INFECTION 2018
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Roseo Hotel Leon d'Oro - Verona

Migranti e malattie infettive

Dr Andrea Angheben

WHO Collaborating Center on strongyloidiasis and other intestinal parasitic infections

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

Disclosure

DICHIARO che non ho mai intrattenuto alcun tipo di rapporto professionale, economico e/o personale con aziende farmaceutiche e/o di strumenti o presidi sanitari, e dunque l'assenza di conflitto di interessi rispetto all'Evento odierno, ai sensi e per gli effetti degli Accordi Stato-Regioni del 05.11.2009 e del 19.04.2012

Migranti e malattie infettive

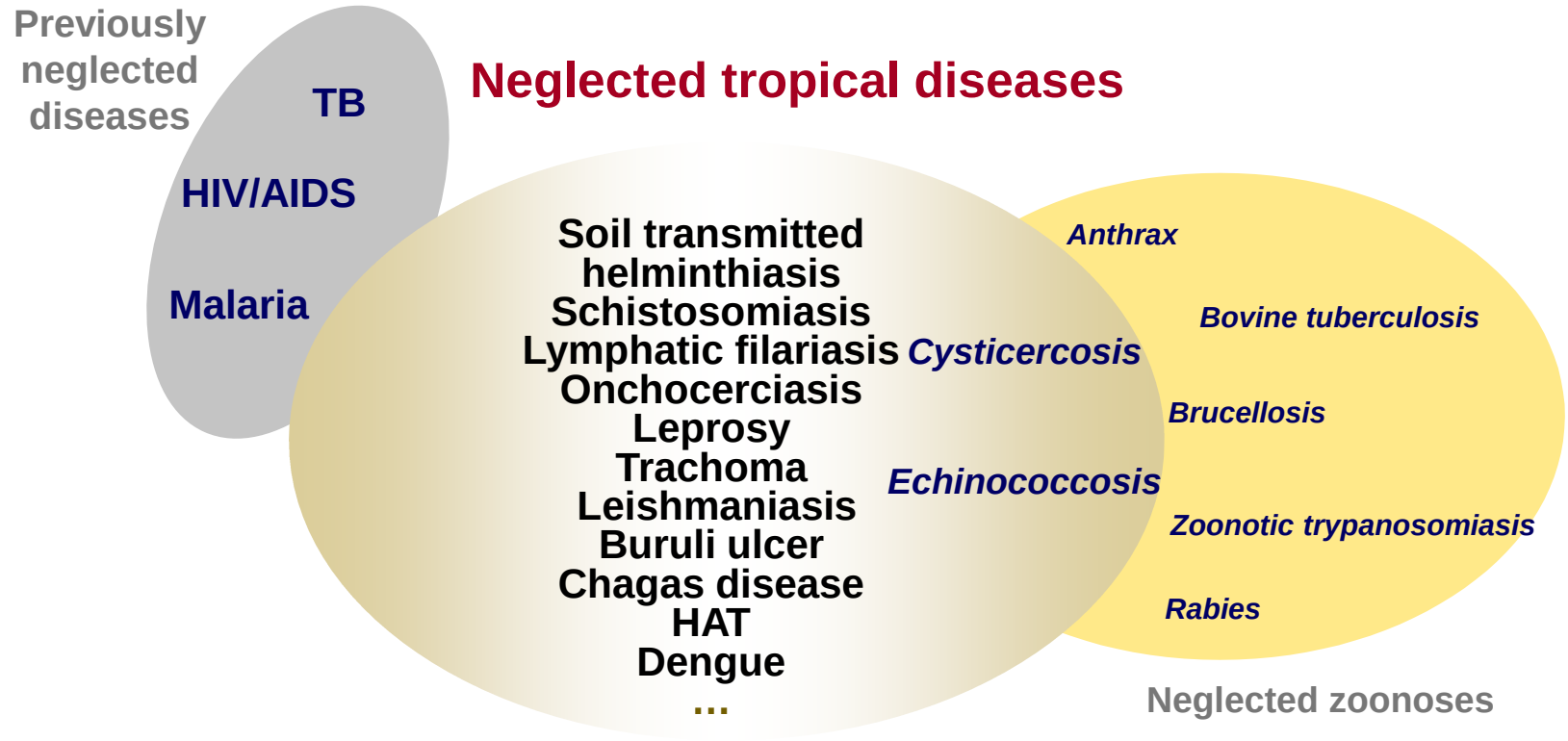
- Il concetto di Neglected Tropical Disease
- Migrazioni ed Effetto migrante esausto
- TBC, HIV, malaria: solo un cenno
- Nuove linee guida ministero salute
- Principali NTDs del migrante in Italia (compresa la scabbia)

prima parte

NTDs: neglected tropical diseases

World Health Organization

NTDs in poor populations



NTDs: several list exist

Table 1. The Major Neglected Tropical Diseases Ranked by Prevalence.*

Disease	Global Prevalence (millions)	Population at Risk
Ascariasis	807	4.2 billion
Trichuriasis	604	3.2 billion
Hookworm infection	576	3.2 billion
Schistosomiasis	207	779 million
Lymphatic filariasis	120	1.3 billion
Trachoma	84	590 million
Onchocerciasis	37	90 million
Leishmaniasis	12	350 million
Chagas' disease	8–9	25 million
Leprosy	0.4	ND
Human African trypanosomiasis	0.3	60 million
Dracunculiasis	0.01	ND
Buruli ulcer	ND	ND

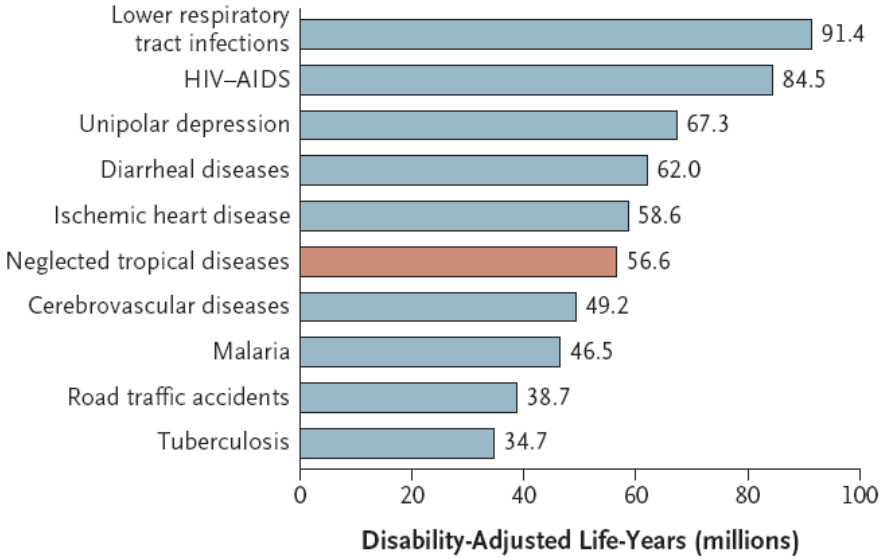


Figure 1. The 10 Leading Causes of Life-Years Lost to Disability and Premature Death.

Hotez et al. N Engl J Med 2007;357:1018-27.

http://www.cdc.gov/globalhealth/ntd/diseases/ntd-worldmap-static.html

WHAT WE CALL “***NEGLECTED DISEASES***” ARE IN FACT

“***DISEASES OF NEGLECTED PEOPLE***”.

AMONG THE NEGLECTED PEOPLE WE FIND THE MIGRANTS

AMONG THE NEGLECTED MEDICAL DISCIPLINES WE HAVE:

“***IMMIGRANT MEDICINE***”.

Manuel Corachan, ECTMIH Verona 2009

PART 2

MIGRAZIONE E SALUTE

Globalizzazione e NTDs

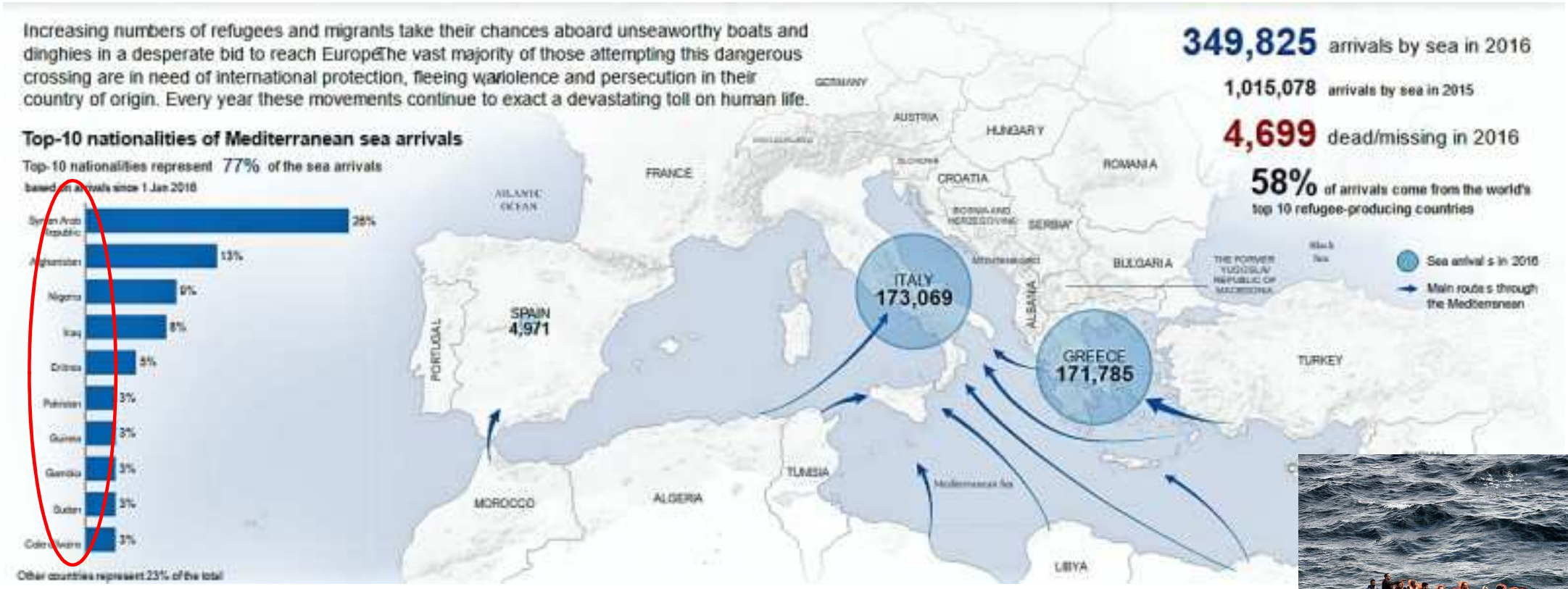
Alcune NTDs: sequele e conseguenze

Malattia	Rischi/sequele
SCHISTOSOMIASI	Pseudocirrosi/ipert. portale; k vescica; aumentata trasmissione HIV
STRONGILOIDIASI	Rischio iperinfestazione/disseminata (immunodepresso)
CISTICERCOSI	Epilessia, Danno neurologico
ECHINOCOCCOSI	Lesioni in sede di localizzazione (fegato, SNC…)
TRACOMA/ONCOCERCOSI	Cecità
FILARIOSI LINFATICA	Infezioni/Linfedema invalidante

Dimensioni del fenomeno migratorio (2015)

- **244 mln** di migranti (**3.3%** della popolazione mondiale)
- **48%** sono donne
- **21,3 mln** di rifugiati
- **3,2 mln** di richiedenti asilo
- **Circa 50 mln** di immigrati irregolari

Flussi migratori nel Mediterraneo nel 2016 (dati UNHCR)



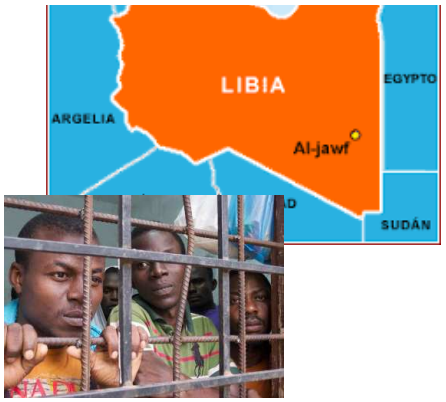
Effetto migrante sano

Meccanismo di **selezione alla partenza di soggetti giovani che possono affrontare il viaggio,** ovvero in condizioni di buona salute e nel pieno dell'efficienza fisica e psichica.

N.B. *Tale meccanismo non vale per chi è costretto a partire in condizioni di particolare vulnerabilità provocate da guerre, persecuzioni, carestie o disastri ambientali* ***(rifugiati, profughi, sfollati).***

Timeline: criticità differenti nei diversi momenti del percorso migratorio

L'effetto migrante sano SFUMA → COMPARE l'effetto migrante esausto



pronto soccorso
malattie diffusive,

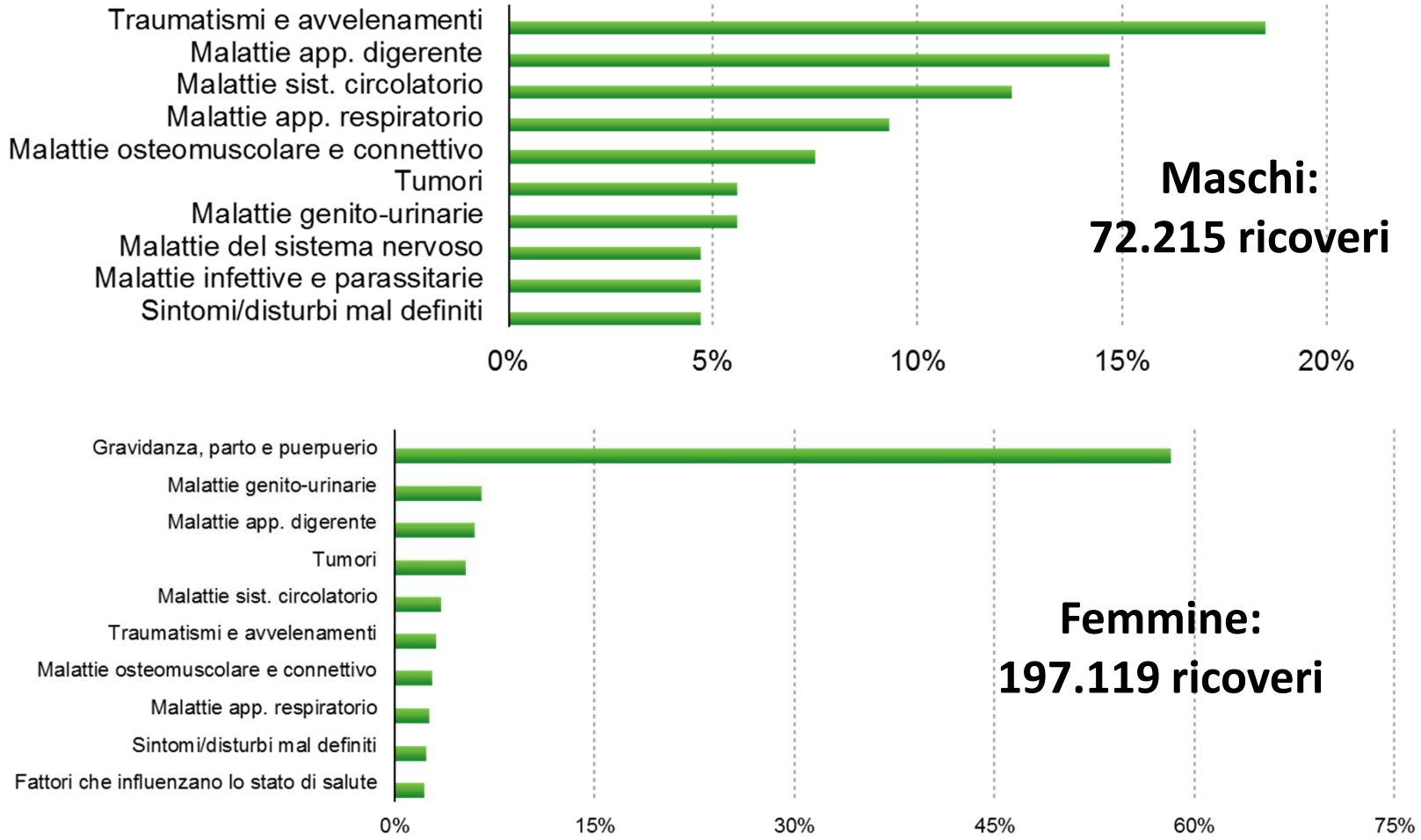
acquisizione/nu
altre patologie di
qualche emergenz
malaria, stress

