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# Evidence of autochthonous transmission of urinary schistosomiasis in Almeria (southeast Spain): An outbreak analysis

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A R T I C L E I N F O

*Keywords:*
Schistosomiasis
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*Schistosoma haematobium*
Urogenital schistosomiasis
*Bulinus truncatus*

A B S T R A C T

*Background:* Schistosomiasis is endemic in 78 countries belonging to tropical and subtropical areas. However, autochthonous transmission of urogenital schistosomiasis was reported in Corsica (France) in 2013. We present evidence of autochthonous transmission of urogenital schistosomiasis in Almería (Spain) in 2003.
*Methods:* Description of the outbreak in farmers and subsequent epidemiological studies aimed at searching for *Bulinus* snails and their genotypic characteristics.
*Results:* The outbreak affected 4 farmers out of a group of 5 people who repeatedly bathed that summer in an irrigation pool in the area. Two of them presented macroscopic hematuria with bilharziomas, showing the presence of *Schistosoma* eggs in bladder biopsies. Two others were asymptomatic but the serology for schistosomiasis was positive. In 2015, the presence of the vector *Bulinus truncatus* was demonstrated in Almería in water collections of appropriate characteristics. DNA sequencing proving that local *B. truncatus* species were base-to-base identical to *B. truncatus* from Senegal.
*Conclusions:* We present a new outbreak of autochthonous transmission of urogenital schistosomiasis in Europe. Although no new cases of autochthonous transmission have been reported, some other cases may have occurred at that time or later on and be unnoticed as many cases of schistosomiasis are asymptomatic or present mild and unspecific symptoms.

## 1. Introduction

Schistosomiasis is a parasitic disease caused by several *Schistosoma* species that show different host specificity. Some species only infect humans, such as *S. haematobium*, which causes urogenital schistosomiasis, some others affect both humans and animals, such as *S. japonicum* in Asia, and others only animals, and therefore, do not apparently present medical interest. There are an estimated 230 million infected people in the world, 93% living in sub-Saharan Africa. In 2013, the existence of autochthonous transmission of urogenital schistosomiasis was reported in Europe (Cavu river, Corsica, France), with transmission continuing until at least 2017, and a total of more than 100 cases reported [1–4]. Indeed, it seems that is no longer restricted only to the Cavu River [5]. In Corsica, as well as in other areas of southern Europe, the presence of an intermediate host, the snail *Bulinus truncatus*, was already known [6]. The parasites implicated in the human cases infected in Corsica were both *S. haematobium* and, surprisingly, *S. bovis*, a parasite typically affecting cattle, as well as hybrids between the two species, *S. haematobium* and *S. bovis*. The genetic molecular analysis located the geographical origin of the implicated parasites in Senegal [2,7].

The Poniente area is an administrative and health region located in the province of Almeria, in southeast Spain (Fig. 1). It holds a population close to 300,000 inhabitants, with a migrant share of 21%, many of them coming from sub-Saharan countries to work in horticultural greenhouses. Schistosomiasis is one of the most prevalent diseases diagnosed among the sub-Saharan migrant population living in the region [8,9]. The presence of *Bulinus truncatus* has recently been demonstrated in this area [10,11] and experimental studies on susceptibility have shown that

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they are capable of being infected by pure strains of *S. haematobium* of African origin and of releasing furcocercariae like other Corsican *B. truncatus* [2,12].

The aim of this study is to present the evidence of autochthonous transmission of urinary schistosomiasis in 2003 in the Poniente area, affecting four people out of a group of 5 Spanish farmers who bathed in an artificial irrigation pool used to water crops growing in the surrounding greenhouses. Two of them developed a clinical disease and sought medical attention between 2004 and 2005. This outbreak was not discovered and fully investigated until 2019 when case number 1 consulted because of infertility.

## 2. Methods

### 2.1. Case definition

The diagnosis of confirmed urogenital schistosomiasis relies on the detection of parasite ova in urine or biopsy samples from bladder. Patients with positive serology but no direct parasitological findings and without laboratory or radiological signs suggestive of schistosomiasis are considered as possible schistosomiasis cases.

