WRAIR Tropical Medicine Course September 16, 2010

Schistosomiasis

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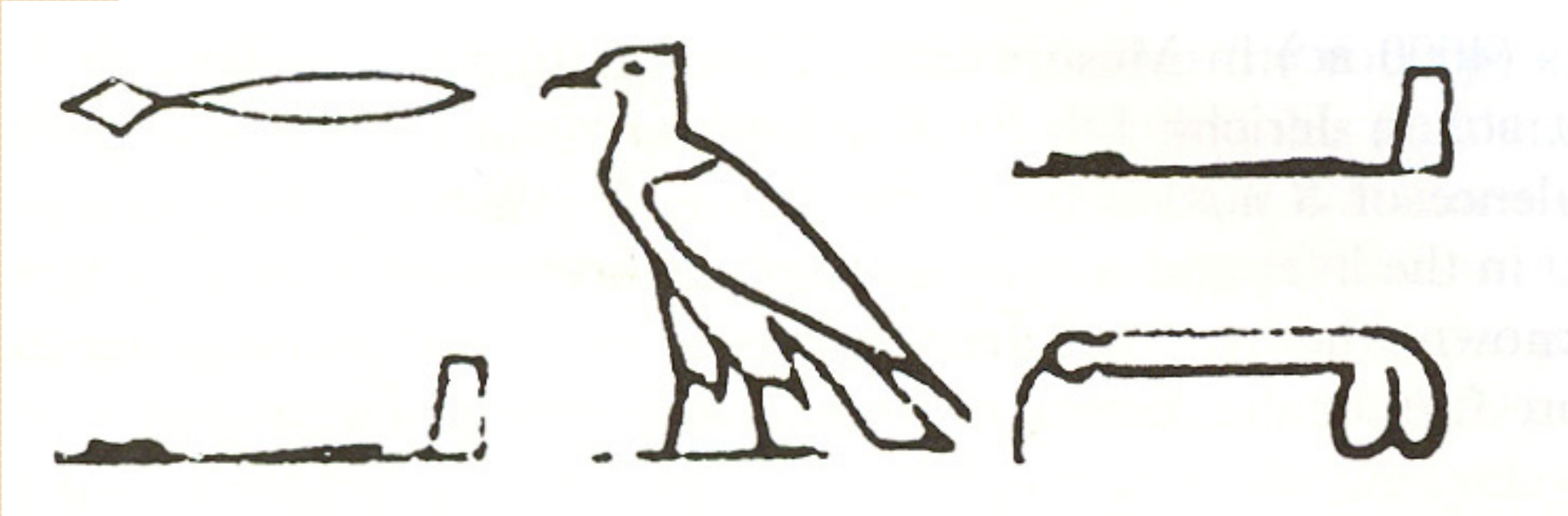
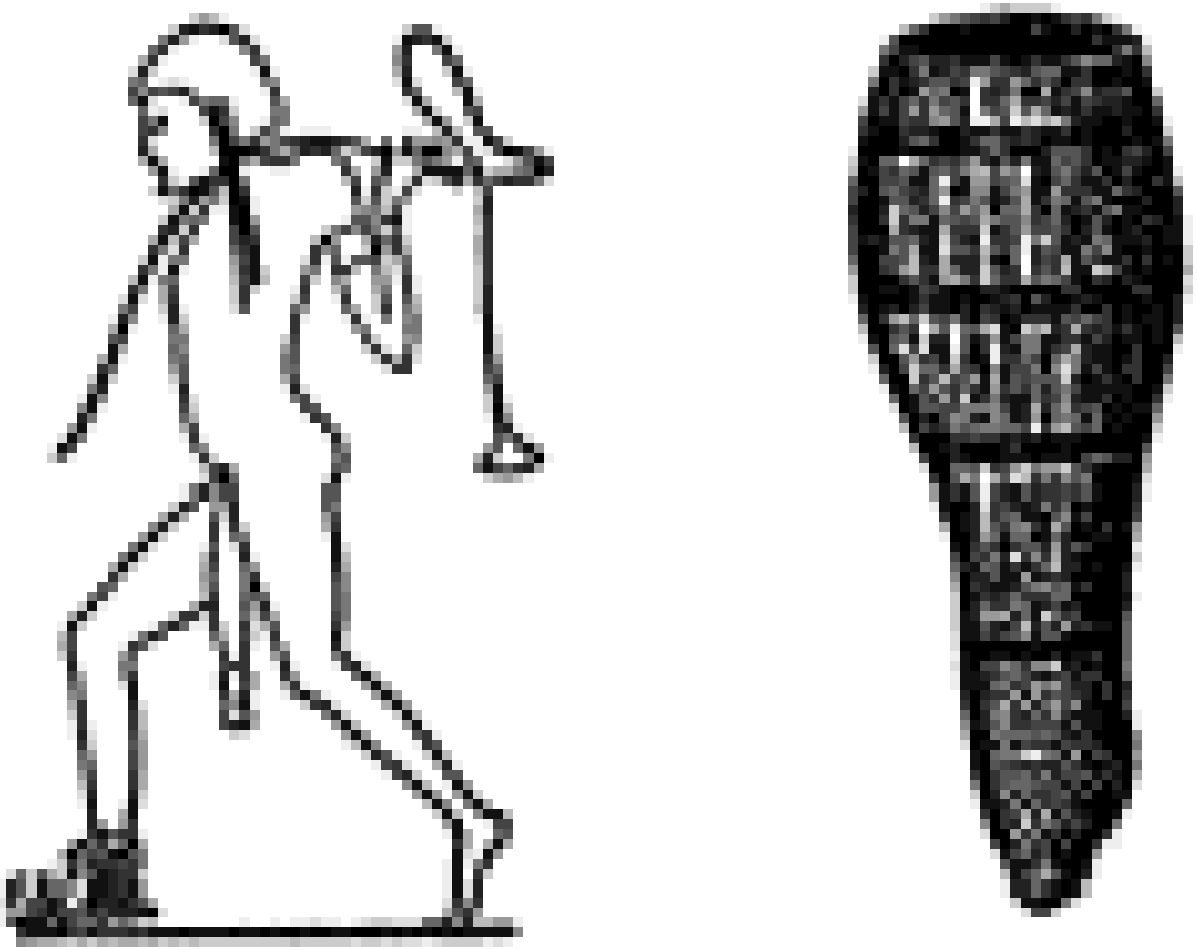
Outline

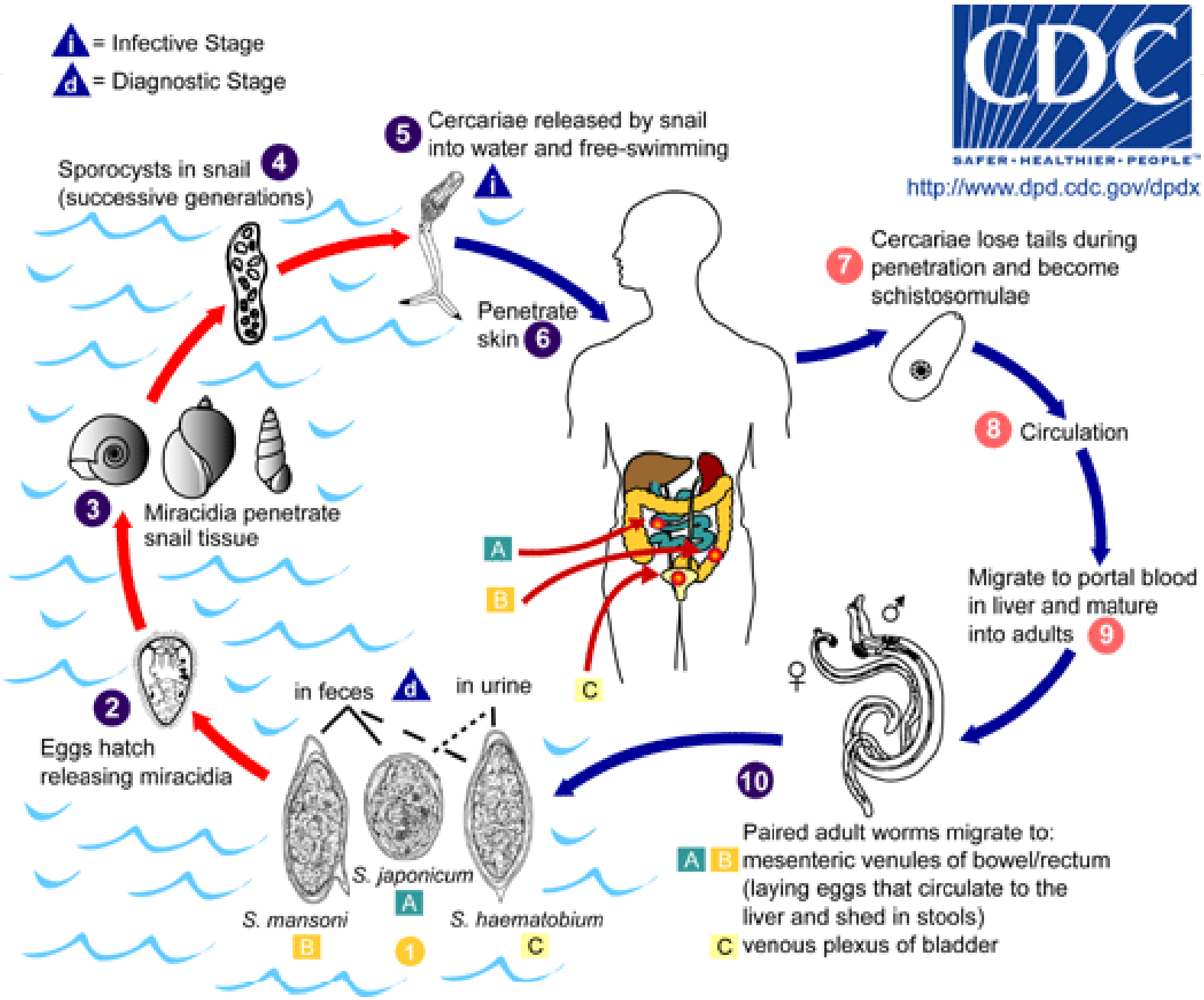
- Schistosomiasis in Antiquity
- Etiology; Schistosome genome
- Epidemiology and Geographic distribution
- Clinical Presentations:
  - Military relevance – Acute Schistosomiasis
  - Chronic disease
  - Management

