Schistosomiasi

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-Vice direttore scientifico

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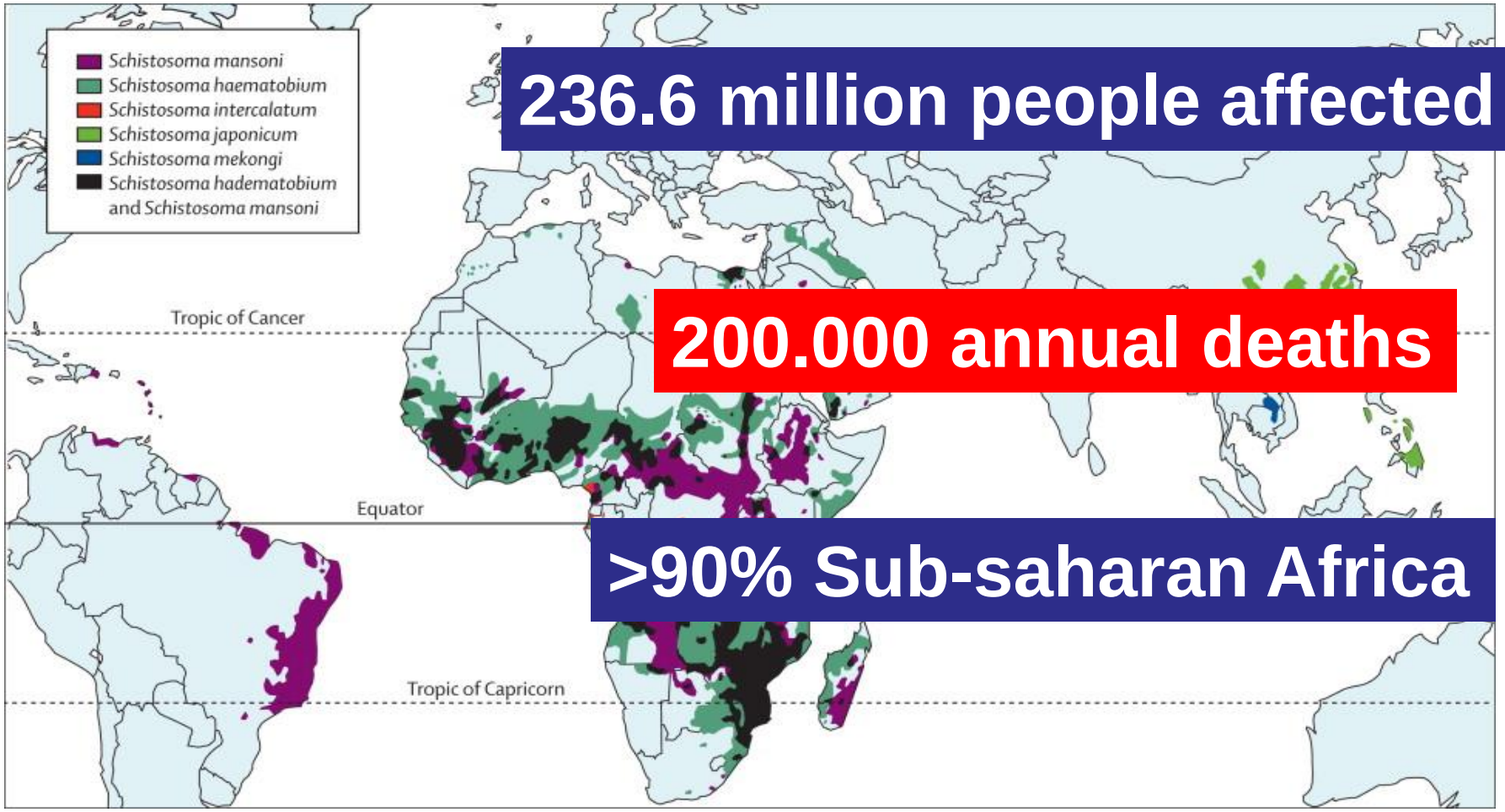
Presidio Ospedaliero Accreditato - Regione Veneto

Distribution of Schistosomiasis



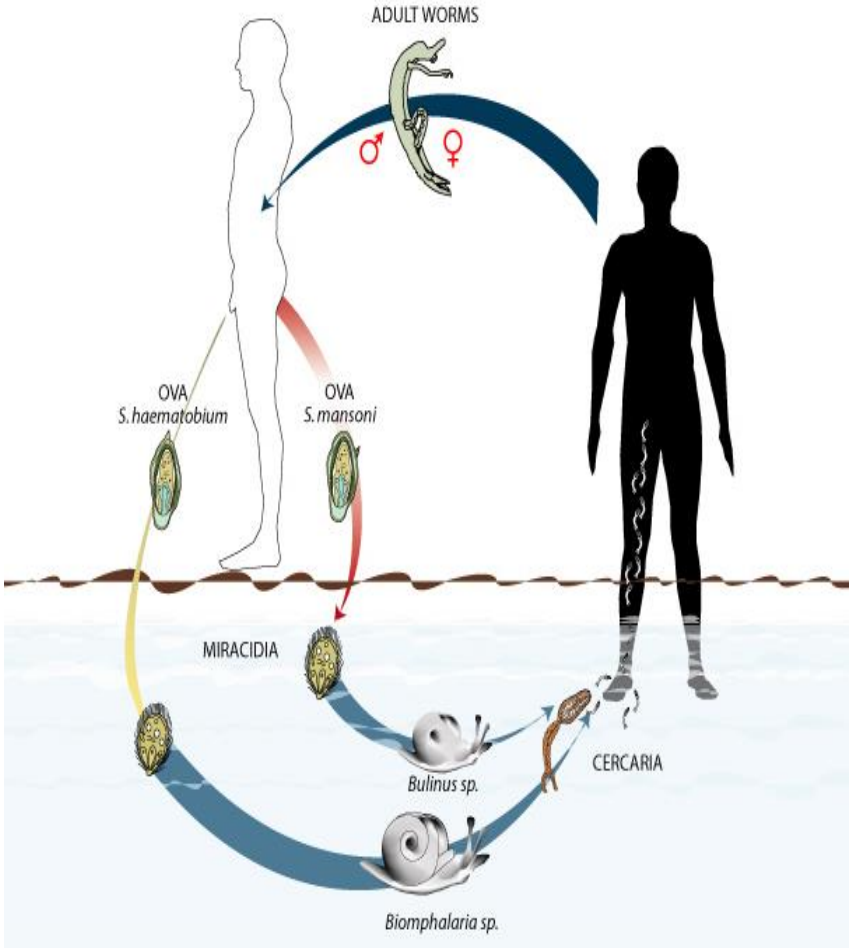
Ferrari TC, Moreira PR.
Neuroschistosomiasis: clinical symptoms and pathogenesis.
Lancet Neurol. 2011 Sep;10(9):853-64

Not endemic area?

Rothe C, Zimmer T, Schunk M, Wallrauch C, Helfrich K, Gültekin F, Bretzel G, Allienne JF, Boissier J
Developing Endemicity of Schistosomiasis, Corsica, France
Emerg Infect Dis. 2021 Jan;27(1):319-21

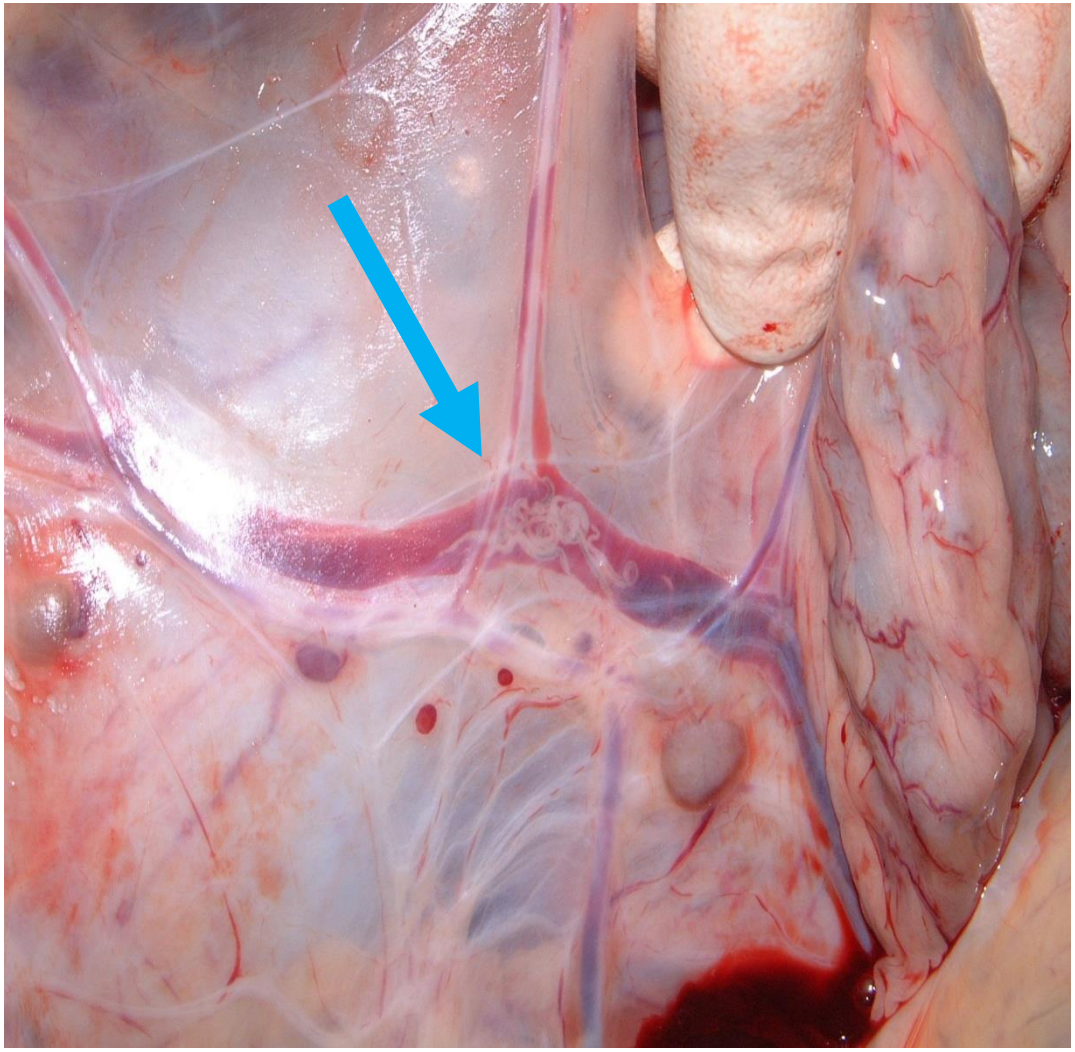
Salas-Coronas J, Bargues MD, Lozano-Serrano AB, Artigas P, Martínez-Ortí A, Mas-Coma S, Merino-Salas S, Abad Vivas-Pérez JI.
Evidence of autochthonous transmission of urinary schistosomiasis in Almeria (southeast Spain): An outbreak analysis
Travel Med Infect Dis. 2021 Nov-Dec;44:102165.

