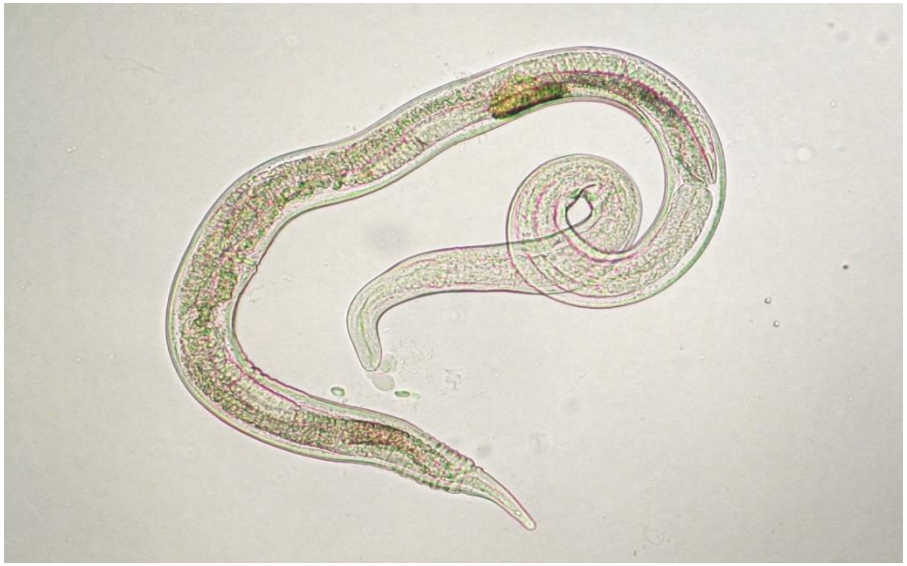
Convegno “Gestione sanitaria dei richiedenti asilo: tubercolosi e le altre”
Venezia, 25/05/2017

Nuove e vecchie problematiche del migrante: le “malattie dimenticate”



Centro Malattie Tropicali
NEGRAR - VERONA - ITALY
Centre for Tropical Diseases

Zeno Bisoffi

WHO Collaborating Center on strongyloidiasis and other intestinal parasitic infections

ccm
Centro nazionale per la prevenzione e il Controllo delle Malattie

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PLOS | NEGLECTED TROPICAL DISEASES

Viewpoints

Strongyloides stercoralis: A Plea for Action

Zeno Bisoffi[1,2*], Dora Buonfrate[1,2], Antonio Montresor[3], Ana Requena-Méndez[2,4], Jose Muñoz[2,4], Alejandro J. Krolewiecki[5], Eduardo Gotuzzo[2,6], Maria Alejandra Mena[2,6], Peter L. Chiodini[2,7], Mariella Anselmi[2,8], Juan Moreira[2,8], Marco Albonico[1,2,9]

➡ Stima di almeno 370 milioni di persone infette nel mondo

Some 30–100 million people are estimated to be infected worldwide (probably an underestimate)”

Journal of
TRAVEL MEDICINE

EDITORIAL

Acute Strongyloidiasis: A Rarity. Chronic Strongyloidiasis: A Time Bomb!

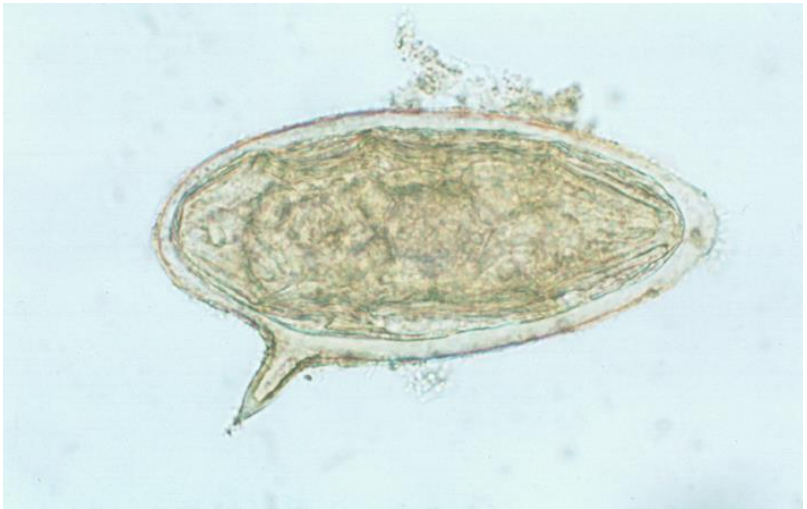
Eric Caumes, MD*† and Jay S. Keystone, MD‡§