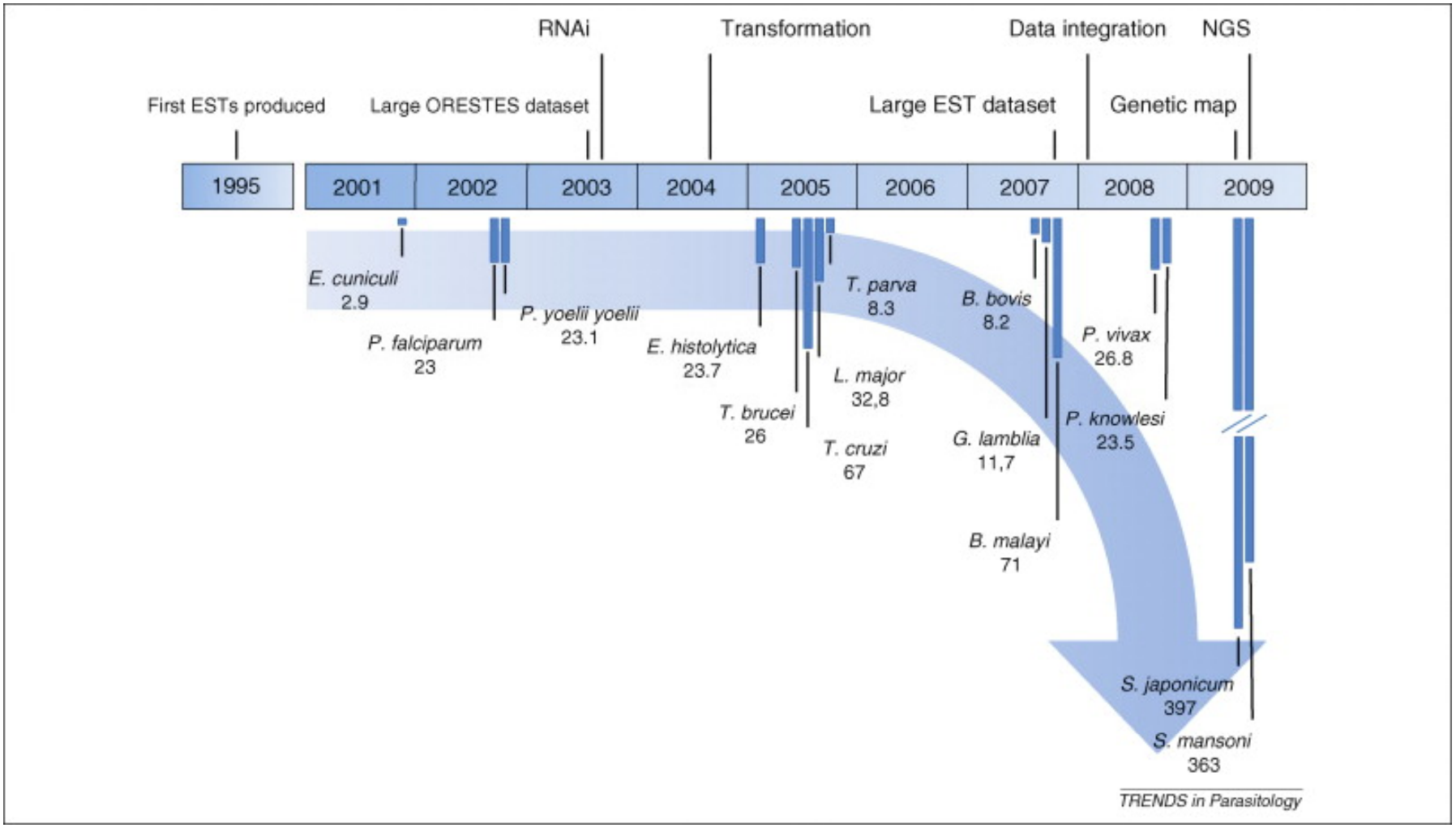


Historical Aspects of Infectious Diseases, Part II 2004, p 211 Fig 3



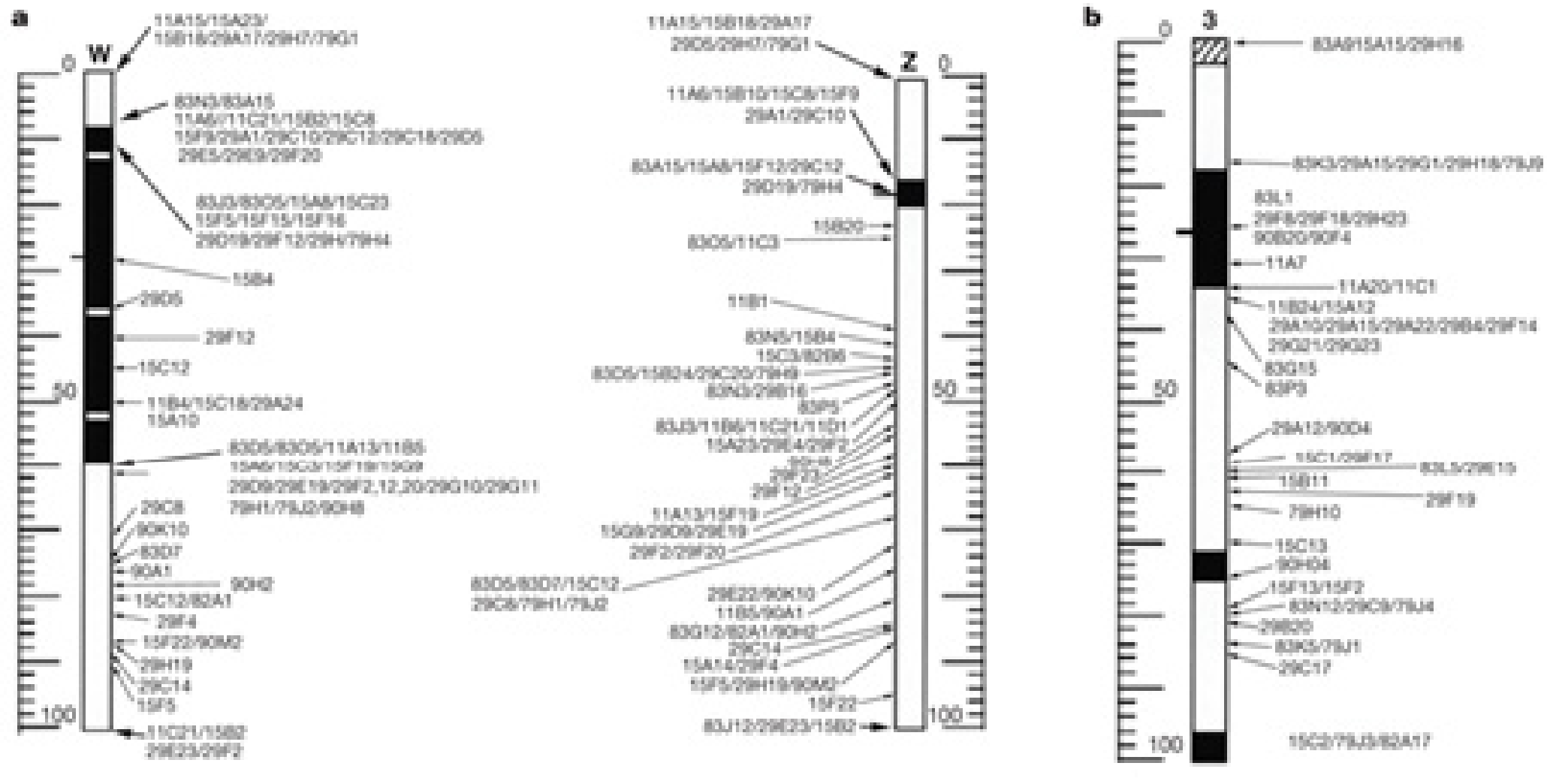
An illustration of the use of penile sheath in Ancient Egypt, circa XIX Dynasty 1350 to 1200 .


= Infective Stage
= Diagnostic Stage
CDC
SAFER · HEALTHIER · PEOPLE™
http://www.dpd.cdc.gov/dpdx
5 Cercariae released by snail into water and free-swimming
Sporocysts in snail 4 (successive generations)
Penetrate skin 6
7 Cercariae lose tails during penetration and become schistosomulae
8 Circulation
3 Miracidia penetrate snail tissue
A
B
C
Migrate to portal blood in liver and mature into adults 9
2 Eggs hatch releasing miracidia
in feces
in urine
S. japonicum
S. mansoni
S. haematobium
10
Paired adult worms migrate to:
A B mesenteric venules of bowel/rectum (laying eggs that circulate to the liver and shed in stools)
C venous plexus of bladder



Source: Webster, JP *et al* (2010) Schistosome genomes: a wealth of information. *Cell* **26**(3):103-106.