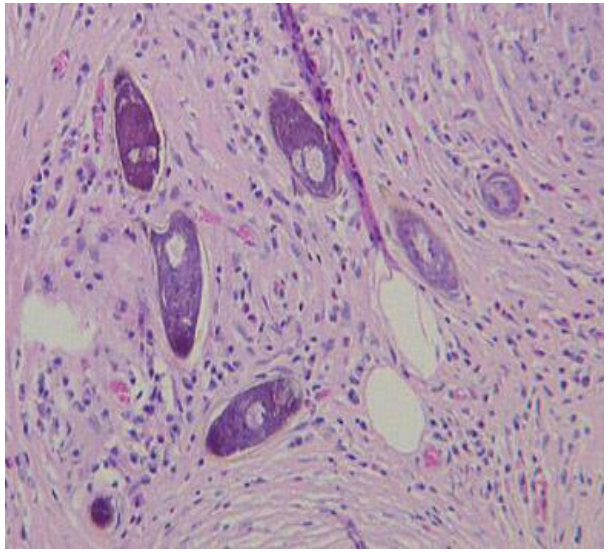
Cycle and clinical manifestations

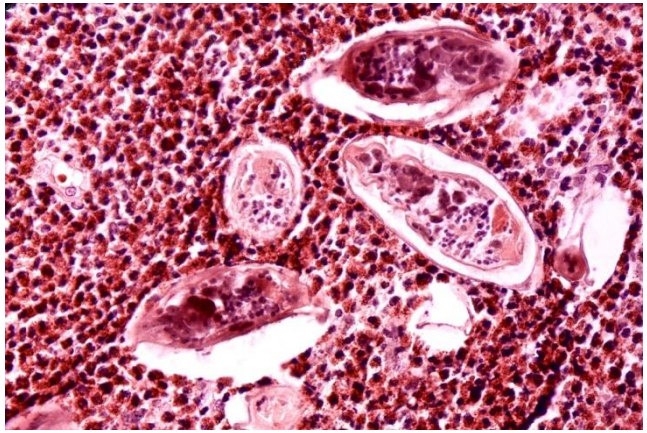


- Clinical manifestations of schistosomiasis are divided into
- **-schistosome dermatitis**
- **-acute schistosomiasis**
- **-chronic schistosomiasis (early phase)**
- **-chronic schistosomiasis (late phase)**

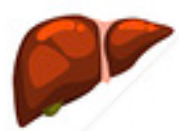
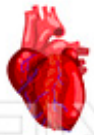
Schistosoma: worms and eggs

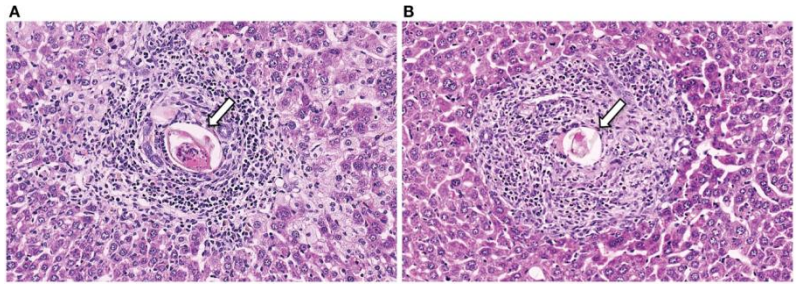




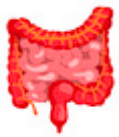


S. mansoni, S. japonicum, S. mekongi S. intercalatum
Schistosomiasi intestinale e epatosplenica

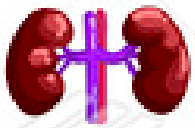



https://doi.org/10.3389/fimmu.2013.00089



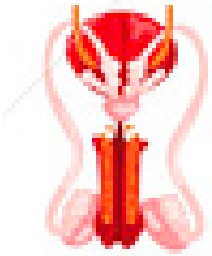
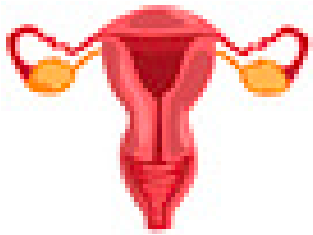
- Sintomi intestinali
- Fibrosi epatica periportale
- **Ipertensione portale con varici e sanguinamento**
- Splenomegalia
- Ipertensione polmonare



S. haematobium
Schistosomiasi genitourinaria

- Ematuria
- Polipi e ispessimento parete vescicale
- Uropatia ostruttiva, idronefrosi, insufficienza renale
- **Cancro della vescica**

- Infertilità
- Ulcere (aumento rischio di HIV)
- Problemi ostetrici

Pulmonary nodules in African migrants caused by chronic schistosomiasis

Federico Gobbi, Dora Buonfrate*, Andrea Angheben, Anna Beltrame, Matteo Bassetti, Luca Bertolaccini, Giuseppe Bogina, Simone Caia, Silvia Duranti, Maria Gobbo, Valentina Marchese, Stefania Marocco, Maria Merelli, Geraldo Monteiro, Alberto Terzi, Zeno Bisoffi*

Schistosomiasis is a neglected tropical disease that can cause mainly hepatic and genitourinary damage, depending on the species. Involvement of the lungs has been commonly described in acute infection (Katayama syndrome) and chronic infection (pulmonary hypertension). Although rarely reported in the scientific literature, cases of lung nodules due to chronic schistosome infection are also possible and are probably more frequent than commonly thought. Here we report seven cases of African migrants who were diagnosed with chronic schistosomiasis and

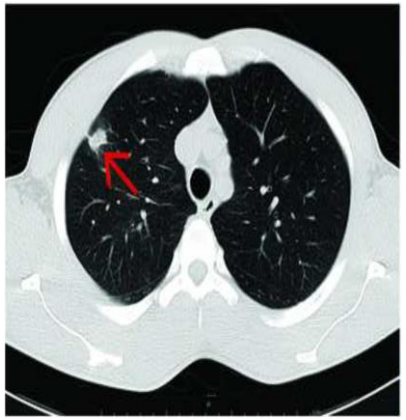
Lancet Infect Dis 2017
Published Online
February 14, 2017
http://dx.doi.org/10.1016/S1473-3099(16)30530-8

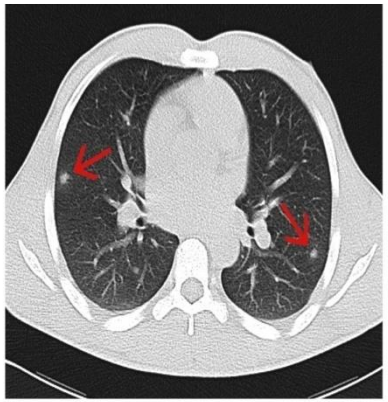
In 18 month-period we found 6 cases of lungs nodules in 120 migrants with chronic schistosomiasis (5%)

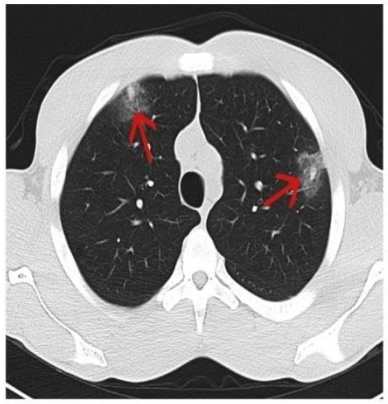
•Migrants (1,2,3,4) from West Africa with schistosomiasis and lung nodules

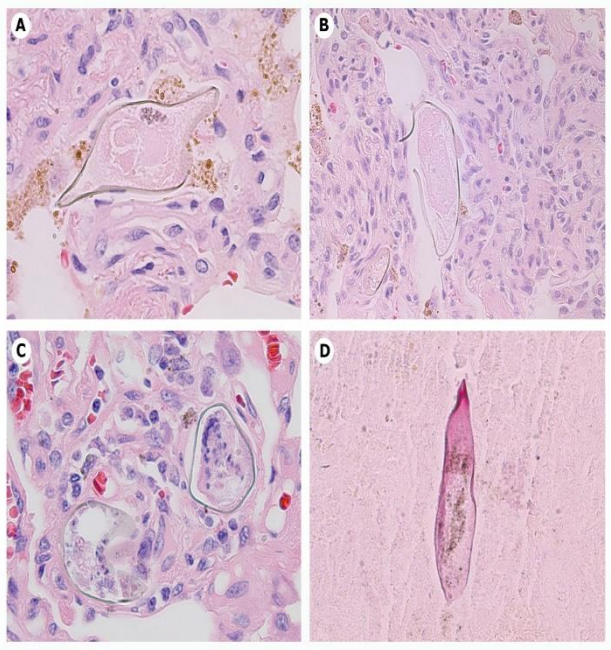
•Pulmonary biopsy positive for Schistosome eggs

