

## Acute schistosomiasis mansoni: revisited and reconsidered

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*Acute schistosomiasis is a systemic hypersensitivity reaction against the migrating schistosomula and eggs. A variety of clinical manifestations appear during the migration of schistosomes in humans: cercarial dermatitis, fever, pneumonia, diarrhoea, hepatomegaly, splenomegaly, skin lesions, liver abscesses, brain tumours and myelodysplasia. Hypereosinophilia is common and aids diagnosis. The disease has been overlooked, misdiagnosed, underestimated and underreported in endemic areas, but risk groups are well known, including military recruits, some religious congregations, rural tourists and people practicing recreational water sports. Serology may help in diagnosis, but the finding of necrotic-exudative granulomata in a liver biopsy specimen is pathognomonic. Differentials include malaria, tuberculosis, typhoid fever, kala-azar, prolonged Salmonella bacteraemia, lymphoma, toxocariasis, liver abscesses and fever of undetermined origin. For symptomatic hospitalised patients, treatment with steroids and schistosomicides is recommended. Treatment is curative in those timely diagnosed.*

Key words: acute schistosomiasis - cercarial dermatitis - FUO - dermatitis - neuroschistosomiasis - pyogenic liver abscesses

Schistosomiasis is endemic in 76 countries and territories (Amaral et al. 2006). Approximately 200 million people are infected and another 600 million are at risk of infection (Chitsulo et al. 2000). In Brazil, the disease ranks higher in prevalence than HIV/AIDS. Brazil, with 25 million people living in endemic areas and 4-6 million infected, is the most affected country in the Americas.

Acute schistosomiasis is not rare in Brazil. Nevertheless, unsupported statements about it pop up in scientific meetings and medical journals: (i) it is uncommon to see patients with acute schistosomiasis in endemic areas. In fact, most people living in big cities of Brazil have never had contact with contaminated waters and if they do, may end up developing acute schistosomiasis; (ii) acute schistosomiasis is a rare event in the course of schistosomiasis. We are aware of several high-risk groups for predictable epidemics of acute schistosomiasis, including soldiers during military manoeuvres, religious organisations that baptise their followers in stream waters, fishermen, canoers and rural tourists (Fig. 1); (iii) the behaviour of schistosomiasis has changed after implementation of mass chemotherapy in Brazil associated with the migration of people from rural areas to the outskirts of large cities. It is most probable that acute cases have been overlooked, misdiagnosed, underestimated and underreported over time (Table I); (iv) there is no good surrogate marker for acute schistosomiasis. In liver tissue obtained by needle biopsy, it is easy to identify the characteristic necrotic-exudative granulomas

of acute schistosomiasis. In Brazil and Africa, where differential diagnoses should include malaria, tuberculosis, typhoid fever, kala-azar, lymphoma, liver abscesses and fever of undetermined origin (FUO), it is worthwhile to consider doing a liver biopsy to be sure of the diagnosis.

*Schistosome life cycle* - Schistosomiasis is caused by flatworms. Adults of *Schistosoma mansoni*, which measure 1-2 cm in length and 0.3-0.6 mm in width, live, mate and feed on blood in the portal and mesenteric vessels. The male worm clasps the female in a gynaecophoric canal so that the pair assumes a nematoid, worm-like shape ideally suited to life in the minor vessels of the portal blood system of the definitive, vertebrate host.

The eggs, measuring 145 x 55 µm, are deposited in the venules, make their way into the faeces and hatch in fresh water, where the miracidium emerges. The miracidium penetrates the body of a snail (*Biomphalaria*) and multiplies asexually. Within 4-6 weeks, hundreds of motile, forked-tail cercariae 0.1-0.2 mm in length burst out. Upon encountering human skin, the cercariae penetrate and change into schistosomula. The newly transformed schistosomulum (Fig. 2) enters a nearby vein and is carried passively in the blood flow to the right heart and on to the pulmonary capillaries (Fig. 3). To develop further, the worms must next reach the liver via the splanchnic vasculature.