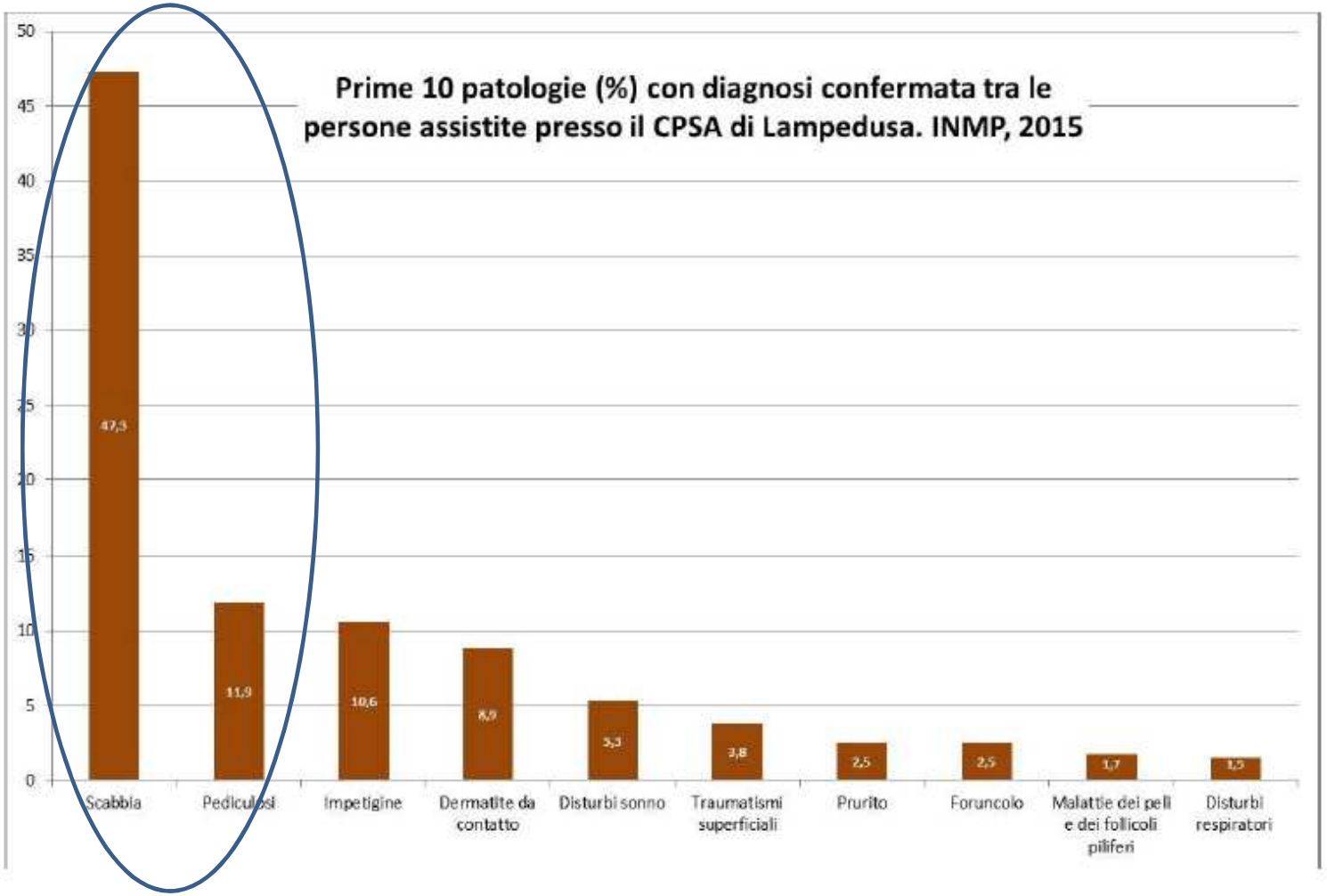
problematiche c
ricorrenti, UGD, p
stress

PART 3

MALATTIE INFETTIVE E MIGRAZIONE: ECTOPARASSITOSI

Motivo di ricovero per gli stranieri in Italia (SIMM, dati da MoH, 2012)





>½ delle visite per scabbia…

Journal of Travel Medicine

International Society of Travel Medicine
Established 1991
Promoting healthy travel worldwide

Journal of Travel Medicine, 2017, 1–8
doi: 10.1093/jtm/tax016
Review

Review

Health problems of newly arrived migrants and refugees in Europe

Dr Androula Pavli, MD, FRACGP, DTM, MPH, PhD*, and Dr Helena Maltezou, MD, PhD

Table 1. Health status of newly arrived migrants

	Study reference[15]		Study reference[10]	
Diagnosis	Number	%	Number	%
Respiratory tract infection	744	23	22	6.7
Rheumatological	591	18	1	0.3
Headache/neurological	325	10	13	4.0
Epigastric pain	297	9		
Dermatological conditions	261	8	7	2.1
Allergic reactions or skin erythema	248	8		
Psychiatric conditions	177	5	7	2.1
Injuries	175	5	66	20.3
Dental problems	99	3		
Cardiac disease	92	3	10	3.1
Gastroenteritis	51	2	34	10.4
Gynaecological/obstetric	43	10	48	14.7
Fever	35	1		
Diabetes mellitus/metabolic	27	1	9	2.8
Genitourinary disease	13	0	4	1.2
Frostbite	5	0		21.9
Unknown			34	10.4
Total	3280	100	326	100

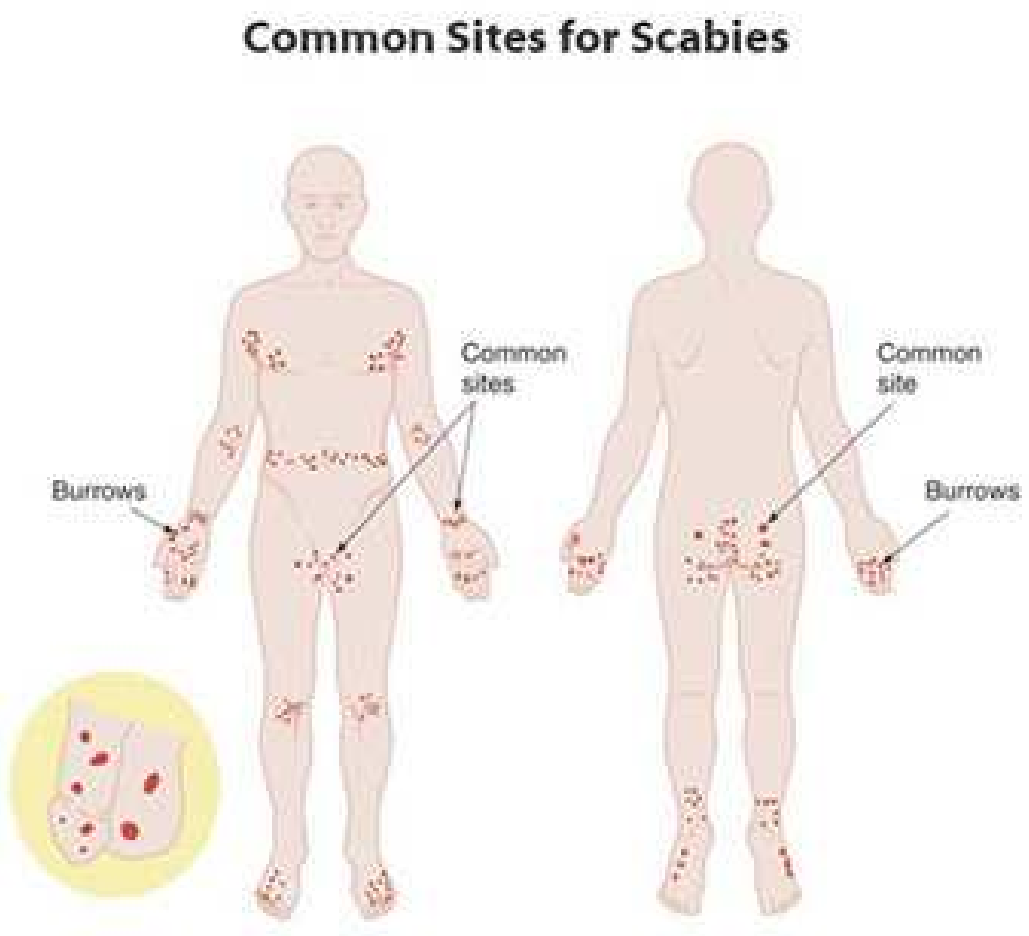
Tabella 1. Distribuzione delle visite effettuate, per diagnosi o sospetto diagnostico, nell'ambito di un intervento di assistenza sanitaria per migranti in transito a Roma. Anni 2014 e 2015.
Table 1. Distribution of medical visits, by diagnosis or diagnostic suspect, in the context of health care intervention for "transient" immigrants in Rome. Years 2014 and 2015.

DIAGNOSI*	ANNO 2014		ANNO 2015	
	n.	%	n.	%
Condizioni generali/sistemiche	176	4,7	519	6,4
sintomi/disturbi	*113*	*3,0*	*256*	*3,2*
malattie infettive	*21*	*0,5*	*108*	*1,3*
Sangue/organi emopoietici e sistema immunitario	3	0,1	10	0,1
Apparato digerente	329	8,8	641	7,9
Occhio	72	1,9	122	1,5
Orecchio	54	1,4	88	1,1
Sistema cardiocircolatorio	25	0,7	47	0,5
Apparato muscolo-scheletrico	93	2,5	301	3,7
Sistema nervoso	114	3,1	250	3,1
Problemi psicologici	5	0,1	8	0,1
Apparato respiratorio	734	19,6	1.040	12,8
sintomi/disturbi	*252*	*6,7*	*371*	*4,6*
infezioni	*468*	*12,5*	*643*	*7,9*
Cute	2.038	54,5	4.912	60,4
infezioni	*1.341*	*35,9*	*3.894*	*47,9*
lesioni traumatiche	*236*	*6,3*	*432*	*5,3*
Endocrino/metabolico/nutrizionale	34	0,9	94	1,2
Sistema urinario	22	0,6	27	0,3
Gravidanza/parto	19	0,5	34	0,4
Apparato genitale femminile	12	0,3	15	0,2
Apparato genitale maschile	7	0,2	24	0,3
Problemi sociali	2	0,1		
Totale	**3.739**	**100,0**	**8.132**	**100,0**

*Per la codifica delle diagnosi è stata utilizzata la Classificazione internazionale delle cure primarie ICPC-2R (traduzione italiana: http://www.kith.no/upload/2705/ICPC-2-Italian.pdf), modificata dall'INMP. / *The International Classification of Primary Care ICPC-2R was used to encode diagnoses, with modified by INMP.*

SCABBIA

- La femmina secerne un liquido cheratolitico che le permette di attraversare gli strati cornei superficiali formando un pozzetto in cui si ferma in attesa di un maschio vagante
- La femmina gravida inizia a scavare il CUNICOLO (al confine tra corneo e granuloso) e semina uova lungo il decorso: 2-3 uova al giorno per tutta la durata della sua vita che è di circa di 30 giorni
- Solo il 10% delle uova matura

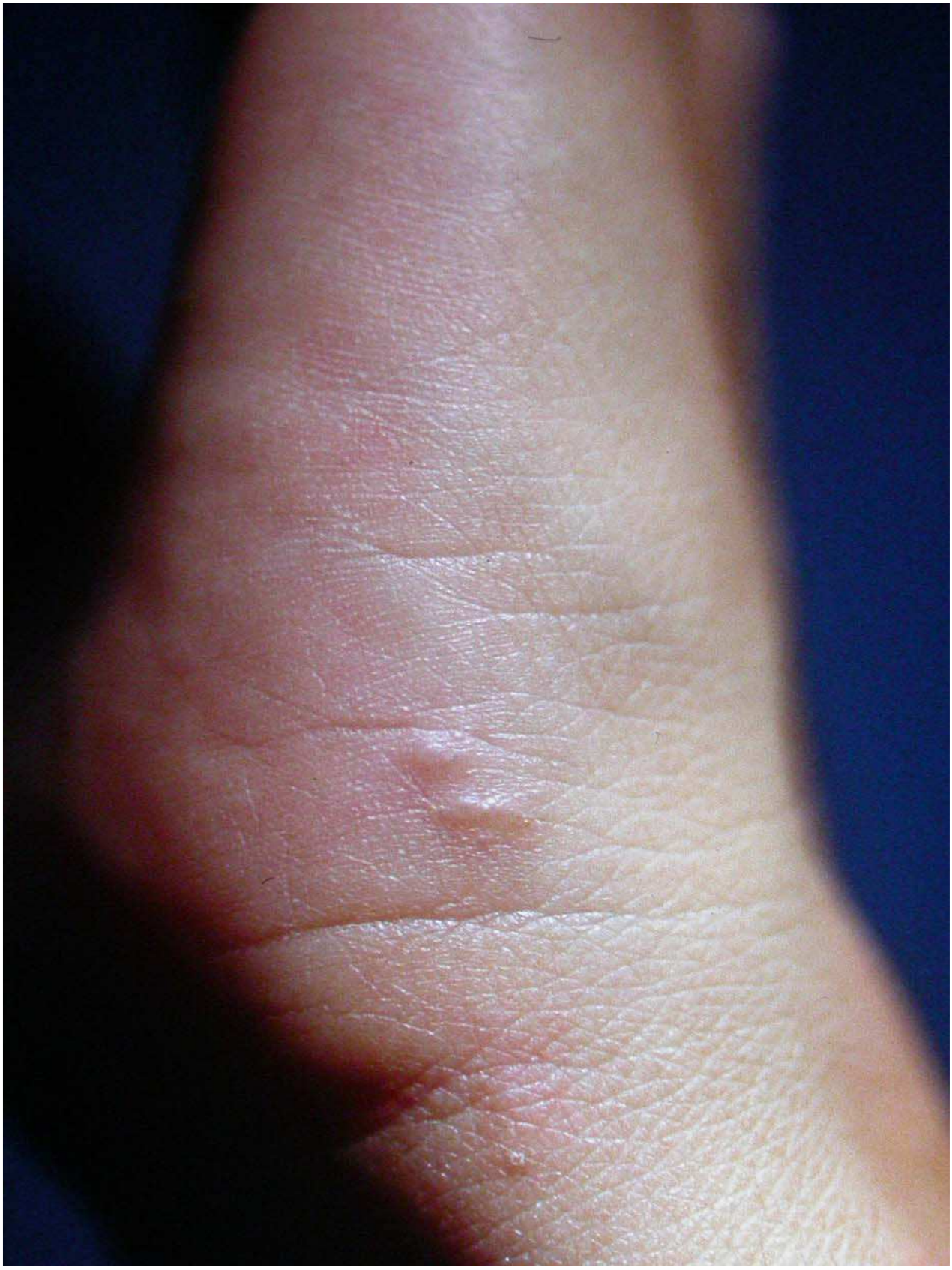


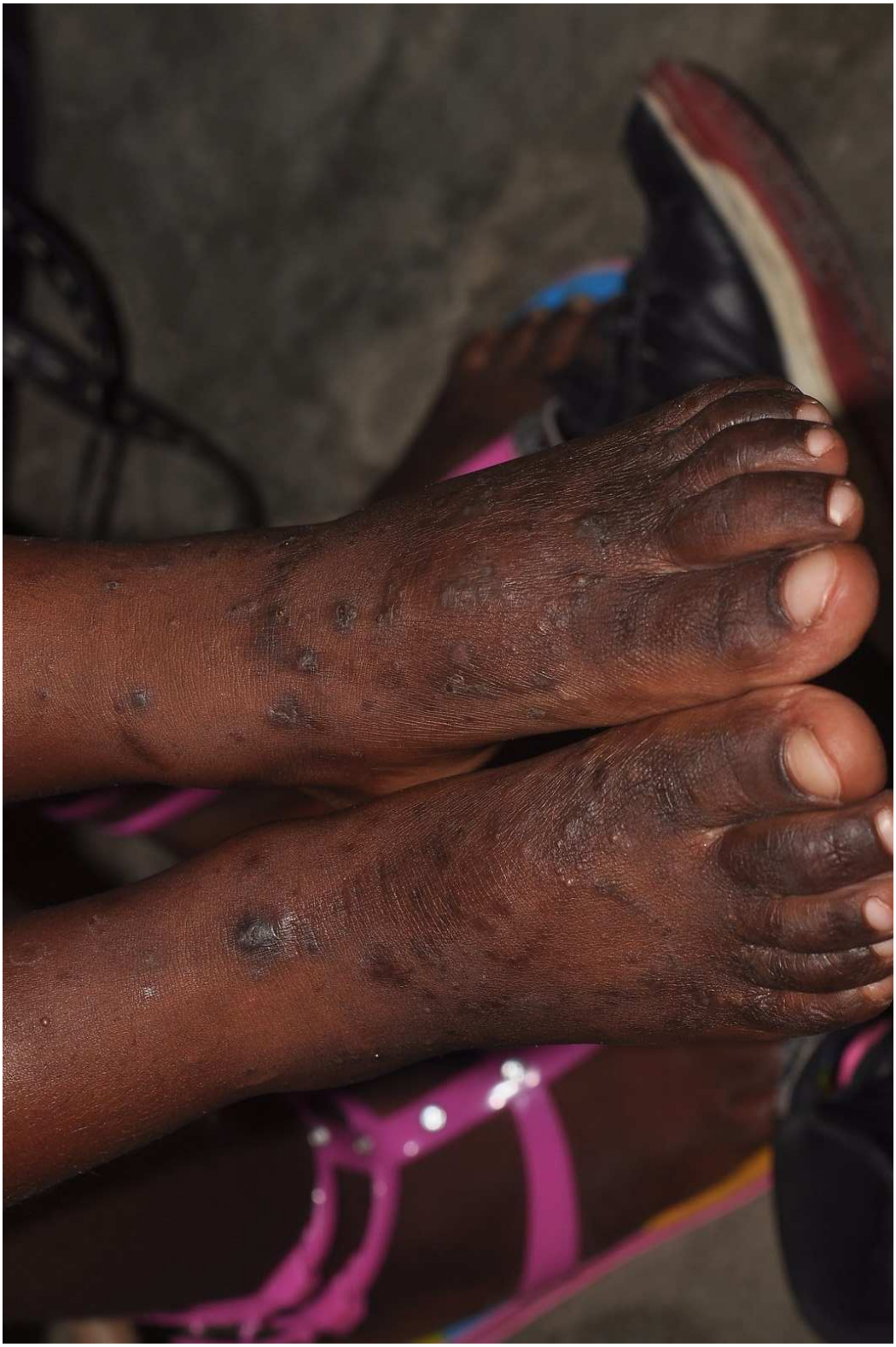
CLINICA

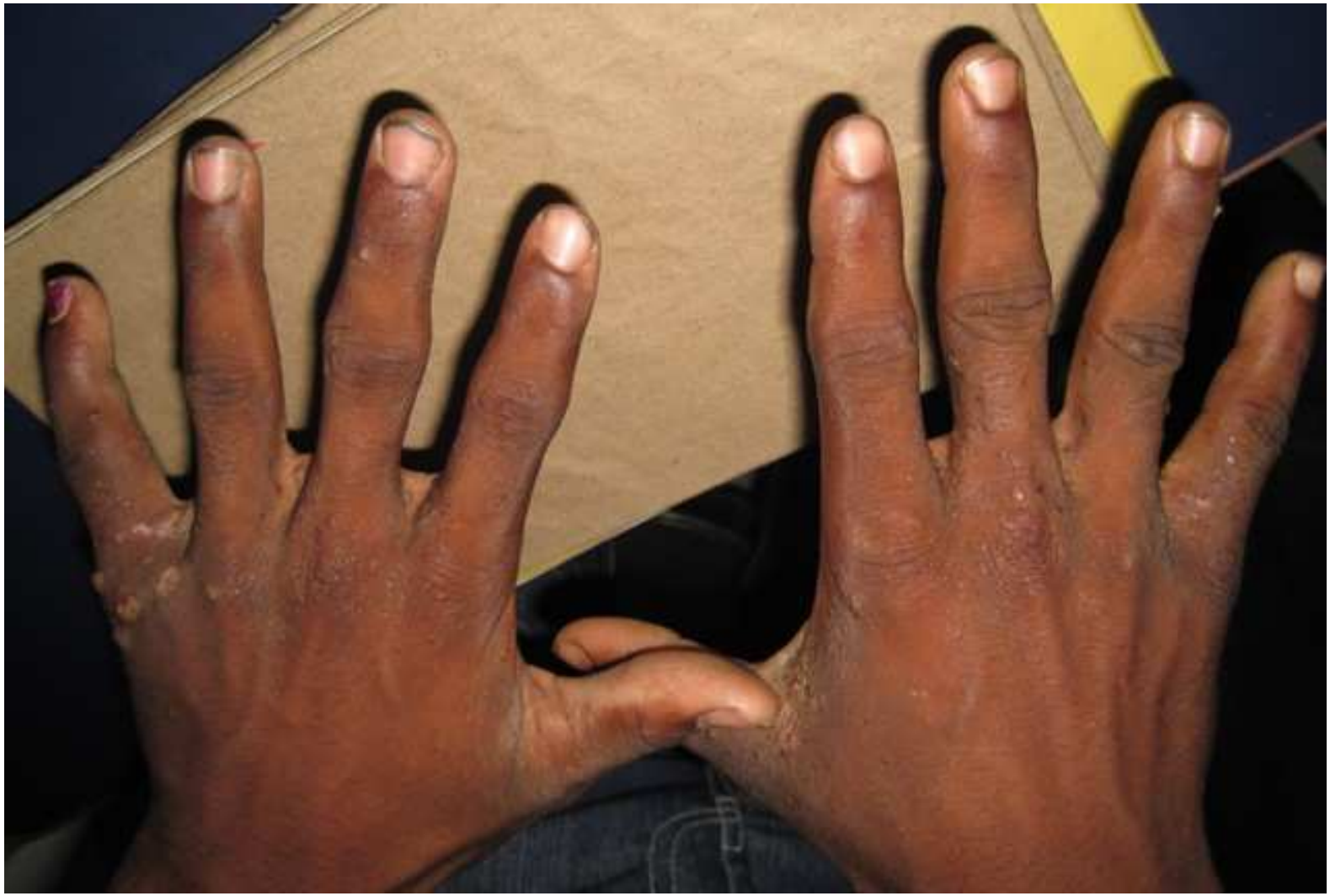
- CUNICOLI
- VESCICOLE
- NODULI
- LESIONI SECONDARIE:
  - lesioni da grattamento
  - impetiginizzazione
- PRURITO: prevalentemente notturno

