test, 26 of which were confirmed by the identification of eggs in the urine [14]. Among the individuals for which the date of exposure is available, 62% reported bathing in the Cavu River during the first two weeks of August 2013 [15].

As of 14 April 2015, no cases had been identified with exposure in 2014 [14,15]. None of 3 534 *Bulinus* snails in the Cavu River tested in summer 2014 were found to be infected. In addition, 38 bathing sites in 19 other rivers in Corsica were investigated for the presence of snails. *Bulinus* snails were found in two bathing sites in Solenzara, two sites in Osu and one site in Tarcu. None were found positive for *Schistosoma* spp. The swimming ban in Cavu River was lifted on 4 June 2015 [15].

Figure 1. Situation map of southern Corsica



A study among 43 Italian travellers seeking medical screening after learning of the risk of acquiring schistosomiasis after freshwater exposure in the Cavu River was published in July 2015 [16]. The authors report 15 cases that they classify as follows, according to the table of the publication [16]:

- Five confirmed cases, defined on the basis of one positive western blot test, four of which were asymptomatic. All five tested negative for *S. haematobium* eggs in urine samples, and all five had negative indirect immunofluorescent antibody test results. Among these five cases, three reported an exposure in the Cavu River in 2013, one in 2011 only and one in 2014 only.
- Two probable cases, defined on the basis of one positive serological test (ELISA or IFAT), reported an exposure in the Cavu River over several years including 2013.
- Eight possible cases, defined on the basis of having signs or symptoms suggestive of schistosomiasis (i.e. urogenital symptoms), eosinophilia (>0.4 × 109 cells/L of blood), or both. Three reported multiple years of exposure in the Cavu River including in 2013. Five cases reported a single year of exposure in the Cavu River (one in 2011, three in 2012 and one 2014).

All 15 cases, considered possible, probable, and confirmed, received praziquantel as treatment.

In addition, another study published in July 2015 by a travel medicine network detected eleven cases among travellers returning from Corsica [17]. None reported exposure to fresh water in schistosomiasis-endemic areas. None of the patients experienced symptoms. One presented with microscopic haematuria. The authors acknowledged that confirmation either by a reference laboratory or by western blot was not done [6]. The authors classified cases as confirmed if presenting with positive results from two different serological testing methods and/or parasite eggs in urine; probable if presenting with a positive result from one serological assay; and suspected if presenting with a borderline result from one serological testing method.

The findings can be summarised as follows:

- Two confirmed cases: one reported an exposure in the Cavu River in 2013, one reported exposure in the Cavu River in 2007, 2009 to 2011 and 2014, but not in 2013.

- Six probable cases:
  - three of them declared an exposure in the Cavu River, of which one in 2013, one between 2011 and 2013, and one in July to August 2014 only;
  - the three remaining probable cases declared having been bathing in several different rivers (Osu, Gaglioli, Solenzara, and Restonica) but not in the Cavu River.
- Three suspected cases: two declared an exposure to the Cavu River, one in 2012 and one in 2014. The third case declared having being exposed in 2007 and 2012 to 2014 in several rivers (Gaglioli, Solenzara, and Restonica) but not in the Cavu River.

Molecular investigation of *S. haematobium* in Corsica

In April 2015, the ANSES (Agence nationale de sécurité sanitaire de l'alimentation de l'environnement et du travail) reported that molecular investigations of parasite eggs from infected patients in the Cavu River showed a large genetic diversity [14,15]. In July 2015, Boissier, et al. reported that 'molecular studies on the Corsican *Schistosoma* strain have shown that, in addition to pure *S. haematobium*, most of the eggs collected from patients are hybrids of *S. haematobium* and the livestock species *S. bovis*' [18]. Whether the hybrid strain has been imported or *S. haematobium/S. bovis* hybridisation has occurred locally remains unknown and should be investigated through further molecular analysis of the parasite eggs.