•PCR for TB negative



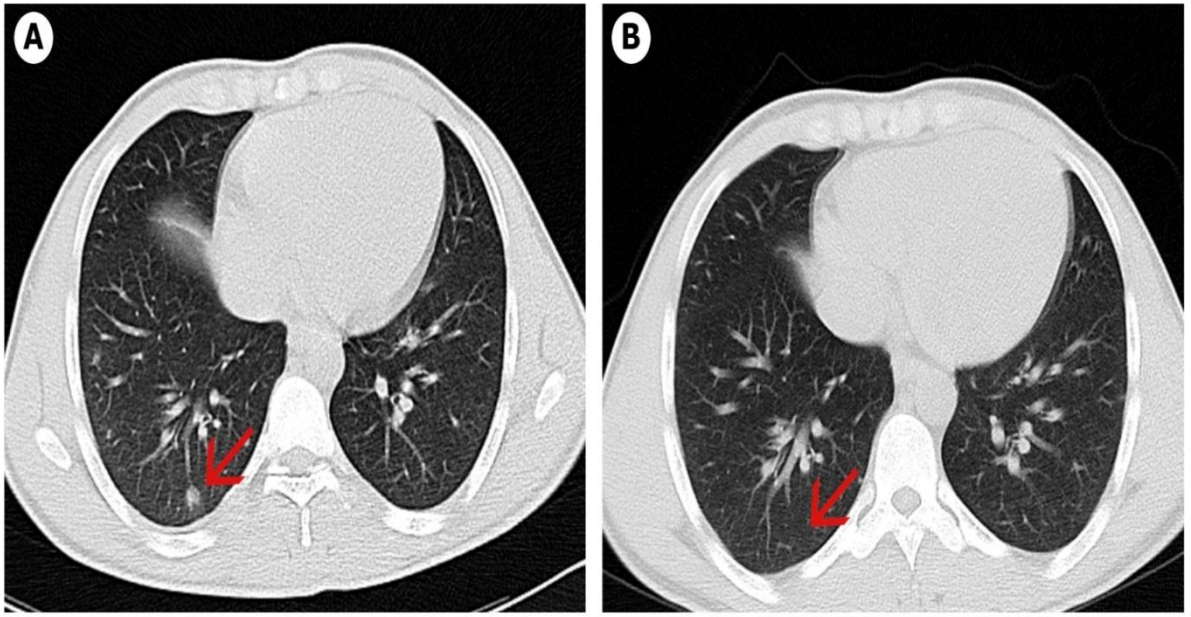






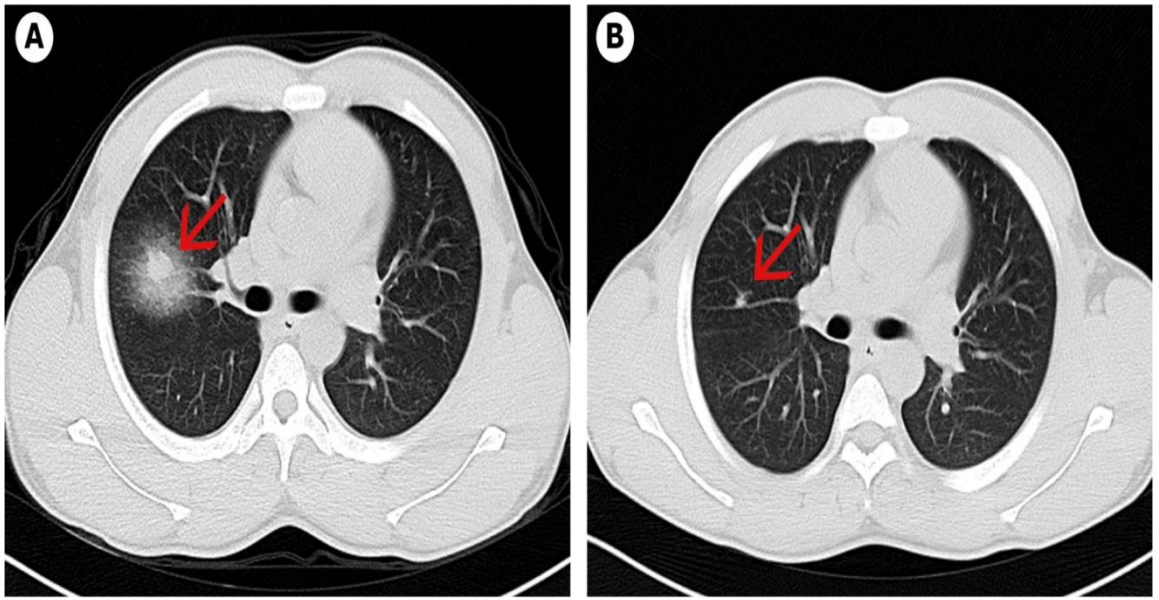
Patient 5

90 days after treatment



Patient 6

50 days after treatment



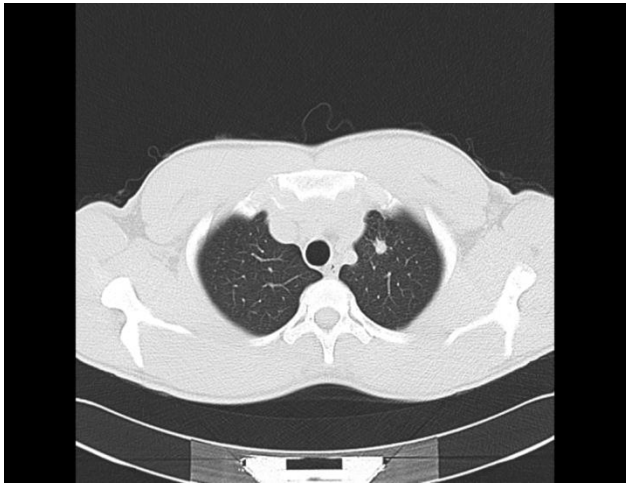
A 22-year-old migrant from Guinea Conakry

March 2016

-Complaining of chest pain

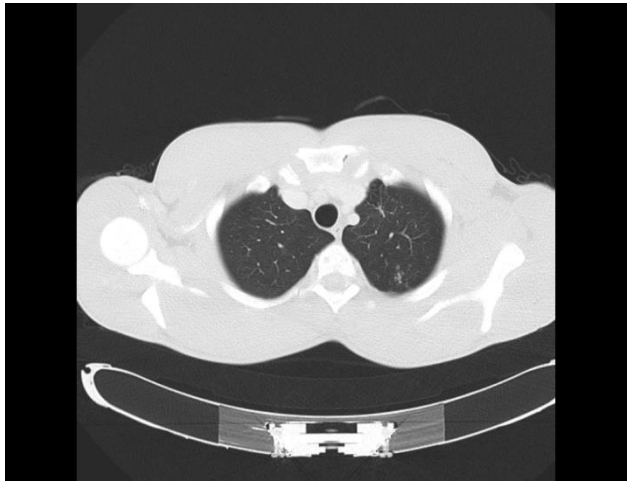
-Lost to follow up

In this period he denied any treatment



January 2017

-recurrent abdominal pain and right chest pain
-900 eosinophils/µl
-Serology for *S. mansoni* (ELISA) resulted positive (Optical Density 3.24, negative <0.9)
-several *S. mansoni* eggs were detected in stool specimens, some *S. haematbium* eggs were detected in urines



Gobbi F, Buonfrate D, Angheben A, Bisoffi Z.
Restaging Pulmonary Schistosomiasis.
Am J Trop Med Hyg. 2019 May;100(5):1049-1051

CellPress
REVIEWS

Opinion

New Insights on Acute and Chronic Schistosomiasis: Do We Need a Redefinition?

Federico Gobbi,[1,*] Francesca Tamarozzi,[1] Dora Buonfrate,[1] Lisette van Lieshout,[2] Zeno Bisoffi,[1,3] and Emmanuel Bottieau[4] on behalf of TropNet Schisto Task Force

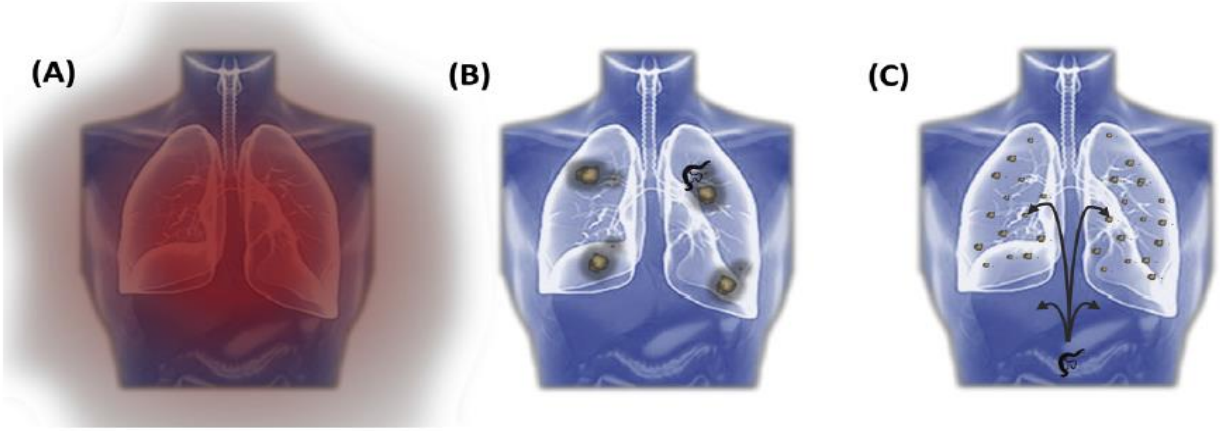


Figure 2. Lung Involvement in Different Phases of Schistosomiasis. (A) A very early systemic Loeffler-like reaction (Katayama syndrome), characterized, when present, by a diffuse interstitial pattern but no nodular lesions on imaging. This is possibly related to the migration of larvae/juvenile worms; the pulmonary symptoms are nonspecific and are part of a more general immunoallergic reaction. (B) Transient lung nodular lesions, most of the time asymptomatic and with a rather typical 'ground-glass' aspect on imaging; they may be present from the very early stage (3 weeks after infection) and throughout the whole period of active schistosomiasis (involving the presence of living adults). These are related to nests of eggs laid during sporadic adult migration. (C) Pulmonary arterial hypertension, with severe morbidity, occurs as a rather late complication of schistosomiasis. This is due to the granulomatous and fibrotic reaction around eggs embolized and stuck in capillaries, following their continuous release by adult worms established in the portal/caval venous system. In this case eggs are homogeneously distributed in the lungs.