INCUBAZIONE

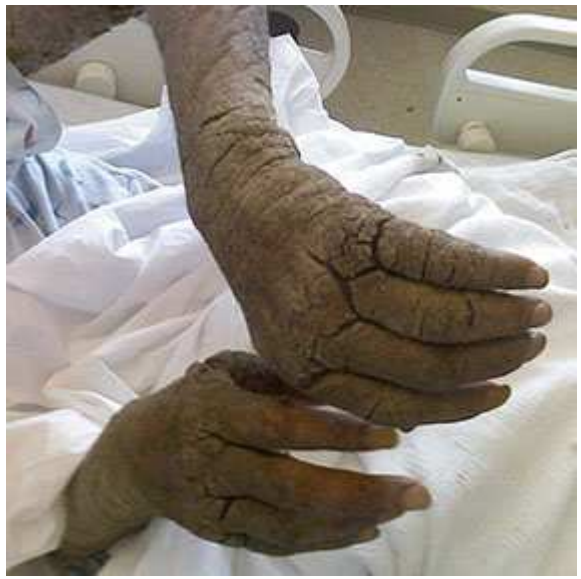
- 2-6 settimane - comparsa di prurito (reazione di ipersensibilità di IV tipo)
- In caso di reinfezione il prurito compare già dopo 48 ore







SCABBIA



VARIANTI CLINICHE

- SCABBIA NORVEGESE

- Pazienti con diminuite difese immunitarie
(soggetti defedati, cachettici, con neuropatie, AIDS*…)
- Assenza di prurito: ritardo nella diagnosi
- Molta contagiosa per elevato numero di acari
-Ipercheratosi palmo-plantare, ipercheratosi subungueale: grande contagiosità per disseminazione di squame
-Eritema e desquamazione del volto, del collo, o generalizzata

* Talora assenza di ipercheratosi

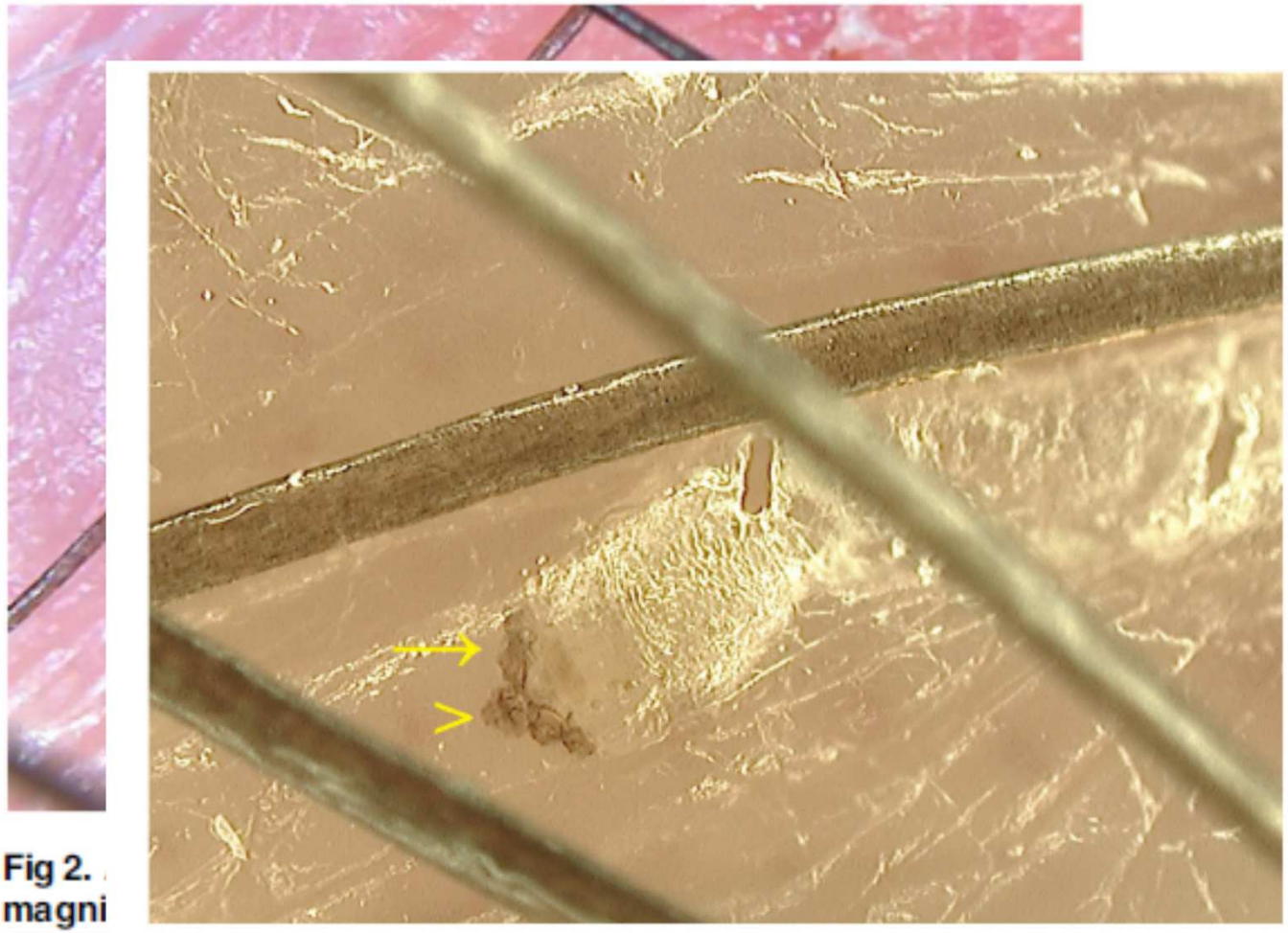


Fig 1. *Sarcoptes scabiei* observed by videodermatoscopy at X400 magnification. The mite, localized at the end of the burrow, has a roundish body and pigmented head (arrowhead) and anterior legs (arrow).

doi:10.1371/journal.pntd.0004691.g001

SCABBIA

TERAPIA

- PERMETRINA in crema al 5%; applicazione serale (12h) per 2 cicli di 2gg intervallati da 7gg di riposo (92-98% EFFICACIA)
- IVERMECTINA* in compresse (200µg/Kg in una unica somministrazione da ripetersi dopo 7 gg attiva anche su pediculosi
- BENZOATO DI BENZILE in crema al 25%; applicazione quotidiana (24h) per cicli di 2 gg intervallati da 7 gg di riposo (50% EFFICACIA)

- IVERMECTINA* in compresse (200µg/Kg in una unica somministrazione da ripetersi dopo 7 gg (74% → 95% DOPO 1 O 2 SOMMINISTRAZIONI)

https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/louse-borne-relapsing-fever-in-eu-rapid-risk-assessment-17-nov-15.pdf

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

RAPID RISK ASSESSMENT

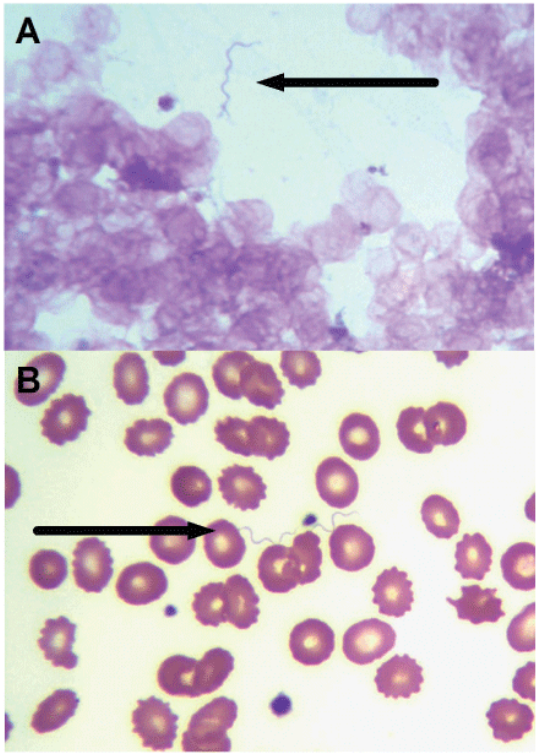
Louse-borne relapsing fever in the EU

17 November 2015

http://www.eurosurveillance.org/content/10.2807/1560-7917.ES2015.20.32.21204

FIGURE 2

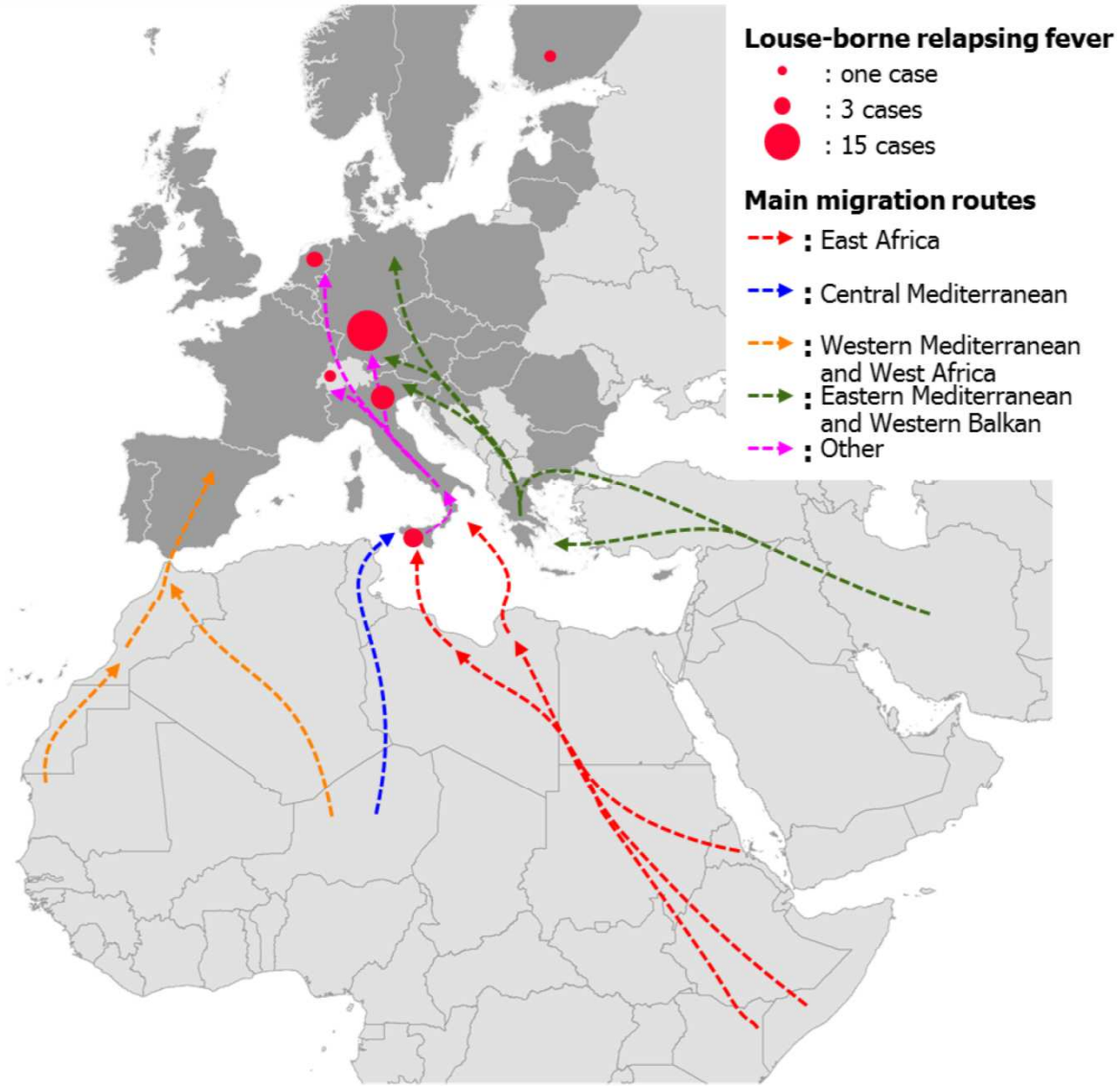
Microscopic detection of spirochetes in blood, louse-borne relapsing fever case, Switzerland, August 2015



Panel A: Giemsa pH 7.2, stained thick film, 1,000-fold magnification.

Panel B: May-Grünwald Giemsa (MGG)-stained blood smear, 1,000-fold magnification.

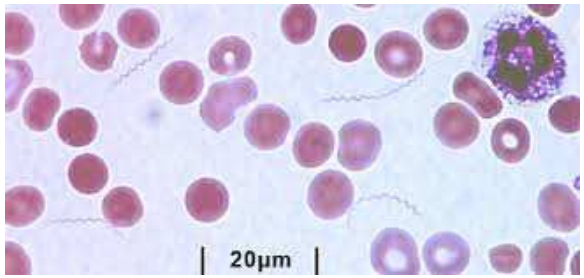
Figure 1. Distribution of the 27 cases of louse-borne relapsing fever in Europe by reporting country in 2015, and main migration routes*



EPIDEMIOLOGY of Relapsing fevers

- **There are two epidemiological forms:**
  - Louse borne relapsing fever
  - Tick borne relapsing fever
- **Louse borne relapsing fever is transmitted**:
  - **ONLY** between humans, by the body louse, ***Pediculus humanus, var corporis*.**
  - It is endemic in Ethiopia, the Sudan, and Rwanda.
  - It is a disease of poverty, overcrowding, poor personal hygiene, and infestation with lice.

PATHOGENESIS



- Portal of entry, infected lice crushed into abraded skin.
- Incubation period, 5-10 days.
- High level spirochetemia.
- Patients' producing neutralizing antibodies,

  clearing of the circulating strain ***Borrelia*** *in 3-5 days*

- New **ANTIGENIC VARIANTS** appear
  - Recurrence of clinical symptom/signs;
  - up to 3-5 relapses may occur

.

CLINICAL FEATURES

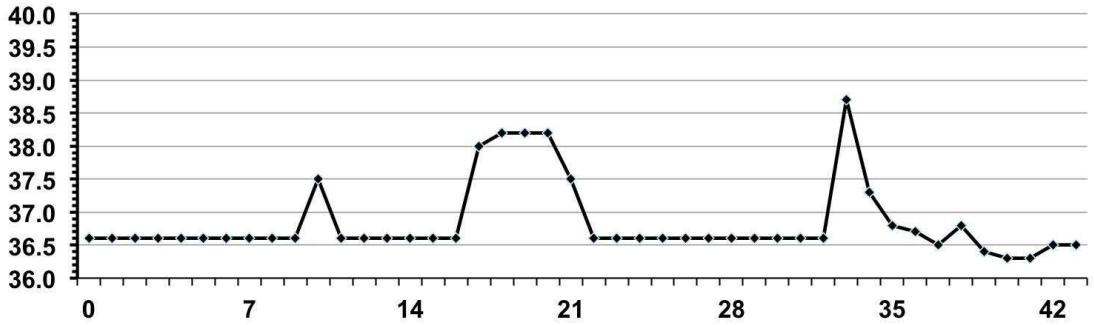
- Incubation period, 5-10 days, average 7 days.
- The range of clinical symptoms/ signs is wide.
- In a typical sever case there is abrupt onset of fever, 39-40.
- The following is the dominant clinical features:

TABLES

Table 1. Manifestations of tick-borne relapsing fever acquired in the northwestern United States and southwestern British Columbia. (Adapted from Dworkin MS, Schwan TG, Anderson DE, Borchardt SM. Tick-borne relapsing fever. Inf Dis N Am 2008;22:449-468.13).

Sign or symptom	%	Sign or symptom	%
Headache	94	Photophobia	25
Myalgia	92	Neck pain	24
Chills	88	Rash	18
Nausea	76	Dysuria	13
Arthralgia	73	Jaundice	10
Vomiting	71	Hepatomegaly	10
Abdominal pain	44	Splenomegaly	6
Confusion	38	Conjunctival injection	5
Dry cough	27	Eschar	2
Eye pain	26	Meningitis	2
Diarrhea	25	Nuchal rigidity	2
Dizziness	25		

Table 2. Antibiotic treatment of tick-borne and louse-borne relapsing fever in adults. (Adapted from Dennis DT, Hayes EB. Relapsing fever. In: Braunwald E, Hauser SL, Fauci AS, Longo DL, Kasper DL, Jameson JL, editors. Harrison's principles of internal medicine. 16th edition. New York: McGraw-Hill: 2005).



ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

RAPID RISK ASSESSMENT

Cutaneous diphtheria among recently arrived refugees and asylum seekers in the EU

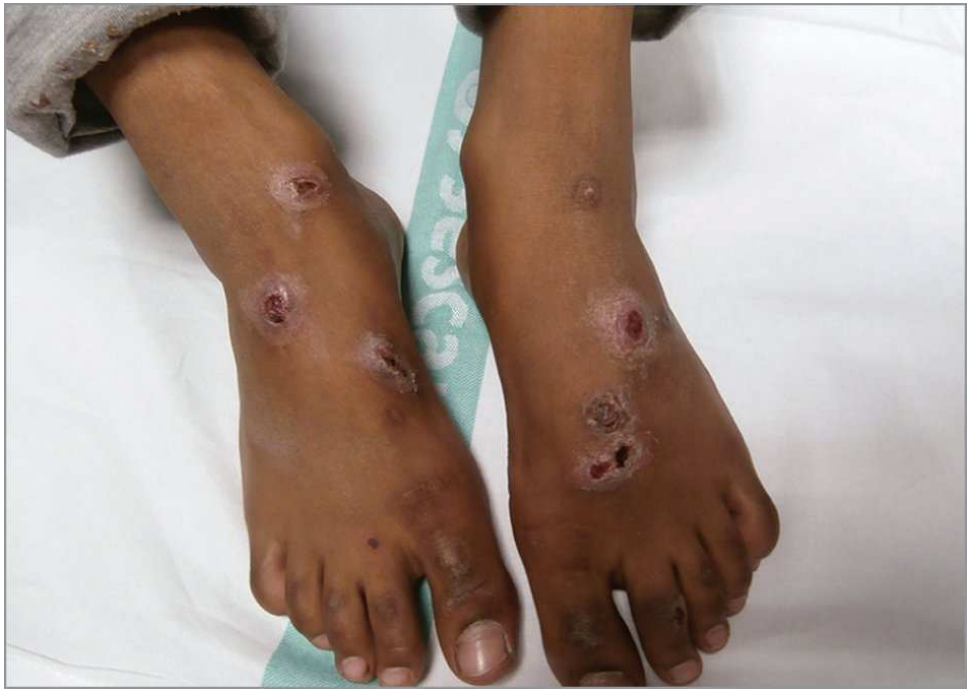
30 July 2015

Table 1: Number of cases of *C. diphtheriae* and *C. ulcerans* reported in the EU/EEA, by year and country, 2009–2014

Year	2009	2010	2011	2012	2013	2014	Total
All diphtheria cases	**10**	**14**	**20**	**27**	**31**	**38**	**140**
C. diphtheriae							
Total	**5**	**3**	**12**	**16**	**19**	**24**	**79**
Reporting country (n)	DE (2), SE (1), UK (2)	DE (1), LV (1), UK (1)	DE (2), FR (3), LV (6), SE (1)	DE (3), FR (2), LV (8), NL (1), SE (2)	LV (14), SE (2), UK (3)	AT (2), DE (3), ES (1) FR (1), LV (12), NL(1), NO (2) SE (2)	AT (2), DE (11), ES (1), FR (6), LV (41), NL(2), NO (2) SE (8), UK (6)
Age range (yrs)	11–74	20–68	11–69	3–75	5–75	2–76	2–76
C. ulcerans							
Total	**3**	**11**	**7**	**11**	**12**	**13**	**57**
Reporting country (n)	FR (1), UK (2)	DE (7), FR (2), LV (1), UK (1)	DE (2), FR (2), SE (1), UK (2)	BE (1), DE (6), FI (1), FR (2), UK (1)	BE (1), DE (4), FR (6), UK (1)	DE (6), FR (5), SE(1), UK (1)	BE (2), DE (25), FI (1), FR (18), LV (1), SE (2), UK (8)
Age range (yrs)	30–87	19–89	59–85	10–92	46–85	13–88	10–92
Unknown type							
Reporting country	DE (2)	0	LT (1)	0	0	LV (1)	4
Age range (yrs)	56–62	—	55	—	—	78	55–78

Countries reporting cases: AT–Austria, BE–Belgium, DE–Germany, ES–Spain, FI–Finland, FR–France, LT–Lithuania, LV–Latvia, NL–Netherlands, NO–Norway, SE–Sweden, UK–United Kingdom.

Of the 79 *C. diphtheriae* cases, 25 were reported as cutaneous infections. Seven of these 25 were indigenous cases from Latvia and 18 cases were imported. In addition to the 25 cases reported as cutaneous infections, 14 imported cases missed information about the clinical manifestations but are likely to be cutaneous infections. The probable origin of the imported cases were Angola, Afghanistan, Cameroon, Cambodia, Ethiopia, The Gambia, India, Kenya, Madagascar, Mozambique, Pakistan, the Philippines, Sierra Leone, Thailand, the Democratic Republic of the Congo, Sri Lanka and Togo. For all but four cases, the vaccination status was reported as unknown or uncertain. The available surveillance data at European level show a wide age range of cases, with a preponderance in adults and the elderly.



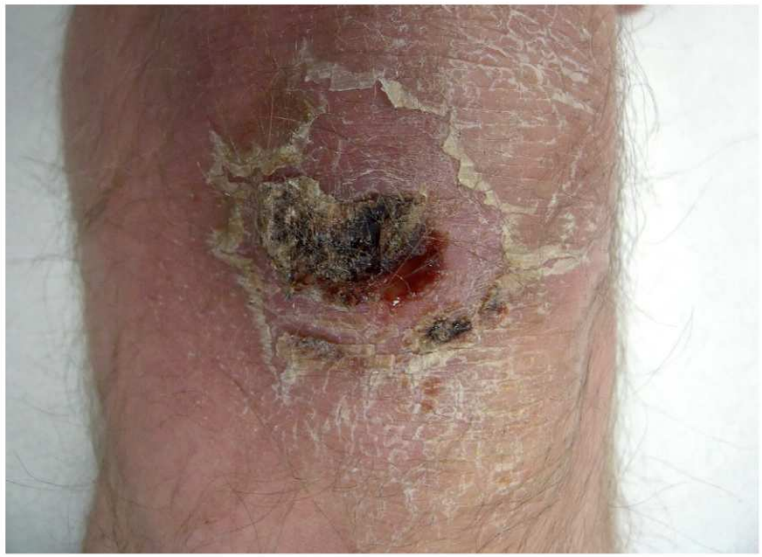
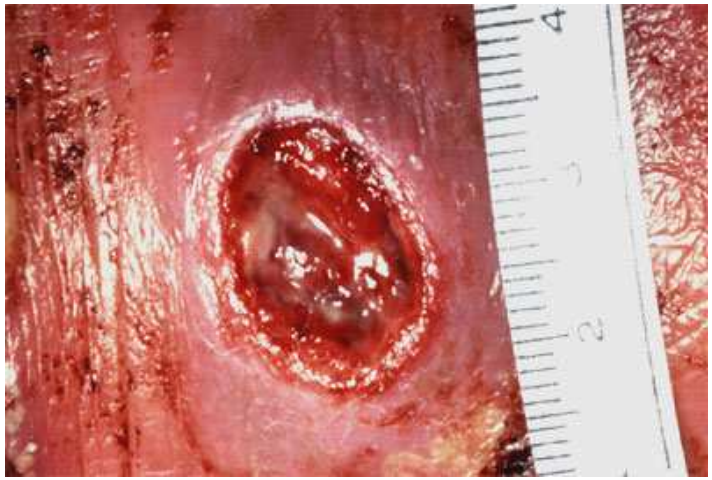


Fig. 1. Ulcer with firm brownish crust and haemorrhage on the left knee.



Part 4

E NON SOLO…

Dalla salute della comunità alla salute del singolo (=beneficio per la comunità)…

REVIEW

Prevalence rates of six selected infectious diseases among African migrants and refugees: a systematic review and meta-analysis

A. Chernet [1,2] · J. Utzinger [1,2] · V. Sydow [1,2] · N. Probst-Hensch [1,2] · D. H. Paris [1,2] · N. D. Labhardt [1,2,3] · A. Neumayr [1,2]

(https://doi.org/10.1007/s10096-017-3126-1)

In this systematic review and meta-analysis, records on six selected infectious diseases among African migrants/refugees were retrieved and reviewed: chronic viral hepatitis B, chronic viral hepatitis C, helminthiasis infections with soil-transmitted helminths (Ascaris lumbricoides, hookworm, and Trichuris trichiura), schistosomiasis (infections with blood flukes of the genus Schistosoma), intestinal protozoa infection (e.g., Entamoeba histolytica and Giardia intestinalis), and syphilis. We intentionally did not include tuberculosis

The median prevalence of syphilis, hepatitis B, and hepatitis C were 4.4%, 10.5%, and 3.4%, respectively, the median prevalences of schistosomiasis, helminthiasis, and intestinal protozoa infection were 13.8%, 13.6%, and 17.0%, respectively.

Clinical Microbiology and Infection 23 (2017) 335.e1–335.e5

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Seroprevalence of five neglected parasitic diseases among immigrants accessing five infectious and tropical diseases units in Italy: a cross-sectional study

G. Martelli [1, *, †], C. Di Girolamo [2, 3, †], L. Zammarchi [4, 5], A. Angheben [6], M. Morandi [7], S. Tais [8], M. Degani [8], I. El Hamad [9], S. Caligaris [10], A. Ciannameo [2], E. Grilli [11], L. Urbinati [10], G.B. Monteiro [6], C. Scarcella [9], N. Petrosillo [11], M. Digaetano [1, 12], L. Rabbi [1], N. Bazzanini [1, 13], F. Cacciatore [2], B.L. Marta [2], M.L. Moro [7], A. Bartoloni [4, 5], P. Viale [1], G. Verucchi [1]

Prevalenze effettive

11,2 % prevalenza di positività ad almeno una malattia

- 56/1011 strongiloidiasi → **5,5%**
- 33/571 schistosomiasi → **5,8%**
- 12/111 toxocariasi → **10,8%**
- 7/56 filariasi → **12,5%**
- 8/226 malattia di Chagas → **3,5%**
- 2/32 leishmaniasi → **6,3%**

G.Martelli courtesy

• Quesito 9 •

È indicata l'esecuzione di un esame parassitologico delle feci come screening delle parassitosi intestinali nei migranti durante il percorso di accoglienza? È indicato un programma di screening dello *Strongyloides*? È indicato un programma di screening dello *Schistosoma*?

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 (anche anamnestica), 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**

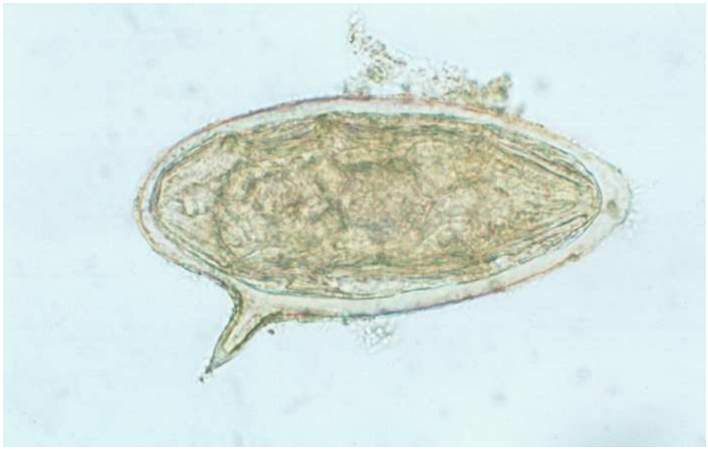
R9.4 – Nei migranti, anche asintomatici, che hanno vissuto o viaggiato in aree endemiche per strongiloidosi * e schistosomiasi (si veda allegato 6), è raccomandato l'esame sierologico, nell'ambito della presa in carico sanitaria. Il riscontro di sierologia positiva per *Strongyloides stercoralis* e *Schistosoma 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.

http://www.salute.gov.it/imgs/C_17_pubblicazioni_2624_allegato.pdf

Schistosomiasi

S. mansoni



S. haematobium

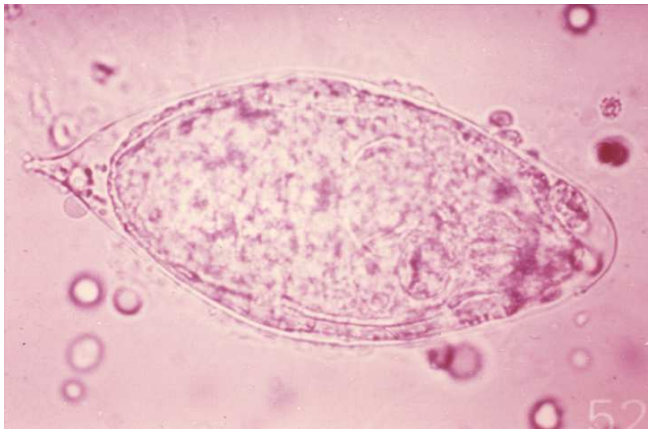


Table 3 Systematic review on schistosomiasis

	Author	Year of publication	African refugees (irrespective of geographic origin)			Sub-Saharan African refugees (SSA)			North African refugees (NA)			Ref.
			No. of individuals tested for *Schistosoma*	No. of individuals tested positive for *Schistosoma*	%	No. of individuals tested for *Schistosoma*	No. of individuals tested positive for *Schistosoma*	%	No. of individuals tested for *Schistosoma*	No. of individuals tested positive for *Schistosoma*	%	
1	Beltrame et al.	2017	373	127	34	374	127	34	–	–	–	[S73]
2	Chernet et al.	2017	107	63	59	107	63	59	–	–	–	[S74]
3	Martelli et al.	2017	393	27	6.9	323	25	7.7	70	2	2.9	[S75]
4	Serre Delcor et al.	2016	171	48	28.1	171	48	28.1	–	–	–	[S19]
5	Monpierre et al.	2016	167	12	7.2	–	–	–	–	–	–	[S35]
6	Cobo et al.	2016	2185	278	12.7	1930	278	14.4	255	0	0	[S1]
7	Monge-Maillo et al.	2015	317	19	5.9	317	19	5.9	–	–	–	[S3]
8	Bocanegra et al.	2014	260	36	13.8	260	36	13.8	–	–	–	[S8]
9	McCarthy et al.	2013	2804	370	13.2	2301	256	11.1	503	114	23	[S22]
10	Norman et al.	2010	1862	27	1.5	1810	26	1.4	52	1	1.9	[S36]
11	Sheikh et al.	2009	168	37	22	168	37	22	–	–	–	[S13]
12	Gibney et al.	2009	206	84	40.8	206	84	40.8	–	–	–	[S37]
13	Brodine et al.	2009	171	46	26.9	171	46	26.9	–	–	–	[S38]
14	Franco-Paredes et al.	2007	42	27	64	42	27	64	–	–	–	[S39]
15	Posey et al.	2007	562	299	53	562	299	53	–	–	–	[S26]
16	Varkey et al.	2007	1547	203	13.1	–	–	–	–	–	–	[S29]
17	Tiong et al.	2006	217	27	12	217	27	12	–	–	–	[S40]
18	Caruana et al.	2006	124	14	11	124	14	11	–	–	–	[S30]
19	Roca et al	2002	1321	200	15.2	1321	200	15.2	–	–	–	[S34]
		Median prevalence [range]:			13.8	[1.5–64.0]		15.2	[1.4–64.0]		2.4	[0.0–23.0]

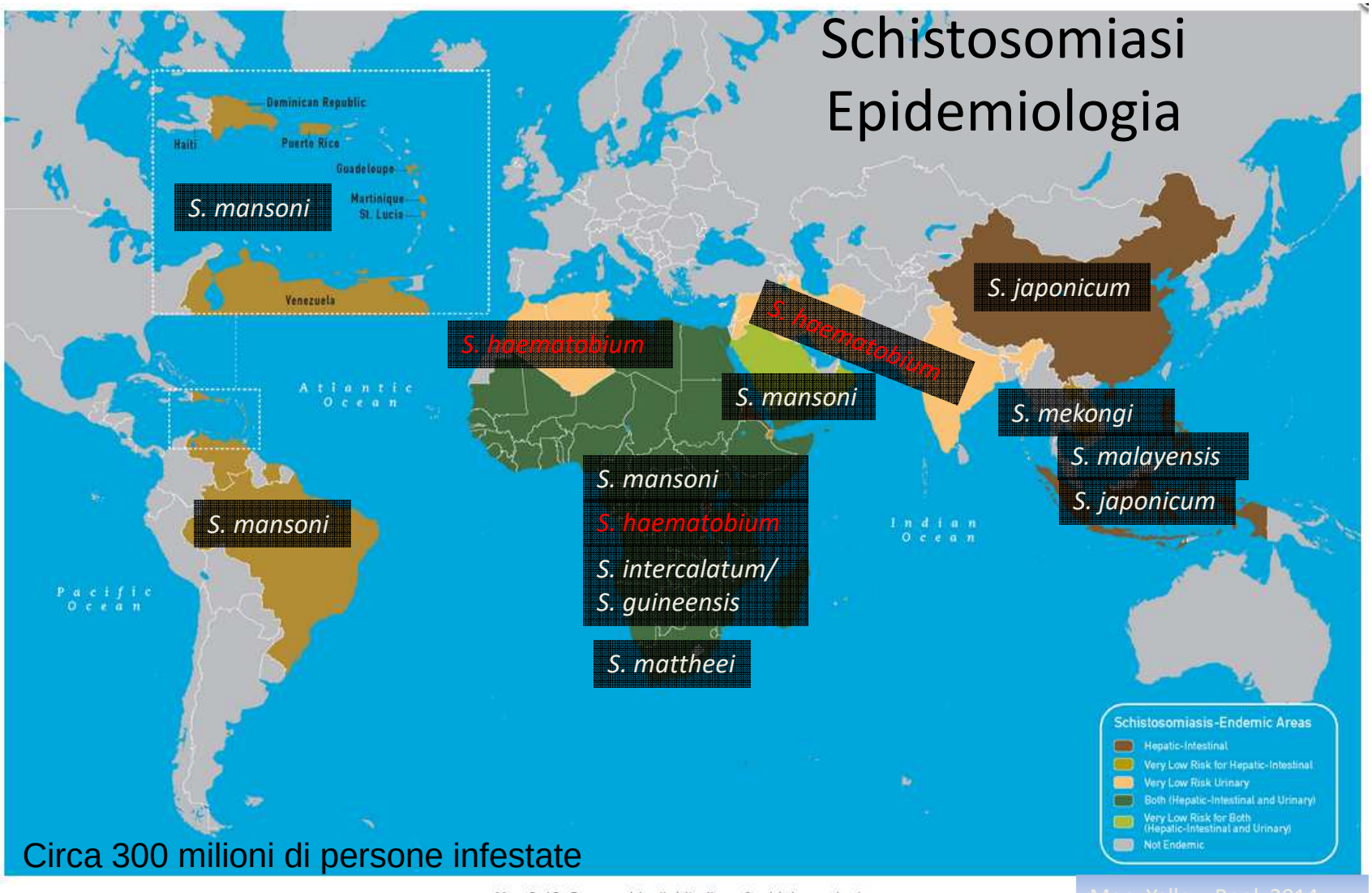
Eur J Clin Microbiol Infect Dis
https://doi.org/10.1007/s10096-017-3126-1

