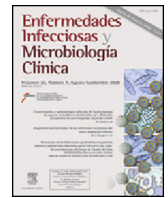




# Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Consensus document

## Executive summary consensus statement of imported diseases group (GEPI) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the Spanish Society of Tropical Medicine and International Health (SETMSI), on the diagnostic and treatment of imported schistosomiasis



Cristina Bocanegra<sup>a</sup>, Miriam J. Álvarez-Martínez<sup>b</sup>, Marta Arsuaga Vicente<sup>c</sup>, Moncef Belhassen-García<sup>d</sup>, Sandra Chamorro Tojeiro<sup>e</sup>, Daniel Camprubí-Ferrer<sup>f</sup>, Pedro Fernández Soto<sup>g</sup>, Elisa García Vázquez<sup>h</sup>, Zaida Herrador Ortiz<sup>i</sup>, Oihane Martín<sup>j</sup>, Antonio Muro<sup>k</sup>, José Luis Pérez Arellano<sup>l</sup>, Marta Reguera Gómez<sup>m</sup>, Joaquín Salas-Coronas<sup>n</sup>, Fernando Salvador<sup>o,p</sup>, Javier Sotillo Gallego<sup>q</sup>, Elena Sulleiro<sup>r</sup>, Diego Torrús Tendero<sup>s</sup>, María Velasco Arribas<sup>t</sup>, Azucena Rodríguez Guardado<sup>u,\*</sup>

<sup>a</sup> Unidad de Medicina Tropical y Salud Internacional Vall d'Hebron-Drassanes, PROSICS Barcelona, Servicio de Enfermedades Infecciosas Hospital Universitario Vall d'Hebron, Spain

<sup>b</sup> Servicio de Microbiología, Hospital Clínic de Barcelona, Departamento de Fundamentos Clínicos, Facultad de Medicina y Ciencias de la Salud, Universidad de Barcelona, ISGlobal, Spain

<sup>c</sup> Unidad de Patología Importada y Salud Internacional (CSUR), Unidad de Alto Aislamiento, CIBERINFEC, Hospital La Paz-Carlos III, Madrid, Spain

<sup>d</sup> Servicio de Medicina Interna, Unidad de Enfermedades Infecciosas, Hospital Universitario de Salamanca, Centro de Investigación en Enfermedades Tropicales de la Universidad de Salamanca (CIETUS), Instituto de Investigación Biomédica de Salamanca (IBSAL), Universidad de Salamanca, Salamanca, Spain

<sup>e</sup> Unidad de Referencia Nacional para Enfermedades Tropicales, Servicio de Enfermedades Infecciosas, Hospital Universitario Ramón y Cajal, Madrid, IRYCIS, CIBERINFEC, Spain

<sup>f</sup> ISGlobal, Hospital Clínic – Universitat de Barcelona, Barcelona, Spain

<sup>g</sup> Grupo Enfermedades Infecciosas y Tropicales (e-INTRO), Instituto de Investigación Biomédica de Salamanca-Centro de Investigación de Enfermedades Tropicales de la Universidad de Salamanca (IBSAL-CIETUS), Facultad de Farmacia, Universidad de Salamanca, Salamanca, Spain

<sup>h</sup> Unidad de Enfermedades Infecciosas, Hospital Clínico Universitario Virgen de la Arrixaca, IMIB, Facultad de Medicina, Universidad de Murcia, Spain

<sup>i</sup> Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid, Spain

<sup>j</sup> Servicio de Microbiología y Parasitología, Hospital Universitario Ramón y Cajal, Madrid, Spain

<sup>k</sup> Grupo de Investigación Enfermedades Infecciosas y Tropicales (e-INTRO), IBSAL, CIETUS, Facultad de Farmacia, Universidad de Salamanca, Salamanca, Spain

<sup>l</sup> Universidad de las Palmas de Gran Canaria, Unidad de Enfermedades Infecciosas y Medicina Tropical, Hospital Insular de Gran Canaria, Spain

<sup>m</sup> Departamento de Parasitología, Facultad de Farmacia, Universidad de Valencia, Valencia, Spain

<sup>n</sup> Unidad de Medicina Tropical, Hospital Universitario Poniente El Ejido, Almería, Spain

<sup>o</sup> Servicio de Enfermedades Infecciosas, Hospital Universitario Vall d'Hebron, PROSICS Barcelona, Barcelona, Spain

<sup>p</sup> Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain

<sup>q</sup> Laboratorio de Referencia e Investigación en Parasitología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Spain

<sup>r</sup> Servicio de Microbiología, Hospital Vall d'Hebron, Barcelona, CIBERINFEC, ISCIII, Universitat Autònoma de Barcelona, Spain

<sup>s</sup> Unidad de Referencia de Enfermedades Importadas y Salud Internacional, Unidad de Enfermedades Infecciosas, Hospital General Universitario Dr. Balmis, ISABIAL, Alicante, Área de Parasitología, Universidad Miguel Hernández, Spain

<sup>t</sup> Sección Infecciosas y Medicina Tropical, Medicina Interna, Hospital Universitario Fundación Alcorcón, Universidad Rey Juan Carlos, Madrid, Spain

<sup>u</sup> Área de Gestión Clínica Medicina Interna, Hospital Universitario Central de Asturias, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain

### ARTICLE INFO

#### Article history:

Received 3 October 2022

Accepted 8 February 2023

### ABSTRACT

Schistosomiasis is a highly prevalent disease, especially in immigrant populations, and is associated with significant morbidity and diagnostic delays outside endemic areas. For these reasons, the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the Spanish Society of Tropical Medicine and International Health (SEMITS) have developed a joint consensus document to serve as a guide for the screening, diagnosis and treatment of this disease outside endemic areas. A panel of experts from

**Abbreviations:** AE, acute schistosomiasis; ACA, anodic circulating antigen; CCA, cathodic circulating antigen; CT, computed tomography; CSF, cerebrospinal fluid; DIGFA, Dot Immunogold Filtration Assay; DNA, deoxyribonucleic acid; ELISA, enzyme-linked immunosorbent assay; HIV, human immunodeficiency virus; IFA, Immunofluorescence assay; IHA, indirect haemagglutination; LAMP, loop-mediated isothermal amplification; MRI, magnetic resonance imaging; OR, odds ratio; OXA, oxamniquine; PAH, acute pulmonary hypertension; PCR, polymerase chain reaction; PNS, peripheral nervous system; POC-CCA, rapid urine screening test; PZQ, praziquantel; SchHAP, acute pulmonary hypertension secondary to schistosomiasis; SSE, schistosomiasis of the spinal cord; WHO, World Health Organisation.