### 2.2. Epidemiologial investigation

#### 2.2.1. Case 1

A 38-year-old male attended the Urology clinic of our hospital in 2019 because of infertility. A previous diagnosis of urinary schistosomiasis in 2005 was found in his old medical records. It was not until 2015 that the presence of *Bulinus truncatus* was confirmed in the Poniente area of Almeria [10] and thereupon a risk assessment note was issued by the Epidemiology Department warning of the risk of autochthonous transmission of schistosomiasis in our area. Consequently, it was decided to review the entire episode.

The patient is a native farmer who was 24 years old in November 2005 when he presented to the Emergency department with a one-month history of recurring terminal gross hematuria. There were no other urinary symptoms nor fever. Laboratory tests at that time showed a white blood cell count of 11,940/mm$^3$ with a differential count of 2734/mm$^3$ (22.9%) eosinophils. Renal function and coagulation tests were within normal range. The urinary sediment was abnormal, with 20–30 red blood cells and 30–40 white blood cells per field. He was prescribed amoxicillin-clavulanate and referred to the Urology outpatient clinic. New laboratory tests confirmed the blood eosinophilia and an ultrasound examination revealed a bladder neoformation. Transurethral resection of a thick papillary tumor with whitish spots was performed one month later. The pathological findings were described as chronic eosinophilic granulomatous cystitis with the presence of Schistosoma ova.

The patient was treated with a single 40 mg/kg dose of praziquantel and hematuria resolved within a few days. In subsequent visits, the disappearance of hematuria and of the bladder tumor was confirmed and no parasites were found in the several samples of urine analyzed. In April 2006, the blood test still showed moderate eosinophilia (1012 eosinophils/mm$^3$) but it disappeared later on (Fig. 2). End of follow-up was then decided because of resolution of the condition. In the current visit of 2019, blood tests showed a white cell count of 7900/mm $^3$ and 340 eosinophils/mm$^3$ (4.3%). The urinary sediment was normal, no parasites were found in urine and Schistosoma serology (SCHISTOSOMA ICT IgG-IgM ®, LDBIO Diagnostics) was positive. X-ray of the abdomen and abdominal and bladder ultrasound examination showed no abnormal findings. Regarding the patient's study of infertility, a testicular ultrasound examination showed a bilateral grade I varicocele and small epididymal cysts, the largest measuring 11 mm. The study of the semen revealed *asthenospermia* but searching for Schistosoma ova was not performed. The patient and his wife were referred to a fertility clinic.

Former laboratory tests performed in Primary Care were reviewed showing no eosinophilia in the blood tests from 2002 and March 2003 (Fig. 2). Soon afterwards, in September 2003, mild eosinophilia (425 eosinophils/mm$^3$) developed, increasing to moderate in February 2004 (total white blood cell count 9270/mm$^3$, eosinophils 1048/mm$^3$,11.3%) and accompanied by the presence of microscopic hematuria in the urinary sediment (15–20 red blood cells/field).

The patient's medical history was irrelevant but for a honeymoon trip to Egypt from the 4th to the 11th of July 2005. He bathed in the swimming pool of a cruise-ship traveling along the Nile River. He also visited the Aswan Dam but had no contact with water. The patient did not present dermatitis or any other symptom suggesting acute schistosomiasis during the trip or upon return. Two years before, in the summer of 2003, while working in intensive greenhouse farming in the Poniente area, he reported having bathed several times in an irrigation pool with