S. haematobium/S. bovis hybrids have been described in West Africa (Niger, Senegal) but the consequences for disease epidemiology, and how modified phenotypic characteristics might affect the transmission pattern and increase the range of intermediate reservoir hosts, are not well understood to date [30-32]. As *S. haematobium* and *S. bovis* can share intermediate hosts (e.g. *Bulinus* snails), it is important to consider the distribution of bovine schistosomiasis in this assessment of potential receptive areas. Bovine schistosomiasis was reported in Corsica throughout the 1960s [19]. In the 1960s and 1970s, bovine schistosomiasis was reported in Spain and Portugal [20], Sicily and Sardinia [21,22], the southern part of Corsica [19] and in some countries from the Maghreb and Middle East (Iraq, Israel) [14,19,23].

The hybrid eggs collected from patients infected in Corsica were found to infect the freshwater molluscan host, supporting the possibility of focal transmission under suitable temperature conditions in the natural environment, at least within one summer season (from Boissier J, unpublished, in [18]). None of the 30 goats and three cows tested in the summer of 2014 were found positive on serological tests or on stool examination for the presence of eggs [15]. None of the investigated local rodents were found to be infected either [14,15]. A larger study of sheep, goats and cattle is ongoing to assess the presence of enzootic *S. bovis* in Corsica.

ECDC threat assessment for the EU

The epidemiological findings from the cluster of cases [9] and results of the French screening survey confirm local transmission of *S. haematobium* in the Cavu River during the summer of 2013.

The two recently published studies of travellers with exposure in Corsica are in line with focal transmission in the Cavu River during 2013 but also raise questions about:

- the possibility of transmission in the Cavu River during years other than 2013, as transmission in the summer of 2011 or 2014 cannot be excluded based on the reported findings,
- the possibility of transmission in other rivers than the Cavu River, as some of the cases described as suspected and probable by Gautret, et al. reported exposure only to the Solenzara, Osu and Tarcu rivers in Corsica where *Bulinus* snails were found in some bathing places during a malacological survey in 2014 [14,15].

Further investigations and laboratory testing are required before these findings can be considered as conclusive evidence of additional transmission having occurred in other places or at other times than those reported in the Cavu River in 2013.

The risk of *S. haematobium* infection in the Cavu River is currently considered to be low in the light of the findings of investigations, including enhanced epidemiological surveillance and malacological surveys, which are ongoing [15]. However, the risk in Corsica would need to be re-evaluated in the event of a confirmation of transmission having occurred in other areas of Corsica or if the presence of the parasite in intermediate snail hosts is documented through the ongoing malacological surveys [14,15].

Given the existence of asymptomatic infections and the usual long delay between infection and symptoms, it is possible that additional cases in people previously exposed to the infested water of the Cavu River will occur.

Risk for the EU

The risk for the occurrence of the parasitic cycle in other areas of Europe is dependent upon the presence of receptive areas where the intermediate host is present in suitable environmental conditions, the introduction of the parasite, and exposure of humans.

The presence of *Bulinus* snails, the intermediate host, has been documented in Portugal, Spain, Italy in Sardinia [24-26], southern France and Corsica (historical records in [27]) and recently in two bathing sites of Solenzara River and two sites in the Osu and Tarcu rivers [14]. Historical foci of *S. haematobium* support the presence of intermediate hosts and were described in southern Europe, notably in Portugal and Maghreb countries [23,28-30]. Detailed information about currently receptive areas in the EU is not available, but historical data support the presence of the intermediate host in rivers in the above-mentioned areas. Suitable environmental conditions for the development of *S. haematobium* in the freshwater snail are likely found during the summer months in Mediterranean areas, coinciding with the high attendance period for recreational activities involving exposure to river water.

The introduction of the parasite into receptive areas may be associated with travellers who have acquired infection while in endemic areas, such as tourists, armed forces personnel returning from deployments or immigrants from endemic areas [27-29]. Recurrent seasonal foci of transmission of *S. haematobium* or *S. haematobium/S. bovis* could occur through the persistence of the parasite in intermediate hosts throughout the winter, or the reintroduction in receptive areas from an individual infected either abroad or locally in a previous season. In addition, there is a theoretical possibility that the hybrid parasite *S. haematobium/S. bovis* identified in Corsica could be reintroduced from an animal reservoir, although ongoing investigations have not yet substantiated this hypothesis.