\* Corresponding author.

E-mail address: [azucenarguardado@gmail.com](mailto:azucenarguardado@gmail.com) (A. Rodríguez Guardado).

<https://doi.org/10.1016/j.eimc.2023.02.008>

2529-993X/© 2023 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights reserved.

**Keywords:**

Schistosomiasis  
*Schistosoma* spp  
*Schistosoma haematobium*  
*Schistosoma mansoni*  
*Schistosoma japonicum*  
*S. mekongi*  
*S. intercalatum*  
 Guidelines

both societies identified the main questions to be answered and developed recommendations based on the scientific evidence available at the time. The document was reviewed by the members from both societies for final approval.

© 2023 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights reserved.

## Resumen ejecutivo del documento de consenso del Grupo de Patología Importada (GEPI) de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) y la Sociedad Española de Medicina Tropical y Salud Internacional (SEMTSI), sobre el diagnóstico y tratamiento de la esquistosomiasis importada

### R E S U M E N

La esquistosomiasis es una enfermedad de elevada prevalencia, especialmente en población inmigrante, asociada a importante morbilidad y retraso diagnóstico fuera de zona endémica. Por estas razones, la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) y la Sociedad Española de Medicina Tropical y Salud Internacional (SEMTSI) han elaborado un documento conjunto de consenso que sirva de guía para el cribado, diagnóstico y tratamiento de esta patología en zonas no endémicas. Un panel de expertos de ambas sociedades identificó las principales preguntas a responder y elaboró las recomendaciones siguiendo la evidencia científica disponible en el momento. El documento fue revisado por los miembros de ambas sociedades para su aprobación final.

© 2023 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

**Palabras clave:**

Schistosomiasis  
*Schistosoma* spp  
*Schistosoma haematobium*  
*Schistosoma mansoni*  
*Schistosoma japonicum*  
*S. mekongi*  
*S. intercalatum*  
 Documento de consenso

## Introduction

### Justification

Human schistosomiasis is a parasitic disease caused by trematodes of the genus *Schistosoma* endemic in tropical and subtropical areas of Africa, the Americas, the Middle East, East Asia and the Philippines, although it is in sub-Saharan Africa where the greatest burden of disease is concentrated; 93% of cases are diagnosed in this region, where it is responsible for between 1.6 and 4.2 million disability-adjusted life years (DALYs).<sup>1</sup> Three species are the main causes of human disease: *Schistosoma haematobium*, present in Africa and the Middle East, *Schistosoma mansoni* in Africa and the Americas, and *Schistosoma japonicum*, which is localised in Asia, mainly in the Philippines and China. Three more geographically localised species are *S. mekongi* in the Mekong River Basin and *S. guineensis* and *S. intercalatum* in Central Africa.

In Europe, two outbreaks of autochthonous transmission have recently been described in Spain and Corsica, in relation to climate change, globalisation and the presence of the intermediate host in these areas.<sup>2,3</sup> However, the vast majority of cases diagnosed in Spain are imported. The prevalence of schistosomiasis in immigrant population from endemic areas varies from 7.5% to 43% according to the diagnostic method used, with higher prevalences described when serology is used.<sup>4</sup> Despite these data, there is still a significant lack of knowledge of the disease, so it is not surprising that the diagnosis of imported schistosomiasis is delayed, especially in the immigrant population which is why screening in this population is currently recommended by European health authorities.<sup>5</sup>

Despite this evidence, there are currently differences in patient management between centres, depending on the screening capacity of the target populations and the diagnostic resources available, as well as access to certain complementary examinations. There are also no national recommendations regarding the follow-up of these patients or the management of possible complications, so that the management of imported schistosomiasis is, in some aspects, a matter of debate among the professionals involved.

### Aim

The aim of this consensus document is to provide the best possible evidence on the management of imported schistosomiasis. Thus, professionals from different fields involved in the care of patients with schistosomiasis in Spain have evaluated the data available in the literature to propose recommendations based on scientific evidence on the different aspects of the disease.

### Method

A systematic review of the literature was conducted to evaluate data concerning the clinical, diagnostic, screening, treatment and follow-up of imported schistosomiasis. PRISMA method was following to reporting the results.<sup>6</sup> Thirty-seven questions were identified and distributed to group members for analysis. For this purpose, a search was carried out in Pubmed until December 2021 for articles in English or Spanish with the search terms “Schistosoma”, “schistosomiasis” associated with each of the items explored (e.g. “screening”, “treatment”, “ELISA”, “praziquantel”, “travellers”, etc.). The search was subject to the PRISMA criteria. It was initially reviewed by the contributors and secondarily by the coordinators of the text. A total of 374 publications were selected, eliminating duplicates and non-relevant publications. All authors have agreed on the content of the document and the final recommendations. Definitions of the different levels of evidence can be found in the [supplementary material](#).

### Clinical manifestations of schistosomiasis

Clinically, schistosomiasis can be divided into three main stages: (a) a stage occurring within 24 h of cercariae penetration of the skin, called cercarial dermatitis (b) a second stage occurring 3–8 weeks after infection, which constitutes acute schistosomiasis and (c) a third chronic stage occurring months or years after infection and resulting from the formation of granulomas around the schistosome eggs retained in the tissues. Although clinical manifestations may occur at other levels, urinary and hepatic schistosomiasis

are the two classic forms of chronic schistosomiasis. The clinical presentation of chronic schistosomiasis may differ between endemic/migrant populations and international travellers. Sometimes the clinical manifestations are indistinguishable from other processes so maintaining a high clinical suspicion is essential.