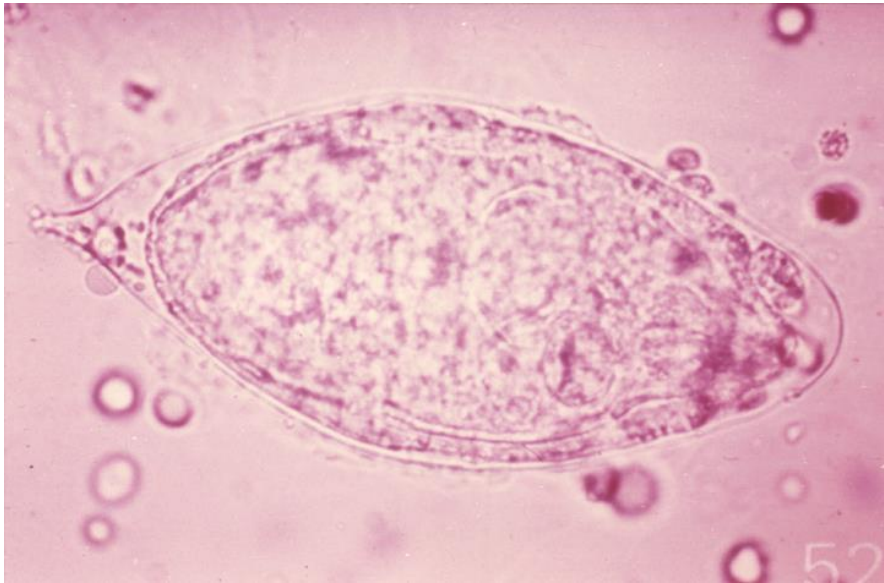
*Service de Maladies Infectieuses et Tropicales, Hôpital Pitié-Salpétrière, Paris, France; †University Pierre et Marie Curie, Paris, France; ‡Tropical Disease Unit, Department of Medicine, Toronto General Hospital, Toronto, Ontario, Canada; §Department of Medicine, University of Toronto, Toronto, Ontario, Canada