REVIEW

Prevalence rates of six selected infectious diseases among African migrants and refugees: a systematic review and meta-analysis

A. Chernet[1,2] · J. Utzinger[1,2] · V. Sydow[1,2] · N. Probst-Hensch[1,2] · D. H. Paris[1,2] · N. D. Labhardt[1,2,3] · A. Neumayr[1,2]

Schistosomiasi Epidemiologia



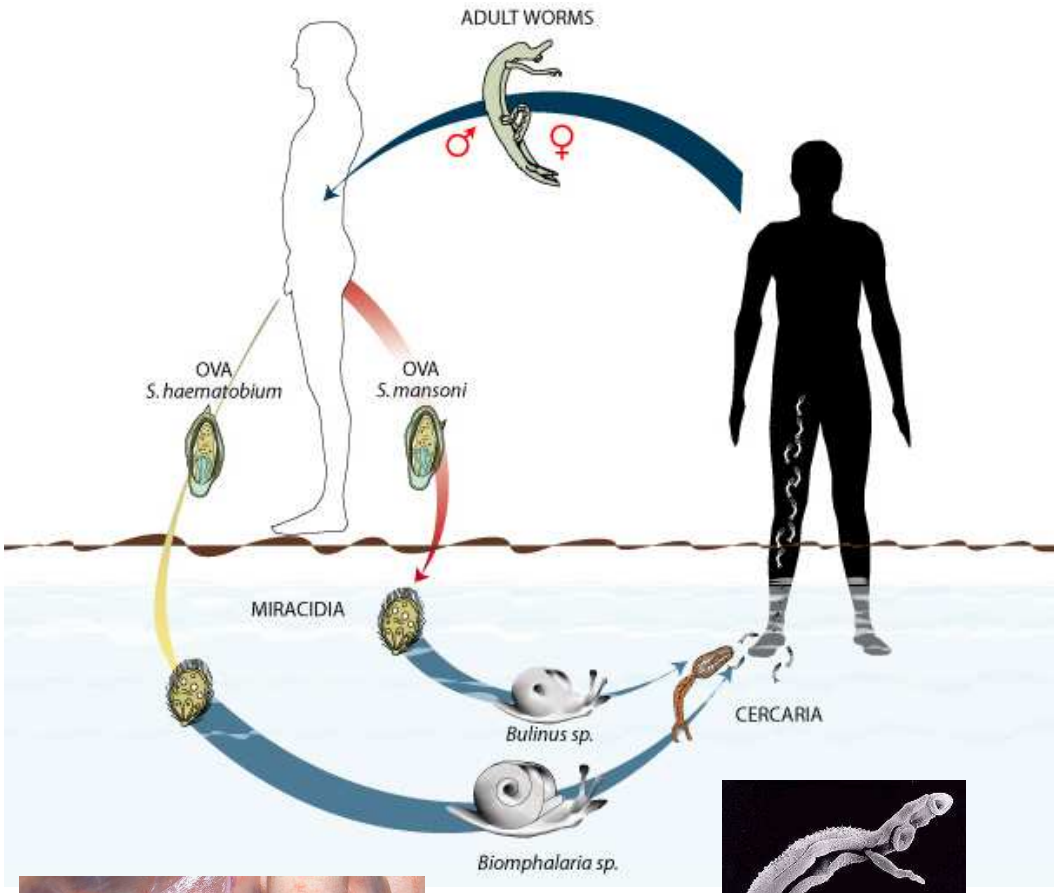
Circa 300 milioni di persone infestate

Map 3-12. Geographic distribution of schistosomiasis

Map: Yellow Book 2014

Schistosomiasi epato-intestinale: *S. mansoni, S. japonicum, S. mekongi, S. intercalatum, S. guineensis*

Schistosomiasi genito-urinaria: *S. haematobium*



LO SCHISTOCICLO nell'uomo

la cercaria infesta derma e mucose

↓

schistosomuli (cute 1-3 giorni)

↓

verme adulto (sistema portale) vita media 3-8 anni

↓

accoppiamento e migrazione
(v. mesenterica inferiore-plesso vescicale e pelvico)

↓

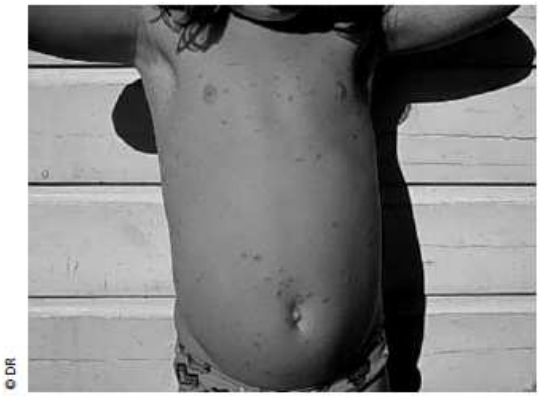
liberazione di uova

Manifestazioni cliniche acute

Manifestazioni iniziali (tutte le specie di Schistosoma su base immuno-allergica)

1. Dermatite da cercarie o prurito del nuotatore (<72h)

2. Febbre (o sindrome) di Katayama (2sett-3 mesi)

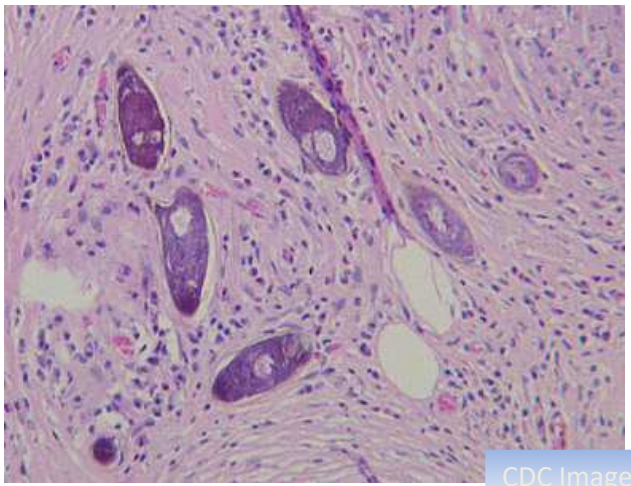


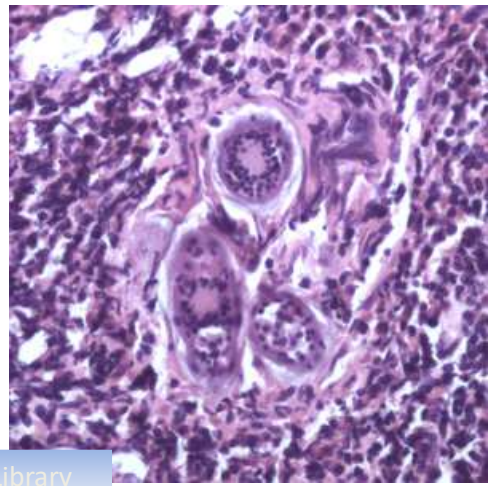
Figures 1 et 2 Dermatite cercarienne : lésions maculo-papuleuses érythémateuses

1. Bourée Presse Med 2004

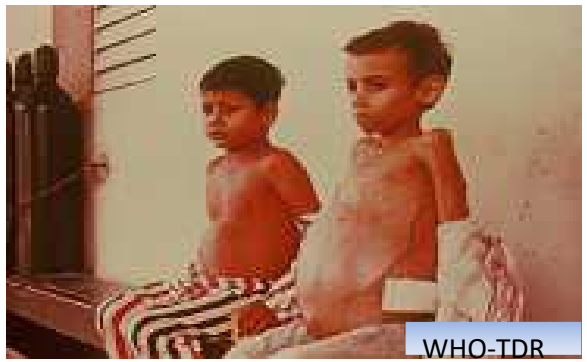
Manifestazioni cliniche croniche

Manifestazioni croniche d'organo (specie-specifiche, conseguenza di reazione granulomatosa-fibrotizzante intorno alle uova presenti nei tessuti)





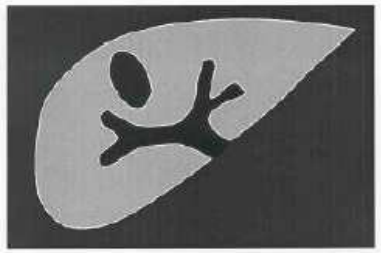
CDC Image Library



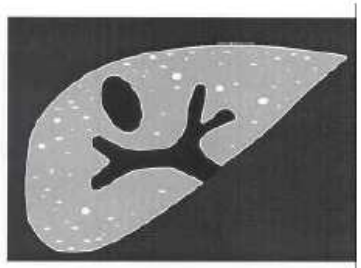
WHO-TDR

ANNEX A: IMAGE PATTERNS IN THE LIVER PARENCHYMA, OBSERVED BY ULTRASONOGRAPHY

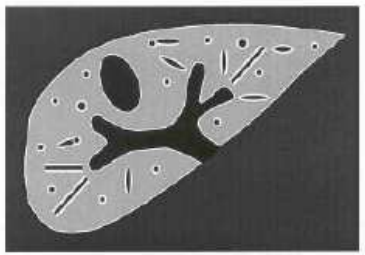
Patterns associated with schistosomiasis (A – F)



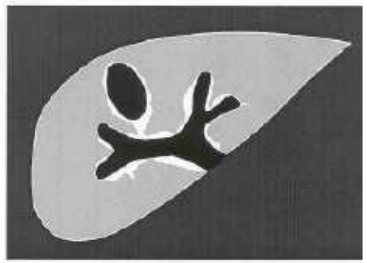
A : normal



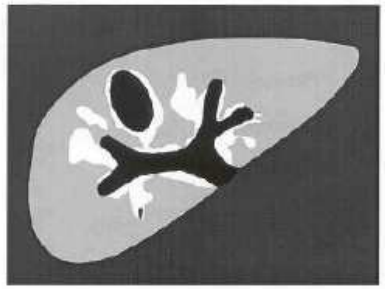
B : "starry sky"



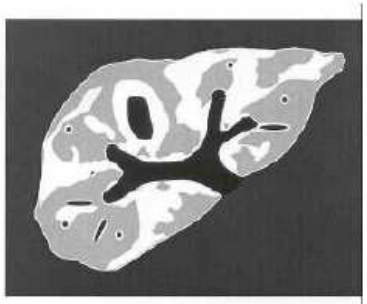
C : "rings and pipe-stems"



D : "ruff" around portal bifurcation



E : "patches"



F : "bird's claw"

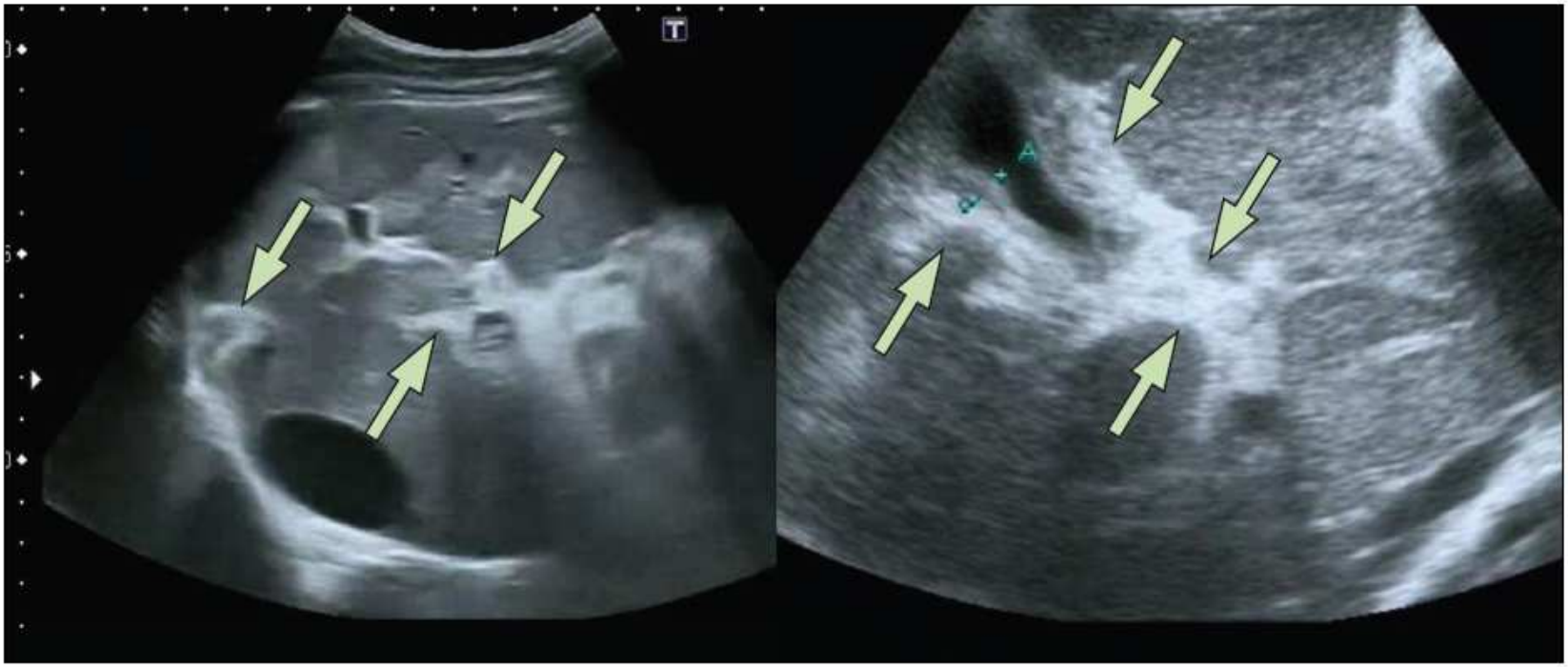
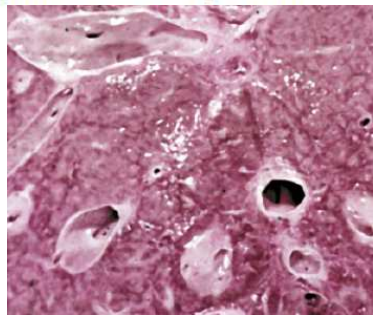
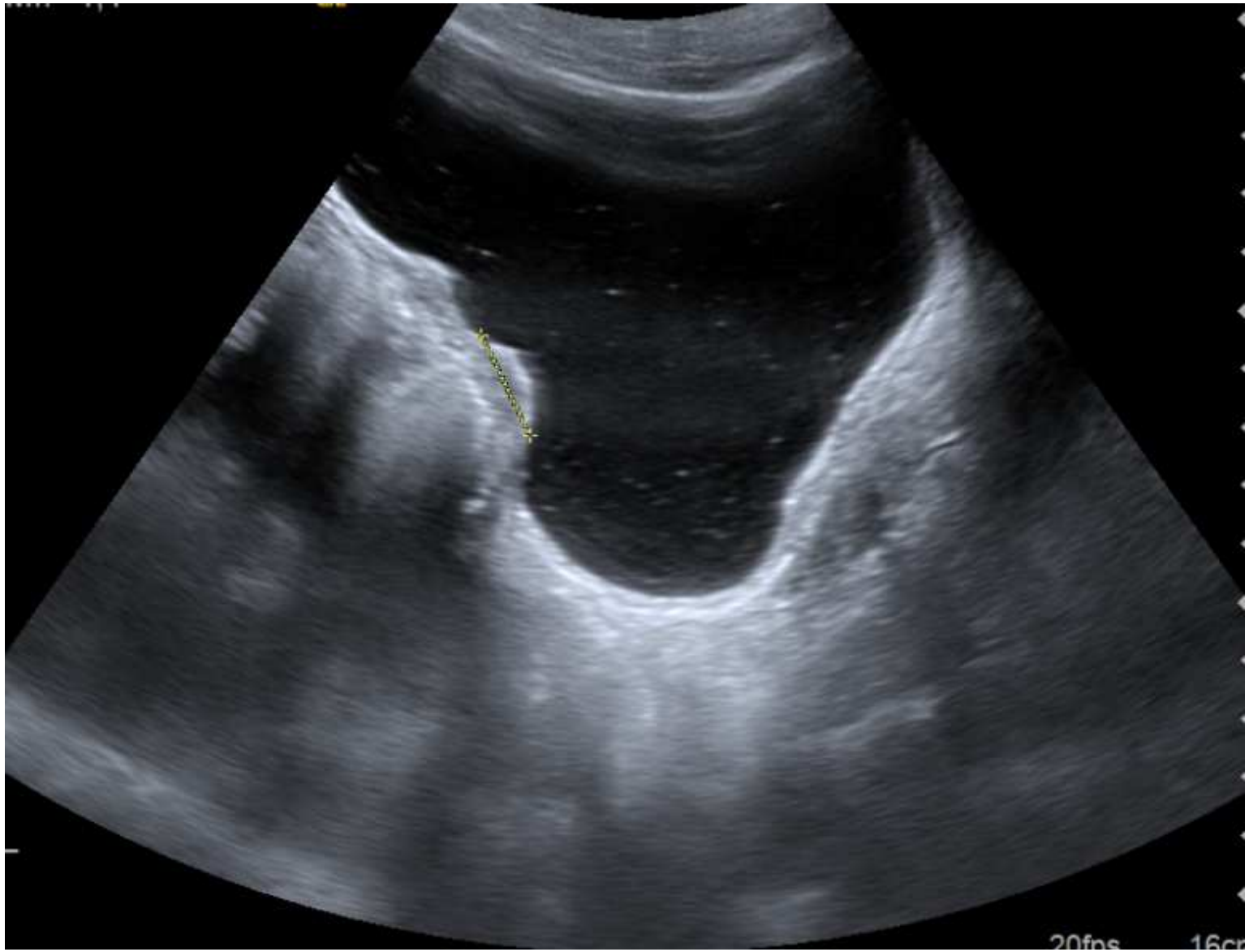
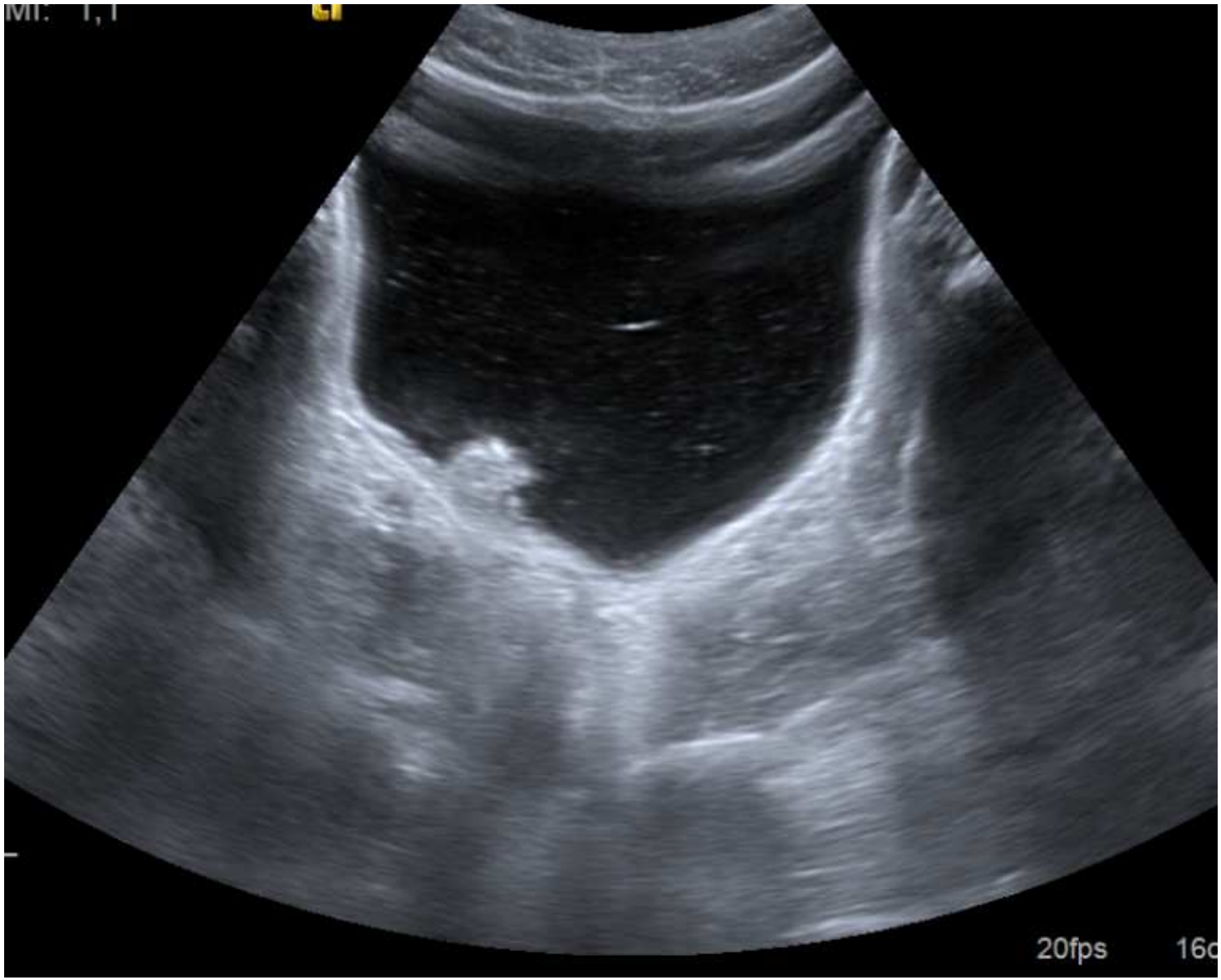