#### When should acute schistosomiasis be suspected?<sup>7</sup>

- All travellers arriving from schistosomiasis endemic areas should be asked about history of skin exposure to freshwater sources (A-I).
- A history of cercarial dermatitis may be an indication of infection (B-I) but its absence does not exclude the diagnosis (B-I).
- An adequate epidemiological history together with compatible clinical features and/or eosinophilia is highly suggestive of acute schistosomiasis (A-I). It should be noted that the absence of eosinophilia does not exclude the diagnosis.
- In patients with a history of exposure who do not develop symptoms, serology should be performed three months after return from the endemic area (A-I).
- Neither a negative serological test nor the absence of eggs in urine or stools alone is sufficient to rule out acute schistosomiasis (A-I).

#### When should genitourinary schistosomiasis be suspected?<sup>8–11</sup>

- Urinary schistosomiasis should be ruled out in patients with urinary symptoms from endemic countries in Africa and to a lesser extent the Middle East (A-I).
- *S. haematobium* infection should be considered in the differential diagnosis of obstructive uropathy and recurrent pyelonephritis in patients from endemic areas (A-I).
- The presence of haematuria and/or haematospermia in a patient from an endemic area should rule out the presence of underlying schistosomiasis (A-I).
- For women and girls with urogenital symptoms who have had contact with freshwater in schistosomiasis-endemic countries, a diagnosis of female genital schistosomiasis (A-I) should be considered.
- The presence of underlying schistosomiasis should be ruled out in women with infertility or dyspareunia from an endemic area (A-I).
- The absence of *Schistosoma* spp. eggs in urine does not exclude the presence of female genital schistosomiasis and diagnosis is based on the presence of characteristic lesions on colposcopy (A-I).
- Given the relationship between genitourinary schistosomiasis and bladder carcinoma, the presence of schistosomiasis should be ruled out in patients from endemic areas with bladder neoplasia (A-I).
- Schistosomiasis should be considered as a cause of end-stage renal failure that may require haemodialysis and renal transplantation (A-I).
- HIV infection should be ruled out in patients with genitourinary schistosomiasis (B-II).

#### When should hepatointestinal schistosomiasis be suspected?<sup>12–14</sup>

- In patients from sub-Saharan Africa and parts of the Caribbean or South America with clinical manifestations of chronic liver disease, especially portal hypertension, *S. mansoni* (A-II) liver schistosomiasis should be ruled out.
- Imaging studies provide important information in the evaluation of this form of schistosomiasis, with ultrasound being the most commonly used technique (A-II).
- Patients with hepatosplenic schistosomiasis should be screened for chronic viral hepatitis given the high prevalence of hepatotropic viruses in schistosomiasis-endemic areas and the implications for progression of periportal fibrosis (A-II).

- Elastography is useful in the evaluation of patients with hepatic schistosomiasis, correlating with ultrasound findings and allowing exclusion of advanced fibrosis (A-II).
- Rectal tenesmus, inflammatory diarrhoea or rectorrhagia in patients from sub-Saharan Africa and some parts of the Caribbean or South America should rule out intestinal schistosomiasis (A-II).

#### What other manifestations should be suspected in chronic schistosomiasis?<sup>15–17</sup>

- Pulmonary arterial hypertension (PAH) secondary to schistosomiasis should be ruled out in individuals with signs and symptoms of progressive right heart failure with risk exposure, previous treatment for schistosomiasis and/or evidence of hepatosplenic abnormalities with fibrosis (A-III).
- If cardiopulmonary involvement is suspected, a directed study with chest X-ray, echocardiography and right heart catheterisation should be performed (the latter would confirm the diagnosis of PAH) (A-II).
- *Schistosoma* spinal cord involvement (SCD) should be suspected in patients from endemic areas or with a history of risky exposure who present with low back pain or lower limb pain, rapidly progressive weakness or sensory impairment associated with autonomic disturbances, especially bladder dysfunction (A-III) even if no *Schistosoma* spp. eggs are detected in stools, urine or cerebrospinal fluid.
- Central nervous system involvement by *Schistosoma* spp. should be suspected in patients from endemic areas or with a history of risk exposure who present with seizures, focal neurological impairment and/or space-occupying brain lesions on CT and/or MRI (A-III) even if no *Schistosoma* spp. eggs are detected in stools, urine or cerebrospinal fluid.
- In case of MRI involvement at any level of the spinal cord, the study should be extended to the other segments, given the likelihood of multilevel involvement (A-II).
- In patients with spinal cord involvement due to *Schistosoma* (EME), CSF serology may be of great diagnostic value (A-II).

#### Diagnosis

For the diagnosis of schistosomiasis, there are direct diagnostic techniques, in which the presence of the parasite is demonstrated, and indirect diagnostic techniques, in which the organism's response to parasitism is revealed. Direct diagnostic techniques include: (i) microscopy to demonstrate the presence of *Schistosoma* spp. eggs in stools or urine, (ii) detection of *Schistosoma* spp. antigens in blood, faeces or urine and (iii) detection of parasite DNA by molecular diagnostic techniques. The indirect diagnostic technique for schistosomiasis is the detection of *Schistosoma* spp. antibodies in serum. In this section, the different microbiological and other diagnostic techniques available are positioned.

#### Are there analytical data for suspected diagnosis of schistosomiasis?<sup>18</sup>

- Eosinophilia is a characteristic, but not constant, sign in patients with schistosomiasis (A-II).
- In case of haematuria and proteinuria in patients with a history of epidemiology, it is recommended to rule out urinary schistosomiasis (A-I).

#### What are the most commonly used parasitological and serological techniques in the diagnosis of schistosomiasis?<sup>19–21</sup>

- Although microscopic examination has high specificity but limited sensitivity, it remains the gold-standard method of choice for the diagnosis of intestinal and urinary schistosomiasis (A-II).

- Serology is a very sensitive technique, useful in the diagnosis of schistosomiasis in non-endemic areas when schistosomiasis is suspected (A-II).
- The detection of ACA in serum and CEC in urine shows the same sensitivity as the parasitological test in areas of high endemicity and can be of complementary use to other techniques in areas of low endemicity (A-II).
- In short-stay travellers in endemic areas, the absence of antibodies and negative microscopy does not exclude recent infection (less than 12 weeks) (A-III).
- In case of positive serology, confirmation with a direct diagnostic method is recommended (A-III).