When the worms reach sexual maturity, pairing takes place. The muscular male folds around and embraces the female, then transports her against the blood flow in the hepatic portal vein to its branches around the intestine.

Both sexes have a weak oral sucker perforated by the mouth and a more muscular ventral sucker, which is especially well developed in the male (Fig. 4). Egg laying can begin within 25-30 days and the first eggs are detectable from day 35 onwards. Each female worm

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TABLE I  
Selected outbreaks of acute schistosomiasis mansoni reported in Brazil from 1939-2003

Reference	Municipality (state)	Locality	Cases (n)	Activity
Martins & Versiani (1939)	Belo Horizonte (MG)	Pampulha's lake	104	Recreation
Marques (1957)	Olinda (PE)	Streams	3	Recreation
Ferreira et al. (1960)	Juiz de Fora (MG)	Swimming pool	12	Recreation
Neves et al. (1965)	Belo Horizonte (MG)	Hospital <sup>a</sup>	50	-
Ferreira et al. (1966)	Belo Horizonte (MG)	Different places	25	Recreation
Leocádio (1969)	Salvador (BA)	Streams	6	Recreation
Coura et al. (1970)	Rio de Janeiro (RJ)	Furnas de Tijuca	22	Recreation
Neves et al. (1970)	Rio de Janeiro (RJ)	Jacarepaguá	2	Recreation
Castro et al. (1971)	Belo Horizonte (MG)	Outskirts of city	13	Recreation
Lambertucci et al. (1980)	Belo Horizonte (MG)	Outskirts of city	11	Recreation
Gonçalves et al. (1992)	Itamaracá (PE)	Island	4	Flood
Rocha et al. (1995a)	Belo Horizonte (MG)	Ribeirão das Neves	34	Military <sup>b</sup>
Rabello (1995)	Belo Horizonte (MG)	Streams	18	Recreation
Silva et al. (2000)	Estância (SE)	Lagoa do Abais	31	Recreation
Barata et al. (1999)	Belo Horizonte (MG)	Outskirts of city	26	Recreation
Barbosa et al. (2001)	Orange Beach (PE)	Flood	13	Flood
Enk et al. (2003)	Ibirité (MG)	Swimming pool	17	Recreation

a: admitted to hospital from different places for investigation of fever of undetermined origin; b: military maneuvers; BA: Bahia; MG: Minas Gerais; PE: Pernambuco; RJ: Rio de Janeiro; SE: Sergipe.

TABLE II

Migration of the worm in humans and parallel morbidity
The stage of invasion (cercarial dermatitis)
Migration through the lungs (pneumonia)
Egg-laying (acme of acute schistosomiasis)
Pulmonary involvement (nodules, pleural effusion)
Intestinal involvement (diarrhoea)
Skin involvement (papules, nodules, plaques)
Pyogenic liver abscess (staphylococci sepsis)
Neuroschistosomiasis (brain and spinal cord involvement)
Acute over chronic schistosomiasis (re-infection)



Fig. 1: rural tourism.

produces approximately 300 eggs per day. *S. mansoni* adults are normally found in the tributaries of the inferior mesenteric veins around the lower bowel, whence eggs are usually voided in the faeces.

*Cercarial dermatitis* - During penetration of cercariae, some previously exposed and unexposed persons experience a prickling sensation and may note a macular rash several hours later. The rash may persist up to 15 days, or even longer if scratching results in secondary infection (Table II). **The rash consists of discrete erythematous raised lesions that vary in size from 1-3 cm (Fig. 5).** Dermatitis is also frequently seen with avian trematode cercariae (Appleton 1984).

In immune mice (already challenged by a previous infection), it has been shown that the eosinophil-enriched accelerated dermal inflammatory response to schistosomula is best regarded as antibody-mediated and that killing of the parasites in the immune host requires contact between leukocytes and schistosomula, with eosinophils probably playing a crucial role (von Lichtenberg et al. 1977).