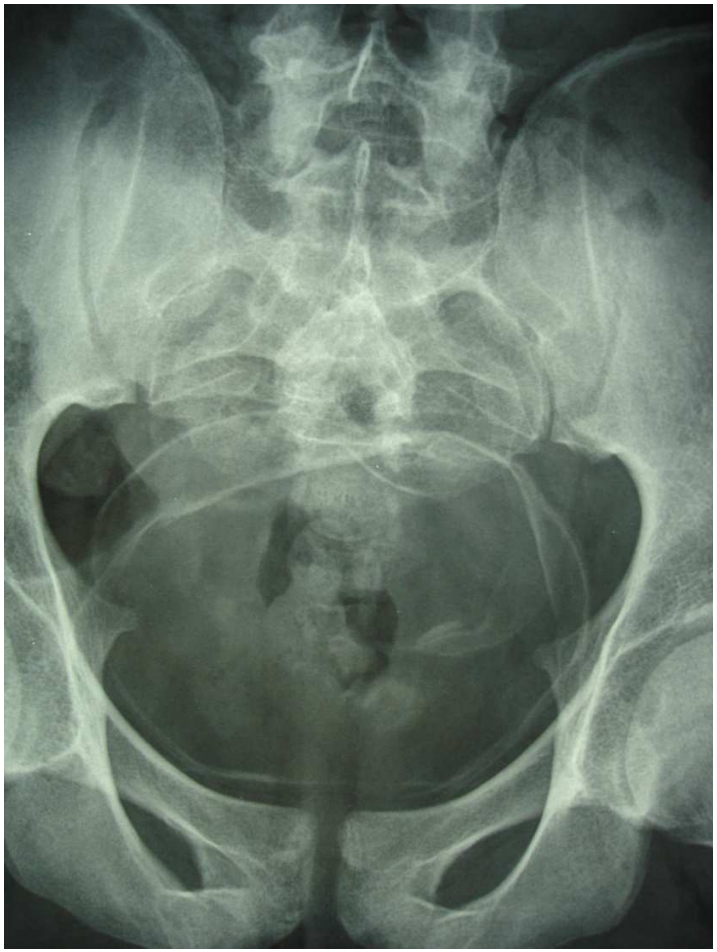
***Figure 1*: Abdominal ultrasonography**

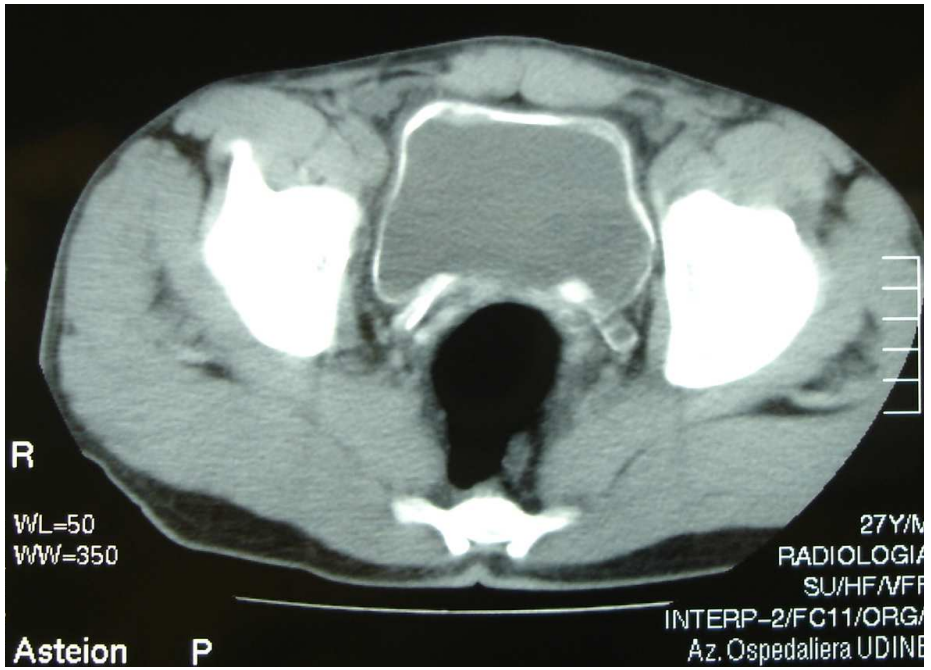
Left, typical echogenic areas (white) along the portal tree. Right, echogenic thickening of the gallbladder wall and neck (white areas); the gallbladder was typically not tender under ultrasound-guided palpation. Arrows point to hyperechogenic areas indicating fibrotic areas in the liver and gallbladder wall and neck.

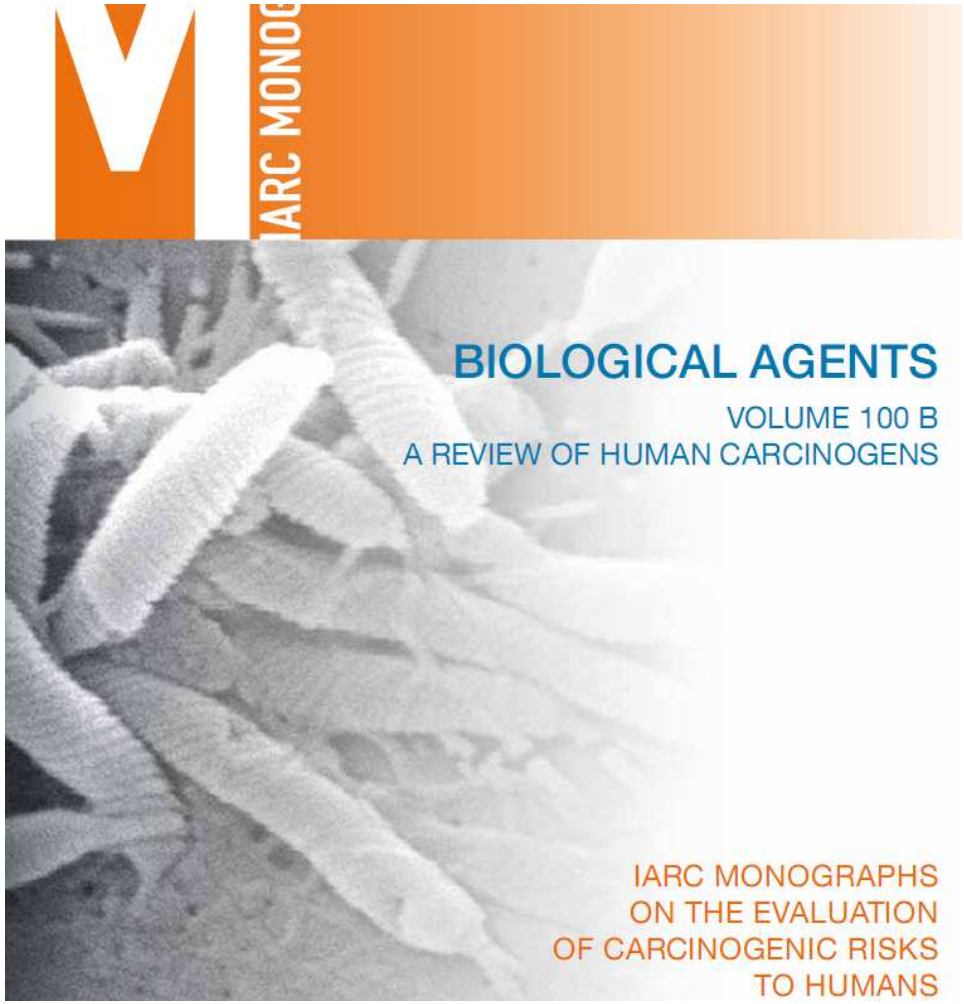



20fps


20fps




R
WL=50
WW=350
27Y/M
RADIOLOGIA
SU/HF/VF
INTERP-2/FC11/ORG
Asteion
P
Az. Ospedaliera UDINE



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 e sintomi (casistica italiana)

- 20 su 35 (57,1%) asintomatici/sintomi aspecifici

Eosinofilia e schistosomiasi

- Schistosomiasi nei pazienti con eosinofilia

  6/82 (7,3%)

- Schistosomiasi nei pazienti senza eosinofilia

  29/489 (5,9%)

Trans R Soc Trop Med Hyg
doi:10.1093/trstmh/tru195

Schistosomiasis presenting in travellers: a 15 year observational study at the Hospital for Tropical Diseases, London

Cordelia E. M. Coltart[a,b,*], Anastasia Chew[a], Neill Storrar[a], Margaret Armstrong[a], Natalie Suff[a], Leila Morris[c], Peter L. Chiodini[a,b] and Christopher J. M. Whitty[a,b]

[a]The Hospital for Tropical Diseases, UCLH, Capper Street, London WC1E 6JB, UK; [b]The London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [c]University College London Medical School, Gower Street, London, WC1E 6BT, UK

Table 3. *Schistosoma haematobium* vs *Schistosoma mansoni* microscopy positive cases: a comparison of eosinophilia, serology results, country of acquisition, and type of patient (i.e., tourist vs other)

	S. *haematobium*	S. *mansoni*
Number (n=275)[a]	204 (74.2%)	61 (21.8%)
Proportion of tourists vs other[b]	98 (48.0%) tourists vs 97 (47.5%) other	18 (29.5%) tourists vs 43 (70.5%) other
Eosinophilia	86/167 (51.5%) No difference observed between tourists and other subgroups	22/47 (46.8%) No difference observed between tourists and other subgroups
Serology	Tourists 86/93 (92.5%) Other 73/93 (78.5%) p=0.007	Tourists 14/14 (100%) Other 34/40 (85.0%) p=0.12
Country of travel[c] (no. of cases)	Malawi (109), Zimbabwe (43), Ghana (25) Countries with 1–10 cases: Somalia, Kenya, Nigeria, Zambia, South Africa, Uganda, Sudan, Botswana, Egypt, Tanzania, Angola, Mozambique, Mali, Sierra Leone, Namibia, Nepal, Madagascar, Swaziland	Uganda (19), Malawi (8) Countries with 1–5 cases: Kenya, Sudan, Ethiopia, Sierra Leone, Zimbabwe, Nigeria, Congo, Rwanda, Tanzania, Ghana, Zaire, Angola, Benin, Brazil, Egypt, Eritrea, Liberia, PNG, Somalia, South Africa, Thailand

[a] Mixed infection with *S. haematobium* and *S. mansoni* was seen in 3 cases (Ghana and Zimbabwe). *S. japonicum* was detected in two cases (both from Philippines). The species of infection was not stated in 2 cases.
[b] Where reason for travel known.
[c] Where patients travelled to more than one endemic country all countries are listed.

Table 2. Symptoms reported in cases of imported schistosomiasis

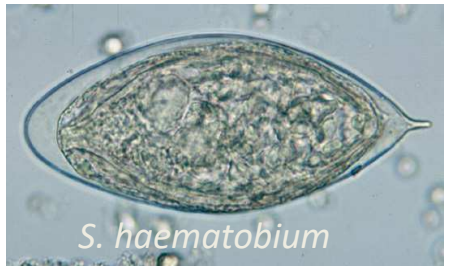
Symptoms	No. patients n=1020	Ova-positive haematobium cases n=181	Ova-positive mansoni cases n=60	Time from exposure to presentation (weeks: mean and range) n=409
Asymptomatic	368 (36.1%)	37 (20.4%)	15 (25.0%)	28 (16–104)

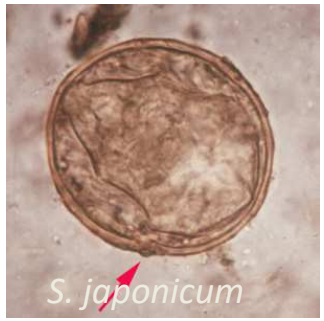
Diagnosi parassitologica

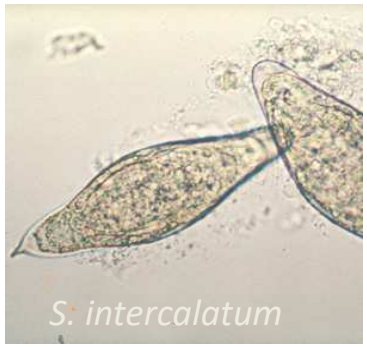
Ricerca Uova su:

1. **Feci** (Kato-Katz o Ritchie mod)
2. **Urine** (dopo esercizio, tarda mattinata)
3. **Campioni bioptici** (rectal snip, biopsia vescicale)

- Gold standard, alta specificità, possibile diagnosi di specie
- Bassa sensibilità
- Utili campioni multipli







Diagnosi sierologic

- Ricerca anticorpi anti *Schistosoma* spp.
- La maggior parte dei test non è specie-specifico
- Vari antigeni (uova, verme adulto…)
- Varie metodiche IHA, IFAT, ELISA, WB
- **Sensibilità migliore** rispetto al parassitologico ma variabile da test a test (40-84.5
- FP per infezioni da altri elminti (soprattutto cestodi)
- Possibile positività persistente in infezione risolta

Altre tecniche diagnostiche

PCR:
Buona specificità e sensibilità (feci).
Non in commercio.

Ricerca antigeni circolanti (<u>anodico</u> e catodico) in urine e <u>sangue</u>:
Poco sensibile in infezioni lievi.
Positivi solo in presenza di verme adulto vitale.
Possibile stima della carica parassitaria.
Alto costo. Non in commercio.

Courtesy of Dr. Lorenzo Zammarchi Malattie Infettive e Tropicali, Università di Firenze

Quale metodica diagnostica?

?

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%	99% (96-100)	100%	98%	74%	77%

Table 2 Accuracy and predictive values according to Composite Reference Standard (CRS) and to Latent Class Analysis (LCA)

Beltrame, Plos NTD, 2017

Schistosomiasi: quale strategia diagnostica?

- Nello **screening** degli asintomatici: **ICT** pare la migliore scelta per il buon profilo (alto NPV, buon PPV);
- **Nel contesto clinico, ICT** come primo test ed **ELISA (PPV 98%)** come test di conferma

Table 3. Predictive values of a combination of positive ICT and a positive (PPV) or a negative (NPV) second test, according to Latent Class Analysis (LCA).