#### Are rapid diagnostic tests available?<sup>21</sup>

- The Schisto POC-CCA cassette-based rapid diagnostic test (Rapid Medical Diagnostics) and Schistosomiasis Rapid Test (Maternova) are recommended for patients with clinical or epidemiological suspicion of *Schistosoma* spp. infection, especially for *S. mansoni* (A-II).
- The *Schistosoma* ICT IgG-IgM test (LDBio Diagnostics) has been shown to have remarkably high sensitivity with acceptable specificity and diagnostic accuracy for the detection of both urinary and intestinal schistosomiasis and is therefore recommended for initial patient screening (A-II).

#### How useful are DNA amplification methods for detecting schistosomiasis?<sup>22</sup>

- The use of molecular techniques increases the positivity rates of microscopy and may be useful as a complementary diagnosis, although they are not widely available at this time (A-II).

#### Other diagnostic techniques

##### Is any imaging technique or other complementary examination indicated in the diagnosis of schistosomiasis in the absence of specific signs and symptoms?<sup>23</sup>

- Complementary examinations (non-microbiological) for schistosomiasis diagnosed by serology without symptoms or focal signs should be guided by epidemiological data and potential exposure to *Schistosoma* species (A-III).
- In all patients with asymptomatic schistosomiasis diagnosed by serology, a basic analytical study (haemogram and biochemistry) is recommended in order to assess the presence of anaemia, eosinophilia, as well as liver and renal function involvement (B-II).
- A basic urine study to assess the presence of microhaematuria and proteinuria is indicated in all cases of possible urinary schistosomiasis, even in the absence of radiological or ultrasound findings of the urinary tract (B-II).
- Chest X-ray, chest CT, echocardiography, pyelography or invasive examinations such as cystoscopy or fibrocolonoscopy are not recommended for asymptomatic schistosomiasis (D-III).

#### Screening

The public health importance of schistosomiasis in endemic regions is evident and is increasing in non-endemic areas, among other factors due to the global migration phenomenon. In the immigrant population from endemic areas, nearly 40% of diagnosed infections occur in asymptomatic patients, which can lead to a delay in diagnosis, sometimes with serious consequences. At present, there is sufficient evidence to justify screening for schistosomiasis in immigrants from endemic areas, although it should be noted that cost-effectiveness studies are needed to compare the

screening and treatment strategy with that of presumptive treatment in immigrants from endemic areas.

#### Is screening of immigrants from endemic areas indicated?<sup>24</sup>

- Imported schistosomiasis represents a significant public health problem in non-endemic areas. All persons arriving from an endemic area should be screened serologically regardless of the presence of symptoms or laboratory abnormalities (A-II).

#### Is screening of travellers from endemic areas indicated?<sup>25</sup>

- Asymptomatic travellers from endemic areas with a compatible epidemiological history (contact with freshwater, etc.) could benefit from screening for schistosomiasis (A-II). In all other asymptomatic travellers from endemic areas, but with no epidemiological history of interest, screening would not be recommended (A-II).

#### What is the recommended technique for screening?<sup>24</sup>

- Antibody detection by serological techniques is currently the technique of choice for screening asymptomatic individuals from at-risk areas (A-II).
- If available, molecular techniques such as PCR have a high sensitivity and specificity for screening asymptomatic patients (A-II).
- Microscopy using concentration techniques may be an alternative for screening when serological techniques are not available (B-III).

#### Are there any special considerations in screening immunocompromised patients?<sup>26–28</sup>

- Serology for *Schistosoma* spp. is recommended for immunocompromised patients from endemic areas (A-II).
- The study should be completed with the search for eggs in urine and faeces, being aware of its low sensitivity in HIV+ patients with low CD4 count. (B-III).
- Serology screening is recommended for solid organ donors with risk factors (stay in tropical and subtropical areas, especially sub-Saharan Africa, even years before). (AIII)
- Serology for schistosomiasis (AII) is recommended for all transplant candidates from endemic areas.

#### Treatment

Praziquantel is the universally accepted treatment for both acute and chronic schistosomiasis.<sup>29</sup> However, in the case of acute schistosomiasis, there are no clinical trials evaluating the different doses needed or the timing of treatment. On the other hand, patients often experience treatment failures, which makes adequate follow-up necessary to ensure early retreatment. This section proposes, based on the available evidence, the approach to be followed in the treatment of all forms of schistosomiasis, both acute and chronic, its follow-up and the guidelines to be followed in case of retreatment.

#### Acute schistosomiasis

##### What is the recommended regimen of praziquantel in acute schistosomiasis?<sup>30,31</sup>

- For the treatment of acute schistosomiasis, treatment with praziquantel at doses of 40 mg/kg for 1 day in cases of *S. mansoni* or *S. haematobium* and 60 mg/kg in cases of *S. japonicum*, repeated of a second dose 1–2 months later, is recommended to eradicate the presence of schistosome after maturation (A-III).
- Praziquantel should always be administered in combination with steroids because of the risk of worsening of the clinical picture with monotherapy (B-III).

- Monitoring of treatment efficacy should be based primarily on the presence of compatible symptoms associated or not with parasitological/histological evidence (B-III).
- Eosinophilia, although it may persist elevated despite successful treatment, is a useful parameter for follow-up (B-III).

What is the role of corticosteroids in the treatment of acute schistosomiasis?<sup>32,33</sup>.

- Corticosteroids are recommended when the patient has at least moderate symptoms (A-III).
- Corticosteroids are recommended concomitant with or prior to praziquantel administration (A-III).
- There is no strong evidence regarding the dose and duration of steroid treatment. One possibility could be the administration of prednisone at a dose of 1 mg/kg body weight for 1–5 days (A-III).
- Strongyloidiasis has to be taken into consideration before the starting high dose treatment with corticosteroids (A-II).

Are there other treatments for acute schistosomiasis?

