

Opinion

Emerging Schistosomiasis in Europe: A Need to Quantify the Risks

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The recent recurrent outbreaks of urogenital schistosomiasis in the south of Europe were unanticipated and caught scientists and health authorities unprepared. It is now time to learn lessons from these outbreaks and to implement concrete procedures in order to better quantify the risks and prevent future outbreaks of schistosomiasis in Europe. In this context, we propose a reflection on the factors that currently hamper our ability to quantify these risks and argue that we are incapable of predicting future outbreaks. We base our reflexion on an ecological two-step filter concept that drives host-parasite interactions, namely the encounter and the compatibility filters.

Schistosomiasis Outbreaks in Europe

Global changes, including both natural and anthropogenic environmental modifications, promote the spread of exotic pathogens worldwide and disease outbreaks [1]. In particular, with the ongoing rise in temperature and the intensification of human activities, it is expected that tropical and subtropical vector-borne diseases will expand to higher latitudes [2–6]. So far, concrete cases of autochthonous transmission of tropical infectious diseases in temperate areas remain scarce. The most alarming examples of pathogen geographical range expansions are the recent cases of locally acquired arthropod-borne diseases such as dengue, malaria, and chikungunya in southern Europe [7–10]. Climate change and trade of car tyres promoted the establishment of the mosquito vector species around the Mediterranean Sea, hence allowing the parasites to complete their life cycles and emerge locally. To face the risk of arthropod-borne diseases, the European Union (EU) established the VBORNET network in 2010. This One Health consortium mobilized both entomological and public health specialists to assist the European Centre for Disease Prevention and Control (ECDC). This network was completed by the VectorNet project in 2014 to include animal disease agents. Today, up-to-date distribution maps of mosquitoes, ticks, and sandflies are freely available on the website of the ECDC. In addition to the risk map, the ECDC has published guidelines for the surveillance of native and invasive mosquitoes in Europe [11,12]. These resources paved the way to concrete and applied operational processes for a better surveillance of mosquitoes and to prevent future outbreaks.

For several reasons, the risks of snail-borne diseases in Europe have been overlooked so far. First, until very recently, freshwater ecosystems received less ecological attention than terrestrial systems [13]. Second, the expansion, and ultimately the establishment, of snail intermediate host species that have coevolved with parasites from tropical countries to Europe is expected to be limited because of the low dispersal ability of freshwater snails. However, in March 2014, clusters of human urogenital schistosomiasis cases, transmitted through freshwater *Bulinus* snails, were simultaneously diagnosed in French and German hospitals [14–16].

Trends

Global changes promote the establishment and spread of infectious diseases worldwide. Several tropical and subtropical vector-borne diseases have recently emerged in more temperate geographical areas, demonstrating that they need further considerations.

An autochthonous urogenital schistosomiasis outbreak has recently been identified in Southern Europe (Corsica, France). The causative parasitic agent is a hybrid between a human-specific and a livestock-specific schistosome species.

Quantifying the emerging risk of vector-borne disease requires knowledge of the ecological characteristics of parasites and their potential vectors as well as of the interactions between protagonists in Northern latitudes.

Host-parasite interactions are driven by an ecological two-step filter concept (the encounter and the compatibility filters). Global changes and hybridization may affect both filters, hence hampering our ability to quantify the risk of future emergence. Thus, we are still incapable of predicting future outbreaks, and new tools need to be developed.

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These patients had never visited a *Schistosoma haematobium*-endemic country (i.e., Africa, Arabian Peninsula), but all the patients had spent their holidays in Corsica in August 2013. Corsica is a favourite destination for tourists from Europe and overseas, and more specifically during summer. All the infected individuals had been in contact with the Cava River (southern Corsica) which is famous for its crystalline and warm natural pools. Subsequently, the INVS (Institut National de Veille Sanitaire) and the ECDC published a rapid risk assessment. Following a massive campaign for diagnosis in April 2015, more than 100 further cases which had contracted the disease during summer 2013 were reported in France. Surprisingly, after intensive screening for the presence of the parasite, no *Bulinus truncatus* snails from the Cava river were found to be infected with schistosomes, highlighting the difficulty of detecting the parasite in the field [17]. Moreover, no potential animal reservoir host was found in the vicinity of the river [17]. However, during the summer of 2015 a new case of acute endemic schistosomiasis was acquired in Corsica, indicating that transmission is persisting locally and pointing out the risk for further infections [18]. In line with this outbreak, the rapid risk assessment of the ECDC stated: “*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.*”. Contrary to arthropod-borne diseases, the emergence of schistosomiasis in Europe was unexpected, and both the scientific community and health authorities were caught unprepared. We discuss here the reasons why we are currently incapable of predicting future outbreaks of this neglected but severe tropical disease in Europe and address several directions that would greatly improve our ability to better evaluate these risks. We base our reflection on the fundamental two-step filter concept, including the encounter and the compatibility filters, as first proposed by Louis Euzet and Claude Combes in the 2000s [19,20] and examine how global changes are expected to alter these filters and hence increase the risk of schistosome parasites establishing and spreading throughout Europe.

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Host-Parasite Association Filters

Host-parasite interactions can be analysed through the concept of association filters. In all systems formed by two organisms, natural selection tends to maximise their fitness independently [21]. In a host-parasite couple, a filter can be seen as a virtual phenotype defined by both the genome of the parasite and the genome of the host [19]. At the parasite level, filters need to be open to accomplish their life cycle, therefore natural selection will tend to select genes allowing both the encounter (encounter filter open) and the survival of the parasite (compatibility filter open) associated with its host. On the contrary, hosts will tend to close these two filters, and natural selection will select genes allowing them to avoid (encounter filter closed) and kill (compatibility filter closed) the parasites. When these filters are synchronously opened in a particular area, and for a particular host-parasite association, there is a potential risk for disease emergence. Evaluating the status of these two filters (open or closed) offers the opportunity to quantify the risk for schistosomiasis emergence in Europe.

Encounter Filter

The encounter requires spatial and temporal overlap between the host and the parasite. Quantifying the risk of emergence and spread of schistosomes in Europe thus partially depends on our knowledge concerning (i) the geographical distribution of all potential intermediate snail hosts for the parasites to complete their life cycle locally, and (ii) the dispersion of parasites through their definitive hosts and in particular humans.

What Do We Really Know about the Distribution of Schistosome Intermediate Snail Hosts in Europe?

The answer is: very little. Among the 2090 freshwater snail species for which the geographical range was documented in Europe, *Planorbis metidjensis* and *B. truncatus* are intermediate

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