Cercarial dermatitis is a seasonal phenomenon. It is most prevalent during the warmer months, when the greatest numbers of people have contact with water and the rate of production of cercariae within the intermediate host is also at a peak.



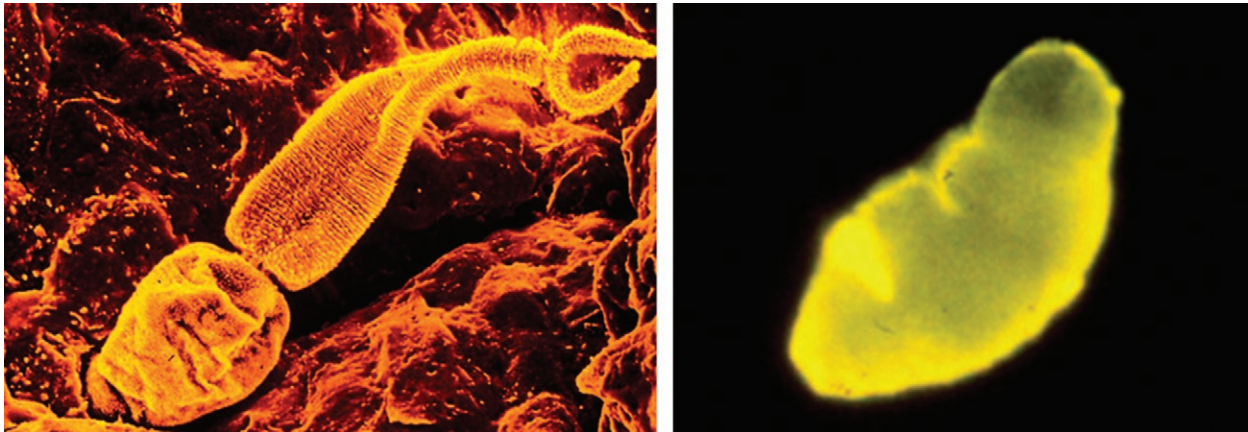


Fig. 2: cercaria of *Schistosoma mansoni* penetrating the skin on the left and schistosomulum after penetration on the right.

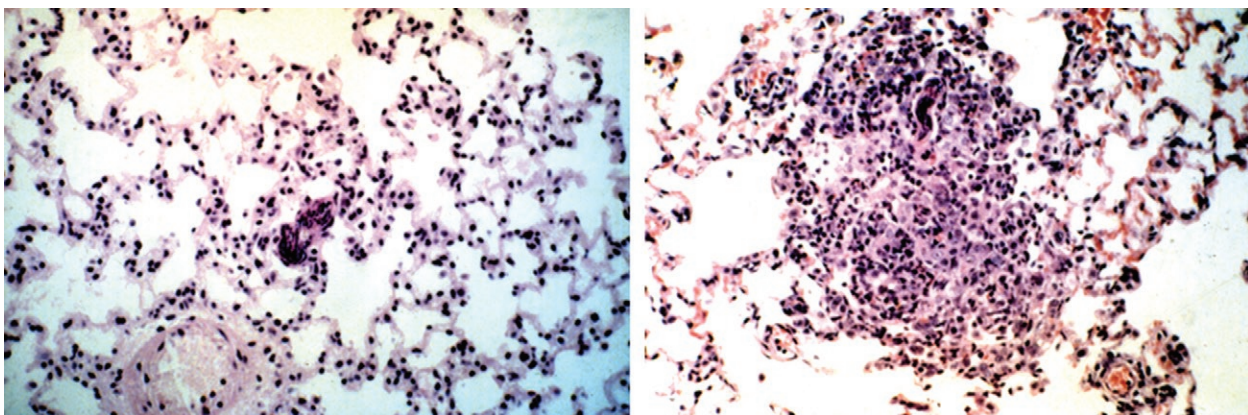


Fig. 3: on the left there is an unnoticed schistosomulum crossing a capillary of the lung of a mouse. On the right, a strong inflammatory reaction is seen around a dead schistosomulum.