- Although the potential is promising, on current evidence the use of artemisinin derivatives for the treatment of acute schistosomiasis (D-III) cannot be recommended.

#### Chronic schistosomiasis

What is the appropriate regimen of praziquantel for the treatment of chronic schistosomiasis?<sup>29,34</sup>.

- Adults and children over 5 years of age with chronic *S. mansoni* infection or those in whom the species has not been identified should be treated with praziquantel 40 mg/kg as a single dose or divided into two doses (B-I). Higher doses may be necessary.
- Adults and children over 5 years of age with chronic *S. haematobium* infection should be treated with praziquantel 40 mg/kg as a single dose or in two doses (A-I).
- Adults and children over 5 years of age with chronic *S. intercalatum* infection should be treated with praziquantel 40 mg/kg as a single dose or in two doses (A-II).
- Adults and children over 5 years of age with chronic infection with *S. japonicum*, *S. mekongi*, should be treated with praziquantel 60 mg/kg as a single dose or in two doses (A-II).

What is the dose in children?<sup>35</sup>.

- Children aged 1–5 years with chronic *S. mansoni* and *S. haematobium* infection should be treated with praziquantel 40 mg/kg as a single dose or divided into two doses (B-I).
- Children aged 1–5 years with chronic infection with *S. japonicum*, *S. mekongi*, *S. guineensis* and *S. intercalatum* should be treated with praziquantel 40 mg/kg as a single dose or in two doses (A-II).

What is the treatment for pregnant women?<sup>36</sup>.

- Praziquantel is considered a Category B drug during pregnancy (probably safe and can be used) (A-I). However, as treatment of chronic schistosomiasis is not usually an emergency, it could be delayed until after delivery (unless there is a risk of loss of follow-up of the patient) (C-III). It can be used during lactation (B-I).

Are there any special considerations in the treatment of immunocompromised patients?<sup>26,37</sup>.

- All candidates for transplantation or immunosuppressive treatments in whom *Schistosoma* spp. infection is demonstrated

should receive pre-transplant treatment with the usual guidelines (A-II).

- In case of transplantation, it is recommended that the donor should be tested if possible and treated if positive (A-II). Positivity is not a contraindication for donation (A-II). Systematic (pre-emptive) treatment is not recommended (D-III). Close follow-up of the recipient is necessary, both in case of confirmed positivity and in case of a donor from an endemic area (A-II). In case of seroconversion or detection of eggs in the recipient, the recipient should be treated with the usual guidelines (A-I). In case of *S. haematobium* infection in renal transplant recipients, data are more controversial (possibility of recurrence of nephropathy) (C-III).
- There are no conclusive data on the effect of HIV infection on the efficacy of praziquantel treatment, although some studies consider that it could be affected (C-II).

Is there any specific treatment for the manifestations of genito-urinary schistosomiasis?<sup>8,29,34</sup>.

- Treatment of complications of genitourinary schistosomiasis is praziquantel at the same doses as in those without complications (A-I).
- Cases of hydronephrosis and bladder carcinoma, in addition to treatment with praziquantel, will require urological and oncological management (A-II).

Is there any specific treatment for the manifestations of hepatosplenic schistosomiasis?<sup>13</sup>.

- Propranolol has been shown to be effective in reducing the risk of the first episode of oesophageal variceal bleeding (primary prophylaxis) (B-II).
- The combination of propranolol and isosorbide mononitrate appears to have better results than propranolol alone in the prevention of first-episode oesophageal variceal bleeding (B-I).
- Propranolol is effective in preventing re-bleeding from oesophageal varices (secondary prophylaxis) (B-I).
- Sclerosis of oesophageal varices has been shown to decrease the risk of re-bleeding from oesophageal varices, especially when oesophagogastric devascularisation with splenectomy is performed simultaneously (B-II).
- Transjugular intrahepatic portosystemic intrahepatic shunt (TIPS) is a technique that can be used to prevent rebleeding from oesophageal varices but is limited by the high frequency of hepatic encephalopathy (C-III).

Is there any specific treatment of the other manifestations?<sup>16,38,39</sup>.

- In chronic pulmonary schistosomiasis with pulmonary hypertension, treatment with praziquantel (A-II) is indicated.
- Treatment with diuretics, oxygen therapy and anticoagulation is recommended in cases of chronic pulmonary schistosomiasis with pulmonary hypertension (B-III).
- In chronic schistosomiasis with secondary pulmonary hypertension, vasodilator therapy with phosphodiesterase-5 inhibitors, prostacyclin analogues or endothelin receptor antagonists (A-II) is indicated.
- Calcium antagonists are not recommended for the treatment of pulmonary hypertension secondary to chronic schistosomiasis (D-III).
- Steroid administration, praziquantel and surgery are the mainstays in the treatment of central nervous system involvement (A-II).
- In the case of neuroschistosomiasis, corticosteroid treatment (prednisone 1 mg/kg/day or equivalent) is recommended and

should be administered prior to initiation of praziquantel treatment and maintained for at least 6 months (B-III).

- In severe cases, initial treatment with methylprednisolone pulses at a dose of 15 mg/kg, with a maximum daily dose of 1 g intravenous for 5 days in conjunction with praziquantel may be considered (B-II).
- Screening for *M. tuberculosis* is recommended in patients with neuroschistosomiasis requiring long-term use of corticosteroids (A-II).
- Strongyloidiasis has to be taken into consideration in patients with neuroschistosomiasis requiring long-term use of corticosteroids (A-II).
- Surgical treatment of neuroschistosomiasis should be assessed on an individual basis and reserved for severe forms refractory to drug treatment or in case of complications such as acute paraplegia or obstruction of cerebrospinal fluid flow (B-III).
- Praziquantel is recommended for the treatment of ectopic cutaneous schistosomiasis (B-III).

#### Retreatment<sup>40</sup>

What are the main causes of retreatment and how is retreatment performed?

- In non-endemic areas, the main reason for retreatment is treatment failure (A-II).
- Patients with viable eggs in control samples three months after correct initial treatment should be re-treated (A-III).
- Patients who, in the absence of viable eggs in control samples, show evidence of treatment failure such as persistent symptoms (B-III) should be screened.
- Retreatment of schistosome infection is performed following the usual regimen with praziquantel (B-II).