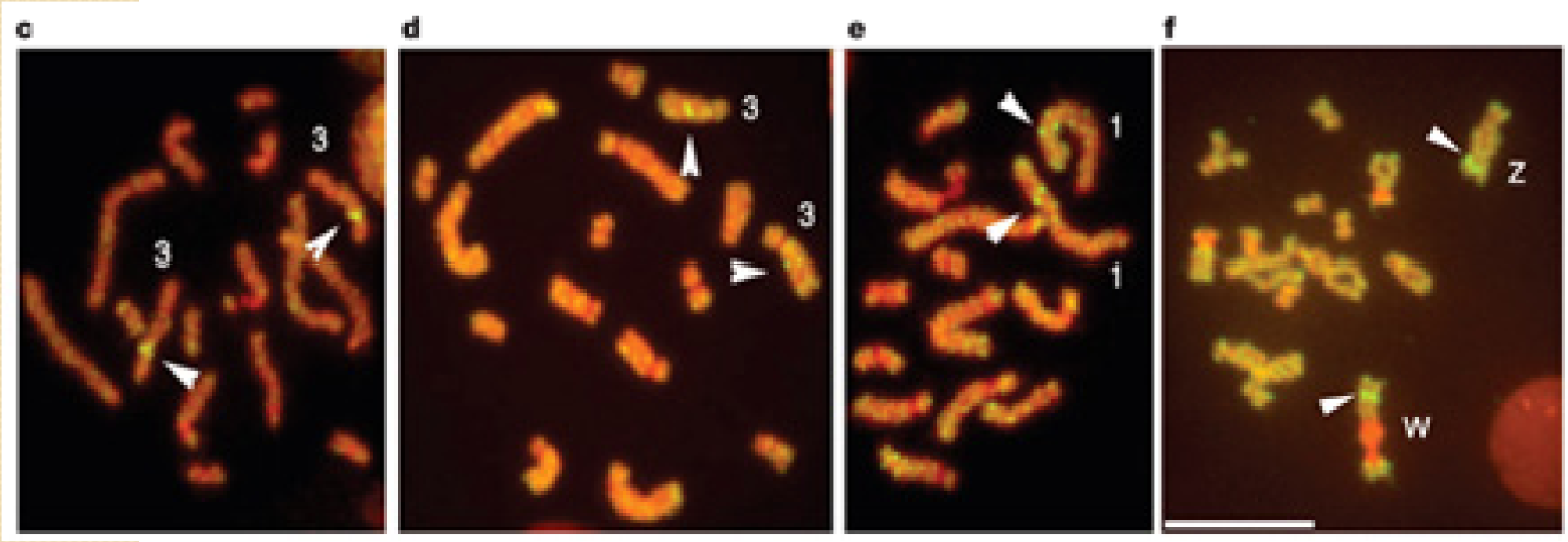
Physical map of *S. mansoni.*



M Berriman *et al. Nature* 460, 352-358 (2009) doi:10.1038/nature08160

nature

Physical map of *S. mansoni.*



M Berriman *et al. Nature* 460, 352-358 (2009) doi:10.1038/nature08160

nature

Table 1. *S. mansoni* genes that match a human gene with marketed drugs.

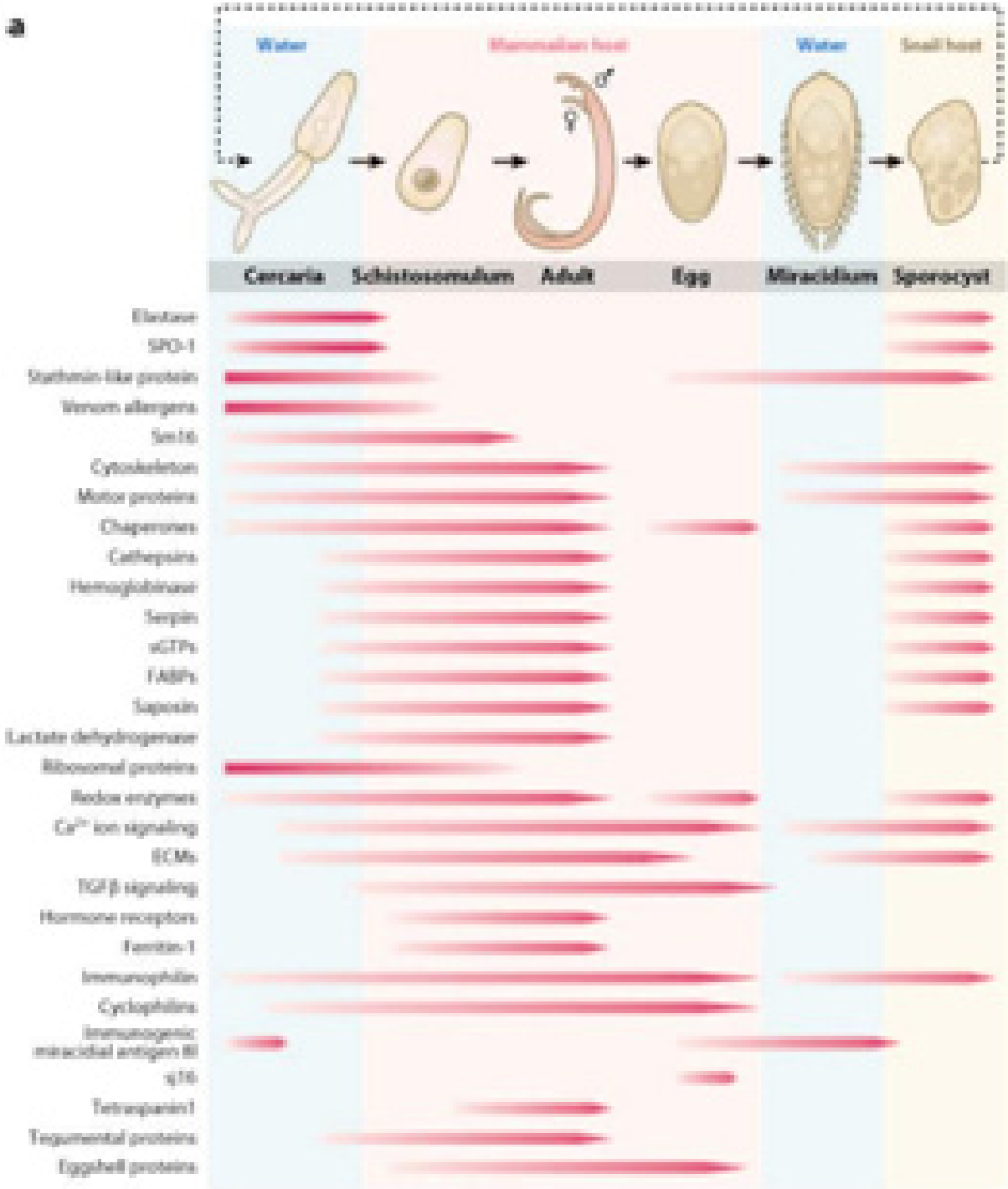
Gene identifier	Protein description	Potential drugs
Smp_005210	Histone deacetylase 1 (HDAC1)	Vorinostat[‡]
Smp_009030	Ribonucleoside-diphosphate reductase, subunit, putative	Fludarabine phosphate[‡]
Smp_012930	Inosine-5-monophosphate dehydrogenase, putative	Mycophenolate mofetil[‡], mycophenolic acid[‡], ribavirin[§]
Smp_015020	Na^+,K^+-ATPase subunit (SNaK1)	Digoxin[‡], digitoxin[‡], acetyldigitoxin[§], deslanoside[§]
Smp_016780[*]	Tubulin chain, putative	Vinblastine[‡], colchicine[‡], vincristine[‡]
Smp_022960	Aldehyde dehydrogenase, putative	Disulfiram[‡]
Smp_026560	Calmodulin, putative	Bepridil[§]
Smp_030730[*]	Tubulin chain, putative	Colchicine[‡], vinblastine[‡], vincristine[‡], albendazole[‡], mebendazole[‡], paclitaxel[‡], thiabendazole[‡], vinorelbine[‡], docetaxel[§]
Smp_040130	Cyclophilin (p17.7)	Cyclosporine[‡]
Smp_040790	Cyclophilin B	Cyclosporine[‡]
Smp_044440	Alcohol dehydrogenase, putative	Fomepizole[‡]
Smp_048430	Thioredoxin glutathione reductase	Auranofin[‡]
Smp_050390	Aldehyde dehydrogenase, putative	Disulfiram[‡]
Smp_053220	Aldo-keto reductase, putative	Tolrestat[‡]

M Berriman *et al. Nature* 460, 352-358 (2009) doi:10.1038/nature08160

Table 1. *S. mansoni* genes that match a human gene with marketed drugs. *Continued*