Highlights

The proportion of patients with chronic schistosomiasis diagnosed with pulmonary nodules seems much higher than previously described in the literature.

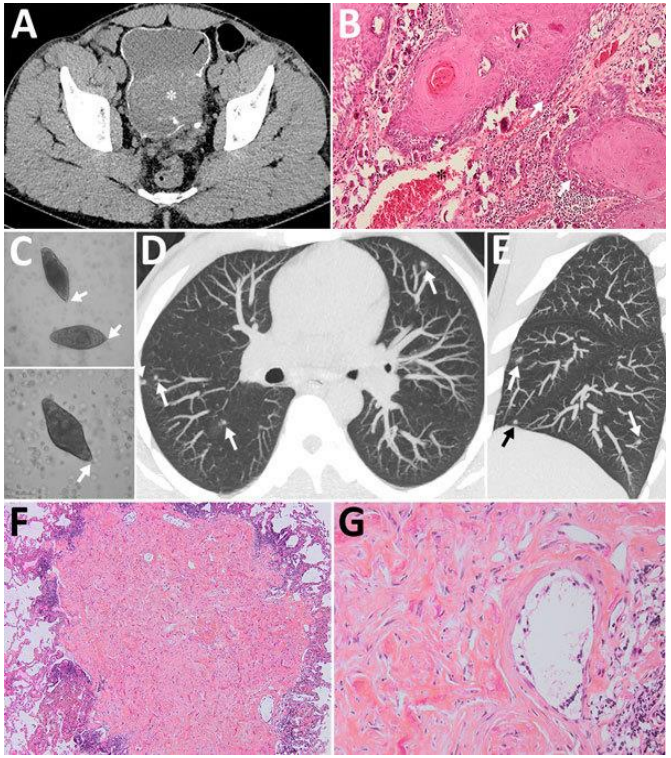
Nodular lesions in chronic schistosomiasis are very similar to those described in acute schistosomiasis; both should be caused by clusters of eggs, and both may be unrelated to the presence of pulmonary symptoms.

Katayama syndrome, which occurs also in patients infected by male parasites only, seems therefore not to be related to egg deposition.

Adult worms can be found all over the body and 'ectopic' sites are more frequent than previously described.

Focal lung lesions incidentally observed during chronic schistosomiasis seem to disappear spontaneously (or clearance may be accelerated by praziquantel), similar to what is known for pulmonary lesions observed during early infection.

- A 30-year-old man from Mali,
- intraluminal mass infiltrating the left ureter
- well-differentiated, keratinized squamous cell carcinoma (SCC)
- calcified eggs with a terminal spine resembling *Schistosoma haematobium*
- Chest CT revealed multiple, bilateral,, diffuse, infracentimetric, pulmonary, ill-defined nodules suggesting metastases.



Saade A, Carton E, Mansuet-Lupo A, Jouffroy R, Damotte D, Yera H, Revel MP, Goldwasser F.
Lung Involvement in Chronic Schistosomiasis with Bladder Squamous Cell Carcinoma.
Emerg Infect Dis. 2018 Dec;24(12):2375-2378

Systemic disease/Ectopic sites

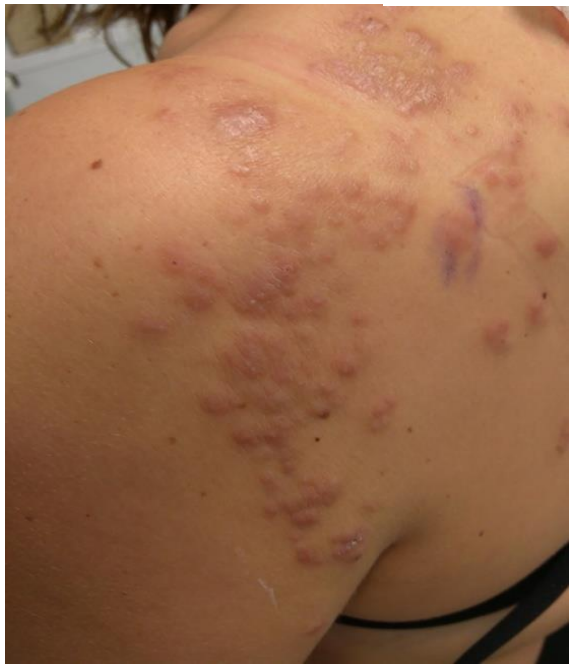
PLOS | NEGLECTED TROPICAL DISEASES

PHOTO QUIZ

A 38-year-old woman with zosteriform skin lesions

Daniel Camprubí[1]*, Ana Requena-Méndez[1], Natalia Rodríguez[1], M. Eugenia Valls[2], Adriana García-Herrera[3], Teresa Estrach[4], Xavier Fustà[4], Juan García-Bernalt Diego[5], Pedro Fernández-Soto[5], Jose Muñoz[1]

1 ISGlobal, Barcelona Ctr. Int. Health Res. (CRESIB), Hospital Clínic-Universitat de Barcelona, Barcelona, Spain, **2** Microbiology and Parasitology, Hospital Clínic, Barcelona, Spain, **3** Pathology Department, Hospital Clinic, Barcelona, Spain, **4** Dermatology Department, Hospital Clinic, Barcelona, Spain, **5** Infectious and Tropical Diseases Research Group (e-INTRO), Biomedical Research Institute of Salamanca-Research Centre for Tropical Diseases at the University of Salamanca (IBSAL-CIETUS), University of Salamanca, Salamanca, Spain



She remained asymptomatic until 2 weeks after her return (**approximately 5 weeks after freshwater exposure**), when she developed pruritic painless erythematous papules grouped on the back part of her left shoulder following the C3-C4 dermatome (Fig 1).

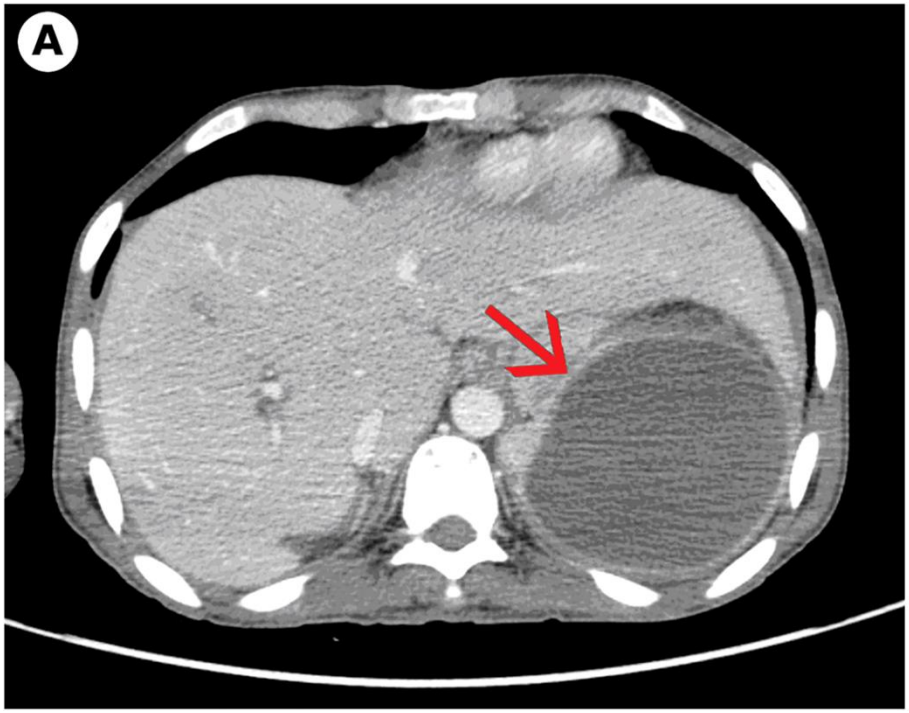
PLOS | NEGLECTED TROPICAL DISEASES

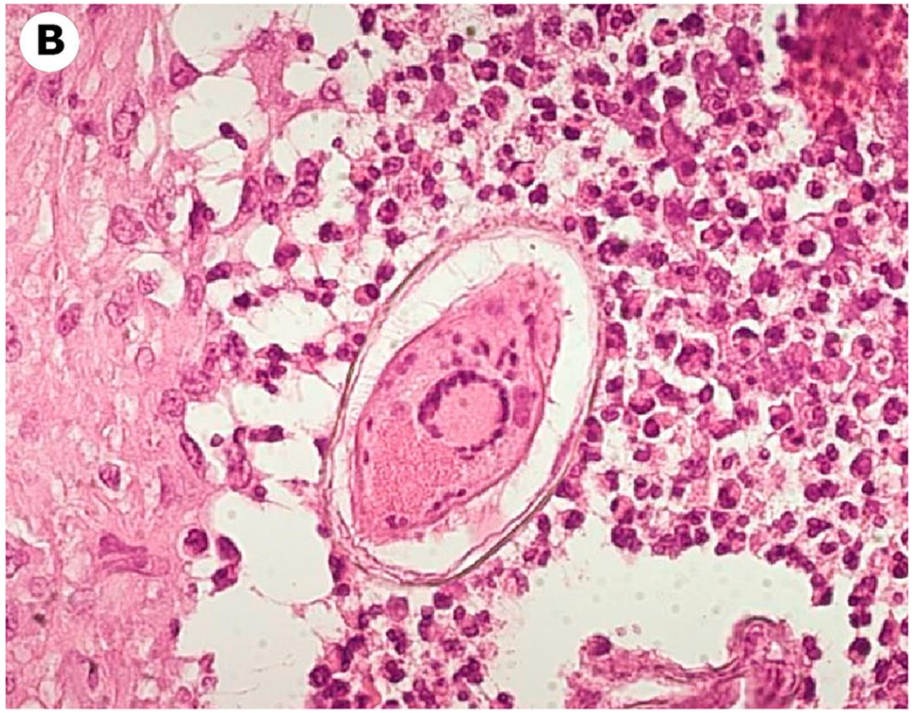
SYMPOSIUM

Schistosoma mansoni Eggs in Spleen and Lungs, Mimicking Other Diseases

Federico Gobbi[1]*, Giulia Martelli[2], Luciano Attard[2], Dora Buonfrate[1], Andrea Angheben[1], Valentina Marchese[1,3], Laura Bortesi[4], Maria Gobbo[1], Elisa Vanino[2], Pierluigi Viale[2], Zeno Bisoffi[1]