**Fig. 1.** Location of the Poniente area (Almería, Spain).

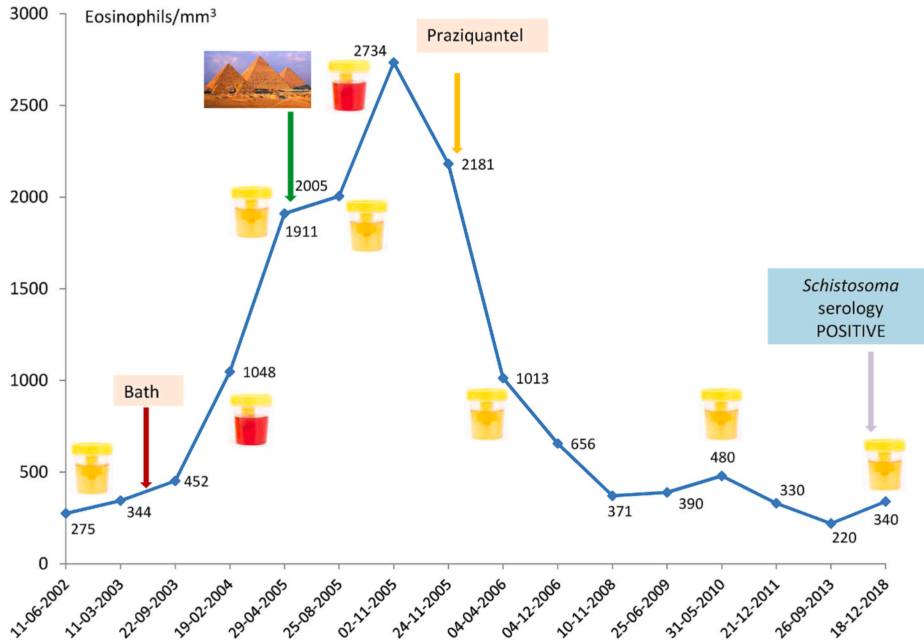


**Fig. 2.** Evolution of laboratory findings (eosinophilia and hematuria) of patient number 1.

4 other workers, without apparent consequences.

Following Case 1 visit in 2019, the other 4 workers were contacted and the epidemiological investigation was completed.

### 2.2.2. Case 2

Another male farmer, who was 29 years old in 2003, confirmed that he belonged to the group of young people who bathed in the irrigation pool in the summer of 2003. After 2–3 months, he began with recurring terminal gross hematuria and dysuria. He consulted at the Emergency department in November 2004 because of macroscopic hematuria. Laboratory tests (Fig. 3) showed a total white cell count of 8200/mm$^3$ (eosionophils 328/mm$^3$, 4%), with normal renal function and coagulation tests. Urinalysis test showed >100 red blood cells/field. He was referred to the Urology outpatient clinic where the ultrasound examination found a bladder tumor. In December, transurethral resection described a prominent 3 cm sessile lesion with whitish spots suggesting schistosomiasis and sited in the urinary bladder fundus. Several samples where obtained with pathological findings being reported as chronic eosinophilic granulomatous cystitis with the presence of Schistosoma ova. The patient's medical history was irrelevant with no trips to schistosomiasis endemic regions. He had just traveled to Russia that very same year of 2003. A single 40 mg/kg dose of praziquantel was administered and symptoms subsided after 2 weeks approximately.

When asked in 2019, he reported that he had been asymptomatic since then. The patient was advised to have several laboratory tests done, including schistosomiasis serology and ultrasound examination, but he never did and neither came back to the scheduled appointment for follow-up.

