

A surprisingly late (and late surprising) diagnosis

TROPICARE 25-11-2024
STEVEN VAN DEN BROUCKE



♀ 28y

- “For 8 years I have fatigue...
- ... menorrhagia's, dysmenorrhea, dyspareunia, vaginal discharge and pain in the lower abdomen. Persistent. Intermittent hematochezia without diarrhea”
- Been abroad?
- Yes, I travelled in several countries in Africa and South America
- Freshwater contact?
- Mali 2010: fallen in the Niger river, ‘abdominal eczema’ for 3 weeks
- Ecuador 2008: fresh water contact
- By the way, for 1,5 year we are failing to conceive



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 - By the way, for 1,5 year we are failing to conceive
- **Physical exam:**
 - Hypogastric palpation moderately painful
 - External genitalia normal
 - Slight cervical motion tenderness
 - Speculum exam normal
 - Digital rectal exam normal
 - **Lab:**
 - Hb 12.6 g/dl
 - WBC 7600/ μ l
 - 50% neutro, 35% lympho, 6% eosino, 2% baso, 7% mono
 - Syphilis, HIV, Chlamydia, Gonorrhoe: neg
 - Urine: 18 RBC/ μ l, no WBCs, mucus +, prot -



Abdominal eczema?

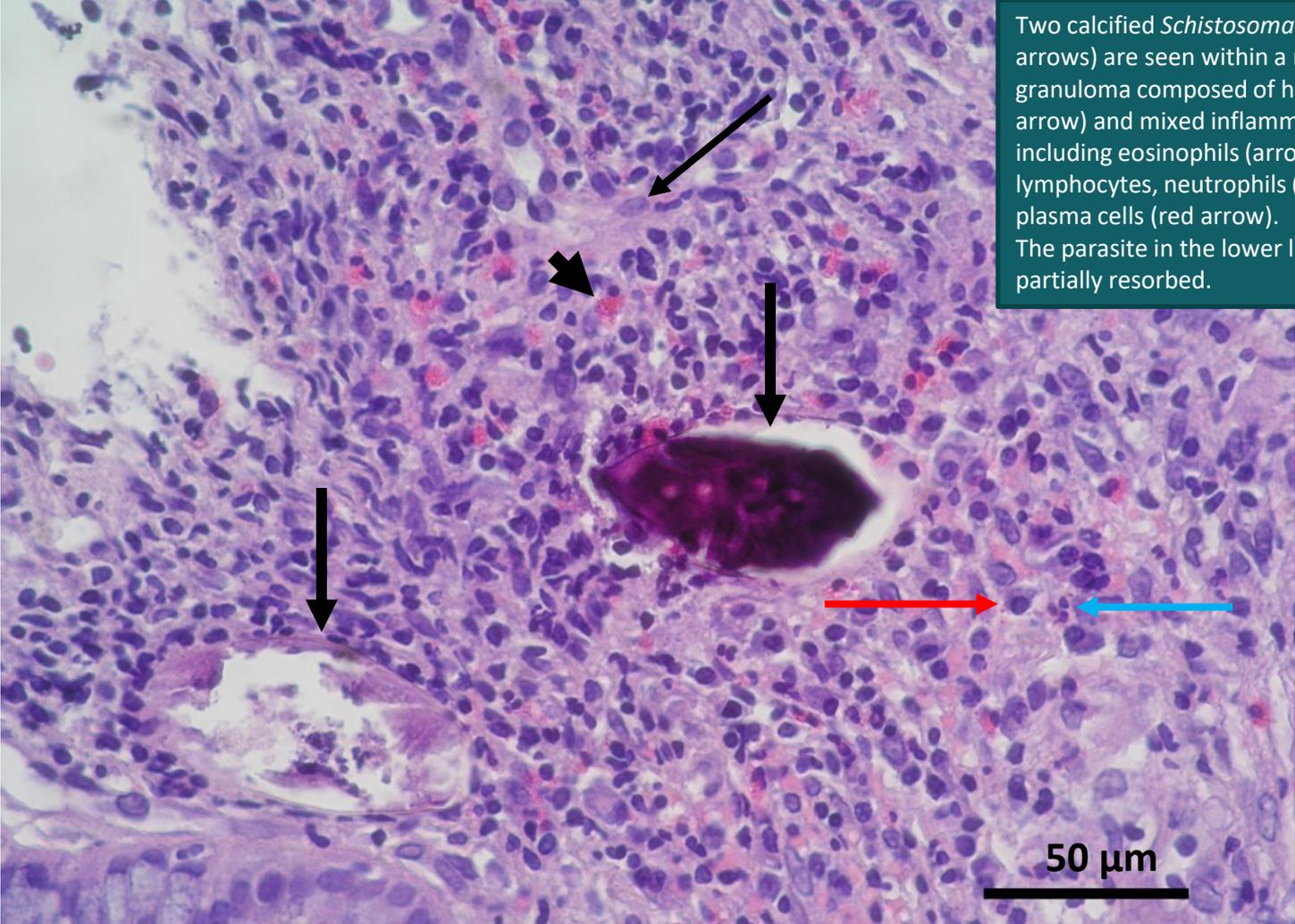
- Cercarial dermatitis
(Swimmer's Itch)