1 Center for Tropical Diseases, Ospedale Sacro-Cuore Don Calabria, Negrar, Verona, Italy, **2** Infectious Diseases Unit, Department of Medical and Surgical Sciences, Ospedale S. Orsola-Malpighi, Alma Mater Studiorum University of Bologna, Bologna, Italy, **3** Acute and Chronic Viral Hepatitis Department, Seconda Università degli Studi di Napoli, Naples, Italy, **4** Department of Pathology, Ospedale Sacro-Cuore Don Calabria, Negrar, Verona, Italy

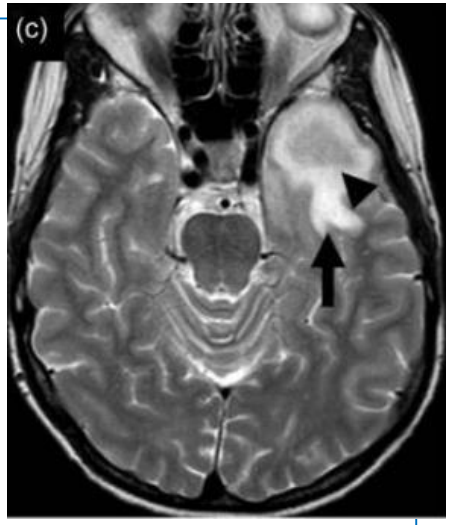




Suthiphosuwan S, Lin A, Gao AF, Munoz DG, Spears J, Bharatha A.
Delayed presentation of cerebral schistosomiasis presenting as a tumor-like brain lesion.
Neuroradiol J. 2017 Jan 1:1971400917703991.

-a 55-year-old Canadian woman who presented with first episode of seizure

-her magnetic resonance imaging scan revealed a **mass-like lesion involving the left anterior temporal lobe**



-she underwent left anterior temporal lobe resection

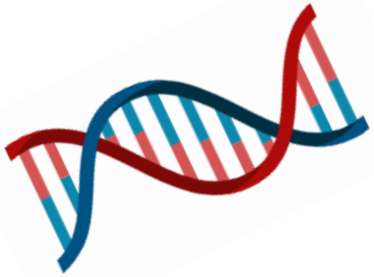
-histologic examination showed **parasitic eggs** with a characteristic lateral spine consistent with **Schistosoma mansoni** infection

-the patient lived in Ghana from the ages of 8-10 years and she visited **Ghana again 10 years prior for two weeks**. She recalled swimming in beaches and rivers

Tools for diagnosis (and follow-up)

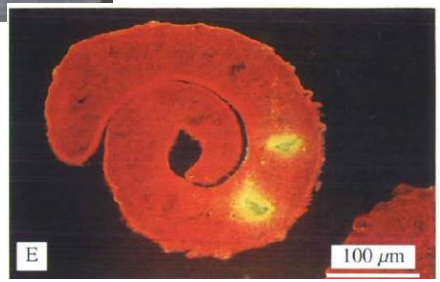
- **Microscopy**
  - Low(er) and variable Se (40-97%)

- **Serology**
  - Many assays available
  - Variable Se (<50-100%) and Sp (<20-100%)
  - Current or past infection?



- **NAAT**
  - More (?) sensitive than microscopy
  - Reference labs
  - No standardization

Van Dam et al 2013
Deelder et al 1996



- **Circulating antigens**
  - POC-CCA [urine]
  - UCP-LF CAA [LUMC]

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Accuracy and predictive values according to Composite Reference Standard (CRS) and to Latent Class Analysis (LCA).

Test	Sensitivity (95% CI)		Specificity (95% CI)		PPV		NPV	
	CRS	LCA	CRS	LCA	CRS	LCA	CRS	LCA
CCA	29% (22–37)	29% (21–37)	95% (91–97)	93% (89–96)	78%	76%	68%	70%
ELISA	71% (63–78)	76% (67–84)	99.6% (98–100)	99.4% (95–100)	99%	99%	84%	88%
WB	92% (86–96)	94% (88–97)	94% (90–97)	91% (85–95)	90%	85%	95%	97%
ICT	96% (91–99)	96% (90–99)	83% (77–87)	79% (73–84)	78%	72%	97%	**97%**
Micro	45% (37–54)	48% (39–57)	100%[1]	99% (96–100)	100%	98%	74%	77%

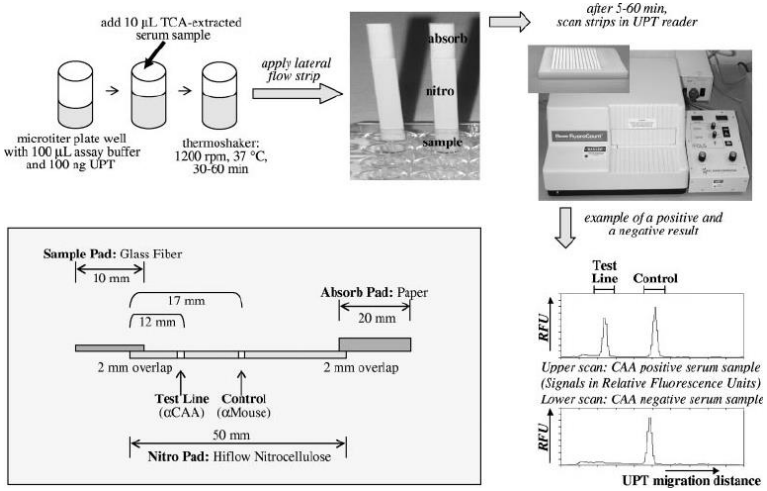
[1] by definition

https://doi.org/10.1371/journal.pntd.0005593.t002

Beltrame A, Guerriero M, Angheben A, Gobbi F, Requena-Mendez A, et al. (2017)
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 Neglected Tropical Diseases 11(6): e0005593

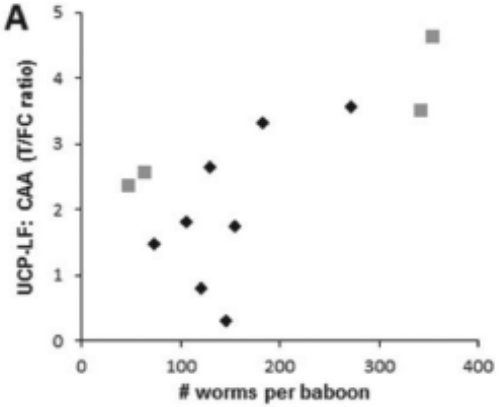
UCP-LF CAA

Better performance when tested in endemic settings for Sm, Sh, Sj, Smek

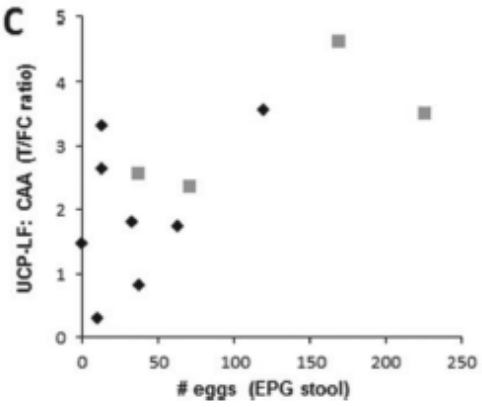


UCP-LF technology Corstjens et al 2008

- Unique polysaccharide structure with no homology → high specificity



Corstjens et al 201

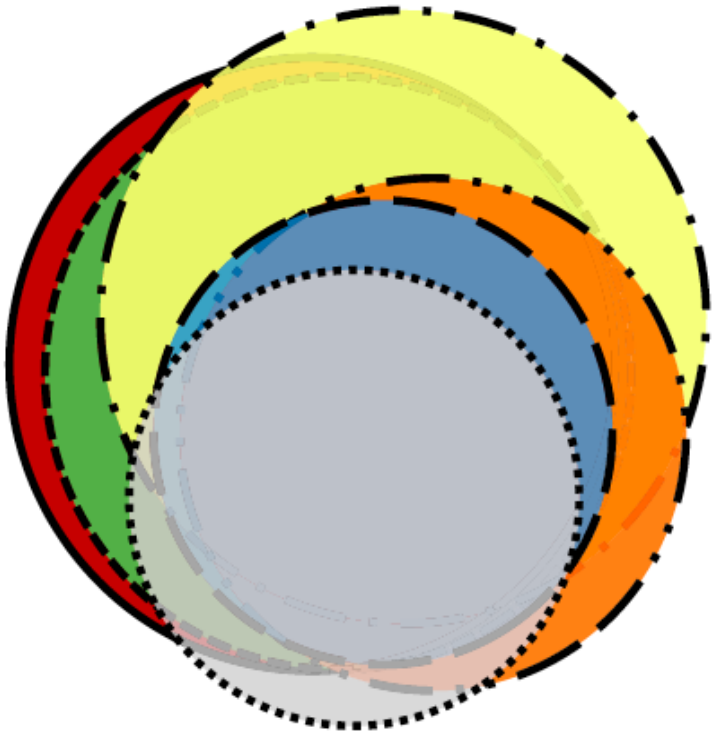


- Levels correlate with worm count and, less well, with egg count (stool; baboon model)