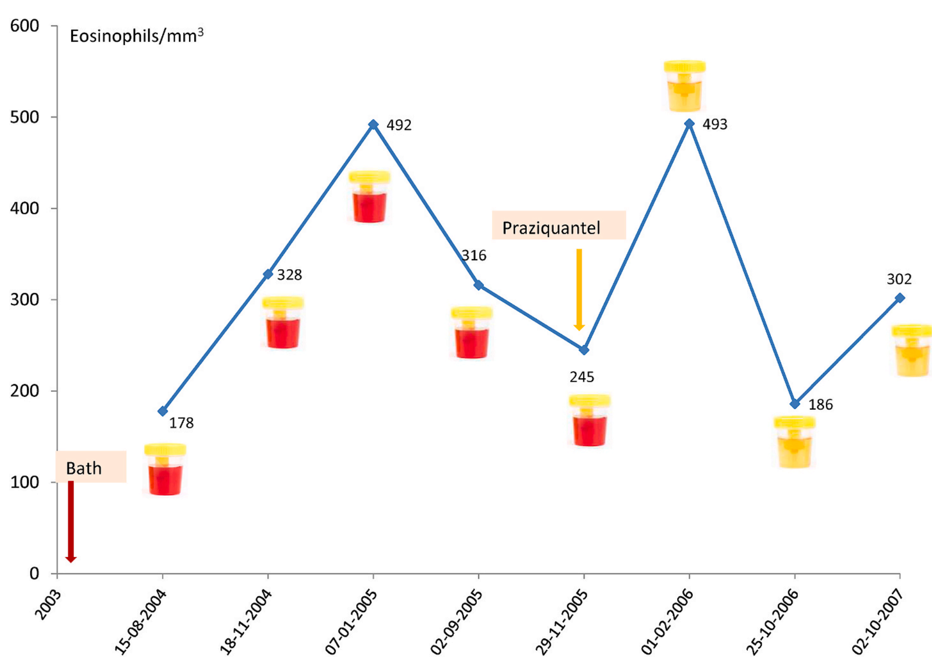


**Fig. 3.** Evolution of laboratory findings (eosinophilia and hematuria) of patient number 2.

### 2.2.3. Case 3

The third patient was another male, who was 24 years old in 2003. He confirmed that he was part of the group but he did not remember well if he actually bathed in the irrigation pool or not. He had been feeling well at all times, with no symptoms suggesting schistosomiasis. He reported no trips outside Spain. There were no available laboratory tests in his medical records until March 2014, showing a normal urinary sediment and a total white blood cell count of 6550/mm$^3$ with 260/mm$^3$ eosinophils.

At the present time, new tests where performed showing 6300 white cells/mm$^3$ (eosinophils 330/mm$^3$, 5.2%), a normal urinary sediment, no urine parasites, and a positive Schistosoma serology (ICT). X-ray of the abdomen and abdominal and bladder ultrasound examination showed no abnormal findings. A single 40 mg/Kg dose of praziquantel was then administered. This patient was considered as possible schistosomiasis case.

### 2.2.4. Case 4

The fourth farmer was 19 years old in 2003. He remembered having bathed several times in the irrigation pool but had always been asymptomatic after that. He had never traveled outside Spain. A single blood test was available in his medical records, without eosinophilia (eosinophils 150/mm$^3$, 1.4%). At the present time, the tests performed showed 11,900 white cells/mm$^3$ (eosinophils 230/mm$^3$, 1.9%), a normal urinary sediment and no urine parasites, but a positive Schistosoma serology (ICT) as well. X-ray of the abdomen and abdominal and bladder ultrasound examination showed no abnormal findings. A single 40 mg/Kg dose of praziquantel was administered. This patient was also considered as possible schistosomiasis case.

### 2.2.5. Case 5

The fifth farmer was the youngest, being 17 years old in 2003. He also remembered bathing in the irrigation pool several times that summer. He had presented no symptoms suggesting schistosomiasis nor had traveled abroad. In his medical records, laboratory tests from 2008 to 2009 showed no eosinophilia and the urinary sediment was normal. In 2019, the tests showed eosinophils 230/mm$^3$, 3.8%, a normal urinary sediment, no urine parasites, and a negative Schistosoma serology (ICT). X-ray of the abdomen and abdominal and bladder ultrasound examination showed no abnormal findings. The patient was discharged without any specific treatment.

## 2.3. Ethics statement

This study has been approved by the Ethics Committee of Almería (protocol PUB_21_21).