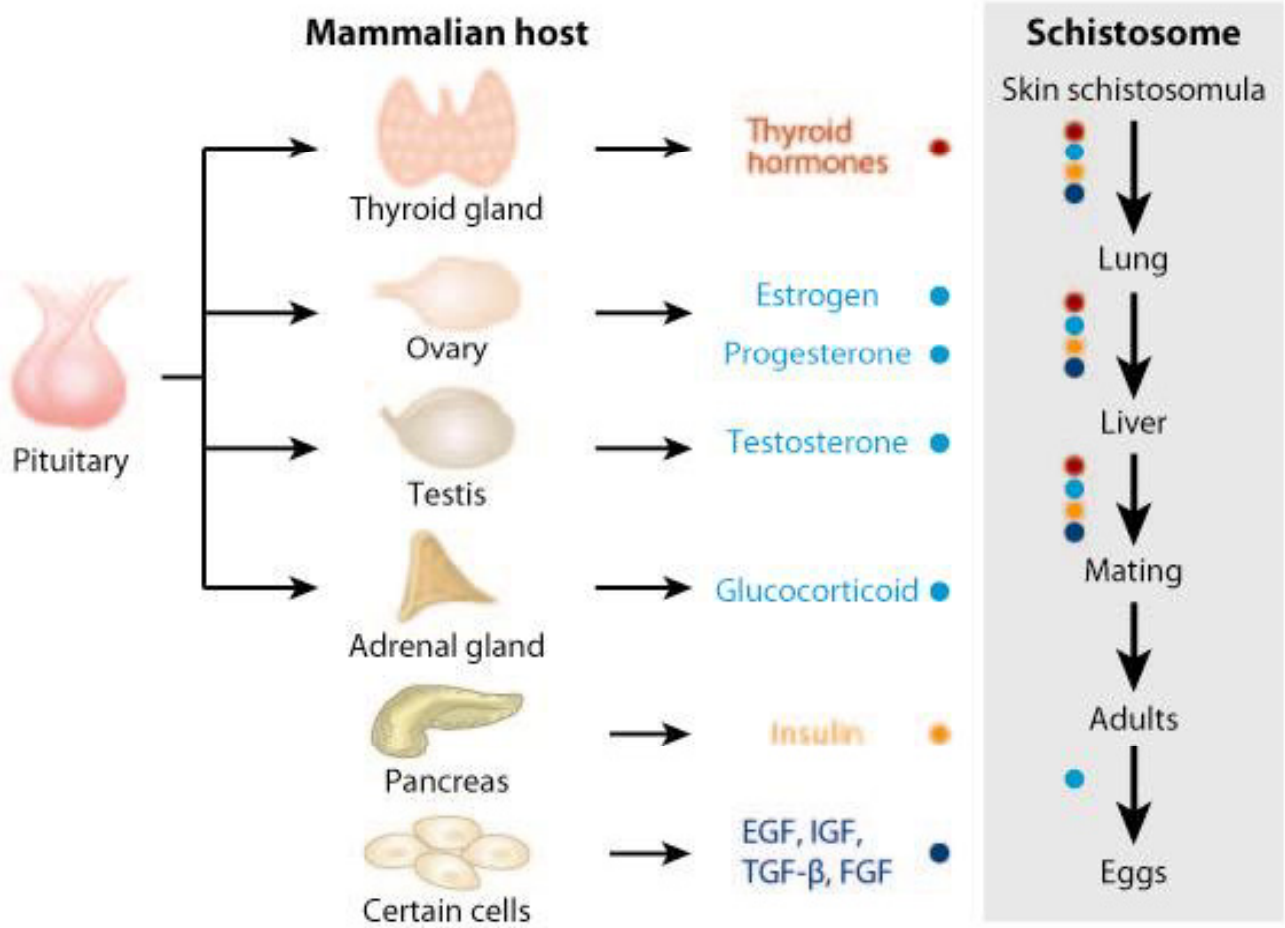
Smp_055890	Ribonucleoside-diphosphate reductase small chain, putative	Hydroxyurea[‡], gemcitabine[‡]
Smp_065120	Deoxyhypusine synthase, putative	Ciclopirox[‡]
Smp_069160	Cyclophilin, putative	Cyclosporine[‡]
Smp_079230	Immunophilin FK506 binding protein FKBP12, putative	Pimecrolimus[‡], temsirolimus[‡], sirolimus[‡], tacrolimus[‡]
Smp_093280	Histone deacetylase 3 (HDAC3)	Vorinostat[‡]
Smp_094810	Cyclophilin E	Cyclosporine[‡]
Smp_121920	Vesicular amine transporter, putative	Rauwolfia serpentina[‡], reserpine[‡], deserpidine[§], rescinnamine[§], alseroxylon[§]
Smp_135460	Bifunctional dihydrofolate reductase-thymidylate synthase, putative	Pemetrexed[‡], flucytosine[‡], floxuridine[‡], capecitabine[‡], gluorouracil[‡]
Smp_136300	Tyrosine kinase 5	Dasatinib[‡]
Smp_147050	ATP synthase subunit vacuolar, putative	Tiludronate[§]
Smp_171580	Aromatic amino acid decarboxylase, putative	Carbidopa[‡]
Smp_173280	Cyclophilin, putative	Cyclosporine[‡]

M Berriman *et al. Nature* 460, 352-358 (2009) doi:10.1038/nature08160



Han Z-G, et al. 2009.
Annu. Rev. Genomics Hum. Genet. 10:211–40

Annual Reviews



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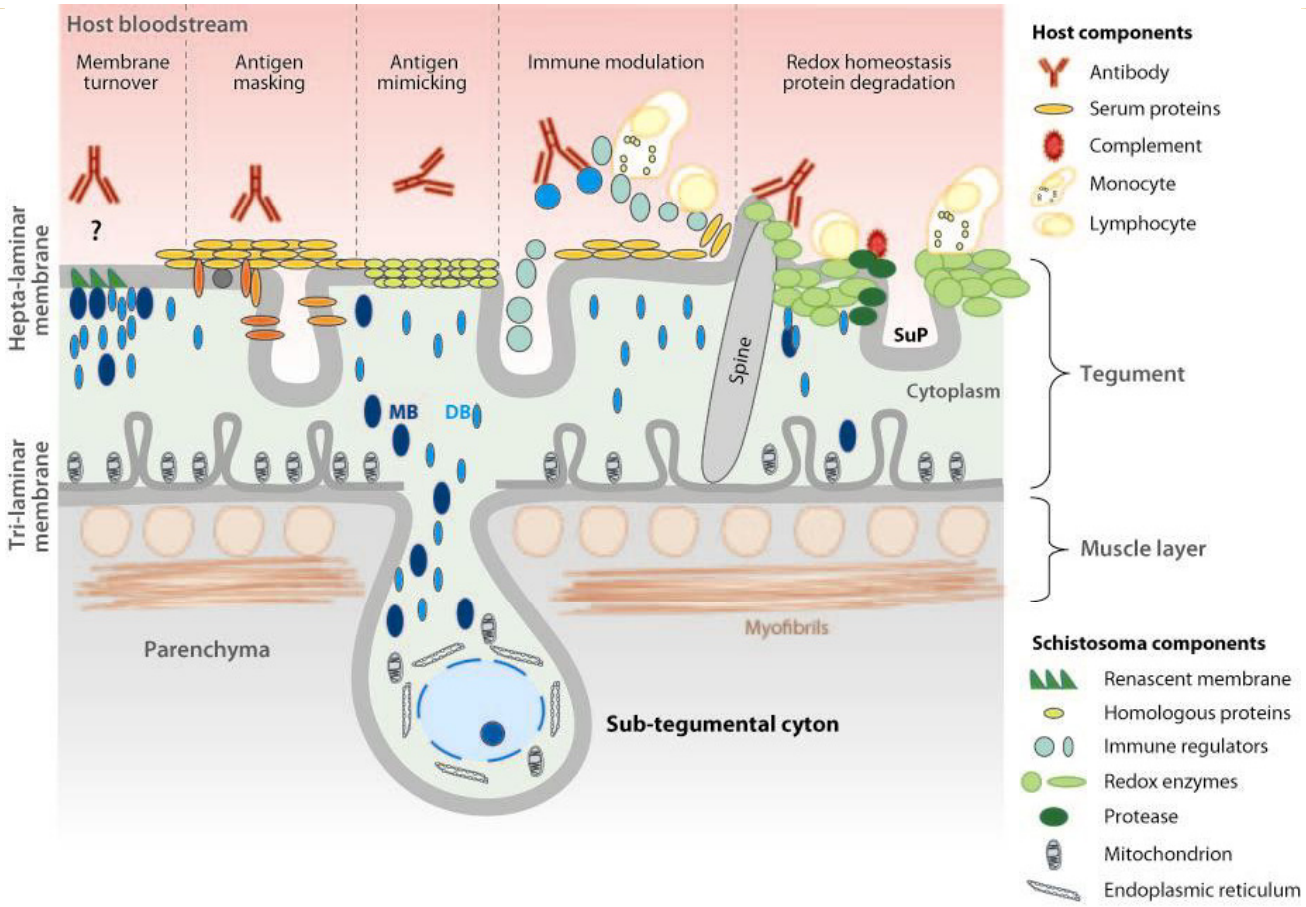
Annual Reviews



Han Z-G, et al. 2009.
Annu. Rev. Genomics Hum. Genet. 10:211–40

Annual Reviews

	Species	Geographical distribution
Intestinal schistosomiasis	Schistosoma mansoni	Africa, the Middle East, the Caribbean, Brazil, Venezuela, Suriname
	Schistosoma japonicum	China, Indonesia, the Philippines
	Schistosoma mekongi	Several districts of Cambodia and the Lao People's Democratic Republic
	Schistosoma intercalatum and related S. guineansis	Rain forest areas of central Africa
Urogenital schistosomiasis	Schistosoma haematobium	Africa, the Middle East