-

UCP-LF CAA

In the imported chronic infection setting – diagnosis



Hoekstra et al 2022

- Van Grootveld et al 2018 **Se 100%**
- Tamarozzi et al 2021 **Se 87%-96%**
- Hoekstra et al 2022 **Se 92%**

- **Detection of CAA+ cases in only-serology+ (egg/PCR neg) individuals!**

No one-test-only approach probably sufficient (CAA + microscopy/PCR)

Available only as a service @ LUMC

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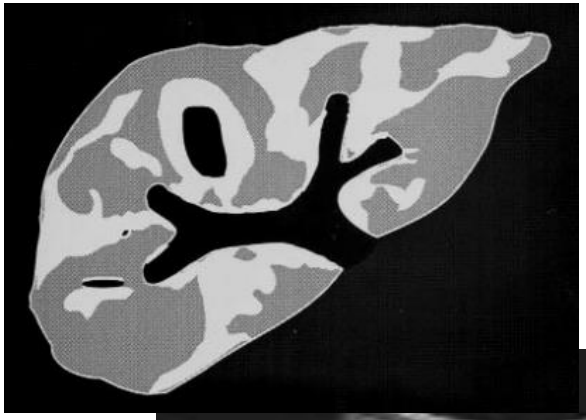
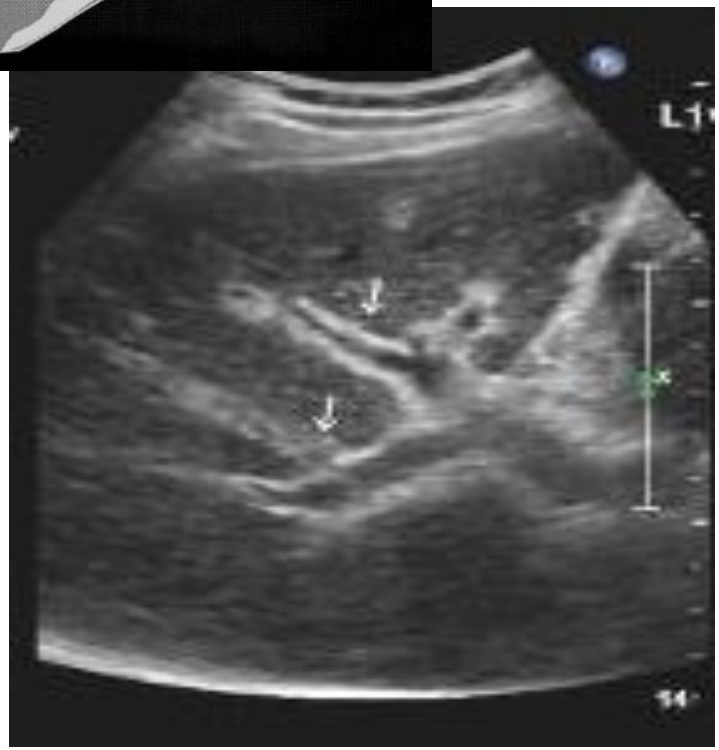
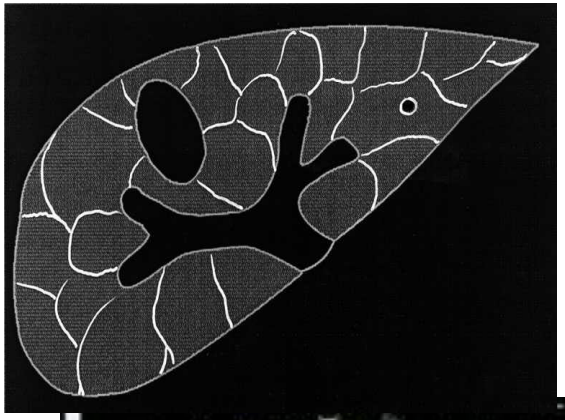
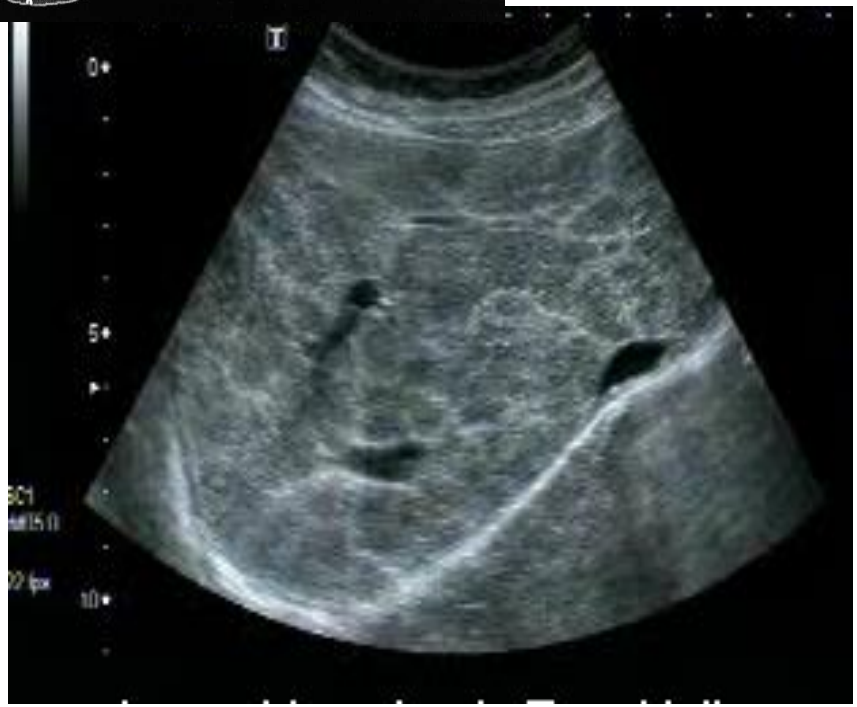


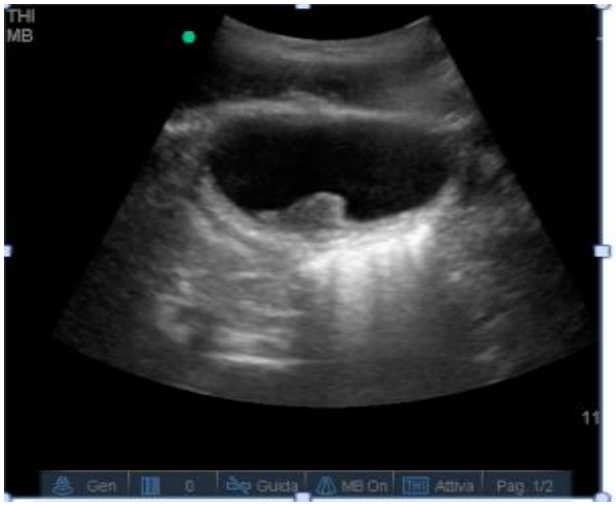


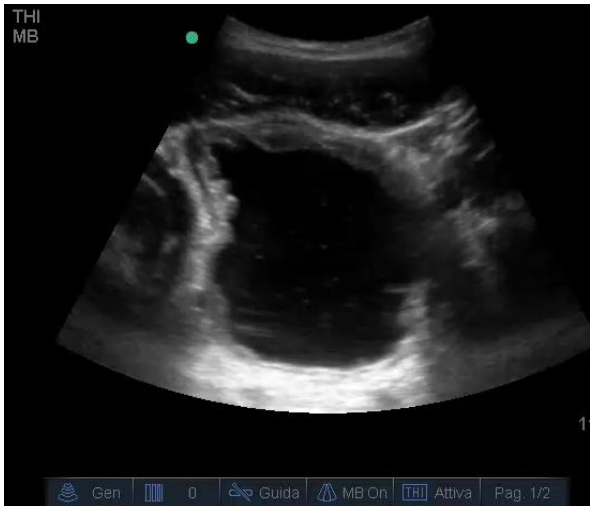
S. mansoni

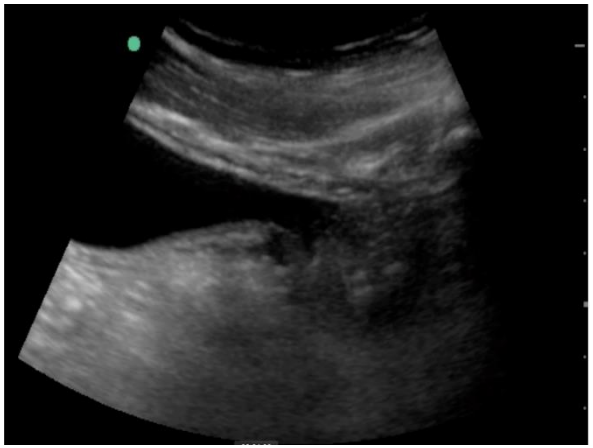


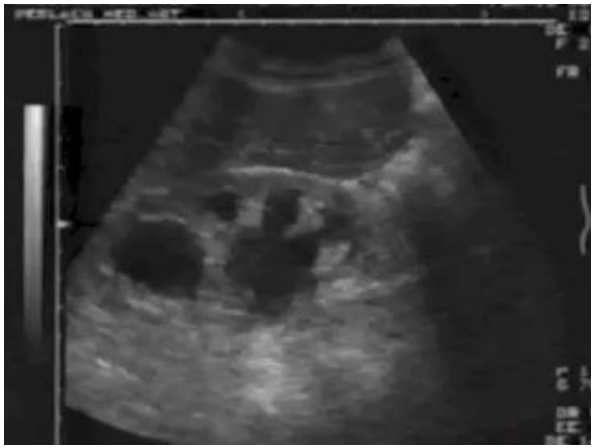


S. japonicum









S. haematobium

***S. haematobium* è cancerogeno**
Associato soprattutto a CARCINOMA SQUAMOCELLULARE DELLA VESCICA

Treatment

World Health Organization

Schistosoma species infection	Praziquantel dose and Duration
Schistosoma mansoni, S. haematobium, S. intercalatum	40 mg/kg per day orally in two divided doses for one day
S. japonicum, S. mekongi	60 mg/kg per day orally in three divided doses for one day

Zwang J, Olliaro PL.