Diagnosis of cercarial dermatitis in humans is difficult. Patients do not seek out medical assistance because they consider the problem to be of minor importance. Differentials include a reaction to insect bites, contact dermatitis, poison ivy, scabies and impetigo (Lambertucci 1993a).

#### Acute schistosomiasis mansoni

Acute schistosomiasis is a systemic hypersensitivity reaction against the migrating schistosomula and eggs and it can occur within 16-90 days after a primary infection (Lambertucci et al. 1987). A pre-egg-laying phase has been described in which the symptoms and signs of acute schistosomiasis are present, together with a non-specific hepatitis (Bogliolo & Neves 1965, Raso & Neves 1965, Lambertucci 1993b).

*Pathological and immunological aspects* - In the cases of acute schistosomiasis in humans in which pathological examination has been performed, the severity of the inflammatory reaction around mature eggs in tissues has been emphasised (Bogliolo 1964). The periovarian granulomas are large, with predominant ne-

crotic-exudative features and they appear as translucent granules disseminated on the serosal surface of the liver and intestines. Other organs, such as the lungs, intra-abdominal lymph nodes, brain, skin and pancreas, are also affected. All granulomas are uniformly at the same phase of formation and this is pathognomonic of acute schistosomiasis. Microscopically, they disclose central necrosis and dense eosinophilic infiltration as predominant characteristics (Fig. 6).

In *S. mansoni*-infected mice, the granuloma size, which may reach 100 times the volume of the egg, decreases with increasing duration of infection. With reduction in granuloma volume comes some relief of the vascular obstruction, resulting in reduced organ size and pathology. Only in the immune modulated state, as in chronic schistosomiasis, when the granulomas are smaller but still protective, do the host's immune response and the disease state maintain an acceptable balance. Some patients never effectively achieve this modulation, leaving them to respond vigorously throughout their infection. This may lead to immunopathogenic reactions that affect fibroblast reactivity and ultimately result in severe hepatic fibrosis (Neves & Raso 1965).

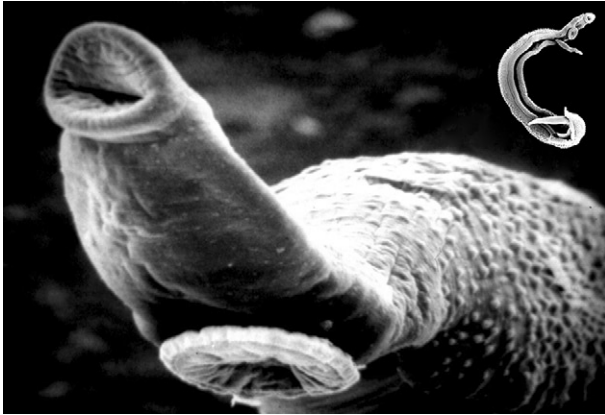


Fig. 4: adult *Schistosoma mansoni* male with two suckers. See also a couple in the insert.



Fig. 5: cercarial dermatitis.

Schistosomal infection, like other parasitic helminth infections, is associated with a strong CD4<sup>+</sup> T-helper (Th2) response. However, in the early stages (the 1st 3-5 weeks), the immunological reaction involves mainly Th1 cells, when proinflammatory cytokines like IL-2, gamma-interferon and TNF-alpha can be measured in the plasma. The Th2 response follows egg laying and causes the production of a series of cytokines, such as IL-4, IL-5, IL-10 and IL-13. The Th2 cells suppress the Th1 proinflammatory response and produce protective eosinophil-rich granulomatous lesions around newly deposited eggs, but they allow the development of fibrosis. The inability to develop a Th2 response to regulate the initial proinflammatory response can be fatal. IL-13 is known to induce not only airway hyper-responsiveness but also endothelial vascular cell adhesion molecule-1 expression, thus playing a role in asthma, acute lung injury and fibrosis (Chiaramonte et al. 1999).