Consulted several gynecologists in the past 8 years

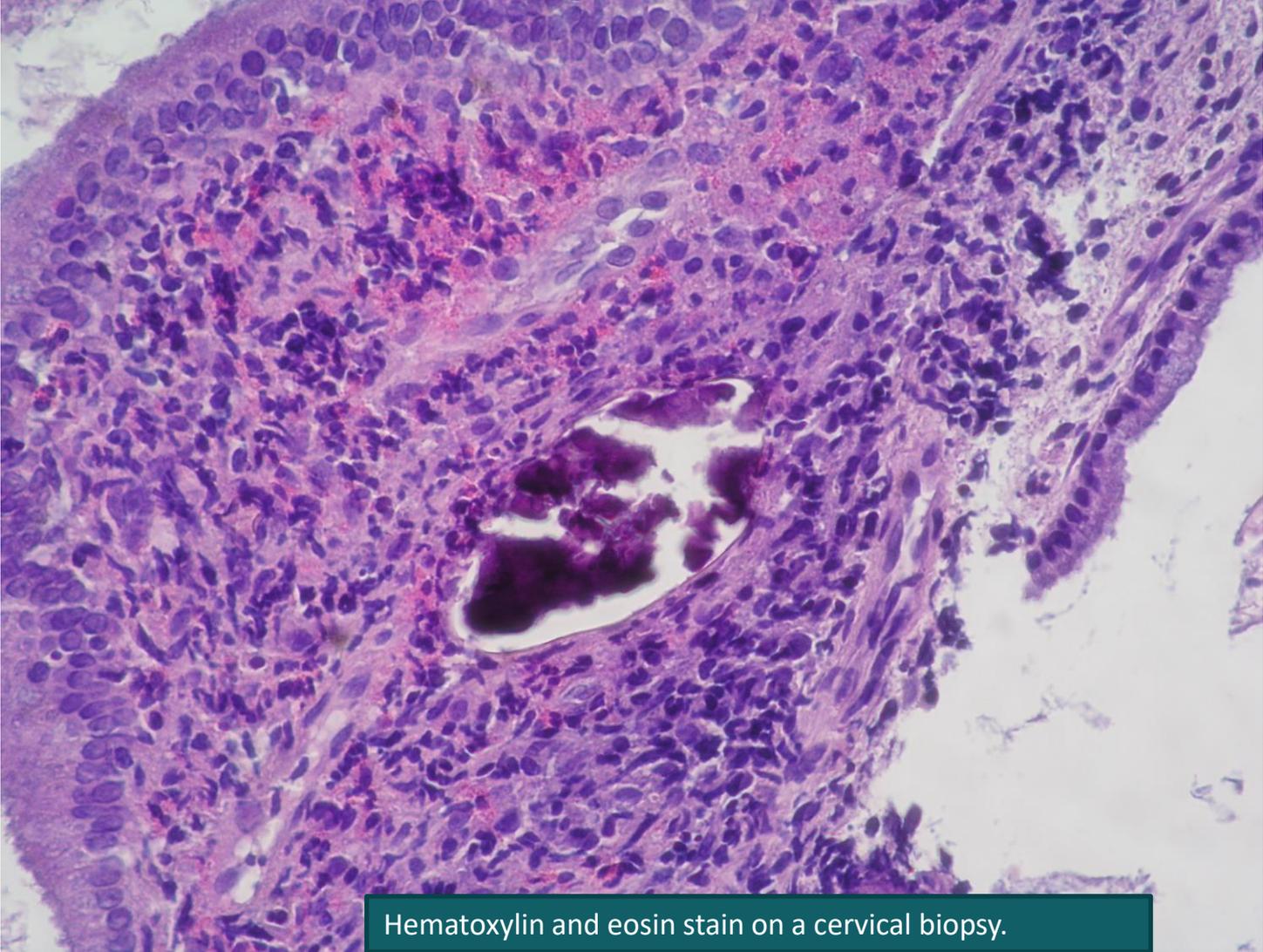
- Extensive work-up including hysterosalpingography normal
- Last PAP-smear: 'atypical inflammation'
- What would you do now?

Cervical biopsy



Two calcified *Schistosoma* eggs (thick arrows) are seen within a nonnecrotic granuloma composed of histiocytes (thin arrow) and mixed inflammatory cells including eosinophils (arrowhead), lymphocytes, neutrophils (blue arrow), and plasma cells (red arrow). The parasite in the lower left granuloma is partially resorbed.

Hematoxylin and eosin stain on a cervical biopsy. Scalebar indicates 50 μm .



Hematoxylin and eosin stain on a cervical biopsy.

Snips: Unstained wet mount preparation

Cervical

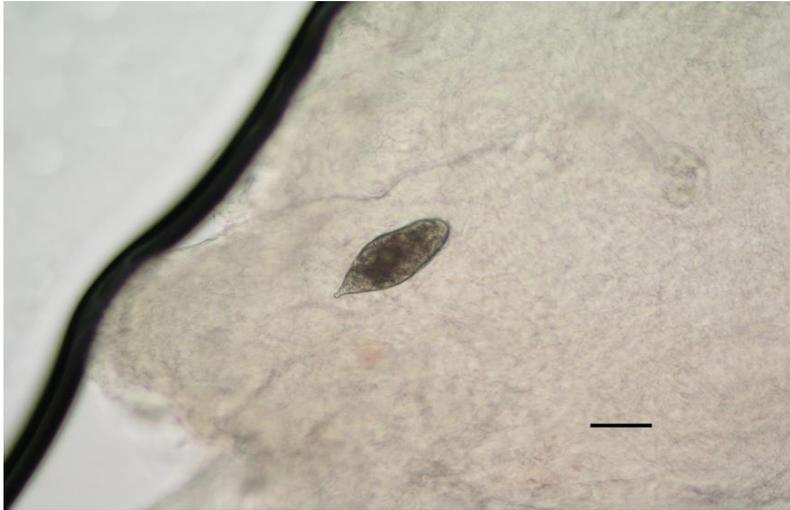


Rectal



Snips: Unstained wet mount preparation

Cervical



Cervical snip, unstained wet mount preparation. A calcified *Schistosoma* egg with terminal spine.

Rectal



Rectal snip, unstained wet mount preparation. A cluster of *Schistosoma* eggs with different stages of calcification (short arrow indicates advanced calcification) having inconspicuous terminal spines (long arrow) and equatorial bulges.

Scale bar indicates 50 μm

Further work-up

- ELISA *Schistosoma* (SEA_{Schistosoma Egg Antigen}): pos, ratio 2,26 (ref range < 1.00)
- IHA *Schistosoma* (WA_{Worm Antigen}): pos, 1/320 (ref range < 1/160)
- Eosinophilia: neg

- Urine Sediment: RBC 18/μl, WBC neg, mucus +, protein -

- Urine: no *Schistosoma* eggs
- Stool: no *Schistosoma* eggs

Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological disease

Vanessa Christinet^a, Janis K. Lazdins-Helds^b, J. Russell Stothard^c, Jutta Reinhard-Rupp^{d,*}

Forty-six publications out of the 193 reviewed papers are from Europe, USA and Oceania describing Female Genital Schistosomiasis in migrants or travellers coming from schistosomiasis endemic countries. The table provides an overview of countries of diagnosis, countries of infection, patient number and age, clinical condition and *Schistosoma* spp.