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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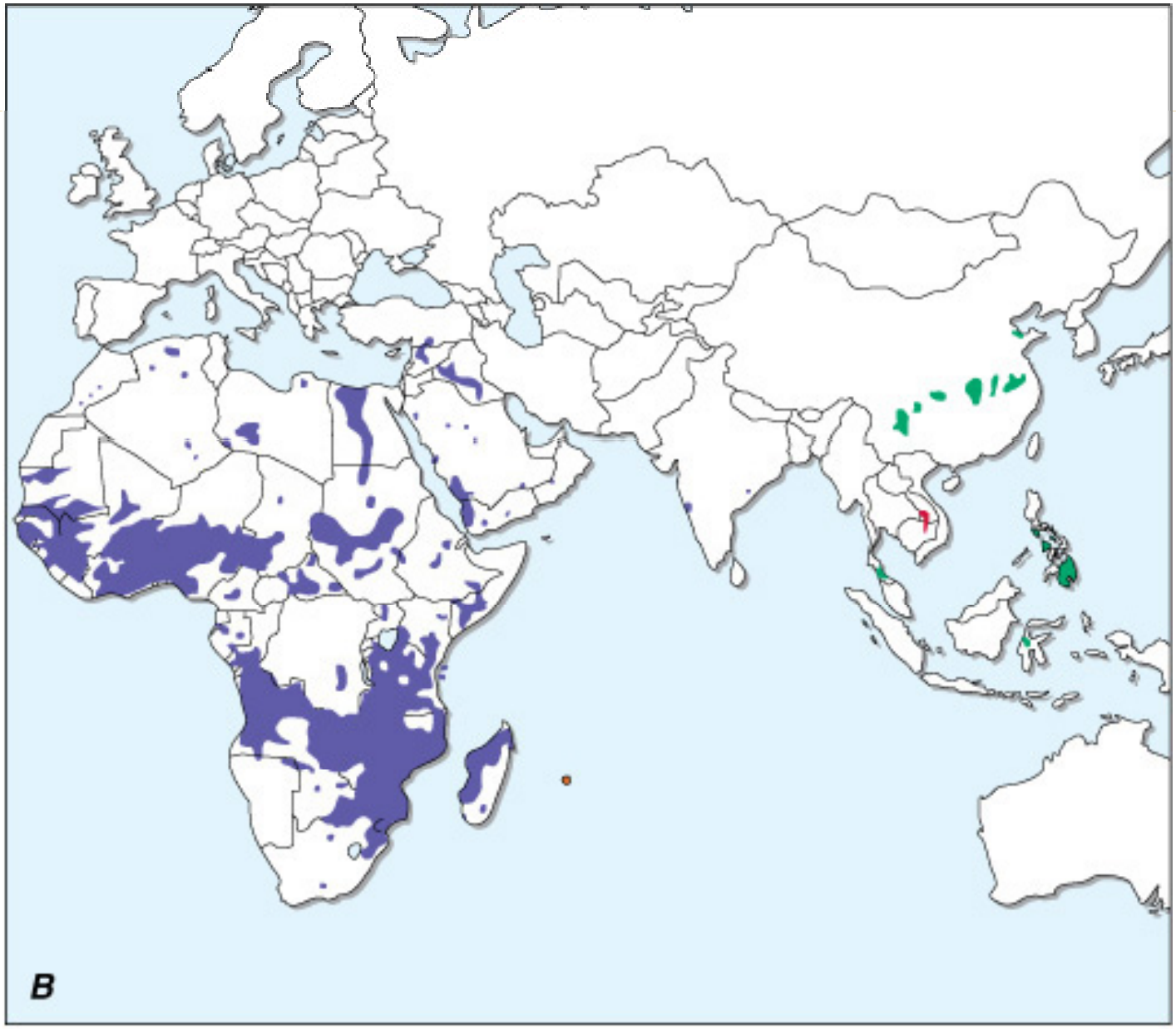

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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Clinical Presentations

Military Significant

- Cercarial dermatitis
- Acute Schistosomiasis
- Hematuria
- Neuroschistosomiasis

ADAM.

Fig. 5: cercarial dermatitis.

Source: José Roberto Lambertucci (2010) Acute schistosomiasis mansoni: revisited and reconsidered. *Mem Inst Oswaldo Cruz,* **105**(4):422-435.

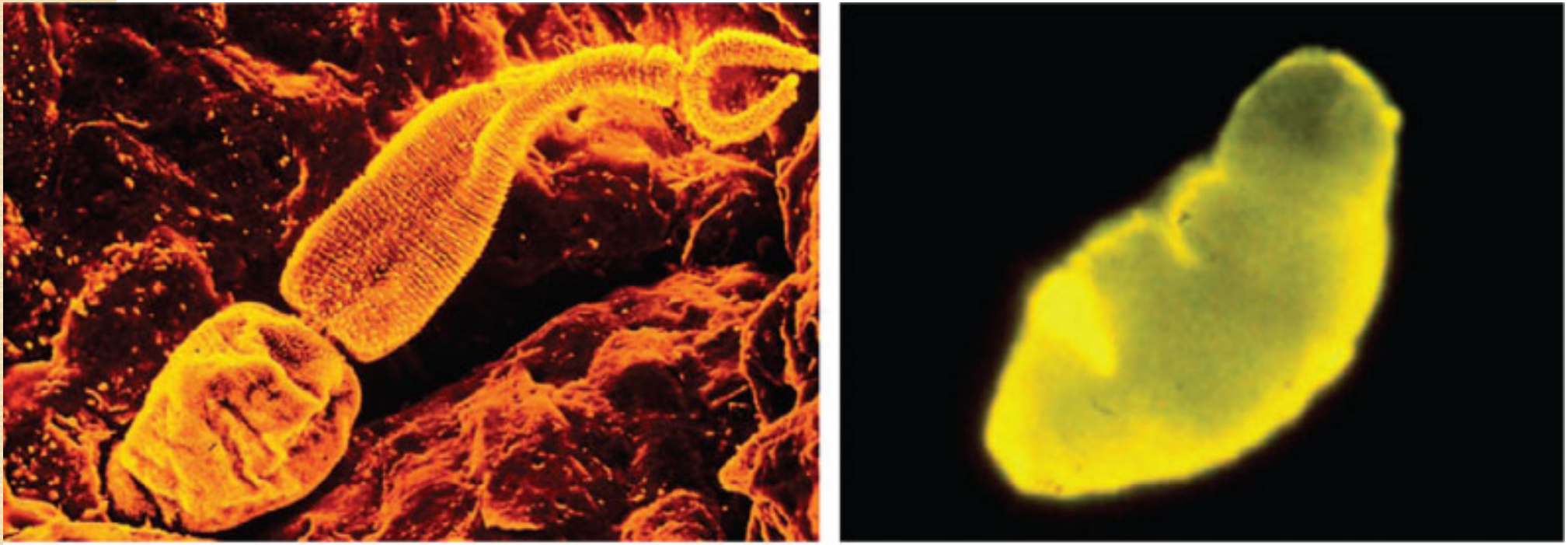


Fig. 2: cercaria of *Schistosoma mansoni* penetrating the skin on the left and shistosomulum after penetration on the right.

Source: José Roberto Lambertucci (2010) Acute schistosomiasis mansoni: revisited and reconsidered. *Mem Inst Oswaldo Cruz,* **105**(4):422-435.

Summary of reports of outbreaks of acute schistosomiasis (involving at least ten patients) among travellers

Year	1995	1995	1996	1996	1998	1998
Exposed persons	29	13	12	16	10	29
Attack rate (%)	96	62	92	100	100	69
Country of infection	Mali	Mali	Burkina Faso	Malawi Mozambique	Ghana	Burkina Faso
Culprit species	*Sh, Sm, Si*	*Sm*	*Sm*	*Sh*	*Sm*	*Sm*
History of CD (%)	36	62.5	NA	13	20	5
Incubation period	2-10 weeks	NA	3-6 weeks	36 days	2-5 weeks	27 days
Acute schistosomiasis (%)	54	54	54	100	80	70

Summary of reports of outbreaks of acute schistosomiasis (involving at least ten patients) among travellers continued

Year	2001	2001	2002	2003	2003	2008
Exposed persons	13	13	31	18	18	27
Attack rate (%)	92	100	100	94	100	81
Country of infection	Brazil	Brazil	Brazil	Brazil	Mali	Tanzania
Culprit species	*Sm*	*Sm*	*Sm*	*Sh*	*Sh*	*Sm*
History of CD (%)	100	NA	NA	100	94	13.6
Incubation period	2-4 weeks	20 days	3-4 weeks	32 days	19 days	3-13 weeks
Acute schistosomiasis (%)	91	92	100	100	77	86

Major signs and symptoms observed during acute schistosomiasis according to the culprit species of Schistosoma

Signs and symptoms (%)	Schistosoma mansoni 95 patients	Schistosoma haematobium 34 patients
Fever	54-100	93-94
Abdominal pain	33-93	0
Dry cough	17-91	44-86
Headache	33-87	31-93
Diarrhoea	25-81	14
Liver enlargement	17-75	0-25
Myalgias	50-74	14-69
Neck pain	64	71
Urticaria	8-17	13-57

Fig. 7: a 17-year-old boy with acute schistosomiasis. Palpable tender liver.

Source: José Roberto Lambertucci (2010) Acute schistosomiasis mansoni: revisited and reconsidered. *Mem Inst Oswaldo Cruz,* **105**(4):422-435.

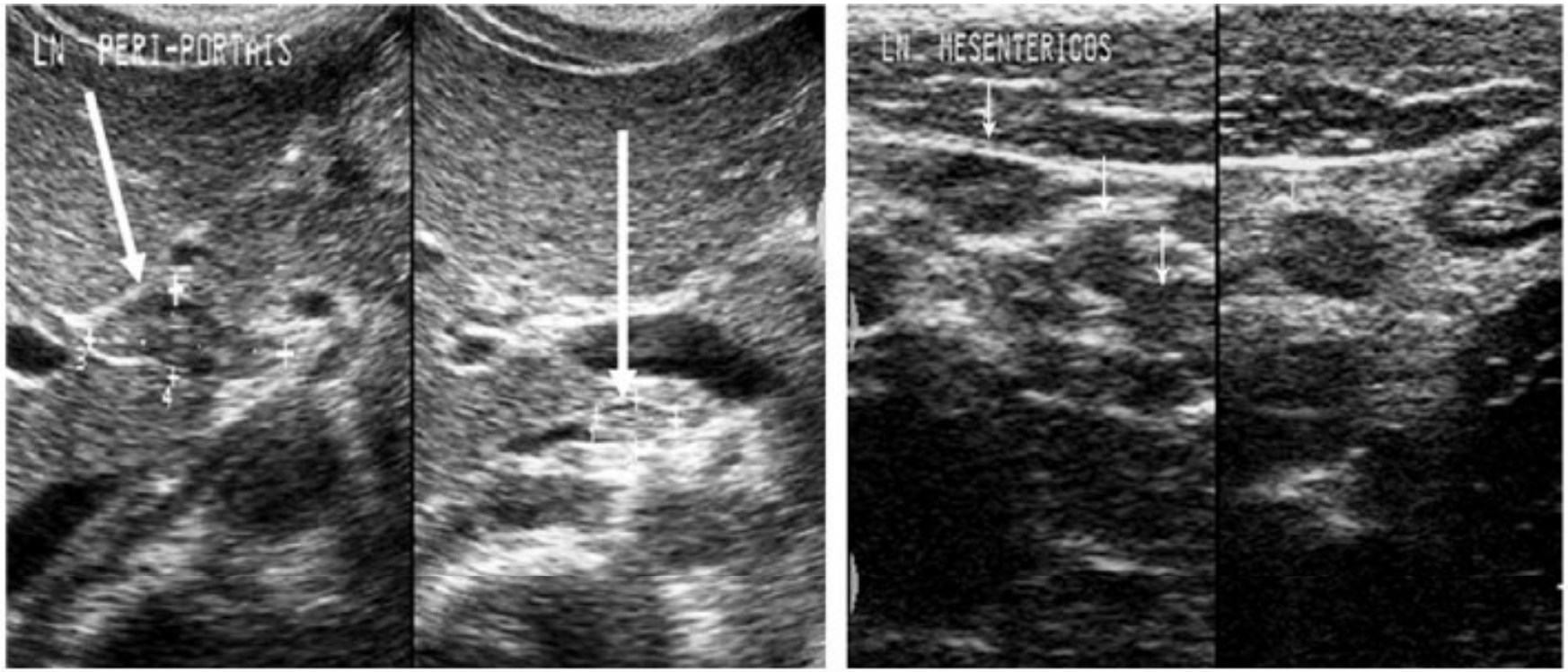


Fig. 9: ultrasound in acute schistosomiasis mansoni: periportal lymph nodes on the left and mesenteric on the right (white arrows).