Conclusions and options for prevention and control

The autochthonous transmission of *S. haematobium* in Corsica in 2013 is a local public health event that highlights a potential risk for other receptive areas of southern Europe. Therefore, there is a need to consider enhancing epidemiological surveillance for schistosomiasis in the EU.

This would entail the following:

- Identifying receptive areas through the conduct of malacological surveys in southern Europe, defining the optimal period of transmission and evaluating factors linked to the introduction of the parasite.
- Raising public awareness in receptive areas and providing information about the symptoms of schistosomiasis symptoms, its prevention and treatment.
- Reminding travellers to schistosomiasis-endemic areas about the risks of acquiring the disease and the means of avoiding it.
- Raising awareness among clinicians of the possibility of schistosomiasis among travellers presenting with unexplained chronic urinary symptoms that have engaged in previous years in recreational water activities in endemic countries or in receptive areas of southern Europe and particularly in the Cavu River.
- Developing an algorithm for testing patients in the EU, criteria for considering presumptive treatment of patients, and a case definition for public health surveillance in the EU.
- Thoroughly investigating cases to confirm the diagnosis by sending samples to reference laboratories and documenting time and location of bathing exposure.
- Informing the country of suspected exposure about the findings of the investigation of the cases for timely implementation of public health prevention and control measures.

References

1. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet. 2014 Jun 28;383(9936):2253-64.
2. Bamgbola OF. Urinary schistosomiasis. Pediatr Nephrol. 2014 Nov;29(11):2113-20.
3. World Health Organization. WHO Recommended Surveillance Standards. Second edition 1999. Available from: http://www.who.int/csr/resources/publications/surveillance/whocdscsrisr992.pdf.
4. Gomes LI, Enk MJ, Rabello A. Diagnosing schistosomiasis: where are we? Rev Soc Bras Med Trop. 2014 Jan-Feb;47(1):3-11.
5. Meltzer E, Schwartz E. Schistosomiasis: current epidemiology and management in travelers. Curr Infect Dis Rep. 2013 Jun;15(3):211-5.
6. Clerinx J, Van Gompel A. Schistosomiasis in travellers and migrants. Travel Med Infect Dis. 2011 Jan;9(1):6-24.
7. Utzinger J, Becker SL, van Lieshout L, van Dam GJ, Knopp S. New diagnostic tools in schistosomiasis. Clin Microbiol Infect. 2015 Jun;21(6):529-42.
8. European Centre for Disease Prevention and Control. Rapid risk assessment: Local transmission of Schistosoma haematobium in Corsica, France – 16 May 2014. Stockholm: ECDC; 2014. Available from: http://ecdc.europa.eu/en/publications/Publications/schistosoma-haematobium-risk-assessment-France-Germany.pdf.
9. Berry A, Mone H, Iriart X, Mouahid G, Aboo O, Boissier J, et al. Schistosomiasis haematobium, Corsica, France. Emerg Infect Dis. 2014 Sep;20(9):1595-7.
10. Patard PM, Debuisson C, Mouttalib S, Berry A, Garnier A, Galinier P, et al. [Urinary schistosomiasis contracted in a child in Corsica]. Archives de pediatrie: organe officiel de la Societe francaise de pediatrie. 2015 Mar;22(3):327-8.
11. Brunet J, Pfaff AW, Hansmann Y, Gregorowicz G, Pesson B, Abou-Bacar A, et al. An unusual case of hematuria in a French family returning from Corsica. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. 2015 Feb;31:59-60.
12. Holtfreter MC, Mone H, Muller-Stover I, Mouahid G, Richter J. Schistosoma haematobium infections acquired in Corsica, France, August 2013. Euro Surveill. 2014;19(22).
13. Ministère des Affaires sociales dlSedDdf. Recommandations pour les personnes potentiellement exposées à la bilharziose après une baignade dans la rivière Cavu (Corse du sud). [Internet]. Paris2014 [cited 2014 June 16]. Available from: http://www.sante.gouv.fr/bilharziose-professionnels-de-sante.html.
14. Agence nationale de sécurité sanitaire de l'alimentation de l'environnement et du travail (ANSES). Note d'appui scientifique et technique de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail relatif aux critères de levée d'interdiction et d'autorisation de la baignade dans la rivière du Cavu (Corse du Sud) suite à la survenue de cas de bilharziose uro-génitale (Saisine n° 2015-SA-036). Maisons-Alfort2015. Available from: https://www.anses.fr/fr/system/files/EAUX2015sa0036.pdf.
15. Agence Régionale de Santé Corse. Dossier de Presse: Bilharziose Urogénitale Rivière du Cavu (Communes de Conca et de Zonza) 2015. Available from: http://www.ars.corse.sante.fr/fileadmin/CORSE/documents_presse/dossier_de_presse/Dossier_Presse_Bilharziose_Uro-genitale_4_juin_2015__V2_.pdf.
16. Beltrame A, Lorenzo Z, Gianluca Z, Federico G, Andrea A, Valentina M, et al. Schistosomiasis Screening of Travelers from Italy with Possible Exposure in Corsica, France. Emerging Infectious Disease journal. 2015;21(10).
17. Gautret P, Frank PM, Frank von S, Camilla R, Michael L, Kristina Van De W, et al. Local and International Implications of Schistosomiasis Acquired in Corsica, France. Emerging Infectious Disease journal. 2015;21(10).
18. Boissier J, Moné H, Mitta G, Bargues MD, Molyneux D, Mas-Coma S. Schistosomiasis reaches Europe. The Lancet Infectious Diseases.15(7):757-8.
19. Calavas D, Martin PM. Schistosomiasis in cattle in Corsica, France. Emerg Infect Dis. 2014 Dec;20(12):2163-4.
20. Martín VR. Contribución al estudio epizootiológico de la esquistosomiasis bovina ("Schistosoma bovis") en la provincia de Salamanca. An Fac Vet León. 1972; 18: 151–214.
21. Nelson GS, Amin MA, Saoud MF, Teesdale C. Studies on heterologous immunity in schistosomiasis. I. Heterologous schistosome immunity in mice. Bull World Health Organ. 1968;38(1):9-17.