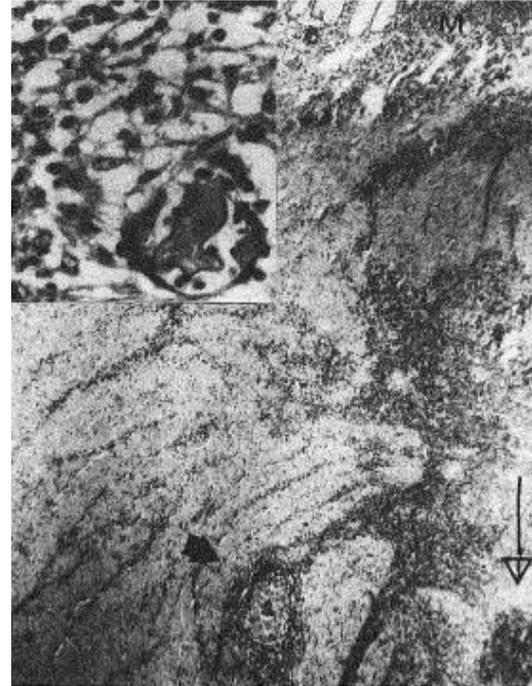
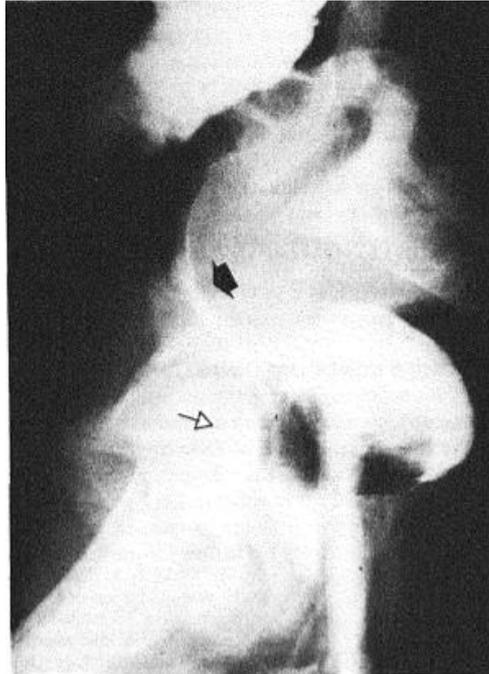
Country of diagnosis	Schistosomiasis infestation origin	Age (years)	Schistosomiasis-associated clinical condition	<i>Schistosoma</i> spp.	Publication reference number
UK	Malawi Lake, Zimbabwe (t), Zambia, Nigeria, Zimbabwe (m)	34, 43, 51, 26, 39, 37, 27, 31, 28, 29, 28, 29	Vulvar granuloma (3 cases), adnexal mass, infertility, tubal carcinoma, ectopic pregnancy, teratoma, HPV/HIV infection, cervicitis, cervical carcinoma in situ	<i>S. haematobium</i>	14, 17, 27
USA	Senegal, East Africa, Liberia, Guinea, South Africa (m)	27, 20, 28, 41, 22, 20, 63, 32, 37	Cervical dysplasia with HPV, cervical dysplasia with HPV/HIV, sandy patches, ectopic pregnancy, salpingitis, infertility, perianal fistula, cervical cancer without HPV	<i>S. haematobium</i> , <i>S. mansoni</i> (1 case)	
France	DRC (m), Mauritania (m), Senegal (ms), Tunisia (m), Mali (m), Mali (t), Senegal (m)	28, 34, 22, 29, 32, 35, 29, 21, 33, 27	Infertility, cervical dysplasia, tubal obstruction, hydrosalpinx, adnexal mass, secondary amenorrhoea, endometritis, ectopic pregnancy	<i>S. haematobium</i> , <i>S. mansoni</i> (DRC, 1 case from Senegal)	
Germany	Angola, Sierra Leone, Togo (m)	24, 30, 21	Ectopic pregnancy, leiomyoma, infertility, adnexal tumour	<i>S. haematobium</i>	86, 118, 161
Netherlands	Malawi Lake, Mali (t)	37, 33	Leiomyoma, infertility	<i>S. mansoni</i> , <i>S. haematobium</i>	29, 79
Spain	Nigeria (m) Mali (t)	26	Infertility, vulvitis	<i>S. haematobium</i>	15, 50
Switzerland	Egypt, Malawi Lake (t)	54, 26	Vulvar granuloma, asymptomatic ovarian and tubal schistosomiasis, vulvar lesion and cervical lesions	<i>S. haematobium</i>	28, 76, 105
Portugal			Ovarian schistosomiasis, external genital mass		104, 179
Australia					91
Belgium	Mali, Senegal (t)	20	Vulvar mass	<i>S. haematobium</i>	39
Czech Rep.	Brazil		Hydrosalpinx, tubal schistosomiasis	<i>S. mansoni</i>	136
Israel	Ethiopia (m)	19	Recto-vaginal fistula		102
Ireland	Nigeria (m)	31	Ectopic pregnancy, tubal schistosomiasis		67
Italy	South Tunisia (t)		Vaginal mass	<i>S. haematobium</i>	23
New Zealand	Malawi Lake	30, 28	Adnexal mass, vulvar lesion	<i>S. haematobium</i>	52, 111

44 FGS cases in migrants and travelers; < 1/2 returning travelers

m, migrants; t, travellers; HPV, human papilloma virus; HIV, human immunodeficiency virus.

Urinary and rectal presentation at the same time?

SCHISTOSOMIASIS AS A CAUSE OF RECTOVAGINAL FISTULA: A BRIEF CASE REPORT



FGS presentations?

- Perineal or vaginal lesions
- Cervicitis
- Endometritis
- Salpingitis
- Infertility
- Fistulae

Snips: Unstained wet mount preparation

Species?

Cervical



Rectal



Question: Which type of *Schistosoma spp.*?

Clinical Infectious Diseases

BRIEF REPORT

Diagnosis and Clinical Management of *Schistosoma haematobium*–*Schistosoma bovis* Hybrid Infection in a Cluster of Travelers Returning From Mali

Patrick Soentjens,^{1,3} Lieselotte Cnops,¹ Tine Huyse,^{2,4} Cedric Yansouni,^{5,7} Daniel De Vos,⁴ Emmanuel Botteiau,¹ Jan Clerinx,¹ and Marjan Van Esbroeck¹

[Parasitology Research](#)