What are the alternatives to praziquantel-resistant schistosomiasis?<sup>41</sup>

- There are currently few alternative treatment options (Oxamniquine, artemisinin derivatives, mefloquine) available to PZQ, which remains the treatment of first choice (A-I).

#### Follow-up

How should the patient with schistosomiasis be followed up?

- Follow-up after treatment of a patient with schistosomiasis should include monitoring of symptoms, monitoring for eosinophilia, detection of eggs in stool or urine and if possible performing AAC (A-II).
- The presence of antibodies or their titre against *Schistosoma* spp. are of no value in the follow-up, so their use is not recommended (A-II).
- In case of initial alterations, abdominal ultrasound is a useful tool to monitor the degree of periportal fibrosis related to *S. mansoni* infection after treatment with praziquantel (A-II).
- In case of initial alterations, abdominal and urinary tract ultrasound is a useful tool to monitor the degree of regression of anatomical alterations of the urinary tract in *S. haematobium* infection after treatment with praziquantel (A-I).
- Liver elastography could be useful in monitoring liver fibrosis after praziquantel treatment (B-III).
- In case of persistence or worsening of clinical, analytical or ultrasound alterations, evaluation with another imaging test depending on the organ affected (e.g. CT, cystoscopy or colonoscopy) is recommended (A-II).

What is the value of analytical markers in follow-up?

- The POC-CCA test is recommended for monitoring patients with intestinal schistosomiasis treated with praziquantel (A-II). Although it is commercially available, its availability in clinical practice is limited.
- Specific qPCR tests have demonstrated their ability to monitor infection and are recommended for post-treatment monitoring if available (B-II).

How long should the patient with schistosomiasis be followed up?<sup>42</sup>

- Follow-up analytical and microbiological tests in schistosomiasis can be performed two to six months after treatment and thereafter if needed 6–12 months after treatment (B-II).
- Eosinophil counts are not useful to guide response to treatment at least in the first 3 months after completion of treatment (A-II).
- In acute schistosomiasis, it must be confirmed that there is no persistence of viable eggs or continued symptoms after 3–6 months of treatment (A-II).
- In chronic schistosomiasis, follow-up with ultrasound should be performed as long as there are symptoms or evidence of organ involvement (A-II). The frequency of monitoring is not well defined and should be adapted to each patient (C-III).
- If there are no analytical or ultrasound findings, follow-up after treatment is recommended for 3 to 6 months to ensure that eosinophilia decreases and that eggs disappear in faeces or urine (B-II).
- In the case of asymptomatic patients diagnosed only by serology, post-treatment follow-up is not recommended (A-II).

When can a patient be considered cured?<sup>42</sup>

- Patients with negative egg detection in previously positive samples and disappearance of clinical and analytical evidence of infection can be considered cured (A-II).

#### Prevention<sup>43</sup>

Schistosomiasis in travellers to an endemic area constitutes a significant proportion of all imported schistosomiasis cases. A European study conducted between 1997 and 2010 showed that 33% of all diagnoses were made in travellers and 16% in long-term expatriates. Only 19% had had a previous consultation. The lack of an effective vaccine makes prophylaxis measures essential

What measures should be taken to avoid schistosome infection during a stay in endemic areas?

- Avoid swimming, bathing, canoeing, fishing or wading in freshwater sources such as lakes, rivers, ponds and wetlands in endemic area (A-I).
- Boil the water to be used for bathing for at least 5 min, then allow it to cool to avoid scalding (B-II).
- Treat the water by allowing it to stand for 48 h before exposure (B-II).

Is chemoprophylaxis with praziquantel indicated for travellers to an endemic area?

- Pre- and post-exposure chemoprophylaxis is not routinely indicated for travellers to risk areas (D-III).

#### Funding

This research has not received specific support from public sector agencies, the commercial sector or non-profit organisations.

## Conflicts of interest

The authors declare no conflict of interest.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eimce.2023.02.008