22. Sadun EH. Intradermal and fluorescent antibody tests on humans exposed to Schistosoma bovis cercariae from Sardinia. Bull World Health Organ. 1962;27:810-4.

23. World Health Organization Eastern Mediterranean Region. Inter-country meeting on strategies to eliminate schistosomiasis. WHO; 2007. Available from: http://www.who.int/schistosomiasis/resources/EMRO_report_Schistosomiasis.pdf.

24. IUNC. The IUCN red list of threatened species. *Bulinus truncatus*: International Union for Conservation of Nature; [13 May 2014]. Available from: http://www.iucnredlist.org/details/156053/0.

25. Perez-Quintero JC, Bech Taberner M, Huertsa Dionisio L. [Freshwater Molluscs of Huelva Province (SW Spain)]. Iberus. 2004;22(2):19-31.

26. Welter-Schultes F. European non-marine molluscs, a guide for species identification. Gottingen: Planet Poster Editions; 2012.

27. Doby JM, Rault B, Deblock S, Chabaud A. [Snails and bilharziasis in Corsica. Distribution, frequency and biology of "Bulinus truncatus"]. Ann Parasitol. 1966 Jul-Aug;41(4):337-49.

28. Fraga de azevedo J, Colaco A. Sobre a morfologia do schistosoma haematobium de Portugal. Anais Inst Med Tropical. 1950;7(7-17).

29. Barkia H, Barkia A, Nhammi H, Belghyti D. La schistosomiase au Maroc: de sa découverte à l'après-élimination. Eastern Mediterranean Health Journal. 2011;17(3):250-6.

30. World Health Organization. Schistosomiasis - Country maps [Internet]. WHO; 2014. Available from: http://www.who.int/schistosomiasis/epidemiology/global_atlas_maps/en/.