Immune complexes, usually cleared by reticuloendothelial cells, are probably responsible for some manifestations of the acute phase, such as cerebral and cutaneous vasculitis (Lambertucci et al. 1997, Jauréguiberry et al. 2007), and pericardial and pleural effusions (Taliberti et al. 1978, Lawley et al. 1979, Rezende et al. 1997).

*Clinical aspects* - The acute phase is usually asymptomatic, but clinical signs of varying intensity may occur (Fig. 7). This stage is most marked in primary infections in non-immune individuals.

The most common manifestations are fever, chills, weakness, weight loss, headache, anorexia, nausea, vomiting, diarrhoea, dry cough, hepatomegaly, splenomegaly and skin lesions (Table III). A smaller proportion of patients also have bloody diarrhoea, urticaria, periorbital oedema and wheezing. Symptoms last for a few weeks to 2-3 months and gradually abate without therapeutic intervention.

Leukocytosis with 10-75% eosinophils is common and aids diagnosis. Immunoglobulins are elevated in the serum, especially IgE, IgG and IgM. Serum alkaline phosphatase may be increased. The absence of *S.*

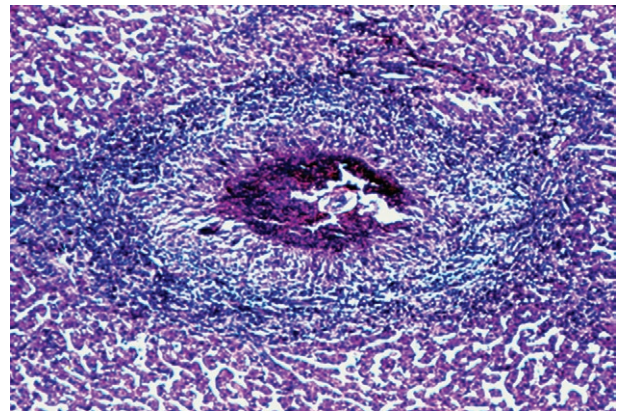


Fig. 6: a large necrotic-exudative granuloma in the liver of a patient with acute schistosomiasis mansoni. Note the isolated central egg surrounded by extensive necrosis.

*mansoni* eggs in the faeces does not rule out the diagnosis. There is usually a miliary distribution of eggs in the organs of the host and laparoscopy frequently reveals whitish nodules (granulomas) on the surface of liver (Fig. 8), intestines and visceral peritoneum.

The finding of necrotic-exudative granulomas in the liver is diagnostic (Table IV). Patients with less well-defined clinical pictures, moderate eosinophilia and/or negative stool examination for parasite ova may pass unnoticed (Rocha et al. 1993).

Reports on abdominal ultrasound results in patients with acute schistosomiasis are still scarce. In a report on 26 patients with acute schistosomiasis, ultrasound showed a non-specific homogeneous size increase of the liver and spleen in all acute patients and easily identified intraabdominal lymph nodes in the periportal region in most cases (Fig. 9). Twenty-four months after successful treatment there was involution of the liver and spleen and lymph nodes, although reduced in size, were still easily recognised (Lambertucci et al. 1994, Barata et al. 1999).



TABLE III

Clinical manifestations in 50 symptomatic in-hospital patients with acute schistosomiasis mansoni described in Belo Horizonte, Minas Gerais, Brazil (Neves et al. 1965)

Clinical manifestations	%
Fever	100
Anorexia	100
Abdominal pain	96
Diarrhoea	90
Coughing	86
Diaphoresis	84
Hepatomegaly	80
Splenomegaly	80
Weight loss	76
Myalgia	72
Headache	56
Prostration	38
Nausea	30
Vomiting	26
Breathlessness	22
Skin involvement	12

### Remarkable clinical presentations of acute schistosomiasis mansoni

In many cases, a particular aspect of the disease dominates the clinical picture.