Second test	PPV	NPV
CCA	90%	47%
ELISA	98%	51%
WB	82%	87%
Microscopy	100%	43%

https://doi.org/10.1371/journal.pntd.0005593.t003

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.

Background

Extensive use of praziquantel for treatment and control of schistosomiasis requires a comprehensive understanding of efficacy and safety of various doses for different *Schistosoma* species.

Methodology/Principal Findings

A systematic review and meta-analysis of comparative and non-comparative trials of praziquantel at any dose for any *Schistosoma* species assessed within two months post-treatment. Of 273 studies identified, 55 were eligible (19,499 subjects treated with praziquantel, control treatment or placebo). Most studied were in school-aged children (64%), *S. mansoni* (58%), and the 40 mg/kg dose (56%); 68% of subjects were in Africa. Efficacy was assessed as cure rate (CR, n = 17,017) and egg reduction rate (ERR, n = 13,007); safety as adverse events (AE) incidence. The WHO-recommended dose of praziquantel 40 mg/kg achieved **CRs of 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) for mixed ***S. haematobium/S. mansoni*** infections. Using a random-effect meta-analysis regression model, a dose-effect for CR was found up to 40 mg/kg for S. *mansoni* and 30 mg/kg for *S. haematobium.* The mean ERR was 95% for *S. japonicum*, 94.1% *for S. haematobium*, and 86.3% for *S. mansoni*. No significant relationship between dose and ERR was detected. Tolerability was assessed in 40 studies (12,435 subjects). On average, 56.9% (95%CI 47.4–67.9) of the subjects receiving praziquantel 40 mg/kg experienced an AE. The incidence of AEs ranged from 2.3% for urticaria to 31.1% for abdominal pain.

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.

Different strategies in all over the Europe/World

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

Colley DG, Bustinduy AL, Secor WE, King CH.
Human schistosomiasis.
Lancet. 2014 Jun 28;383(9936):2253-64.

Coltart CE, Chew A, Storrar N, Armstrong M, Suff N, Morris L, Chiodini PL, Whitty CJ.
Schistosomiasis presenting in travellers: a 15 year observational study at the Hospital for Tropical Diseases, London.
Trans R Soc Trop Med Hyg. 2015 Jan 8.

S. mansoni and *S. haematobium*
Praziquantel 40 mg/kg
Oral, single day, in two divided doses 4 to 6 hours apart

S. Japonicum and *S. mekongi*
Praziquantel 60 mg/kg

Holtfreter MC, Moné H, Müller-Stöver I, Mouahid G, Richter J.
Schistosoma haematobium infections acquired in Corsica, France, August 2013.
Euro Surveill. 2014 Jun 5;19(22).

- The boy was treated with a single standard dose of praziquantel (40mg/kg body weight) and re-treated three weeks later with the same dose, to be sure to achieve complete cure of the infection.

Dusseldorf, Germany

Brunet J, Pfaff AW, Hansmann Y, Gregorowicz G, Pesson B, Abou-Bacar A, Candolfi E.
An unusual case of hematuria in a French family returning from Corsica.
Int J Infect Dis. 2015 Feb;31:59-60.

- The patient and the two serologically positive family members received two treatments of praziquantel (40 mg/kg) with a 1-month interval.

Strasbourg, France

S. mansoni and *S. haematobium*
Praziquantel 40 mg/kg
Oral, three days, in two divided doses 4 to 6 hours apart

CTD Negrar, Verona, Italy

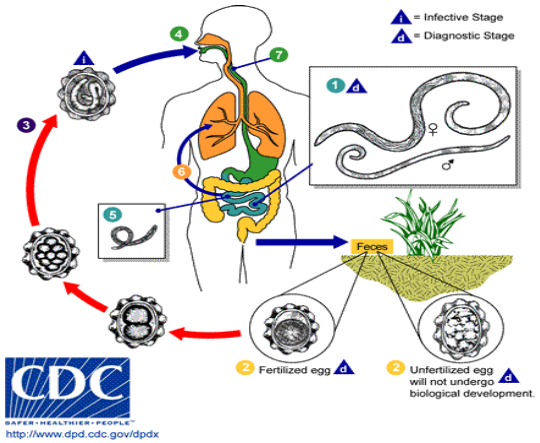
S. mansoni and *S. haematobium*
Praziquantel 40 mg/kg
Oral, single day, in two divided doses 4 to 6 hours apart,
repeated every 1 to 4 months until normalization of eosinophilia and disappearance of eggs
Possible increased dosage (60 mg/Kg) for 2-3 days

Antwerp, Belgium

Table 2 Systematic review on infections from intestinal helminths

	Author	Year of publication	African refugees (irrespective of geographic origin)			Sub-Saharan African refugees (SSA)			North African refugees (NA)			Ref.
			No. of individuals tested for helminths	No. of individuals tested positive for helminths	%	No. of individuals tested for helminths	No. of individuals tested positive for helminths	%	No. of individuals tested for helminths	No. of individuals tested positive for helminths	%	
1	Abu-Madi et al.	2016	261	14	5.4	123	6	4.9	138	8	5.8	[S18]
2	Serre Delcor et al.	2016	171	48	28.1	171	48	28.1	–	–	–	[S19]
3	Belhassen-García et al.	2016	231	1	0.4	164	1	0.6	64	0	0	[S20]
4	Abdel Hamid. et al.	2015	171	48	32.6	171	48	32.6	–	–	–	[S21]
5	McCathy et al.	2013	2804	370	13.2	2301	256	11.1	503	114	23	[S22]
6	Swanson et al.	2012	18,666	406	2.2	18,666	406	2.2	–	–	–	[S23]
7	Abu-Madi et al.	2011	424	56	13.2	220	42	19.1	204	14	6.9	[S24]
8	Abu-Madi et al.	2008	175	12	6.9	175	12	6.9	–	–	–	[S25]
9	Posey et al.	2007	562	276	49.1	562	276	49.1	–	–	–	[S26]
10	Gbakima et al.	2007	581	97	16.7	581	97	16.7	–	–	–	[S27]
11	Mohammed et al.	2007	80	34	42.5	80	34	42.5	–	–	–	[S28]
12	Varkey et al.	2007	1547	203	13.1	–	–	–	–	–	–	[S29]
13	Caruana et al.	2006	124	19	15	124	19	15	–	–	–	[S30]
14	Garg et al.	2005	142	12	8.5	–	–	–	–	–	–	[S31]
15	Anosike et al.	2005	755	66	8.7	755	66	8.7	–	–	–	[S32]
16	Geltman et al.	2003	1254	174	14	–	–	–	–	–	–	[S33]
17	Roca et al	2002	1321	200	15.2	1321	200	15.2	–	–	–	[S34]
		Median prevalence [range]:			13.2	[0.4–49.1]		15.1	[0.6–49.1]		6.35	[0.0–23.0]

GEOELMINTI



Eur J Clin Microbiol Infect Dis
https://doi.org/10.1007/s10096-017-3126-1

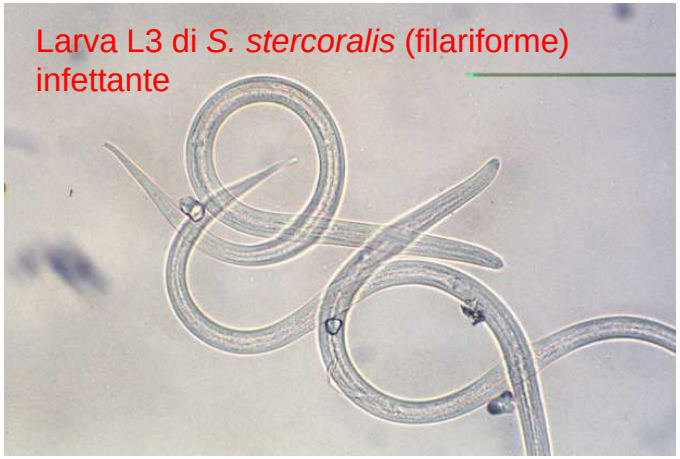
CrossMark

REVIEW

Prevalence rates of six selected infectious diseases among African migrants and refugees: a systematic review and meta-analysis

A. Chernet[1,2] · J. Utzinger[1,2] · V. Sydow[1,2] · N. Probst-Hensch[1,2] · D. H. Paris[1,2] · N. D. Labhardt[1,2,3] · A. Neumayr[1,2]

STRONGILOIDOSI



Un geniale ospite

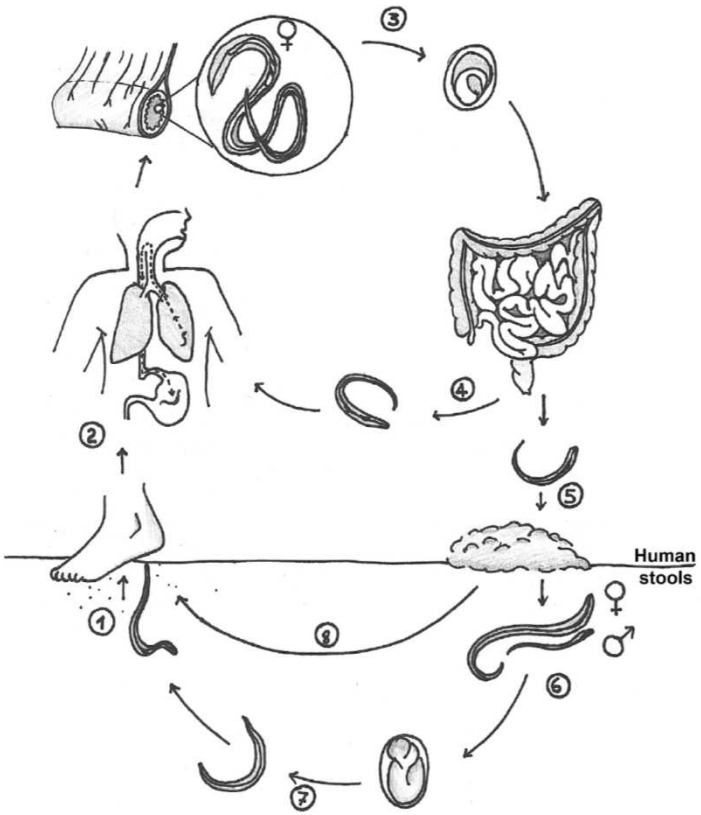


FIG. 1. Life cycle of *Strongyloides stercoralis*. 1, Filariform larvae (450 nm) penetrate human skin. 2, Larvae migrate to the lungs, trachea, and pharynx, and are swallowed. 3, Parthenogenetic adult females (2 mm) penetrate the small-bowel mucosa and release eggs. 4, Rabdiform larvae (250 nm) mature into autoinfective filariform larvae, and enter the circulation. 5, Rabdiform larvae are shed in stools. 6, Free-living 1-mm male and female adults develop in the soil. 7, Sexual reproduction in the soil (indirect development). 8, Filariform larvae develop in the soil—infective for humans (direct development).

Peculiarità:

- Replicazione asessuata

(no sex we are British…)

- Cicli di autoinfestazione

↓

- Cronicizzazione di malattia, che si automantiene senza nuove esposizioni ambientali

- Quasi il 50% dei soggetti colpiti è asintomatico (Concha et al.)

Una bomba a orologeria…

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

Eric Caumes MD[1,2,*], Jay S. Keystone MD[3,4.] 2011; 18(2):71–72

Journal of TRAVEL MEDICINE

1) **Dobbiamo individuare quelli che hanno in corpo la "bomba" senza saperlo**

1) **Il trattamento non può avere altro obiettivo se non di rimuovere completamente la "bomba"**

OPEN ACCESS Freely available online

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]

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

→ Estimate of at least 370 million people infected (or at least 50% hookworm global prevalence)

Figure 4. Prevalence of S. stercoralis infection by country based community-based studies.

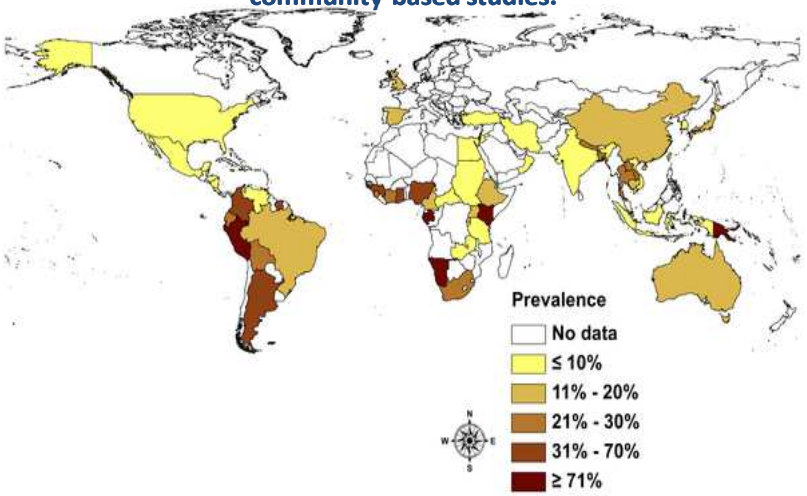
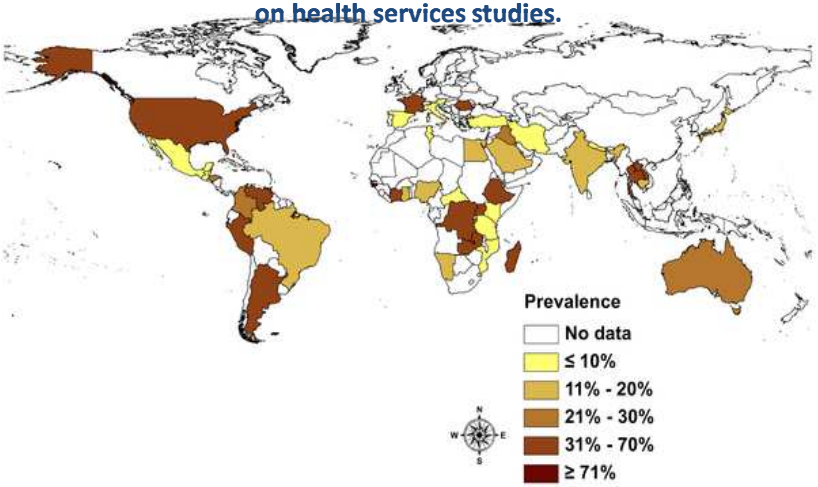


Figure 5. Prevalence of S. stercoralis infection by country based on health services studies.



Schär F, Trostdorf U, Giardina F, Khieu V, Muth S, et al. (2013) Strongyloides stercoralis: Global Distribution and Risk Factors. PLOS Neglected Tropical Diseases 7(7): e2288. https://doi.org/10.1371/journal.pntd.0002288
http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002288

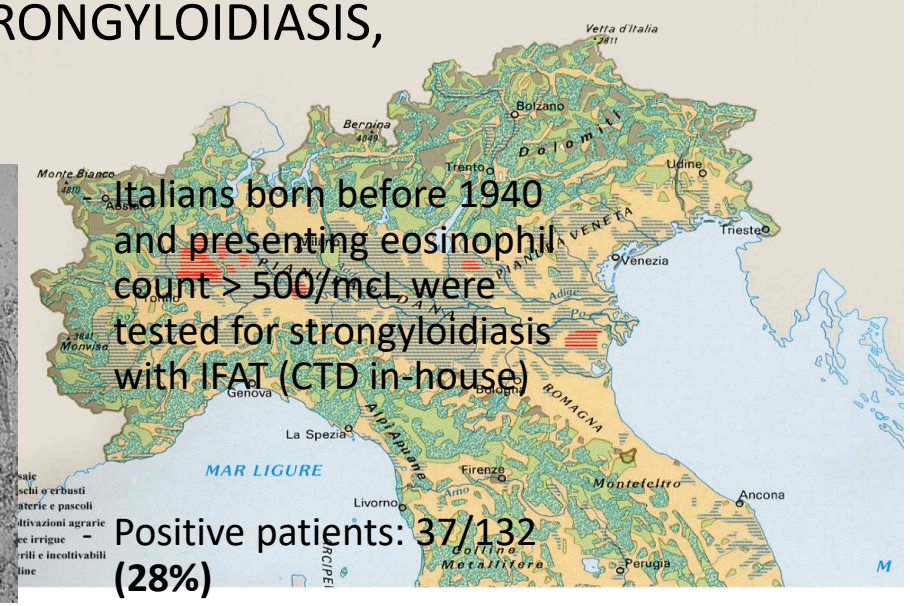
Prevalence in Italy: memories of the past…

PILOT STUDY

Risaie in Italia del Nord

REEMERGENCE OF STRONGYLOIDIASIS, NORTHERN ITALY

Silvana Mang



- Italians born before 1940 and presenting eosinophil count > 500/mcL were tested for strongyloidiasis with IFAT (CTD in-house)

- Positive patients: 37/132 **(28%)**

F. Abrescia et al

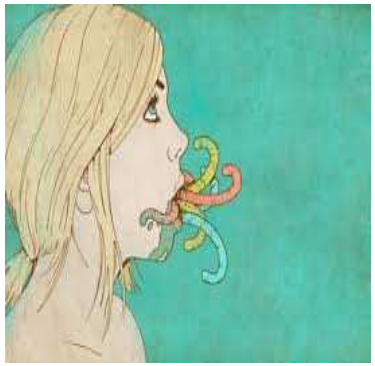
Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 9, September 2009

CLINICA

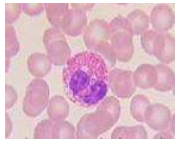
Sintomi cronico-ricorrenti:

- Cutanei (orticaria, prurito)
- Respiratori (tosse secca, asma ricorrente)
- Gastrointestinali (dolore addominale, epigastrico, pseudoappendicite, diarrea)
- Sistemici (perdita di peso, cachessia)