Schistosomiasi

S. haematobium

S. mansoni

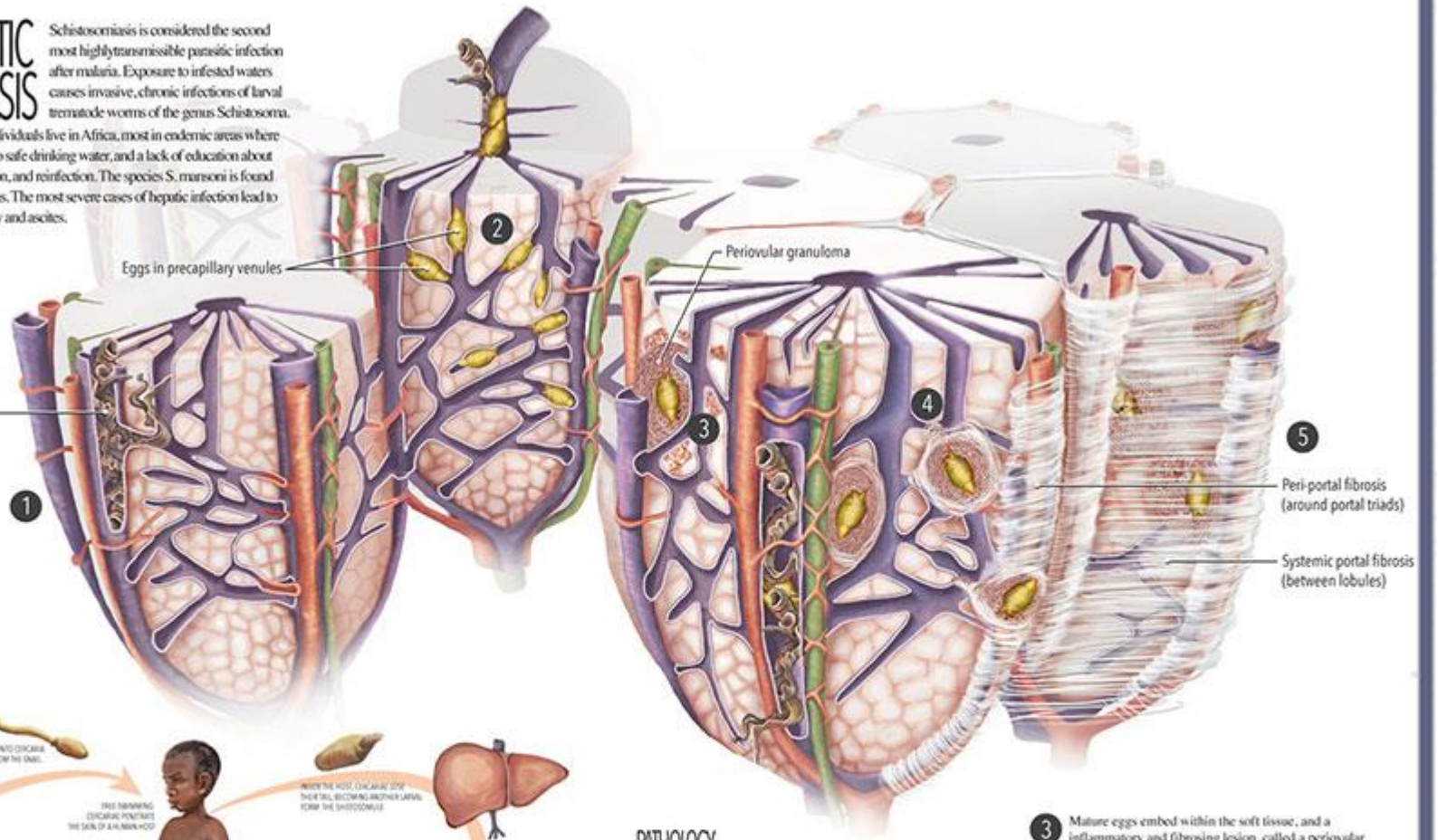




HEPATIC SCHISTOSOMIASIS

Schistosomiasis is considered the second most highlytransmissible parasitic infection after malaria. Exposure to infested waters causes invasive, chronic infections of larval trematode worms of the genus Schistosoma.