**Pulmonary involvement** - A 17-year-old boy presented severe cercarial dermatitis after bathing in stream waters of an endemic area in Belo Horizonte (MG), Brazil. Two weeks after admission to hospital, he developed a clinical picture of bronchopneumonia (dyspnoea and mucous sputum), fever, diarrhoea, hepatosplenomegaly and eosinophilia. A chest x-ray showed micronodules and pulmonary condensations, particularly in the right lung (Fig. 10). **Stool examination was repeatedly negative for *S. mansoni* ova**, but it became positive two weeks later. A liver biopsy revealed a non-specific hepatitis. A control chest x-ray taken four weeks later was normal (Pedroso et al. 1984). This is a probable case of bronchopneumonia caused by schistosomula.

After egg laying, the importance of lung involvement has been described by many authors in different countries (Sami 1951, Bogliolo 1964, Gelfand 1966, Neves et al. 1965, Rocha et al. 1995a, Cooke et al. 1999, N'Goran 2003). Bogliolo (1964), during autopsy of four patients who died during the acute phase of schistosomiasis, found a miliary distribution of eggs in the lungs of three and one had pleural effusion. In 1995, 115 Brazilian Army recruits had contact with schistosome-infected natural waters on the outskirts of Belo Horizonte, during training military manoeuvres.



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

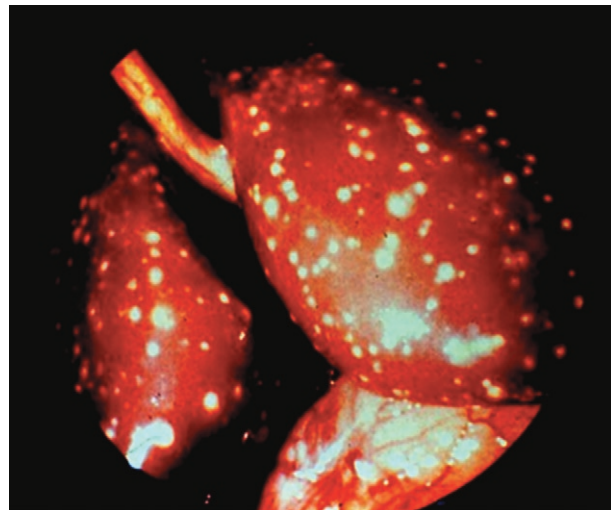


Fig. 8: surface of the liver during laparoscopy in acute schistosomiasis mansoni. A group of eggs appear as whitish areas.

Thirty recruits developed symptoms of acute schistosomiasis and 19 (63.3%) presented respiratory signs or symptoms (cough, wheezing, thoracic pain, dyspnoea and rhinorrhoea). Radiological pulmonary alterations, such as thickening of bronchial wall and beaded micronodulation, were common (Rocha et al. 1995a).

More recently, with routine computerised tomography scans of the lungs, we have been able to describe micro and macronodules in all patients with acute schistosomiasis, even in those without symptoms referred to the lungs. The presence of pleural and pericardial effusion has also been reported (Lambertucci et al. 2007a, Taliberti et al. 1978) (Fig. 11).

*Intestinal involvement* - There are few reports of small bowel involvement in acute schistosomiasis. Castro et al. (1971), using peroral biopsy of the jejunum in 13 patients with acute schistosomiasis, found ova in eight (61%). The authors concluded that, in the acute phase, eggs are laid with great frequency and continuously in the submucosa of the small intestine. Pedrosa et al. (1987) reported the results of a radiological study of the small intestine in 17 untreated patients with acute schistosomiasis; 12 (70%) had jejunal alterations similar to those described for patients with malabsorption syndromes (Fig. 12). The findings described by both sets of researchers are complementary and may explain the diarrhoea reported in the course of acute schistosomiasis. In such patients, the absorption of drugs given orally may be impaired.