Clinical efficacy and tolerability of praziquantel for intestinal and urinary schistosomiasis-a meta-analysis of comparative and non-comparative clinical trials.

PLoS Negl Trop Dis. 2014 Nov 20;8(11):e3286.

CURE RATE:

94.7% (95%CI 92.2–98.0) for ***S. japonicum*****,**

77.1% (68.4–85.1) for ***S. haematobium***,

76.7% (95%CI 71.9–81.2) for ***S. mansoni,*** *and*

63.5% (95%CI 48.2–77.0) ***S. haematobium/S. mansoni*** infections.

Conclusions/Significance

The large number of subjects allows generalizable conclusions despite the inherent limitations of aggregated-data meta-analyses. The choice of praziquantel dose of 40 mg/kg is justified as a reasonable compromise for all species and ages, although in a proportion of sites **efficacy may be lower than expected** and age effects could not be fully explored.

DPDx – CDC

http://www.cdc.gov/dpdx/schistosomiasis/tx.html

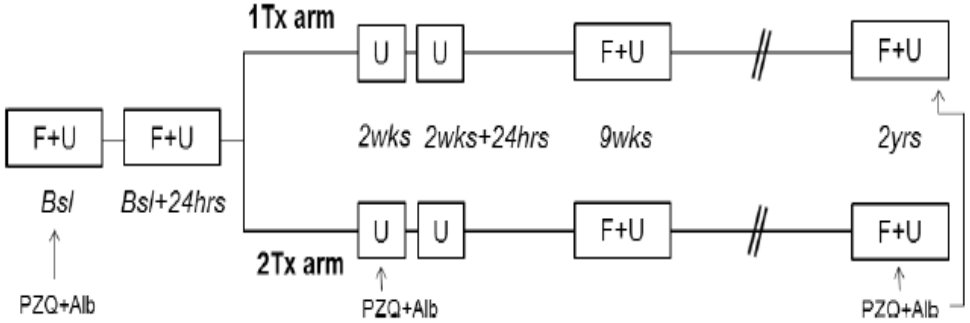
Although a single course of treatment is usually curative, the immune response in lightly infected patients may be less robust, and **repeat treatment may be needed after 2 to 4 weeks to increase effectiveness**. If the pre-treatment stool or urine examination was positive for schistosome eggs, follow up examination at 1 to 2 months post-treatment is suggested to help confirm successful cure.

Schistosoma species infection	Praziquantel dose and Duration
Schistosoma mansoni, S. haematobium, S. intercalatum	40 mg/kg per day orally in two divided doses for one day
S. japonicum, S. mekongi	60 mg/kg per day orally in three divided doses for one day

Kildemoes AO, Vennervald BJ, Tukahebwa EM, Kabatereine NB, Magnussen P, de Dood CJ, Deelder AM, Wilson S, van Dam GJ.

Rapid clearance of Schistosoma mansoni circulating cathodic antigen after treatment shown by urine strip tests in a Ugandan fishing community - Relevance for monitoring treatment efficacy and re-infection.

PLoS Negl Trop Dis. 2017 Nov 13;11(11):e0006054.



significantly lower CCA scores (p = 0,001, n = 399) and fewer eggs (p<0,001, n = 428) were observed at nine weeks in the two treatments arm compared to the one treatment arm.

Hoekstra PT, Casacuberta Partal M, Amoah AS, van Lieshout L, Corstjens PLAM, Tsonaka S, Assaré RK, Silué KD, Meité A, N'Goran EK, N'Gbesso YK, Roestenberg M, Knopp S, Utzinger J, Coulibaly JT, van Dam GJ.
Repeated doses of Praziquantel in Schistosomiasis Treatment (RePST) - single versus multiple praziquantel treatments in school-aged children in Côte d'Ivoire: a study protocol for an open-label, randomised controlled trial.
BMC Infect Dis. 2018 Dec 14;18(1):662.

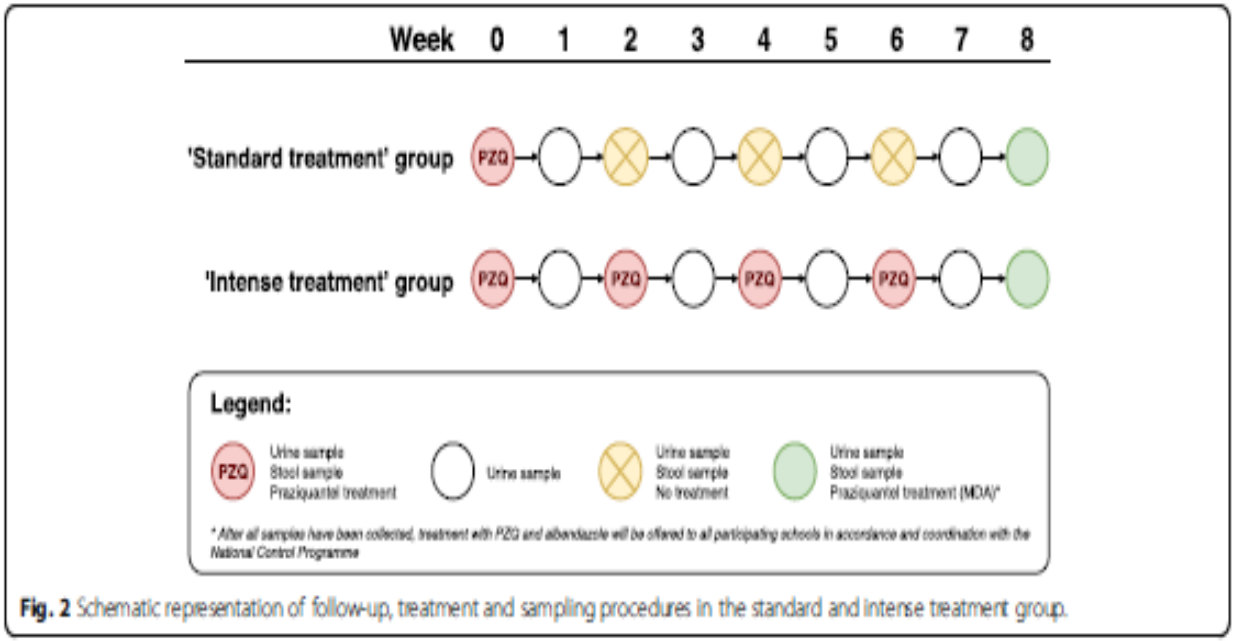
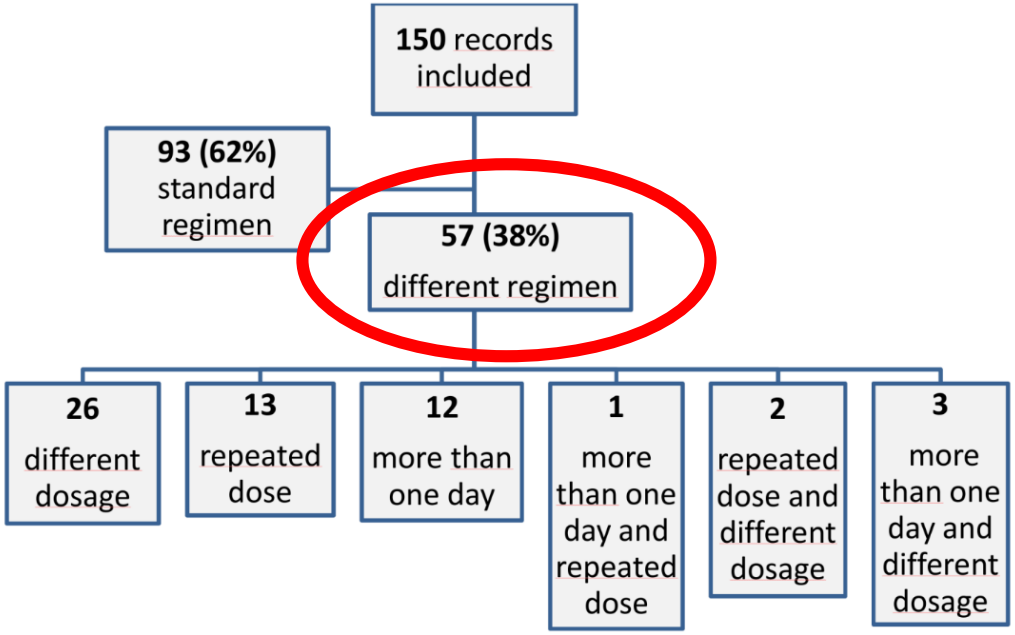


Fig. 2 Schematic representation of follow-up, treatment and sampling procedures in the standard and intense treatment group.

Figure 2. Flow chart describing regimens in the included papers.



Legend:

- Standard regimen: 40 mg/kg of praziquantel for one day (in one or two administrations) for *S. mansoni, S. haematobium* and *S. intercalatum* and 60 mg/kg of praziquantel for one day for *S. mekongi* and *S. japonicum,* according to World Health Organization (WHO) guidelines
- Different regimen: other praziquantel-based treatment schedules
- Different dosage: from 20 mg/kg to 80 mg/kg of praziquantel for one day
- Repeated dose: when the dose of praziquantel was repeated some days/week apart
- More than one day: when praziquantel was given for two or three consecutive days

Cucchetto G, Buonfrate D, Marchese V, Rodari P, Ferrari A, Zanotti P, Bottieau E, Silva R, Bisoffi Z, Gobbi F.
High-dose or multi-day praziquantel for imported schistosomiasis? A systematic review
J Travel Med. 2019 Oct 14;26(7):taz050.