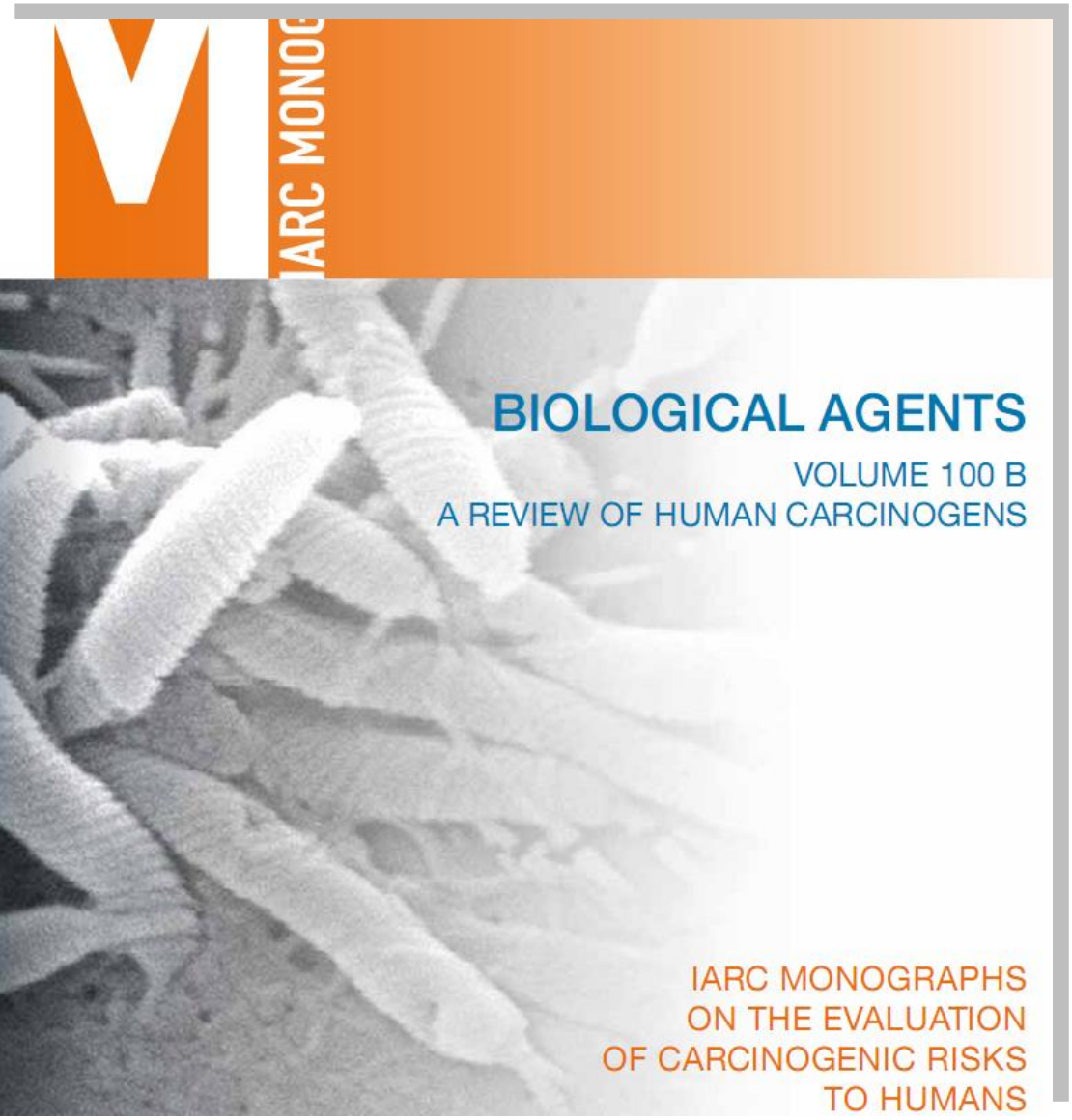
It is estimated that 90% of infected individuals live in Africa, most in endemic areas where inadequate sanitation, limited access to safe drinking water, and a lack of education about hygiene are the main factors ininfection, and reinfection. The species S. mansoni is found in most every case of hepatic infections. The most severe cases of hepatic infection lead to portal hypertensionwith splenomegaly and ascites.