## 2.4. Outbreak control measures

Different types of freshwater collections are present in the area where our study takes place, including natural ponds and lagoons receiving subterraneous water running on phreatic layers descending from the northern Sierra Nevada mountainous chain, and numerous artificial ponds and pools used as water reservoirs for the irrigation of surrounding intensive greenhouse farming. The studies performed so far allowed for the detection of *Bulinus truncatus* in those bodies of water with appropriate characteristics (temperature: 16.0–34.6 °C; conductivity: 320–1250 μS). One point worth mentioning is the presence of small ruminant livestock (sheep, goats), which may play a role in the passive local dissemination of the bulinid snails from one natural water collection to another. Sheep and goat tracks and faecal samples are usually found on the muddy ground around these natural lagoons and ponds. Moreover, several birds well known as frequenters of water collections, may also be involved in the dissemination of the snails, including also to the aforementioned artificial ponds. Bird species present in the area comprise the Common coot *Fulica atra* (Linnaeus, 1758), the Little egret *Egretta garzetta* (Linnaeus, 1766), the Gray heron *Ardea cinerea* (Linnaeus, 1758), and the Black-winged stilt *Himantopus himantopus* (Linnaeus, 1758). Results of preliminary eDNA studies presently under way confirm these assumptions of snail exchange between different local water collections. Additionally, among the present studies to assess the schistosomiasis transmission potential at local level, DNA sequencing results should be highlighted, as indeed the mtDNA *cox*1 marker of the *B. truncatus* specimens from this area proved to be base-to-base identical to *B. truncatus* from Senegal, i.e. the same geographical African origin of the schistosomes introduced in Corsica.

# 3. Discussion

We present in this paper the evidence of autochthonous transmission of urinary schistosomiasis happening in southern Spain in 2003 by describing an outbreak that affected four people. No other new cases have been detected since then. The special conditions of the Poniente area in the province of Almeria, where a big sub-Saharan migrant community lives and where the presence of the intermediate host, the *Bulinus truncatus* snail has been demonstrated [10], made it possible for this particular outbreak of local schistosomiasis to happen.

Two outbreaks of autochthonous transmission of schistosomiasis have been reported in Europe in the last century. The first one was an outbreak of urogenital schistosomiasis described in southern Portugal between 1920 and 1967. It was thought to be probably due to the introduction of the parasite by people who traveled from Angola, where schistosomiasis is endemic, to Portugal. Experimental studies demonstrated the compatibility of local strains of aquatic snails and some African strains of *S. haematobium* [13]. Much more recent is the outbreak of urogenital schistosomiasis that was reported in Corsica island (France) in 2013, affecting more than 100 people [2,5] and persisting for several years. Although the possibility of a zoonotic transmission cannot definitely be ruled out, investigational data point towards humans being at the origin and maintenance of the local transmission. The most likely hypothesis is that local people initially infected in 2013 re-contaminated the river during subsequent summers [4], however potential episodic reintroductions by traveling Senegalese has to be considered as well. After the Corsican outbreak there is no evidence of new sources of schistosomiasis autochthonous transmission in Europe. Nevertheless, active epidemiological surveillance continues in areas where the snail *Bulinus* spp. is present, like Spain, Portugal, Greece, Cyprus, Corsica and Sardinia [11,14,15].

Since no parasitological samples were kept, it was not possible to identify in our series whether the parasites were pure species (*S. haematobium* or *S. bovis*) or hybrids, as happened in Corsica. In Spain the presence of *S. bovis* has also been described [16]. On the other hand, Schistosome eggs are complex structures playing a central role in the diagnosis of the disease. A new standardised methodology, based on geometric morphometric analysis, capable of discerning morphologically close eggs, as is the case inside the haematobium group, was applied to the eggs eliminated by migrants residing in our area. A great morphoanatomic variability was observed providing different phenotypic patterns, (typical and non-typical *S. haematobium* eggs) compatible with both pure forms of *S. haematobium* as well as with even potential intermediate forms [17] This phenomenon has not only been reported in Corsica but also in several West African countries [2,7], among them Senegal and Mali, homeland of many of the African migrants settled in our province.

It has been demonstrated experimentally that *B. truncatus* from Mediterranean areas (captured in our area in Spain and in Corsica), both uninfected and infected with pure *S. haematobium* (African origin) and *S. haematobium-bovis* hybrid forms (Corsican origin) can survive at low temperatures (4 °C and 8 °C) for several weeks and that shedding of viable cercariae starts over again when returned to optimal temperatures [12]. These results indicate that the snails are locally adapted to non-tropical climates but also that schistosomes can overwinter under temperate climates, and therefore, the risk of new outbreaks in the Mediterranean region is more than a theoretical threat. Although none of the *B. truncatus* specimens sampled in freshwater collections of the Poniente area was so far showing infection by human schistosomatids, aspects such as cercarial shedding under controlled laboratory conditions and their morphological and genetic characterization are part of a wide multidisciplinary project presently ongoing in that area.