Source: José Roberto Lambertucci (2010) Acute schistosomiasis mansoni: revisited and reconsidered. *Mem Inst Oswaldo Cruz,* **105**(4):422-435.

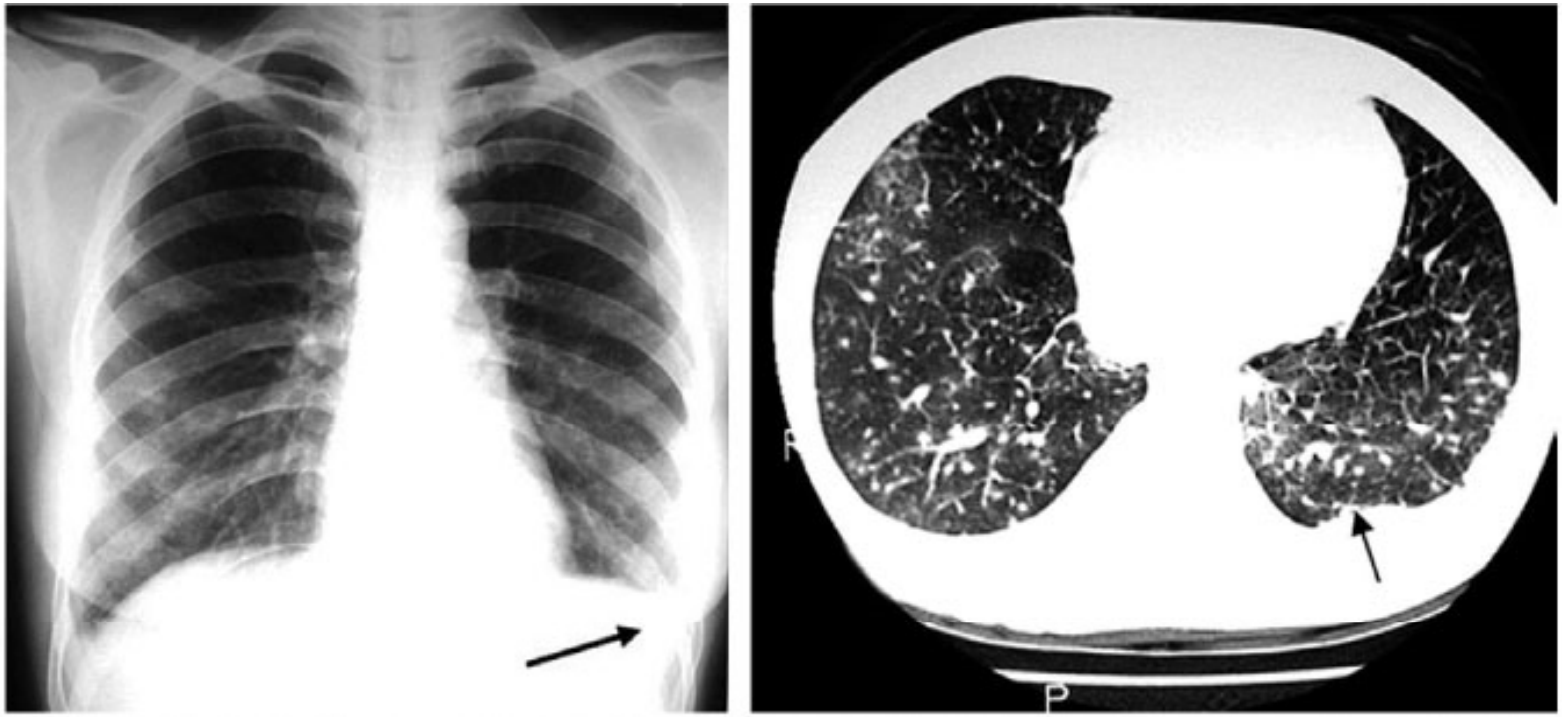


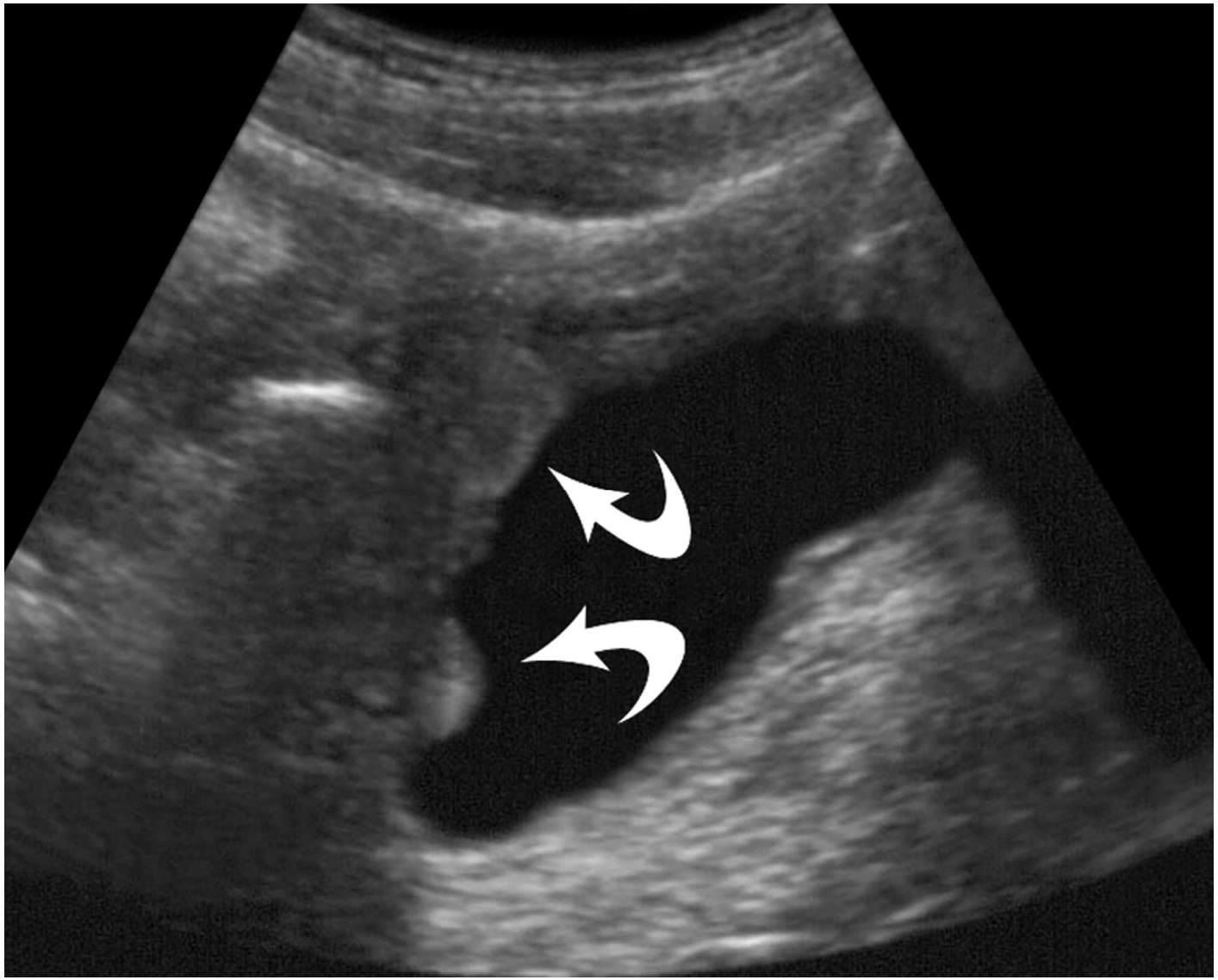
Fig. 11: a 26-year-old female patient with pleural effusion (arrow) on the left and micronodules on the right lung. A computerised tomography scan of the chest on the right with micro nodules and pleural effusion (arrow).

Source: José Roberto Lambertucci (2010) Acute schistosomiasis mansoni: revisited and reconsidered. *Mem Inst Oswaldo Cruz,* **105**(4):422-435.

Frequency of bladder symptoms associated with *S. haematobium* infection

Symptom	Prevalence with light infection (<100 eggs/10 mL urine)		Prevalence with heavy infection (>100 eggs10 mL urine)
Dysuria	55%		55-70%
Hematuria	60%		80-95%
Frequency		56%	
Urinary colic		37%	
Urinary incontinence		20%	
Urinary retention		13%	

Figure 22. Schistosomiasis.