LIFE CYCLE OF S. MANSONI

PATHOLOGY

1. Schistosomulae living in the venous portal-mesenteric system mate, with the female laying upwards of 300 eggs per day in the soft tissues. How severely the disease progress is correlated with worm-load: more worms, more severe.
2. Eggs migrate to precapillary venules, taking 5-7 days to differentiate and produce lytic and antigenic secretions. These secretions flow through micropores in the egg's shell, and are the cause of tissue reaction. They become the local point of infection.
3. Mature eggs embed within the soft tissue, and a inflammatory and fibrosing lesion, called a periovular granuloma, is formed.
4. The periovular granuloma soon becomes encapsulated by the formation of concentric collagen rings at its periphery. Vascular endothelium responds by proliferation, involving both endothelial cells and their associated pericytes, and affecting hepatocytes.
5. Disease begins as periportal granulomatous inflammation and progresses to systemic portal fibrosis with granulomatous chronic inflammation. Severe vascular lesions obstruct intra- and inter-hepatic blood flow.



It is well established that *S. haematobium* with egg deposition in the tissue leads to severe inflammation of the urinary bladder wall with accumulation of inflammatory cells resulting in increased oxidative stress. Overall, the studies summarized above suggest that the observed increased levels of oxidative stress in the schistosomiasis-associated bladder carcinomas correlate with genotoxicity and activation of repair genes, and point towards a relationship between oxidative stress induced by continuous and chronic inflammation due to schistosome infection and possibly nitric-oxide-mediated DNA genotoxicity. The excess of DNA alterations could result from nitric oxide produced by the inflammatory response provoked by Schistosoma eggs, and alkylation of DNA by *N*-nitroso compounds.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of chronic infection with *Schistosoma haematobium*. Chronic infection with *Schistosoma haematobium* causes cancer of the urinary bladder.

IARC Monogr Eval Carcinog Risks Hum 2012;100(PtB):371-382.
IARC working group on the evaluation of carcinogenic reisks to human

Schistosomiasi
Epidemiologia in area non endemica

Prevalenza in gruppi di soggetti in area non endemica		
Rifugiati Sudan (USA) [1]	Sierologia ELISA	44%
Rifugiati Somalia (USA) [1]	Sierologia ELISA	73%
Rifugiati la maggior parte da Africa Sub Sahariana (USA) [2]	Es. parassitologico feci	3%
Viaggiatori/espatriati con storia di bagno nel lago Malawi[3]	Sierologia ELISA	32%

Cortesia Lorenzo Zanmarchi, UFDID Firenze)

1. Posey et al CID 2007
2. Lifson et al Public Health Rep 2002
3. Cetron et al Lancet 1996

Schistosomiasi in richiedenti asilo, CMT 2015-2016

Country of origin	Number of patients tested	Antibodies detection (ELISA)	Ova detection (microscopy)	Schistosoma Antigen detection (CCA)	At least one positive test
Mali	43	24 (55.8%)	19 (44.2%)	9 (20.9%)	31 (72.1%)
Ivory Coast	25	11 (44%)	11 (44%)	7 (28%)	12 (48%)
Senegal	38	13 (34.2%)	7 (18.4%)	5 (13.2%)	15 (39.5%)
Ghana	47	13 (27.7%)	7 (14.9%)	7 (14.9%)	18 (38.3%)
Gambia	30	4 (13.3%)	3 (10%)	5 (16.7%)	7 (23.3%)
Somalia	13	1 (7.7%)	1 (7.7%)	2 (15.4%)	3 (23.1%)
Nigeria	104	11 (10.6%)	6 (5.8%)	5 (4.8%)	15 (14.4%)

Beltrame A. et al. Eur J Epidemiol 2017 (in press)