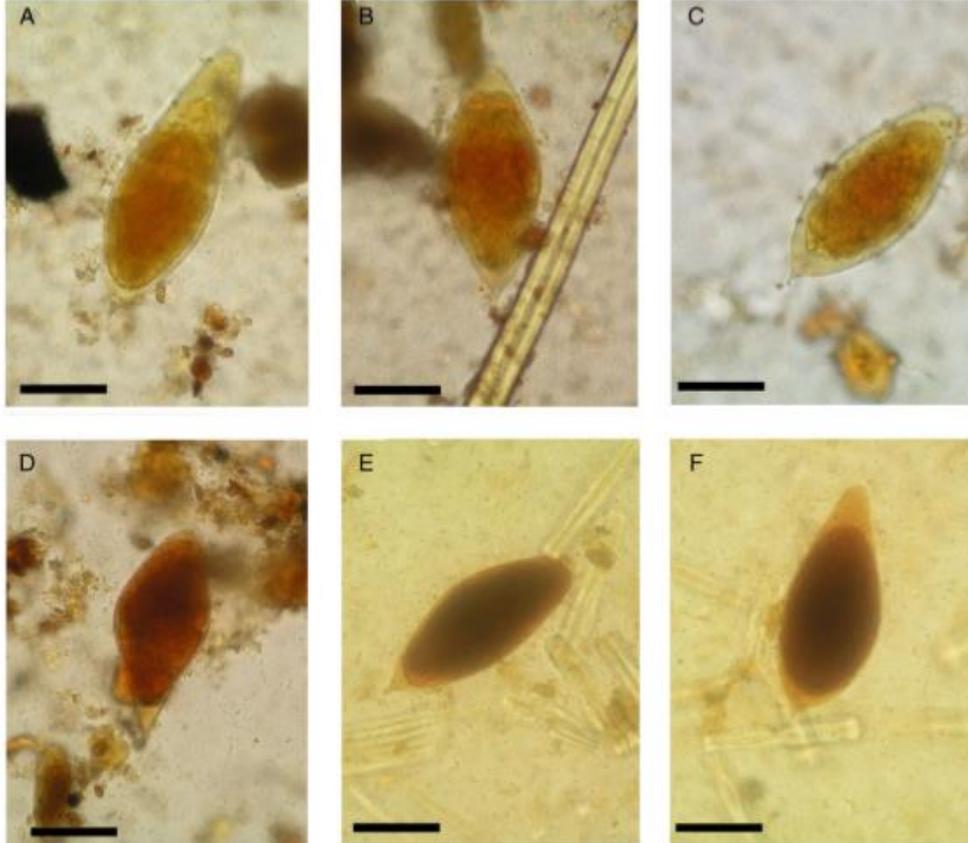
November 2015, Volume 114, Issue 11, pp 4127–4133 | [Cite as](#)

Introgressive hybridizations of *Schistosoma haematobium* by *Schistosoma bovis* at the origin of the first case report of schistosomiasis in Corsica (France, Europe)

G Patient	Time From Exposure to Diagnosis, d	Eosinophil Count, $\times 10^9/L$	ELISA	IHA	Eggs in Stool, No./g	Genus PCR (Stool)	Microscopy (Urine)	Genus PCR (Urine)	Dra PCR (Serum)	Sm1–7 PCR (Serum)
1	39	2.13	Positive	Negative	Negative	NA	Negative	NA	Positive	Positive
2	58	0.88	Negative	1/640	Negative	NA	Negative	NA	Positive	Negative
3	88	1.78	Negative	Negative	360	Positive	Negative	NA	Positive	Positive
4	88	3.94	Negative	Negative	40	Positive	Negative	NA	Positive	Negative
5	81	4.51	Negative	1/160	10	Positive	Negative	NA	Positive	Positive
6	95	0.67	Negative	1/1280	80	Positive	Negative	Negative	Positive	Negative
7	109	1.02	Negative	Negative	60	Positive	Negative	Negative	Positive	Negative
8	109	0.59	Negative	1/160	580	Positive	Positive	Positive	Positive	Negative
9	116	0.3	Negative	Negative	140	Positive	Positive	NA	Positive	Positive
10	719	0.95	Positive	1/160	Negative	NA	Positive	Positive	Positive	Positive



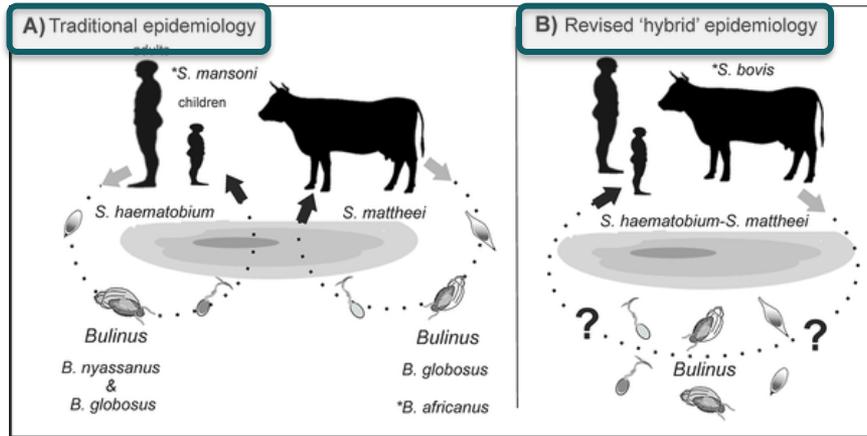
Schistosoma haematobium-*bovis* Hybrids



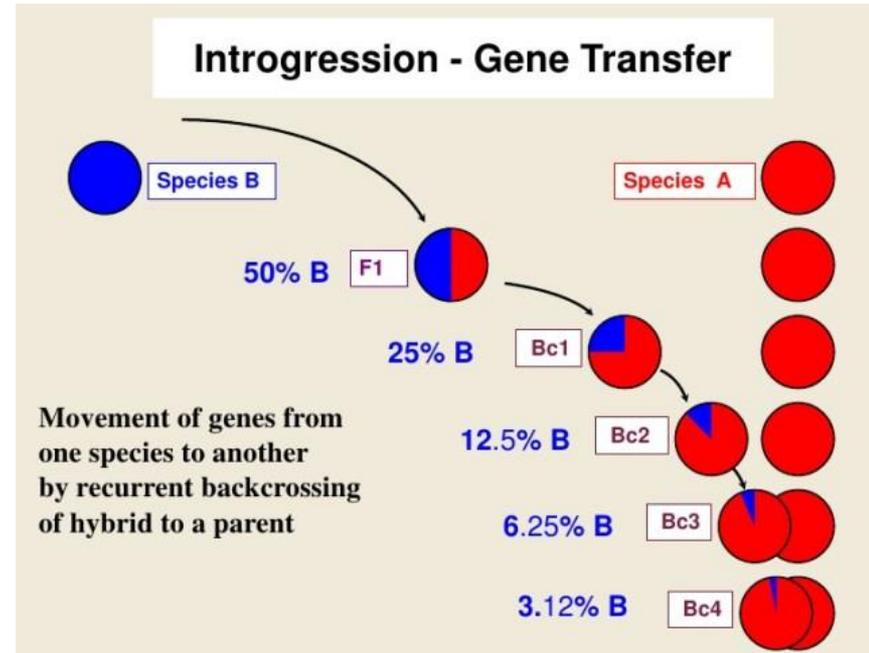
Polymorphic eggs seen in parasitological examination of stool sample from patient 8. The eggs looked similar to those of *Schistosoma guineensis* (formerly *Schistosoma intercalatum*) (140–240 μm); but were smaller, 135–175 μm in length. Their shape was intermediate **between the typical round to oval *Schistosoma haematobium* and the more elongate, spindle-shaped *Schistosoma bovis* eggs**. Some eggs were more stretched, with an oval to diamond shape (D, E), and were larger (A) than the typical *S. haematobium* type, 110–170 μm long; some other eggs were smaller (B, C). Although *S. haematobium* has a characteristic small terminal spine (C, F), some eggs had a somewhat enlarged terminal spine (A, D). Scale bars represent 50 μm .