Abrescia et al., EID 2009

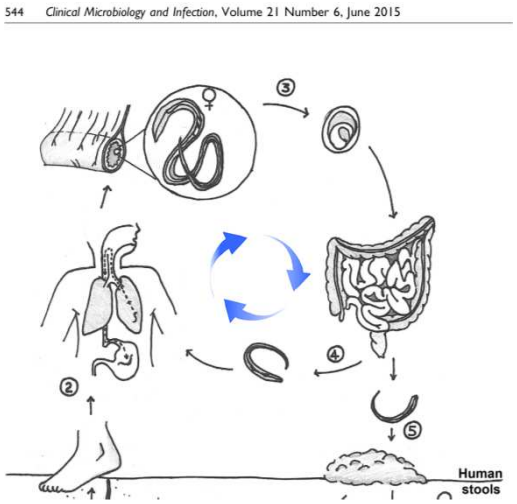


Immunodepressione



iperinfestazione - disseminazione

(autoinfestazione accelerata) **(altri organi)**



Letalità: 50-86%

Segarra Newnham. Annals of Pharmacotherapy 2007

Strongiloidosi severa: 67% dei pz erano sotto tx steroidea

Buonfrate *et al. BMC Infectious Diseases* 2013, **13**:78
http://www.biomedcentral.com/1471-2334/13/78

Table 1 Patients under steroid treatment: reasons for prescription

Condition	N (%)	References
COPD/asthma/lung fibrosis	30 (18.3)	[48,49,52,57-59,68,99,101,118,121,123,128,137,146,153,180-183,185,187,188,192-196]
Leukemia/lymphoma	13 (7.9)	[9,17,23,25,37,47,56,98,111,126,162,186]
SLE	9 (5.5)	[41,64,66,86,151,176,197,198]
Rheumatoid arthtritis	4 (2.4)	[83,103,199,200]
IBD	6 (3.6)	[59,147,148,164,177,201]
Sarcoidosis	2 (1.2)	[65,132]
Cancer	8 (4.8)	[30,54,93,97,112,160,169,202]
Organ/bone marrow transplant	25 (15.2)	[21,25,29,31,39,48,51,54,60,70,71,74,76,81,87,88,90,92,94,142,145,150,184]
Glomerulonephritis/CRI	6 (3.6)	[16,18,20,129,130,154]
"Idiopatic" eosinophilia	3 (1.8)	[7]
Multiple myeloma/myelodisplasia	6 (3.6)	[72,185,203-206]
Aspecific symptoms	2 (1.2)	[85,166]
Other clinical conditions	46 (28)	[17,22,34,36,54,59,66,84,89,100,102,110,113,124,125,127,133-135,140,155,159,171-174,207-213]
HIV-related opportunistic infections/IRIS	4 (2.4)	[24,26,36,105]

Other conditions (no steroids):

HTLV 1

HIV

Alcoholism

Malnutrition

Transplant

RESEARCH ARTICLE

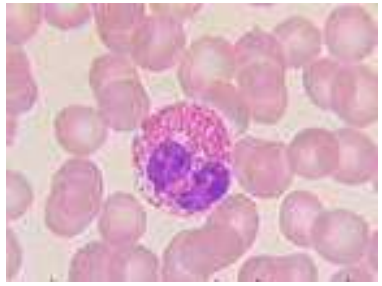
Epidemiology of *Strongyloides stercoralis* in northern Italy: results of a multicentre case–control study, February 2013 to July 2014

D Buonfrate [1], M Baldissera [2], F Abrescia [3], M Bassetti [4], G Caramaschi [5], M Giobbia [6], M Mascarello [7], P Rodari [8], N Scattolo [9], G Napoletano [2], Z Bisoffi [1], on behalf of the CCM Strongyloides Study Group [10]

1. Centre for Tropical Diseases, Sacro Cuore Hospital, Negrar (Verona), Italy
2. Prevention Department, ULSS20, Verona, Italy
3. Medici per la Pace Onlus, Verona, Italy
4. University Hospital of Udine, Udine, Italy
5. Servizio di Medicina di Laboratorio, Azienda Ospedaliera Carlo Poma, Mantova, Italy
6. Infectious Diseases Department, Ca' Foncello Hospital, Treviso, Italy
7. Department of Infectious Diseases, University Hospital of Trieste, Trieste, Italy
8. University Department of Infectious and Tropical Diseases, University of Brescia and Spedali Civili General Hospital, Brescia, Italy
9. Laboratorio Analisi, Ospedale Fracastoro, San Bonifacio (Verona), Italy
10. Members of the group are listed at the end of the article

Correspondence: Dora Buonfrate (dora.buonfrate@sacrocuore.it)

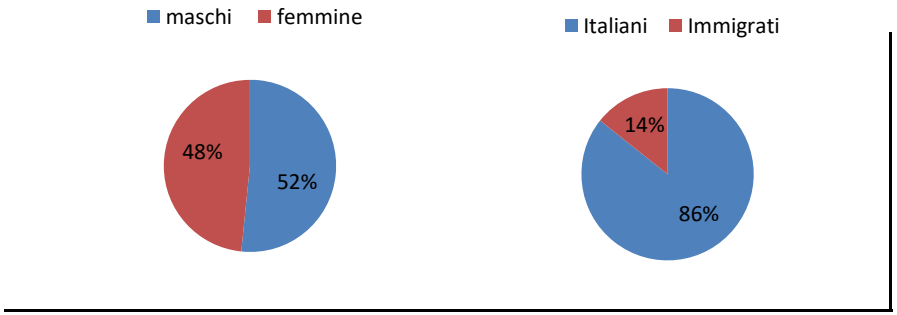
Citation style for this article:
Buonfrate D, Baldissera M, Abrescia F, Bassetti M, Caramaschi G, Giobbia M, Mascarello M, Rodari P, Scattolo N, Napoletano G, Bisoffi Z, on behalf of the CCM Strongyloides Study Group. Epidemiology of Strongyloides stercoralis in northern Italy: results of a multicentre case–control study, February 2013 to July 2014. Euro Surveill. 2016;21(31):pii=30310. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.31.30310



ccm
Centro nazionale per la prevenzione e il Controllo delle Malattie

Positivi: soggetti con e senza eosinofilia

Pazienti sottoposti a screening: 2714



- Nelle province esaminate, la prevalenza di strongiloidosi negli **italiani** nati prima del 1951 e con **eosinofilia** è rilevante (**8%**)
- La prevalenza risulta ancora maggiore negli **immigrati** (**17%** dei soggetti con **eosinofilia**)
- In entrambi i gruppi (italiani e immigrati), i soggetti con eosinofilia presentano probabilità significativamente maggiore (**O.R: 8,82**) di essere affetti da strongiloidosi, rispetto ai soggetti senza eosinofilia

Sottogruppo	Eosinofilia	Positivi	No eosinofilia	Positivi	Odds Ratio (95% C.I.)
Italiani	1145	93 (8%)	1181	13 (1%)	**7,49** (4,39-15,56)
Immigrati	216	37 (17%)	172	3 (1.7%)	**11,64** (3,57-59,85)

Centro nazionale per la prevenzione e il Controllo delle Malattie

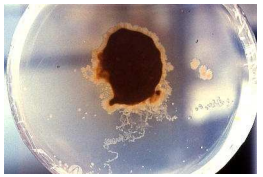
Parassitosi sottodiagnosticata

Bassa sensibilità

Esame diretto delle feci

Esame delle feci con metodi di arricchimento

Coltura in agar



Sierologia

Alta sensibilità

(non eccezionale)

REVIEW

Novel approaches to the diagnosis of *Strongyloides stercoralis* infection

D. Buonfrate, F. Formenti, F. Perandin and Z. Bisoffi

Centre for Tropical Diseases, Sacro Cuore Hospital, Negrar, Verona, Italy

Clin Microbiol Infect 2015; **21:** 543–552

TABLE 1. Accuracy of conventional, faecal-based methods for *Strongyloides stercoralis* diagnosis according to recent, selected studies

Reference	Test(s) assessed	Sensitivity (%)	Specificity (%)	Study characteristics
[31]	Baermann	47	78.4	Accuracy assessed with PCR results as the reference standard
	Baermann	83.6	100	Accuracy assessed with a composite reference standard (PCR plus Baermann). Specificity assumed to be 100% for both methods
	Baermann	28.3	75.2	Accuracy assessed with a Bayesian approach to cope with the lack of a reference standard
[45]	Direct examination	21	100	Meta-analysis of papers published between 1908 and 2013. Specificity considered to be 100% by definition. Reference standard based exclusively on the results of conventional methods
	FECT	48	100	
	APC	89	100	
	Baermann	72	100	
[26]	C-FECT	48.1	100	Reference standard based on a combination of the three methods. Specificity considered to be 100% by definition. Study designed to assess the sensitivity of a modified FECT as explained in the text
	M-FECT	95.2	100	
	APC	94.2	100	

APC, agar plate culture; C-FECT, conventional formol–ether concentration; FECT, formol–ether concentration; M-FECT, Modified formol–ether concentration.

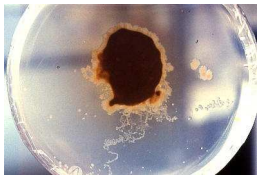


TABLE 2. Accuracy of serological methods for *Strongyloides stercoralis* diagnosis according to selected studies published after 2005

Reference (year)	Test(s) assessed	Sensitivity (%)	Specificity (%)	Study characteristics
[36] (2014)	Bordier ELISA[a]	90.8	94.1	Study using a composite reference standard of faecal and serological tests (denominator for positives: samples with positive stool or ≥3/5 positive serological tests) to cope with the lack of a reference standard. Limits: retrospective study design
	IVD-ELISA[b]	92.3	97.4	
	NIE-ELISA[c]	70.8	91.1	
	IFAT[d]	94.6	87.4	
	NIE-LIPS[c]	83.8	99.6	
[37] (2014)	SciMedx ELISA[e]	85.5	82.6	Study mainly aimed at assessing percentage agreement of the three tests. Reference standard for positives: samples with ≥2/3 positive serological tests—faecal results not considered
	InBios-Strongy ELISA[f]	83.6	91.3	
	NIE-LIPS[c]	89.1	89.1	
[41] (2007)	AMC-ELISA[d]	93.3	95.0	Study using a panel of serum specimens from a population composed of patients with proven strongyloidiasis, healthy controls, and patients with various parasitic and other diseases. Faecal results used as a unique reference standard
	Dipstick[d]	91.1	97.7	
	Bordier ELISA[a]	83.3	97.2	
	IVD-ELISA[b]	88.9	97.2	
[42] (2010)	IVD-ELISA[b]	91.2	93.3	As above
[44] (2010)	Crude Ag-ELISA[d]	97.0	100	Specificity predetermined at 100% for all methods by the use of cut-off values obtained from ROC curves for 90 samples from patients with positive stools and ten healthy controls from a non-endemic area
	NIE-ELISA[c]	84.0	100	
	NIE-LIPS[c]	97.8	100	
[43] (2008)	NIE-ELISA[c]	97	95	Prospective design. Specificity assessed in a small group of healthy controls, but also confirmed (for LIPS) in samples from patients with filarial and other helminth infections
	NIE-LIPS[c]	97	100	
[47] (2007)	IFAT[d]	74.1	98.4	Accuracy (high titre) determined with latent class analysis to cope with the lack of a reference standard. Coprological methods used for the model not optimal for *S. stercoralis*
[49] (2006)	IFAT[d]	97.4	97.9	Reference standard for sensitivity: samples from patients with *S. stercoralis* larvae in stools. Reference standard for specificity: samples from controls with no risk of infection and negative stools. Cross-reactivity assessed separately
[55] (2011)	IFAT[d]	73	NA	Study on HIV-positive subjects, with average CD4 count of 373/μL

Ag, antigen; HIV, human immunodeficiency virus; IFAT, immunofluorescence antibody test; LIPS, luciferase immunoprecipitation system; NA, not available; ROC, receiver operating characteristic.
[a]Crude Ag (*S. ratti*), commercially available.
[b]Crude Ag (*S. stercoralis*), commercially available.
[c]Recombinant Ag, in-house.
[d]Crude Ag (*S. stercoralis*), in-house.
[e]Commercially available for study purpose only.
[f]Recombinant Ag, commercially available.

TABLE 3. **Main characteristics of molecular biology techniques for *Strongyloides stercoralis* diagnosis according to recent studies**

Reference (year)	Test assessed/ region targeted	Extraction/type of specimen	Sensitivity	Specificity (%)	Study characteristics
[28] (2011)	Fret-PCR/18S rRNA	QIAamp DNA stool MiniKit/ 100 mg unpreserved	LOD 4 × 10^2 copies/ reactions (40 larvae per gram)	100	Sensitivity calculated as LOD Specificity evaluated in a control group of negative stool samples from healthy adults plus stool samples positive for other parasites
[30] (2013)	RT-PCR/18S rRNA	Comparison of five methods: four manual and one automatic	10^{-2} dilution LOD	100	Sensitivity calculated as LOD in serial dilutions of *Strongyloides ratti* larvae spiked into stools Specificity calculated in 58 definitely negative samples
[52] (2009)	RT-PCR/18S rRNA, cytochrome c oxidase, sequence repeat	QIAamp DNA stool MiniKit/ 100 mg unpreserved; 2% PvPP	33/38[a] (87%) or 33/54[b] (61%)	100	For sensitivity, the denominator was: positive Baermann or single[a] or duplicate[b] APC. RT-PCR also detected 12 samples negative with both techniques Specificity was calculated by checking the oligonucleotide sequences on BLAST and in 145 definitely negative stool samples
[54] (2011)	Single and nested PCR/ ITS1-5.8S-ITS-2	QIAamp DNA stool MiniKit/ 3 g preserved sample (EtOH 70%)	Single PCR 100% Nested PCR 75%	100	Sensitivity calculated in 16 APC-positive samples Specificity calculated in stool-negative control group (35 APC-negative samples)
[59] (2014)	RT-PCR/18S rRNA	QIAamp DNA stool MiniKit/ 200 mg unpreserved	LOD 0.1 pg	100	Sensitivity calculated as LOD Specificity calculated in 13 definitely negative samples
[73] (2014)	LAMP/28S rRNA	QIAamp DNA stool MiniKit/ 100 mg unpreserved; 2% PvPP	LOD <10 copies	100	Sensitivity calculated as LOD Specificity calculated in 38 stool samples definitely negative for *S. stercoralis*
[87] (2011)	RT-PCR/18S rRNA	QIAamp DNA stool MiniKit	LOD 10 copies	100	Sensitivity calculated as LOD Specificity tested against DNA controls derived from a wide range of intestinal microorganisms

LAMP, loop-mediated isothermal amplification; LOD, limit of detection; PvPP, Polyvinylpolypyrrolidone.

Figure 1

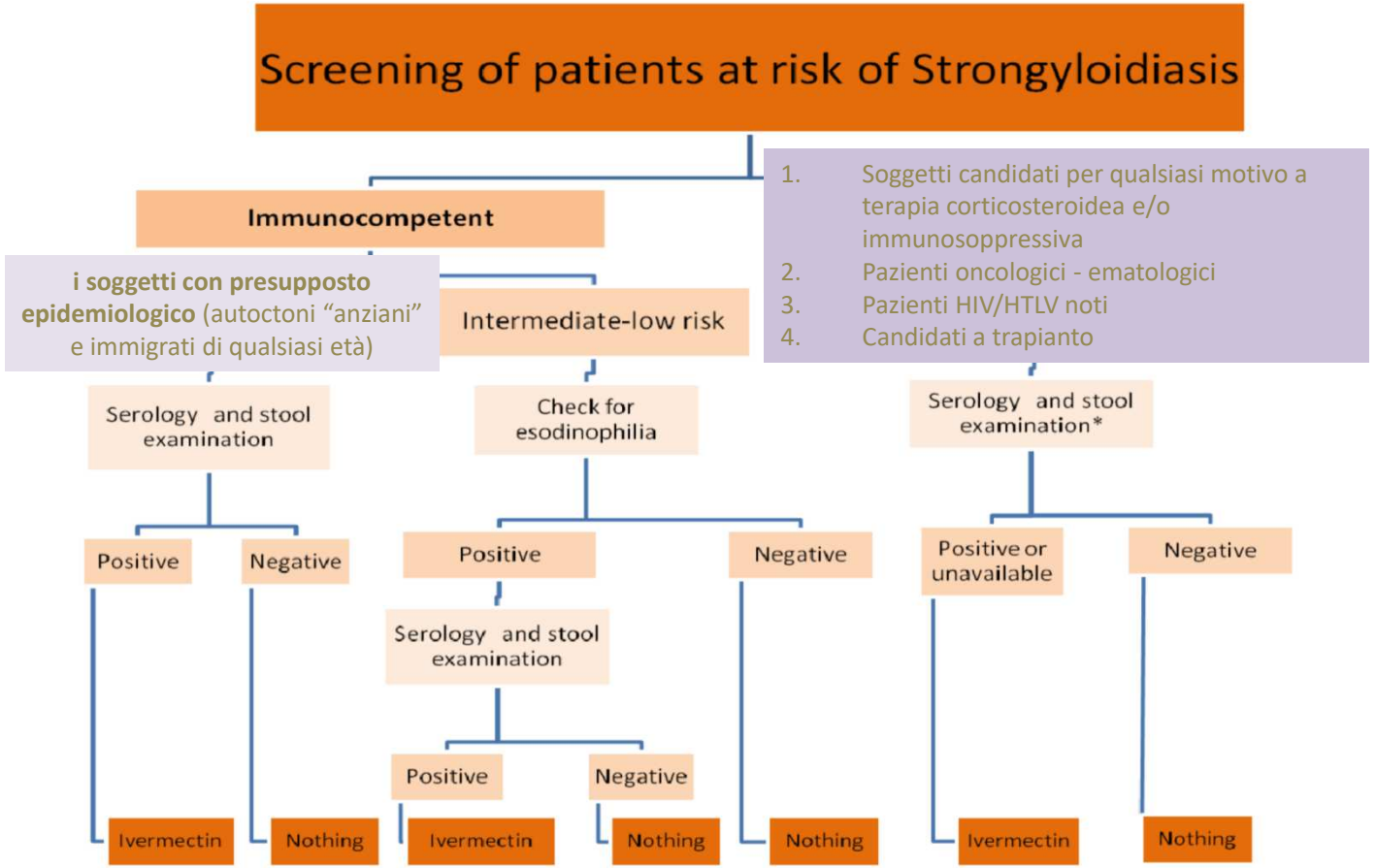


FIGURE 1. Algorithm diagnosis of screening. * When serology or more sensitive stool techniques (Baermann or stool culture) are not available, consider empiric treatment with ivermectin. This figure appears in color at www.ajtmh.org.

Requena-Méndez A et al. Evidence-Based Guidelines for Screening and Management of Strongyloidiasis in Non-Endemic Countries. Am J Trop Med Hyg. 2017 Sep;97(3):645-652.

http://www.simetweb.eu/document/3963

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