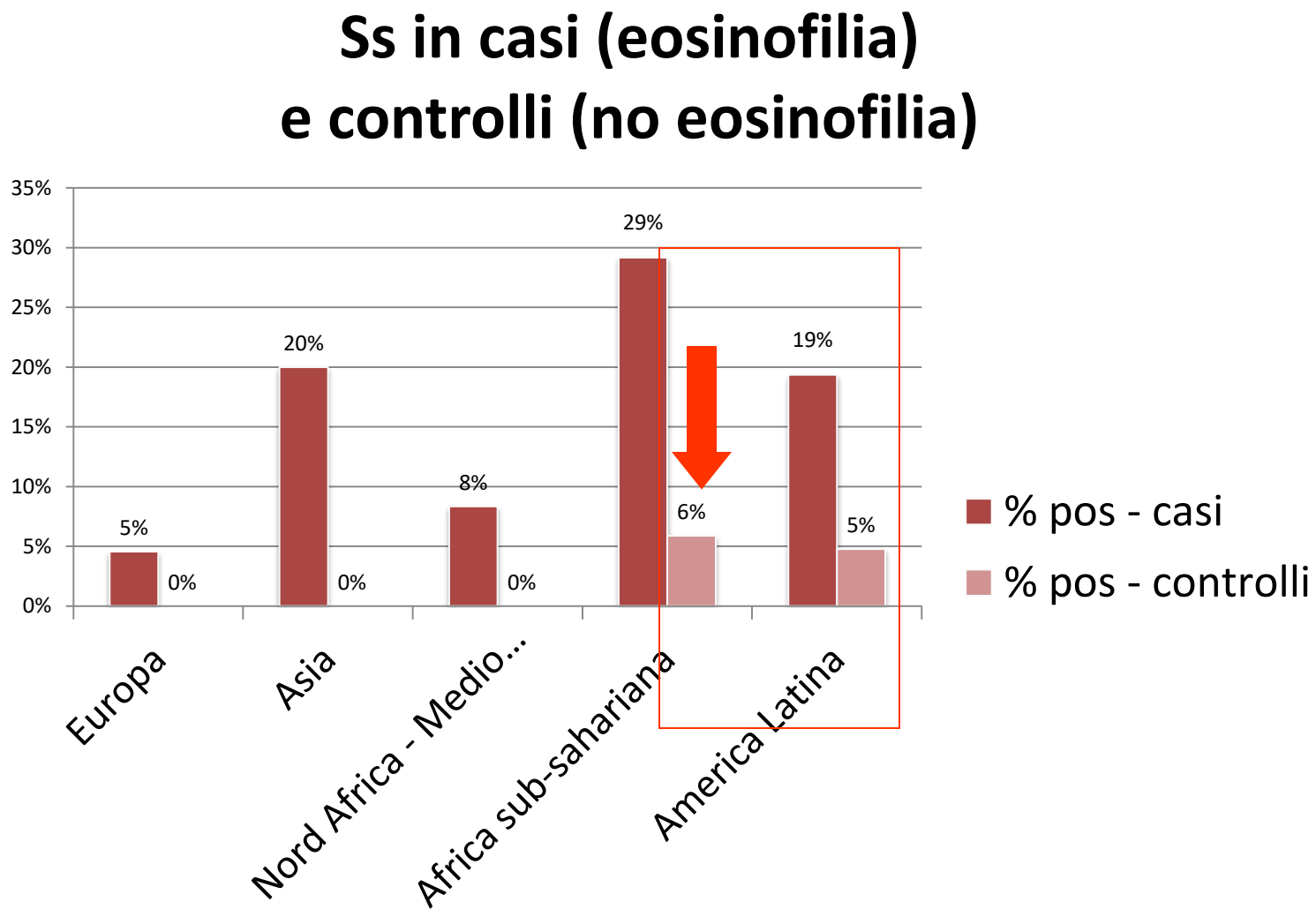
Strongiloidosi e schistosomiasi: questioni aperte per lo screening

1. Eosinofilia utile?

2. Es. microscopico delle feci?

3. Sierologia?

Eosinofilia e *Strongyloides* in immigrati



Buonfrate D, Baldissera M, Abrescia F, Bassetti M, Caramaschi G, Giobbia M, Mascarello M, Rodari P, Scattolo N, Napoletano G, Bisoffi Z; CCM Strongyloides Study Group..
Euro Surveill. 2016 Aug 4;21(31). doi: 10.2807/1560-7917.ES.2016.21.31.30310.