So, to the present, no new cases of autochthonous transmission of urogenital schistosomiasis have been reported and thus, we may suppose that the outbreak described here was an isolated phenomenon of local transmission. Nevertheless, some other cases may have occurred at that time or later on and be unnoticed. Owing to the fact that a significant percentage of patients with schistosomiasis are asymptomatic or do only present mild and unspecific symptoms, we cannot rule out the existence of cases who did not seek medical attention or whose symptoms were wrongly attributed to other more common conditions. Actually, 66% of the people affected in the Corsican outbreak remained asymptomatic [18].

With regard to the infertility problem of patient number 1, it is widely demonstrated the association between schistosomiasis and both male and female infertility. Male infertility is related to epididymitis, prostatitis, hematospermia and/or to secondary infections affecting the prostate and the seminal vesicles. The underlying mechanisms can be multiple: i) direct damage of the testicle by granuloma formation or by vascular occlusion leading to necrosis; ii) post-testicular, due to obstruction of the seminal conducts, and/or affection of the prostate by granulomatous formation and inflammation. It has also been hypothesized that schistosomiasis can induce hypogonadism mediated by schistosome-derived estradiol - like molecules acting as antagonists of human estradiol [19]. Although schistosomiasis cannot be definitively ruled out as the cause of his infertility, it does not seem likely given the lack of genital symptoms in the past and the results of the laboratory and urogenital imaging tests.

A limitation of our study is the serological diagnosis of the two patients with possible schistosomiasis (patients number 3 and 4). The different serological tests commercialized show variable figures for sensibility and specificity, they cannot differentiate between active and past infections (serological titles remain positive for a long time), are not useful to evaluate the response to treatment, and may present cross-reactions with other helminthic infections [20,21]. For our study, we have used a test (SCHISTOSOMA ICT IgG-IgM ®, LDBIO Diagnostics) that has both high sensibility (96%) and specificity (83%) [21]. Regarding patients 1 and 2, the positive results of the serology corroborate its high sensibility and the fact that it remains positive for long periods of time. For patients 3 and 4, they are thought to be asymptomatic infections, with low parasitological burden and possibly spontaneous resolution; the only evidence of infection nowadays being the positive results of the serological test. As these two patients did no travel abroad and the risk of helminthic infections is very low in our country, the chance of a serological cross-reaction is negligible.

In conclusion, the combination of both the presence of a competent intermediate host and the chance of schistosomes being imported by migrants and travelers returning from sub-Saharan Africa make susceptible Mediterranean areas, like the Poniente area, potential foci for autochthonous transmission of schistosomiasis. The response of local public health authorities to such a threat should include several measures: to promote knowledge of the disease among Primary Care physicians in order to increase their index of clinical suspicion; to carry out field studies aimed to locate the presence of the snails and, subsequently, to eradicate them; to launch public campaigns warning against bathing in irrigation pools; and finally, to advise all physicians in the area to rule out schistosomiasis in any patient presenting with suggesting symptoms regardless the absence of fresh water exposure in endemic areas.

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## CRediT authorship contribution statement

**Joaquín Salas-Coronas:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **María Dolores Bargues:** Investigation, Data curation, Writing – review & editing, Visualization. **Ana Belén Lozano-Serrano:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing, Visualization. **Patricio Artigas:** Investigation, Data curation, Writing – review & editing. **Alberto Martínez-Ortí:** Investigation, Data curation, Writing – review & editing. **Santiago Mas-Coma:** Investigation, Data curation, Writing – review & editing. **Sergio Merino-Salas:** Investigation, Data curation, Writing – review & editing. **José Ignacio Abad Vivas-Pérez:** Investigation, Data curation, Writing – review & editing.

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