Wong-You–Cheong J J et al. Radiographics 2006;26:1847-1868

RadioGraphics

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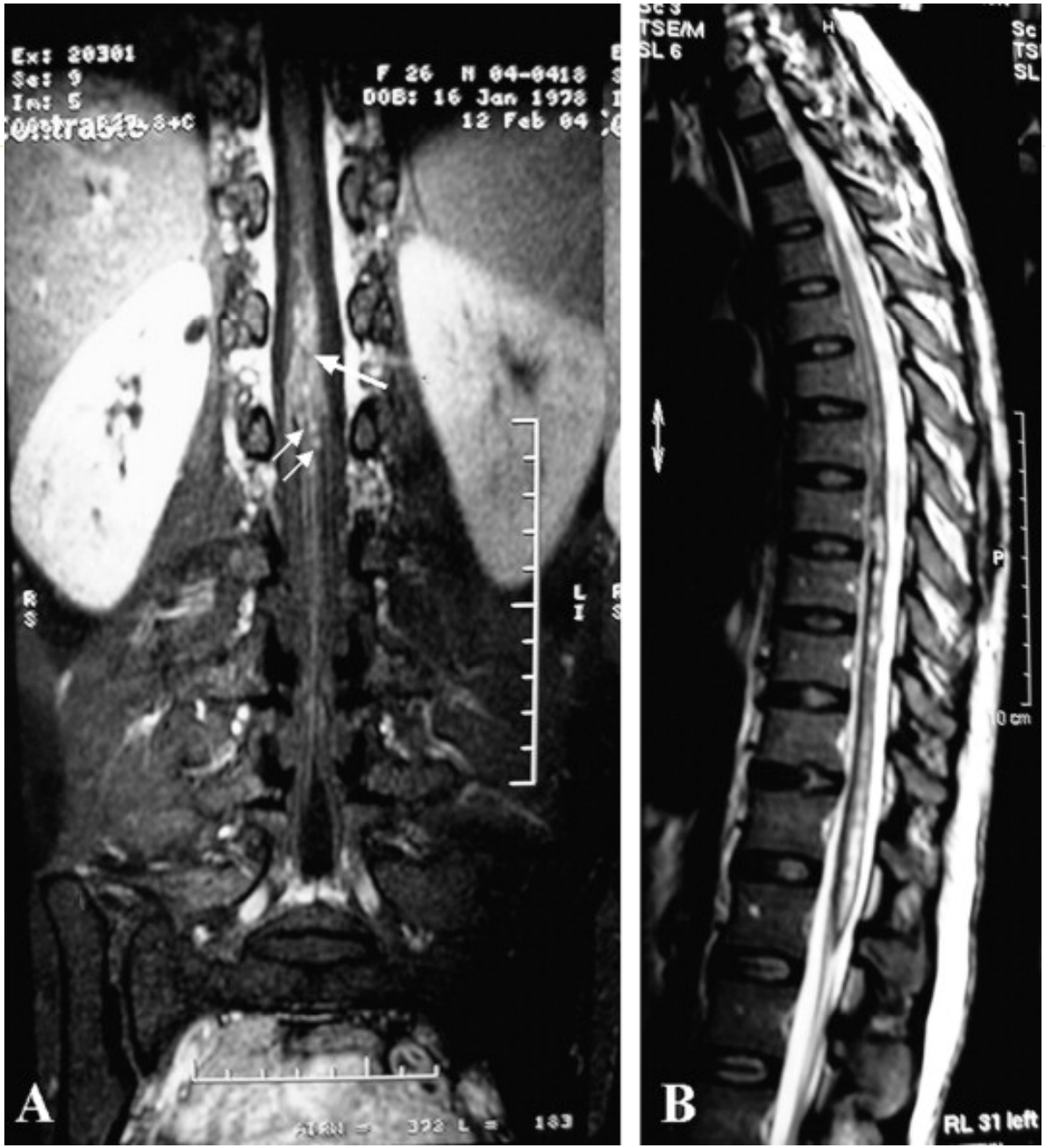
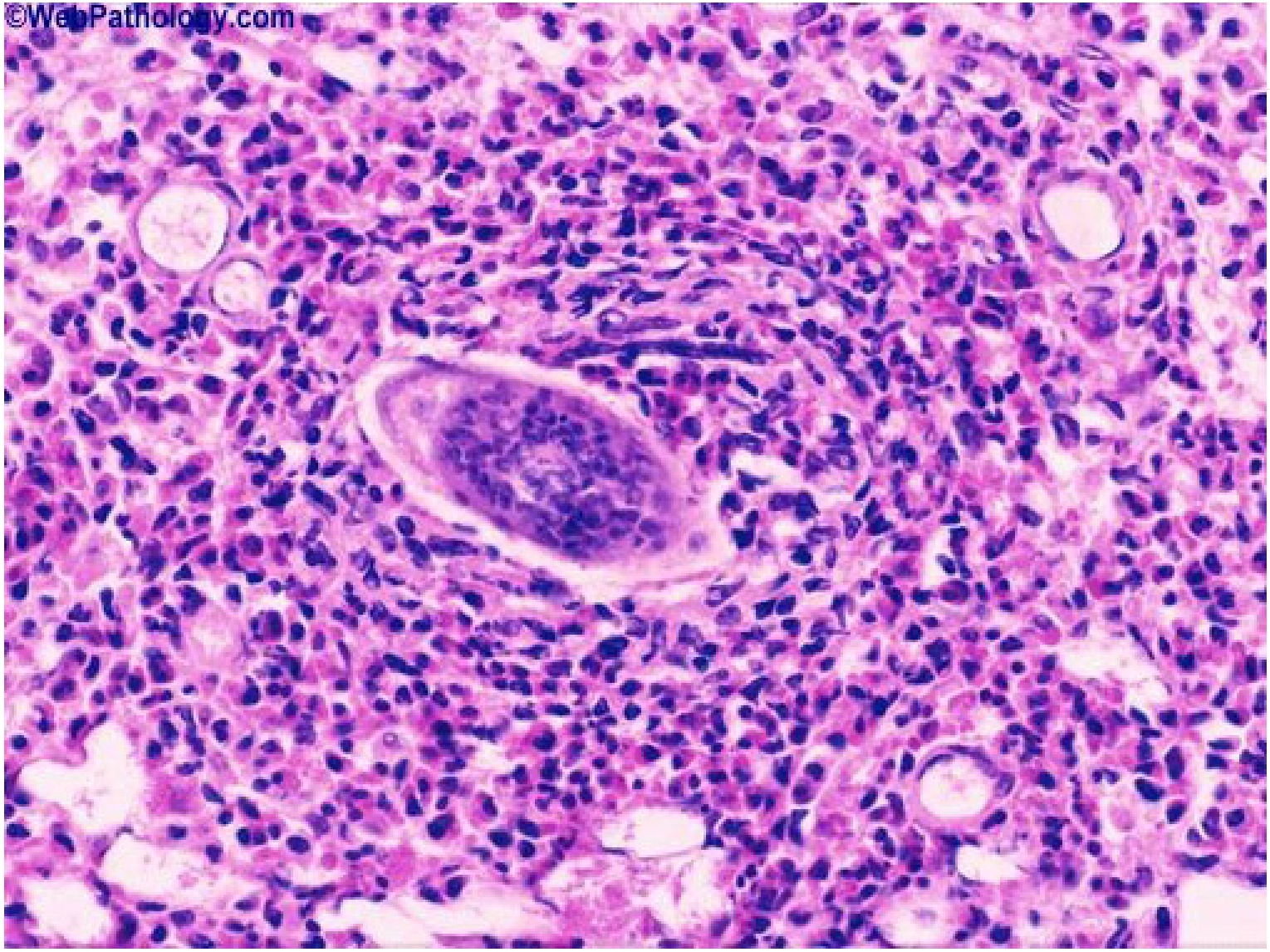


Source: Ferrari, T.C. *et al* (2008) Clinical characterization of neuroschistosomiasis due to Schistosoma mansoni and its treatment. *Acta Tropica* **108:**89-97.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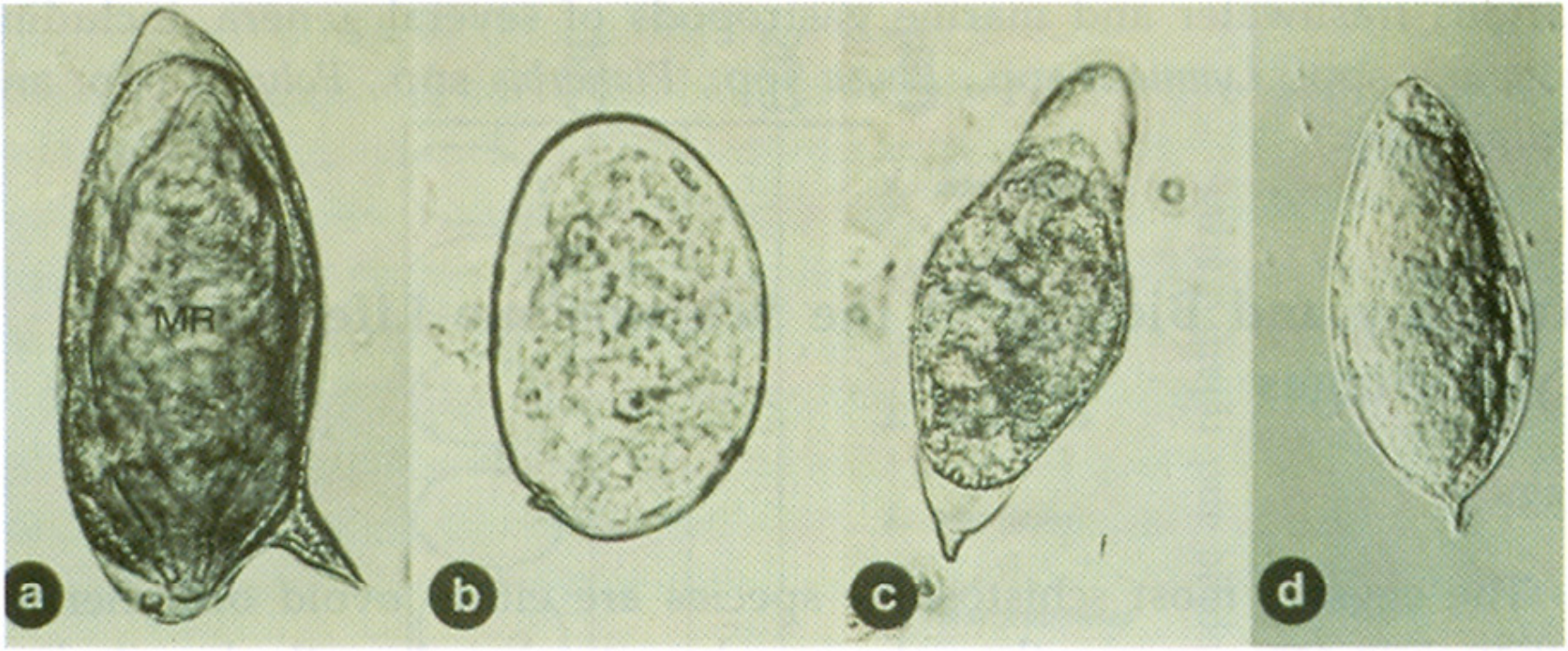