Schistosomiasi (CMT)

Da 01/01/2010 a 31/12/2014 (CMT Negrar): 272 casi
234 immigrati: 46 *S. mansoni*
47 *S. haematobium*
7 *S. mansoni* + *S. haematobium*
134 Schistosoma specie (sierologia)

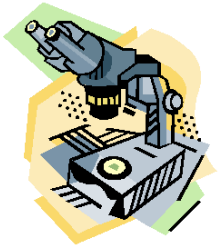
Eosinofili (media)	**410.25/µL (SD 366.55) (IQ range 20-2020)**
Increased AEC (≥400/µL)	**98 (41.9%)**
Total IgE (mean)	**1291.49 (SD 2637) (IQ range 5-25500)**

58.1%
non eosinofilia!

Strongiloidosi: tecniche diagnostiche

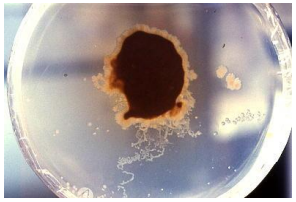
Bassa sensibilità

Microscopia diretta



Baermann

Coprocoltura in agar



Sierologia (obbligatoria per screening)

Alta sensibilità

Bisoffi Z et al. PLoS Negl Trop Dis. 2014; 8(1): e2640

Schistosomiasi, tecniche diagnostiche

Table 2. Accuracy and predictive values according to CRS and to 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%	48%	100%[7]	99%	100%	98%	74%	77%

Beltrame A. et al. PlosNTD 2017 (in press)

Linee guida Ministero della Salute 2017 (documento provvisorio, non ufficialmente approvato)

Parassitosi intestinali

R9.1 - Si raccomanda di considerare, nel contesto della valutazione medica iniziale e durante tutte le fasi del percorso di accoglienza, la presenza di sintomi quali diarrea, dolori addominali, nausea, vomito, prurito, ematuria, in quanto suggestivi di parassitosi. [Grado A]

R9.2 - Nel corso degli accertamenti clinici, il riscontro di eosinofilia deve essere considerato quale possibile marcatore indiretto di elmintiasi. [Grado A]

R9.3 - In presenza di segni e sintomi compatibili con parassitosi intestinale e/o di eosinofilia, si raccomanda di offrire l'esame coproparassitologico per rilevare l'eventuale presenza di parassiti intestinali. [Grado A]

R9.4 - Nei migranti, anche asintomatici, che hanno vissuto o viaggiato in aree endemiche per strongiloidiasi e schistosomiasi*, è raccomandato l'esame sierologico, nell'ambito della presa in carico sanitaria. Il riscontro di sierologia positiva per *Strongyloides* e *Schistosoma*, in soggetti non trattati di recente, deve essere considerato come infezione in atto e come tale meritevole di trattamento. [Grado A]

Linee guida ECDC 2017
(documento provvisorio, non ufficialmente approvato)

Should migrants be screened for Strongyloidiasis?

Recommendation	Serological screening for strongyloidiasis in newly arriving migrants and refugees to Europe from Asia, Africa and Latin America in holding or reception centres. If positive, treat with ivermectin. If patients are immunosuppressed, screened should be performed with a serological test plus parasitological tests. If positive, treat with ivermectin. For strongyloidiasis, if there are no tests or delay in diagnostic methods, presumptive treatment with ivermectin may be recommended

Linee guida ECDC 2017
(documento provvisorio, non ufficialmente approvato)

Should migrants be screened for Schistosomiasis?

Recommendation	Screen all newly arriving migrants/ refugees from high *Schistosoma spp* endemic areas (sub-Saharan Africa , Asia, Southeast Asia and South America) in reception or holding centre with a serological test. If positive, treat with praziquantel. Whenever possible, screen refugees and migrants from high endemic areas with serological test + parasitological techniques for schistosomiasis.