CID 2016:63 (15 December)

Fig 1. Reconciling schistosome hybridization with epidemiological models of schistosomiasis transmission.

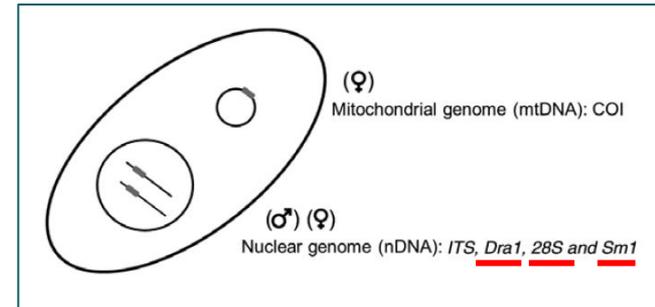


(A) The current model of urogenital schistosomiasis in Malawi involves discrete transmission cycles and does not formally take into account the importance of multi-species coinfections. (B) A revised model of urogenital schistosomiasis with overlapping transmission potentials with schistosome worms also being influenced or interacting with other species present (e.g., *S. mansoni* within coinfecting people or *S. bovis* in cattle). Note **S. mansoni*–intestinal schistosomiasis is now emerging along the Lake Malawi shoreline and is transmitted by *Biomphalaria* (which is not depicted here for brevity), **B. africanus* has now been detected in the lake (MH Al-Harbi *personal observation*) and is a known intermediate host of several other *S. haematobium* group species, which might drive novel environmental transmission opportunities. <https://doi.org/10.1371/journal.pntd.0008201.g001>



PCR Results on cervical smear, rectal- and cervical snips

- Genus PCR: CT 33,69 (all *Schistosoma* species), targets 28S rRNA
- Dra 1 PCR: CT 22,78 (*Haematobium* complex)
- Sm1-7 PCR: **neg** (*Mansoni* complex)
- Sequencing



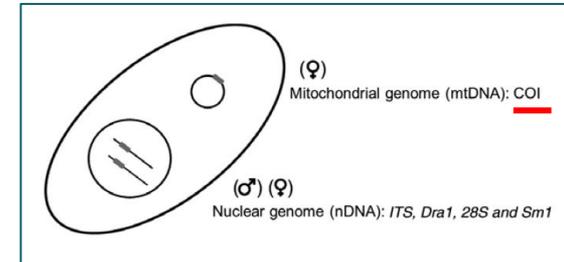
Cnops L, Tannich E, Polman K, Clerinx J, Esbroeck M Van. Schistosoma real-time PCR as diagnostic tool for international travellers and migrants. *Trop Med Int Heal*.

Cnops L, Soentjens P, Clerinx J, Esbroeck M Van. A Schistosoma haematobium-Specific Real-Time PCR for Diagnosis of Urogenital Schistosomiasis in Serum Samples of International Travelers and Migrants. *PLoS Negl Trop Dis*. 2013;7(8):1-7. doi:10.1371/journal.pntd.0002413

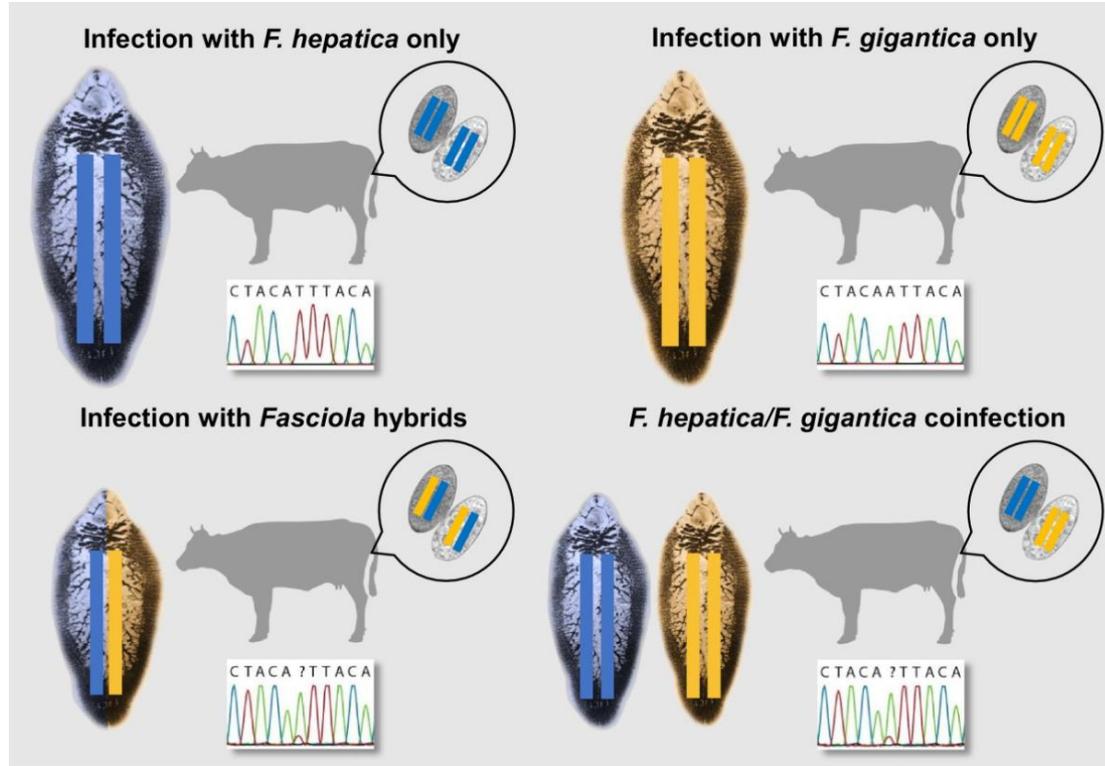


Further testing

- 28S rRNA fragment sequencing -- > Could not distinguish between *S. haematobium*, *S. bovis*, or *S. intercalatum* / *S. guineensis*
- RD-PCR on **cervical** biopsy: strong *S. bovis* band and weak *S. haematobium* band
 - Sequencing: 100% *S. bovis* match
- **Rectum** snip CO1 (cytochrome oxidase subunit I) fragment sequenced
 - 99.76% *S. haematobium*



Explanation?