Figure 3. Human schistosome eggs: (a) *S. mansoni*, (b) *S. japonicum*, (c) *S. intercalatum* and (d) *S. haematobium*. Parasites in human feces. (*Courtesy H. Melhorn.*)

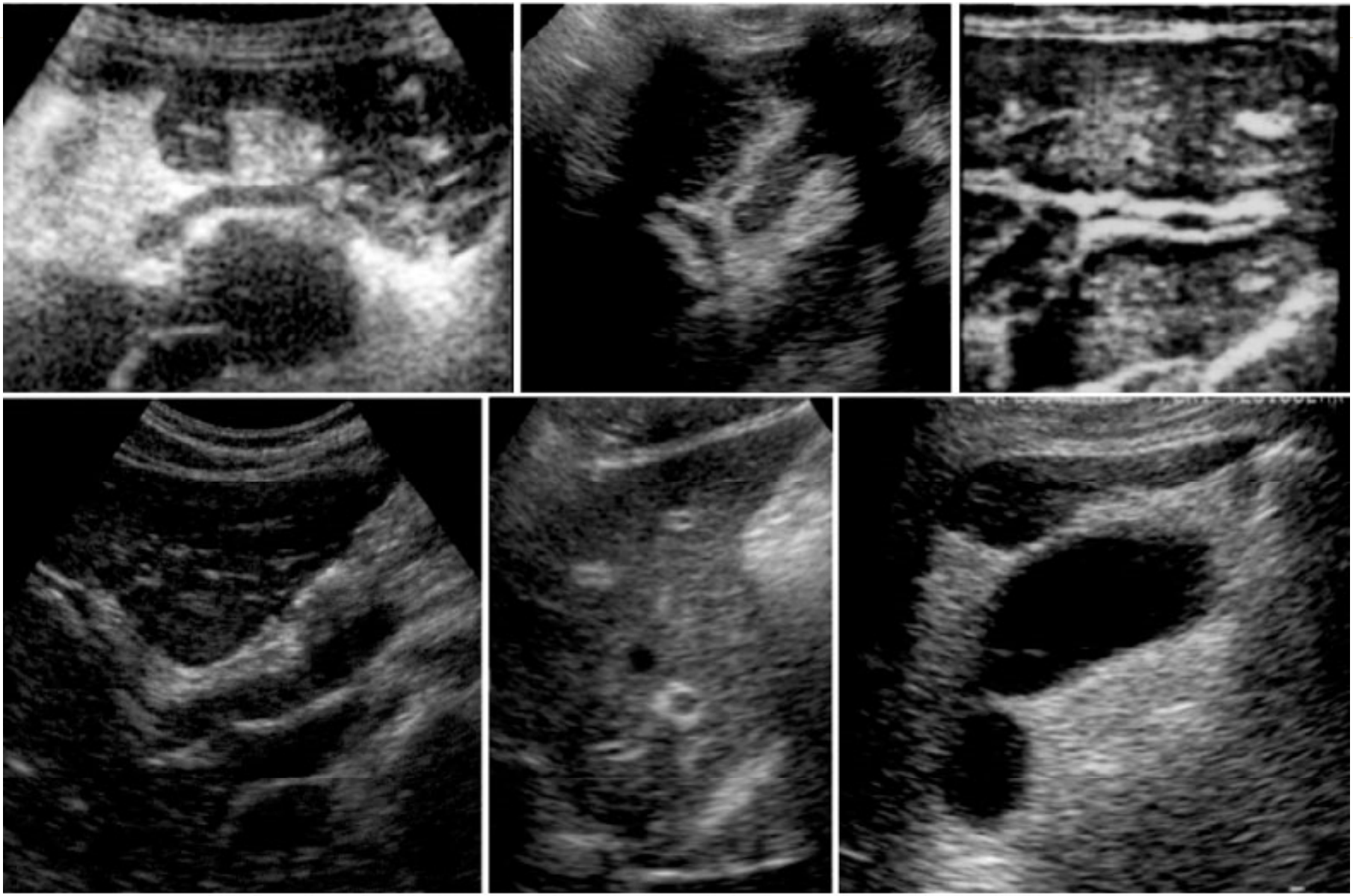

Fig. 1: periportal and gallbladder echogenic thickening in hepatosplenic schistosomiasis mansoni.

Source: Pinto-Salva, R.A. *et al.* (2010) Ultrasound in schistosomiasis mansoni. *Mem Inst Oswaldo Cruz* **105**(4):479-484.

Ultrasound findings in Symmers' fibrosis

Periportal thickening
Echogenic thickening of the gallbladder wall
Liver right lobe reduction
Liver left lobe reduction
Splenomegaly
Portal tract vessels dilation
Hepatofugal collateral circulation
Portal thrombosis (5-10% of cases)

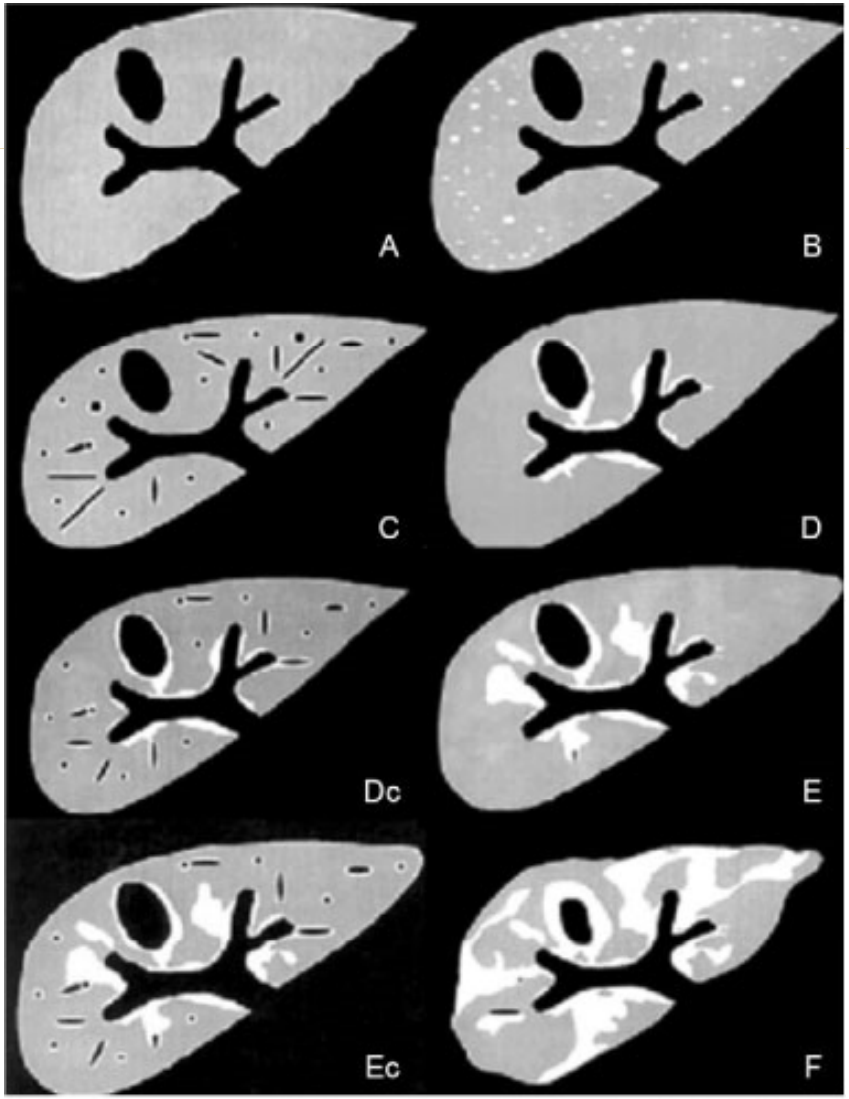

Fig. 3: sonographic standardization of the liver in schistosomiasis mansoni. A: normal; B: starry sky (peripheral fibrosis); C: rings and pipe-stems (initial fibrosis of segmentary branches); D: "ruff" around portal bifurcation, also known as central fibrosis; Dc: mixed form; E: patches, fibrosis around primary and segmentary portal branches; Ec: mixed form; F: bird claws, corresponding to marked central and peripheral fibrosis.

Source: Pinto-Salva, R.A. *et al.* (2010) Ultrasound in schistosomiasis mansoni. *Mem Inst Oswaldo Cruz* **105**(4):479-484.

Drug therapy for human trematode infections

Infection	Drug of choice	Adult dose and duration
Blood Flukes		
S. Mansoni	Praziquantel	20 mg/kg, 2 doses in 1 day
S. intercalatum		
S. haematobium		
S. Japonicum	Praziquantel	20 mg/kg, 3 doses in 1 day
S. mekongi		

Schistosomiasis

Prevention and Control

Individuals

- No contact with fresh water bodies
- How to handle water splashes
- Diagnosis and chemotherapy

Population

- Avoiding fresh water bodies
- Chemotherapy
- Mulluscicides
- Environmental conditions
- Vaccine?