Tamarozzi *et al. Parasites Vectors* (2021) 14:149
https://doi.org/10.1186/s13071-021-04655-z

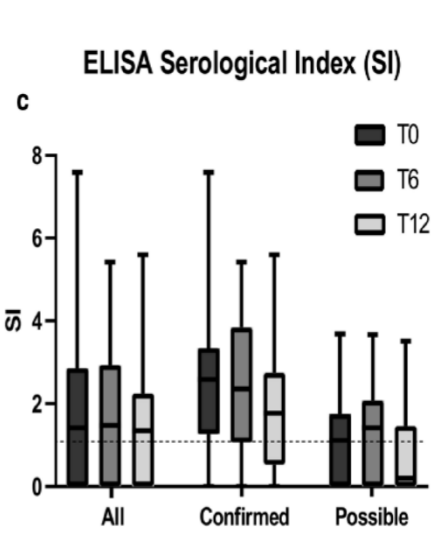
Parasites & Vectors

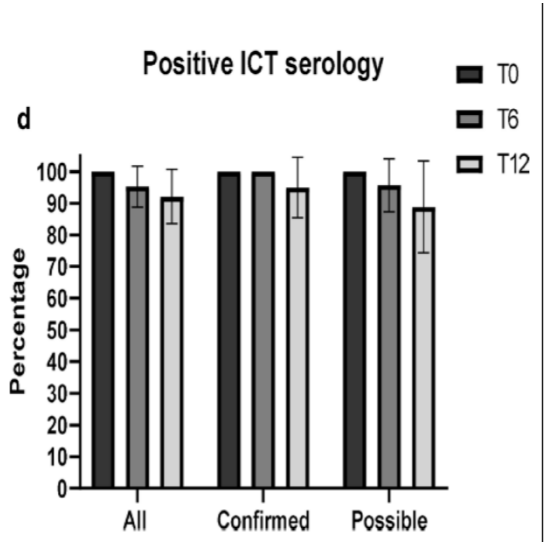
Follow-up

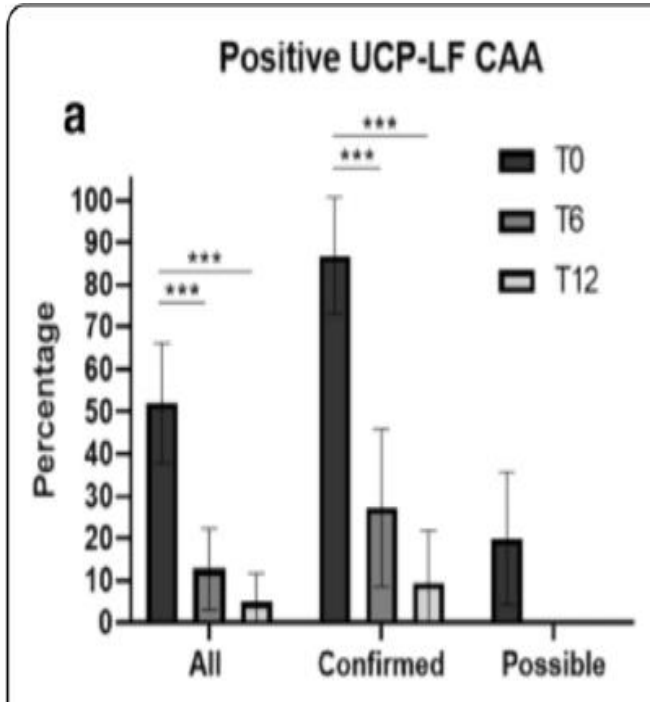
RESEARCH Open Access

Evaluation of microscopy, serology, circulating anodic antigen (CAA), and eosinophil counts for the follow-up of migrants with chronic schistosomiasis: a prospective cohort study

Francesca Tamarozzi[1†], Tamara Ursini[1†], Pytsje T. Hoekstra[2], Ronaldo Silva[1], Cecilia Costa[3], Federico Gobbi[1], Gerardo B. Monteiro[1], Leonardo Motta[4], Govert J. van Dam[2], Paul L. Corstjens[5], Lisette van Lieshout[2] and Dora Buonfrate[1*]





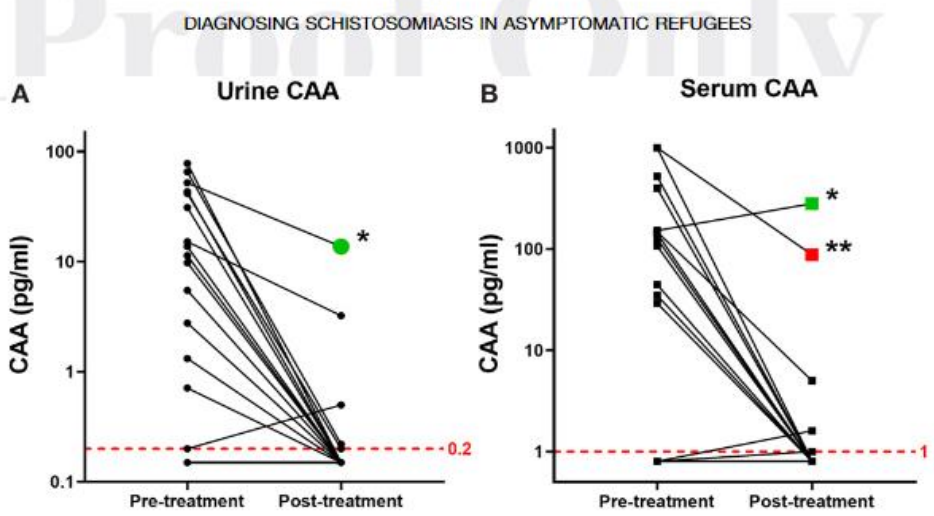


Hoekstra PT, Chernet A, de Dood CJ, Brienen EAT, Corstjens PLAM, Labhardt ND, Nickel B, Wammes L, van Dam GJ, Neumayr A, van Lieshout L.

Sensitive Diagnosis and Post-Treatment Follow-Up of Schistosoma mansoni Infections in Asymptomatic Eritrean Refugees by Circulating Anodic Antigen Detection and Polymerase Chain Reaction

Am J Trop Med Hyg. 2022 Feb 28:tpmd210803.

The CAA test confirmed all microscopy positives, except for two cases that were also negative by all other diagnostic proce-dures

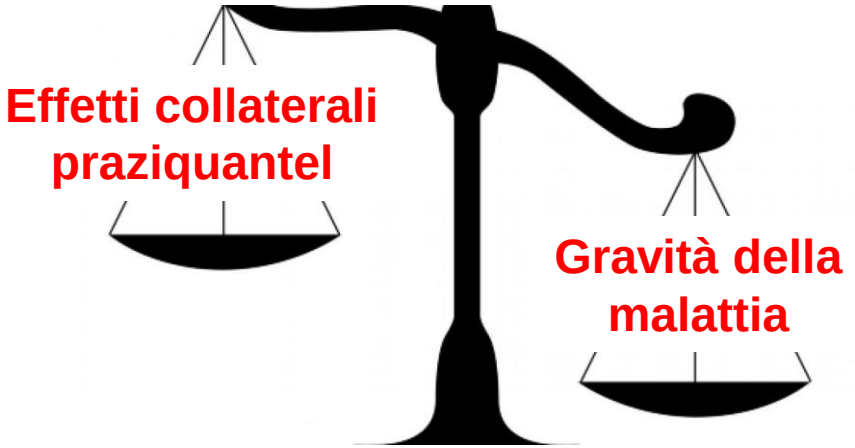


Individuals who were found positive by any of thesemethods were treated with **two doses** of praziquantel (**60 mg/kg** body weight/dose)

Screening

R9.4 – Nei migranti, anche asintomatici, che hanno vissuto o viaggiato in aree endemiche per strongiloidosi * e schistosomiasi (si veda allegato 6), è raccomandato l'esame sierologico, nell'ambito della presa in carico sanitaria. Il riscontro di sierologia positiva per *Strongyloides stercoralis* e *Schistosoma spp*, in soggetti non trattati di recente, deve essere considerato come infezione in atto e come tale meritevole di trattamento. Grado A

* Lo *S. stercoralis* è tendenzialmente ubiquitario e comunemente distribuito nei paesi tropicali e subtropicali, con elevata endemia nel Sud-Est asiatico, in Africa e in Sud America.



Prevalence of strongyloidiasis and schistosomiasis among migrants: a systematic review and meta-analysis

Archana Asundi, Alina Beliavsky, Xing Jian Liu, Arash Akaberi, Guido Schwarzer, Zeno Bisoffi, Ana Requena-Méndez, Ian Shrier, Christina Greenaway

Pooled schistosomiasis prevalence **18.4%** and stool based prevalence **0.9%**

Sub-Saharan African migrants had the highest prevalence **24.1%**

JTM Journal of Travel Medicine
International Society of Travel Medicine
Established 1991
Promoting healthy travel worldwide
Journal of Travel Medicine, 2019, 1–7
doi: 10.1093/jtm/taz075
Original Article

Original Article

Delay in schistosomiasis diagnosis and treatment: a multicenter cohort study in Italy

Agnese Comelli, MD[1,*], Niccolò Riccardi, MD[2], Diana Canetti, MD, DTM&H (LSTM)[2], Michele Spinicci, MD[3], Giovanni Cenderello, MD[4,5], Paola Magro, MD[1], Laura Ambra Nicolini, MD, PhD[6], Valentina Marchese, MD, PhD[1], Lorenzo Zammarchi, MD[3], Francesco Castelli, MD[1], Alessandro Bartoloni, MD, DTM[3], Antonio Di Biagio, MD[6], Silvio Caligaris, MD[1], Giovanni Gaiera, MD[2]

The median diagnostic delay from arrival in Italy was **31 months**:

110 for asymptomatic group and **16 months for symptomatic patients**


THANK
YOU
ASANTE
ASANTE
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DANKON
MULTUMESC
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