■ So either:

1. Mixed *S. bovis* + *S. haematobium* infection
- vs
2. Hybrid infection



Hybrid

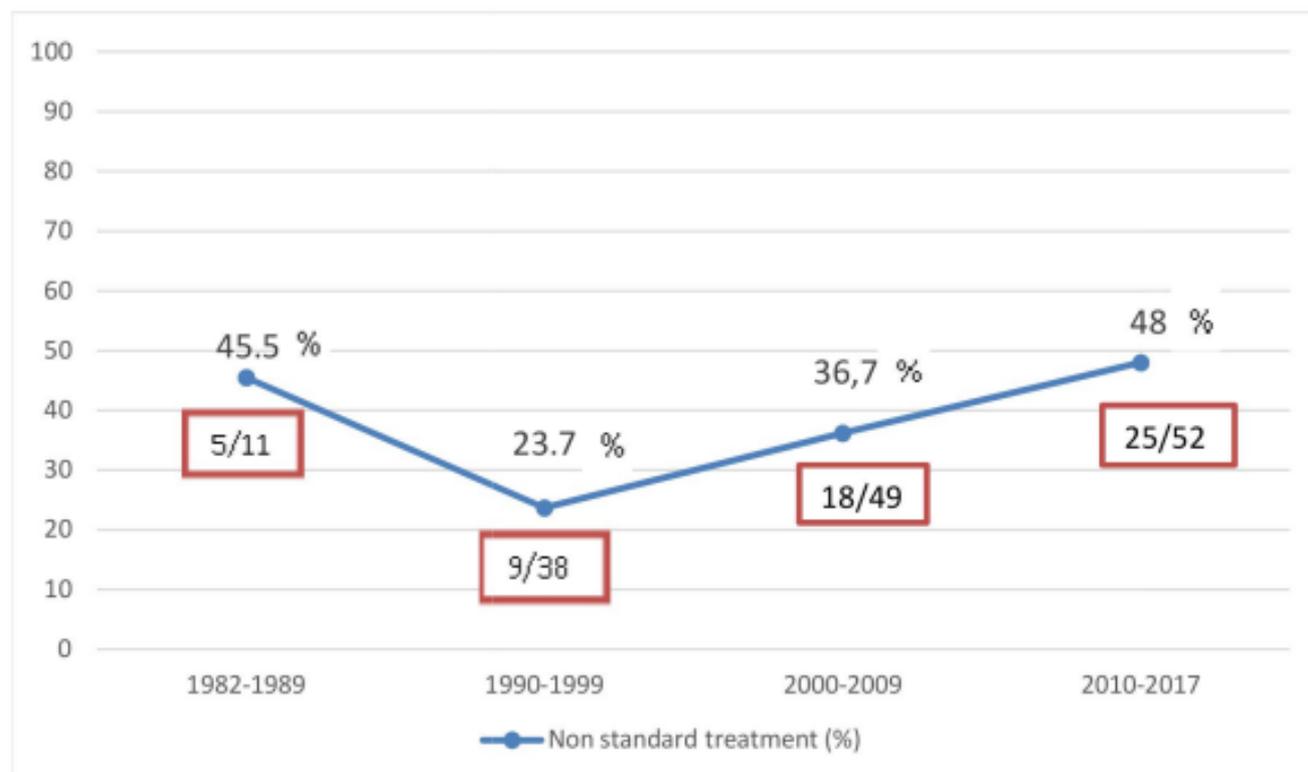
Treatment?

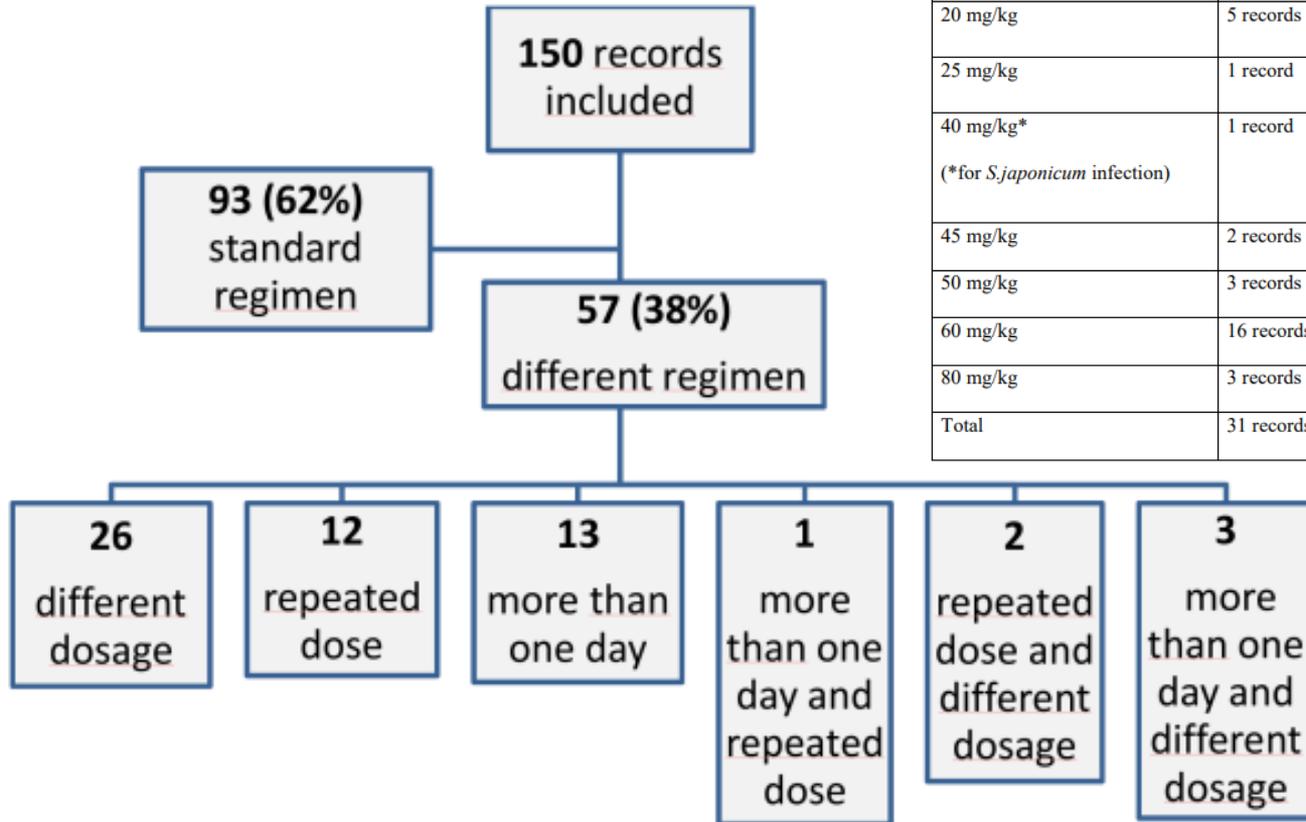
PZQ is the first-line medication for chronic schistosomiasis. According to the WHO recommendations, the treatment regimens are: 40 mg/kg/day orally, in single dose or divided in two doses, for *S. haematobium* and *S. mansoni*, 60 mg/kg/day in three divided doses for *S. japonicum* and *S. mekongi*.^{7,8} The CDC guidelines suggest, in particular in lightly infected patients, to give a second course of treatment after 2 to 4 weeks.⁸ Current recommendations and guidelines for the treatment of schistosomiasis are based on trials conducted in endemic countries, where morbidity control is the main objective. No trials have been performed in non-endemic areas where, in absence of possible re-exposure to an infective source, cure should be the goal of treatment.