## References

- Onasanya A, Bengtson M, Oladepo O, Van Engelen J, Diehl JC. Rethinking the top-down approach to schistosomiasis control and elimination in Sub-Saharan Africa. *Front Public Health*. 2021;9:622809. <http://dx.doi.org/10.3389/fpubh.2021.622809>.
- Ramalli L, Mulero S, Noel H, Chiappini JD, Vincent J, Barré-Cardi H, et al. Persistence of schistosomal transmission linked to the Cavu river in Southern Corsica since 2013. *Euro Surveill*. 2018;23. <http://dx.doi.org/10.2807/1560-7917.ES.2018.23.4.18-00017>, 18-00017.
- Salas-Coronas J, Bargues MD, Lozano-Serrano AB, Artigas P, Martínez-Orti A, Mas-Coma S, et al. Evidence of autochthonous transmission of urinary schistosomiasis in Almería (southeast Spain): an outbreak analysis. *Travel Med Infect Dis*. 2021;44:102165. <http://dx.doi.org/10.1016/j.tmaid.2021.102165>.
- Asundi A, Beliaevsky A, Jian Liu X, Akaberi A, Schwarzer G, Bisoffi Z, et al. Prevalence of strongyloidiasis and schistosomiasis among migrants: a systematic review and meta-analysis. *Lancet Glob Health*. 2019;7:e236–48. [http://dx.doi.org/10.1016/S2214-109X\(18\)30490-X](http://dx.doi.org/10.1016/S2214-109X(18)30490-X).
- ECDC. Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA. Stockholm; 2018. <https://www.ecdc.europa.eu/en/publications-data/public-health-guidance-screening-and-vaccination-infectious-diseases-newly> [consulted 15.12.21].
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *BMJ*. 2009;339:b2700. <http://dx.doi.org/10.1136/bmj.b2700>.
- Meltzer E, Artom G, Marva E, Assous MV, Rahav G, Schwartz E. Schistosomiasis among travelers: new aspects of an old disease. *Emerg Infect Dis*. 2006;12:1696–700. <http://dx.doi.org/10.3201/eid1211.060340>.
- Neves PDMM, Jorge LB, Cavalcante LB, Malheiros D, Woronik V, Dias CB. Schistosomiasis-associated glomerulopathy: clinical aspects, pathological characteristics, and renal outcomes. *Clin Nephrol*. 2020;93:251–61. <http://dx.doi.org/10.5414/CN110013>.
- Tilli M, Gobbi F, Rinaldi F, Testa J, Caligaris S, Magro P, et al. The diagnosis and treatment of urogenital schistosomiasis in Italy in a retrospective cohort of immigrants from Sub-Saharan Africa. *Infection*. 2019;47:447–59. <http://dx.doi.org/10.1007/s15010-019-01270-0>.
- Kjetland EF, Leutscher PD, Ndhlovu PD. A review of female genital schistosomiasis. *Trends Parasitol*. 2012;28:58–65. <http://dx.doi.org/10.1016/j.pt.2011.10.008>.
- Zirimanya L, Mahmud-Ajeigbe F, McQuillan R, Li Y. A systematic review and meta-analysis to assess the association between urogenital schistosomiasis and HIV/AIDS infection. *PLoS Negl Trop Dis*. 2020;14. <http://dx.doi.org/10.1371/journal.pntd.0008383>, e0008383.
- Richter J, Hatz C, Campagne G, Bergquist NR, Jenkins Jennifer M, et al. Ultrasound in schistosomiasis: a practical guide to the standard use of ultrasonography for assessment of schistosomiasis-related morbidity. In: *Second International Workshop*. 2000. Revised and updated. World Health Organization. <https://apps.who.int/iris/handle/10665/66535>
- Tamarozzi F, Fittipaldo VA, Orth HM, Richter J, Buonfrate D, Riccardi N, et al. Diagnosis and clinical management of hepatosplenic schistosomiasis: a scoping review of the literature. *PLoS Negl Trop Dis*. 2021;15. <http://dx.doi.org/10.1371/journal.pntd.0009191>, e0009191.
- Li Y, Mei L, Qiang J, Ju S, Zhao S. Magnetic resonance spectroscopy for evaluating portal-systemic encephalopathy in patients with chronic hepatic schistosomiasis. *Japonicum*. *PLoS Negl Trop Dis*. 2016;10. <http://dx.doi.org/10.1371/journal.pntd.0005232>, e0005232.
- Nunes MC, Guimarães Júnior MH, Diamantino AC, Gelape CL, Ferrari TC. Cardiac manifestations of parasitic diseases. *Heart*. 2017;103:651–8. <http://dx.doi.org/10.1136/heartjnl-2016-309870>.
- Butrous G. Saudi guidelines on the diagnosis and treatment of pulmonary hypertension: schistosomiasis and pulmonary arterial hypertension. *Ann Thorac Med*. 2014;9:S38–41. <http://dx.doi.org/10.4103/1817-1737.134019>.
- Ferrari TC, Moreira PR, Cunha AS. Clinical characterization of neuroschistosomiasis due to *Schistosoma mansoni* and its treatment. *Acta Trop*. 2008;108:89–97. <http://dx.doi.org/10.1016/j.actatropica.2008.04.007>.
- Carranza-Rodríguez C, Escamilla-González M, Fuentes-Corripio I, Perteguer-Prieto MJ, Gárate-Ormaechea T, Pérez-Arellano JL. Helminthosis y eosinofilia en España (1990–2015). *Enferm Infecc Microbiol Clin*. 2018;36:120–36. <http://dx.doi.org/10.1016/j.eimc.2015.11.019>.
- Álvarez-Martínez MJ, Belhassen-García M, Flores-Chavez MD, Pérez de Ayala A, Sulleiro Igual E. 69. Diagnóstico de parasitosis importadas en España. *Procedimientos en Microbiología Clínica*. In: *Procedimientos en Microbiología, Clínica, Sociedad Española de Enfermedades Infecciosas, Microbiología Clínica (SEIMC): Álvarez-Martínez, M.J., (coordinadora)*, 2020.
- Beltrame A, Guerriero M, Angheben A, Gobbi F, Requena-Mendez A, Zammarchi L, et al. Accuracy of parasitological and immunological tests for the screening of human schistosomiasis in immigrants and refugees from African countries: an approach with Latent Class Analysis. *PLoS Negl Trop Dis*. 2017;11:e0005593. <http://dx.doi.org/10.1371/journal.pntd.0005593>.
- van Lieshout L, Polderman AM, Deelder AM. Immunodiagnosis of schistosomiasis by determination of the circulating antigens CAA and CCA, in particular in individuals with recent or light infections. *Acta Trop*. 2000;77:69–80. [http://dx.doi.org/10.1016/S0001-706X\(00\)00115-7](http://dx.doi.org/10.1016/S0001-706X(00)00115-7).
- Frickmann H, Lunardon LM, Hahn A, Loderstädt U, Lindner AK, Becker SL, et al. Evaluation of a duplex real-time PCR in human serum for simultaneous detection and differentiation of *Schistosoma mansoni* and *Schistosoma haematobium* infections – cross-sectional study. *Travel Med Infect Dis*. 2021;41:102035. <http://dx.doi.org/10.1016/j.tmaid.2021.102035>.
- Castillo-Fernández N, Soriano-Pérez MJ, Lozano-Serrano AB, Sánchez-Sánchez JC, Villarejo-Ordóñez A, Cuenca-Gómez JA, et al. Usefulness of ultrasound in sub-Saharan patients with a serological diagnosis of schistosomiasis. *Infection*. 2021;49:919–26. <http://dx.doi.org/10.1007/s15010-021-01612-x>.
- Agbata EN, Morton RL, Bisoffi Z, Bottieau E, Greenaway C, Biggs BA, et al. Effectiveness of screening and treatment approaches for schistosomiasis and strongyloidiasis in newly-arrived migrants from endemic countries in the EU/EEA: a systematic review. *Int J Environ Res Public Health*. 2018;16. <http://dx.doi.org/10.3390/ijerph16010011>.
- Pérez-Arellano JL, Górgolas-Hernández-Mora M, Salvador F, Carranza-Rodríguez C, Ramírez-Olivencia G, Martín-Echeverría E, et al. Executive summary of imported infectious diseases after returning from foreign travel: consensus document of the Spanish Society for Infectious Diseases and Clinical Microbiology (SEIMC). *Enferm Infecc Microbiol Clin*. 2018;36:187–93. <http://dx.doi.org/10.1016/j.eimc.2017.02.009>.
- Documento de prevención y tratamiento de infecciones oportunistas y otras coinfecciones en pacientes con infección por VIH. Versión 1.0. Febrero 2022.
- Len O, Los-Arcos I, Aguado JM, Blanes M, Bodro M, Carratalà J, et al. Executive summary of the Consensus Document of the Transplant Infection Study Group (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the National Transplant Organization (ONT) on the Selection Criteria of Donors of Solid Organs in relation to Infectious Diseases. *Enferm Infecc Microbiol Clin*. 2020;38:379–438. <http://dx.doi.org/10.1016/j.eimc.2019.10.016>.
- Christopeit M, Schmidt-Hieber M, Sprute R, Buchheidt D, Hentrich M, Karthaus M, et al. Prophylaxis, diagnosis and therapy of infections in patients undergoing high-dose chemotherapy and autologous haematopoietic stem cell transplantation. 2020 update of the recommendations of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). *Ann Hematol*. 2021;100:321–36. <http://dx.doi.org/10.1007/s00277-020-04297-8>.
- World Health Organization. Library Cataloguing-in-Publication Data. Preventive chemotherapy in human helminthiasis: coordinated use of anthelmintic drugs in control interventions: a manual for health professionals and programme managers. 2006 May 26. Technical report. <https://apo.who.int/publications/i/item/9241547103> [accessed 16.9.21].
- Grandiere-Pérez L, Ansart S, Paris L, Faussart A, Jaureguierry S, Grivois JP, et al. Efficacy of praziquantel during the incubation and invasive phase of *Schistosoma haematobium* schistosomiasis in 18 travellers. *Am J Trop Med Hyg*. 2006;74:814–8.
- Coelho PM, Enk MJ, Katz N. Treatment of clinical schistosomiasis at the prepatent phase: an option? *Trends Parasitol*. 2009;25:299–300. <http://dx.doi.org/10.1016/j.pt.2009.04.001>.
- Vázquez ML, Jung H, Sotelo J. Plasma levels of praziquantel decrease when dexamethasone is given simultaneously. *Neurology*. 1987;37:1561–2. <http://dx.doi.org/10.1212/wnl.37.9.1561>.
- Boggild AK, Libman M, Greenaway C, McCarthy AE, Committee to Advise on Tropical Medicine, Travel (CATMAT). CATMAT statement on disseminated strongyloidiasis: Prevention, assessment and management guidelines. *Can Commun Dis Rep*. 2016;42:12–9. <http://dx.doi.org/10.14745/ccdr.v42i01a03>.
- CDC. Schistosomiasis Infection. Treatment. [https://www.cdc.gov/parasites/schistosomiasis/health\\_professionals/index.html#tx](https://www.cdc.gov/parasites/schistosomiasis/health_professionals/index.html#tx) [accessed 16.9.21].
- Munisi DZ, Buza J, Mpolya EA, Angelo T, Kinung'hi SM. The efficacy of single-dose versus double-dose praziquantel treatments on schistosoma mansoni infections: its implication on undernutrition and anaemia among primary schoolchildren in two on-shore communities, Northwestern Tanzania. *Biomed Res Int*. 2017;2017:7035025. <http://dx.doi.org/10.1155/2017/7035025>.
- Olveda RM, Acosta LP, Tallo V, Baltazar PI, Lesiguz JL, Estanislao GG, et al. Efficacy and safety of praziquantel for the treatment of human schistosomiasis during pregnancy: a phase 2, randomised, double-blind, placebo-controlled trial. *Lancet Infect Dis*. 2016;16:199–208. [http://dx.doi.org/10.1016/S1473-3099\(15\)00345-X](http://dx.doi.org/10.1016/S1473-3099(15)00345-X).
- Malinis M, Boucher HW, AST Infectious Diseases Community of Practice. Screening of donor and candidate prior to solid organ transplantation—Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33:e13548. <http://dx.doi.org/10.1111/ctr.13548>.
- Lambertucci JR, Silva LC, do Amaral RS. Guidelines for the diagnosis and treatment of *Schistosoma* myelo-radicalopathy. *Rev Soc Bras Med Trop*. 2007;40:574–81. <http://dx.doi.org/10.1590/S0037-86822007000500016>.

39. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Guide for Surveillance and Control of Schistosomal Myeloradiculopathy. Ministério da Saúde, Secretaria de Vigilância em Saúde. Brasília: Ministerio da Saúde; 2006.
40. Magnussen P. Treatment and re-treatment strategies for schistosomiasis control in different epidemiological settings: a review of 10 years' experiences. *Acta Trop.* 2003;86:243–54. [http://dx.doi.org/10.1016/s0001-706x\(03\)00045-7](http://dx.doi.org/10.1016/s0001-706x(03)00045-7).
41. Liu R, Dong HF, Guo Y, Zhao QP, Jiang MS. Efficacy of praziquantel and artemisinin derivatives for the treatment and prevention of human schistosomiasis: a systematic review and meta-analysis. *Paras Vect.* 2011;4:201. <http://dx.doi.org/10.1186/1756-3305-4-201>.
42. Hoekstra PT, van Esbroeck M, de Dood CJ, Corstjens PL, Cnops L, van Zeijl-van der Ham CJ, et al. Early diagnosis and follow-up of acute schistosomiasis in a cluster of infected Belgian travellers by detection of antibodies and circulating anodic antigen (CAA): a diagnostic evaluation study. *Travel Med Infect Dis.* 2021;41:102053. <http://dx.doi.org/10.1016/j.tmaid.2021.102053>.
43. Brunette GW, Kozarsky P, Magill AJ, Shlim DR. CDC health information for international travel 2010. Elsevier Health Sciences; 2009.