High-dose or Multi-day Praziquantel for Imported Schistosomiasis? A Systematic Review.

Cucchetto G^{1,2}, Buonfrate D³, Marchese V⁴, Rodari P³, Ferrari A⁵, Zanotti P⁴, Bottieau E⁶, Silva R³, Bisoffi Z^{2,3}, Gobbi F³.





Dosage of praziquantel	Number of records
20 mg/kg	5 records
25 mg/kg	1 record
40 mg/kg* (*for <i>S.japonicum</i> infection)	1 record
45 mg/kg	2 records
50 mg/kg	3 records
60 mg/kg	16 records
80 mg/kg	3 records
Total	31 records

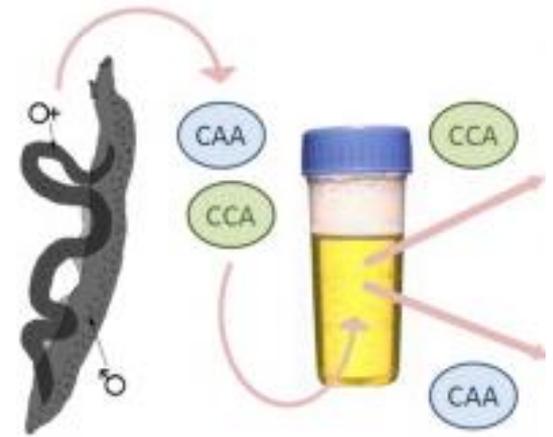


Treatment patient

- Praziquantel 20 mg/kg 3x/d D1 and D14
- Improvement for 6 weeks, but recurrence of symptoms
- What would you do?
- Are the complaints due to established fibrosis?

Circulating anodic antigen (CAA)

- 5 Months after 1° treatment:
 - Serum CAA: 1.44 pg/ml (ref range < 1.00 pg/ml)
 - Urine CAA: negative
- Praziquantel 40 mg/kg single dose
- 11 Months after 1° treatment:
 - Serum CAA: 0,88 pg/ml
 - All complaints have disappeared
 - In follow-up in fertility center



31y old immigrant from Sierra Leone, since 20 years in Belgium

Picture of a Microorganism

Intestinal schistosomiasis: a very long-lived tropical parasite

I. Potters^{1,*}, L. Van Duffel², G. Broeckx³, E. Bottieau¹



ER: acute slightly bloody diarrhea, abdominal pain and vomiting

Schistosoma mansoni egg after glycerol sedimentation of stools. The egg has a large lateral spine, typical for *S. mansoni*, and has a clearly defined miracidium inside. Scale bar represents 50 μm .

LONGEVITY OF PARASITIC WORMS:
THE TERM OF LIVING EXISTENCE OF SCYTOSSOMA
HEMATORIUM IN THE HUMAN BODY.

By J. B. CHRISTOPHERSON, C.B.E., M.D. CAMB.,
F.R.C.P. LOND.,
ASSISTANT PHYSICIAN TO THE CITY OF LONDON HOSPITAL,
VICTORIA PARK; LATE MEDICAL DEPARTMENT,
SUDAN GOVERNMENT.

LONGEVITY in biology is the term of living existence, without reference to its being a long or a short term, or comparatively a long or a short term. The word needs definition, because, being one about which dictionaries are not precise, its meaning is ambiguous. In an essay on comparative longevity, published about 1870, Ray Lankester¹ found it necessary to define its uses. Chalmers-Mitchell, in his Notes on the Theory of Longevity,² accepts Ray Lankester's definitions, and we cannot do better than accept them also.

Longevity: Normal and Potential.

Ray Lankester refers to "specific longevity" as the average span of life of the species, and "potential longevity" as the possible length of life of the individual. Specific longevity is the longevity of the species, the length of time a living being may expect to survive under natural conditions—the "expectation of life at birth." This is a problem of mathematics rather than physiology, is largely determined by accidents and external conditions, and does not interest us here. Potential longevity, on the other hand, depends on the inherent vitality of the individual. Accidents, diseases, and external conditions have no relation to it. It is said to be normal or absolute. If all untoward external conditions, diseases, and accidents could be eliminated, the animal surviving as long as his store of vitality lasts, no longer and no shorter, we should have absolute potential longevity, and the biologist could study longevity without any qualifications.

Absolute potential longevity is rarely if ever attained; we must therefore examine longevity as we find it, normal potential longevity, length of life under normal conditions. Although the subject of potential longevity has been much studied by philosophers and biologists, no great distance has been traversed, possibly because investigations have been limited in the main to man and the higher animals. The question as to why one animal lives longer than another is still without a satisfactory answer. Is there in truth any causative relation between high longevity and complex structure or anything whatever to do with potential longevity? Why is the distribution of "vitality" apparently so arbitrary?

Practically speaking, little is known of the potential longevity of the higher animals; of that of wild animals nothing. Of potential longevity we know little concerning domesticated animals and still less

longevity of a have been stud increasing the of tissue and longevity, ex influences are in fluke parasit hule longevity in other living

The Lancet 1924, viable worms 28 years after exposure

The Bilharzia Worm.

The potential longevity of the bilharzia worm in the human body is well worth attention. It is a tissue and blood parasite, and as such little subject to change in environment, surroundings, or external conditions. G. M. Vevens,³ in a review of the entozoa collected from animals which died in the Zoological Gardens of London during eight months in 1919, reporting a case of *Gastrodiscus agypticus*, the trematode of equine sites of various groups in their hosts. (*Gastrodiscus agypticus* is a species of parasite not altogether unrelated to bilharzia.) Dr. Vevens found this parasite in a Grevy's zebra which had been in the Gardens for six years. As it does not breed in the host, but requires an intermediary host to complete the life-cycle (*Cleopatra bulimoides*, a fresh-water snail), and as an intermediary host has not yet been reported in this country, the parasite must have been six years old at least at the death of the zebra. Further, as the zebra was in Hagenbeck's collection at Hamburg for three years previously we may fairly certainly assume that the potential longevity of *Gastrodiscus agypticus* is at least nine years—probably longer. This is a long time for a parasite to live in the body of the host, and, as Dr. Vevens points out, the more remarkable in that the parasite lived in the intestines, where the vicissitudes of existence are greater and more numerous than in the blood or tissues. But remarkable as is this evidence of great longevity in a small living thing, it is not so remarkable as the long span of life of the bilharzia worm.

During the South African war many British soldiers contracted bilharzia disease. In 1920, 18 years after, many of the survivors, who had not been out of England and so could not have been re-infected, were passing live ova in the urine; in other words, were passing worms which the men had acquired in South Africa in 1902 were alive in 1920. The potential longevity of the bilharzia worm must therefore be 18 years. It is in point of fact longer. A well-known zoologist and doctor of medicine, living in England, contracted bilharzia in 1878, when he was 28 years of age, between the Limpopo and Zambesi rivers, whilst on a naturalist's expedition. He was probably infected in the Northern Transvaal on the borders of the Kala Hari river. He read a thesis on Endemic Hematuria in 1881, for which he obtained his M.D. degree, and became an acknowledged authority on bilharzia disease. Thompson

was, as usual, taking the summer holiday.

In question of the longevity a, practically speaking, is into the bilharzia adult worm having a potential longevity of 28 years. Can this be explained in general terms?

Conclusion.

To conclude, it seems clear that bilharzia worms have a long potential longevity, and do not conform to the conditions which Ray Lankester has laid down as favouring longevity. Their individuality is not high, their structure is not complex or their bulk large. They display considerable energy throughout their (frequently) long life, traversing the portal veins between the liver and bladder (or rectum). Their generative energy is great, commencing early and continuing through life; they deposit enormous numbers of eggs.

It is probable that the study of the life-history of living things shorn of most of the obscuring and overwhelming external conditions of environment will bring us nearer to fundamental principles which apply to more complex and more developed organisms and lead to a revision of our present conclusions regarding potential longevity.

IDIOSYNCRASY TO ADRENALIN,

WITH REFERENCE TO ITS EMPLOYMENT WITH LOCAL ANESTHETICS AND IN GORTSCH'S TEST FOR HYPERTHYROIDISM.*

By H. E. SYMES-THOMPSON, M.D. CAMB.,
M.R.C.P. LOND.,
PHYSICIAN TO THE ROYAL CHEST HOSPITAL, CITY ROAD.

AT the joint meeting of various Sections of the Royal Society of Medicine on cocaine substitutes, as reported in THE LANCET of Dec. 15th, 1923, adrenalin, which is often given with drugs of this class, received little notice when toxic effects were being reviewed. Adrenalin is not a cocaine substitute, and it was not, strictly speaking, under discussion. It seems, therefore, a suitable time to consider its toxic effects.

The Employment of Adrenalin with Local Anesthetics.

The following instance of the occurrence of disquieting symptoms after the injection of novocaine and adrenalin for the extraction of teeth has recently come to my notice. Incidentally, the patient gave a positive reaction to Gortsch's test for hyperthyroidism, though the dentist did not have this test in view when making the injection.

A married woman of average nervous stability, aged 38, had novocaine and suprarenin injected into the gum by Mr. S. D. Corbett for the extraction of two lower incisor teeth on July 2nd, 1923, and the following symptoms appeared almost immediately after the injection: Impass and stiffness, succeeded by mental agitation, severe palpitation, cold anæmic breathers. flushing of the face, and tremor



A Woman With Chronic Lower Abdominal Pain, Vaginal Discharge, and Infertility After a Stay in Mali

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¹Department of Clinical Sciences, Institute of Tropical Medicine Antwerp, Antwerp, Belgium, ²Department of Pathology, University Hospital Antwerp, Antwerp, Belgium, ³Department of Biology, Royal Museum for Central Africa, Tervuren, Belgium

Keywords. female genital schistosomiasis; *Schistosoma* infection.

A 28-year-old Belgian woman presented with hypogastric pain, vaginal discharge, menorrhagia, dysmenorrhea, dyspareunia, and fatigue, which persisted over 8 years. These complaints started a few weeks after an accidental fall in the Niger river during a trip to Mali, after which she had noticed an itching rash localized on the abdominal wall. There were no urinary complaints. Various attempts to conceive in the previous 2 years had failed. She also reported intermittent hematochezia but no diarrhea. During the past 8 years, the patient consulted several gynecologists and had extensive investigations, including a hysterosalpingography without diagnostic yield.

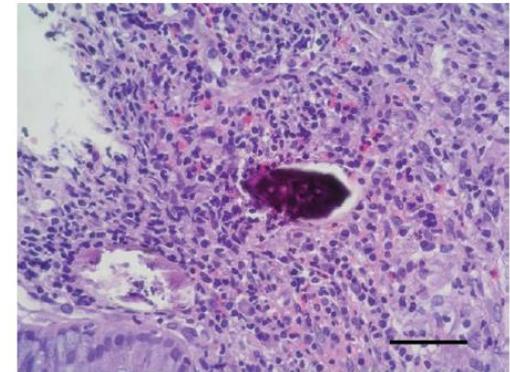
There was no significant medical history except for hay fever for which no maintenance treatment was required. Further travel history revealed a 1-month stay in Ecuador 10 years ago

erythrocytes/ μL , no leucocytes, and the presence of mucus. No proteinuria was detected. Atypical inflammation was reported on a Pap smear, and a cervical biopsy was performed by the treating gynecologist and showed calcified structures within nonnecrotic granulomas (Figure 1).

WHAT IS YOUR DIAGNOSIS?

ANSWER: GENITAL SCHISTOSOMIASIS

The biopsy of the cervix showed calcified *Schistosoma* eggs in the center of granulomas containing eosinophils and other inflammatory cells (Figure 1). We performed cervical,



Thank you!

Spooning:

Schistosomiasis is a distinctly one-sided **love affair**. The male worm is shorter and fatter and equipped with a groove, a **love canal** where the longer, thinner female lodges, enabling the pair to mate for decades.





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