Neves et al. (1993) reported two cases of ischaemic necrosis of the sigmoid colon in two brothers aged seven and four years. Laparotomy disclosed, in both children,

extensive necrosis of the descending colon and sigmoid. The histopathological findings were similar: extensive ischaemic necrosis extending to the muscular layer and serosa, in which granulomas in the necrotic-exudative phase were seen. Eggs and granulomas were also found in regional lymph nodes.

*Skin involvement* - Andrade Filho et al. (1998) reported two cases of ectopic cutaneous schistosomiasis, of which one had acute schistosomiasis. They also reviewed the publications of 25 other cases with skin involvement. In 19 of the 25 cases (76%), skin lesions were located on the trunk. Clinical presentation of skin lesions varied (papules, nodules and plaques), but they most frequently had a zosteriform appearance (Fig. 13). In one case, a skin biopsy unveiled the diagnosis of a patient who presented with acute schistosomiasis and neurological symptoms, which preceded the dermatitis (Wood et al. 1976). Approximately 40% of the skin le-

TABLE IV

Clinical and laboratory findings in acute schistosomiasis mansoni
A history of contact with stream waters in endemic areas in the last 60 days
Fever, diarrhoea, hepatosplenomegaly, dry cough, urticaria
Similar clinical picture in other members of the group who bathed together
Eosinophilia
Laparoscopy: nodules on the surface of the liver
Ultrasound (abdomen): hepatosplenomegaly, periportal lymph nodes
Chest x-ray: interstitial pattern with micronodules, pleural effusion, pericardial effusion
CT scan of the lungs: micronodules and macronodules disseminated in both lung fields
Neurological involvement: transverse myelitis or brain tumor
Stool examination or rectal biopsy: eggs of <i>Schistosoma mansoni</i>
Liver biopsy: huge necrotic-exudative granulomas in portal tracts around <i>S. mansoni</i> ova
Immunology: Th1 cytokines during the first migration phase followed by Th2 cytokines after egg-laying
Serology: enzyme-linked immunosorbent assay using keyhole limpet haemocyanin antigen, soluble egg antigen or worm antigen

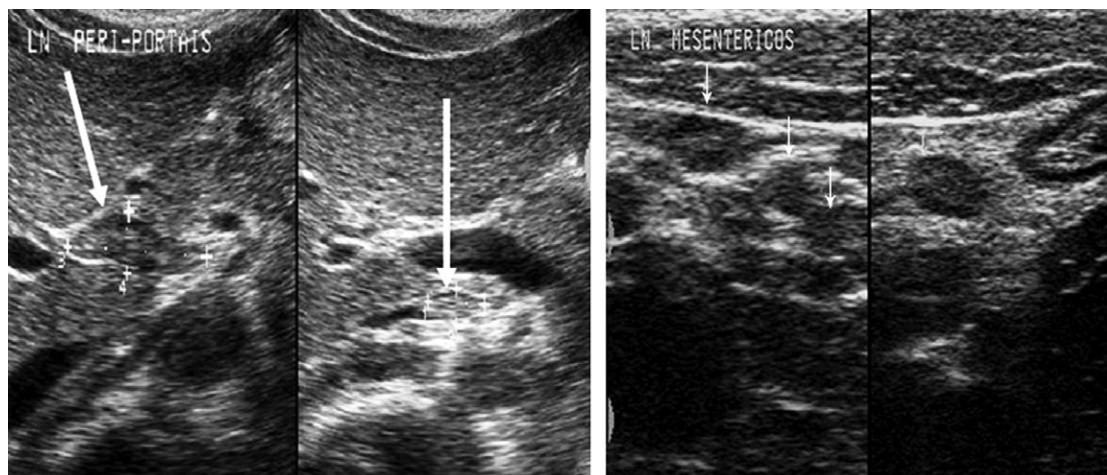


Fig. 9: ultrasound in acute schistosomiasis mansoni: periportal lymph nodes on the left and mesenteric on the right (white arrows).

sions occurred in the acute phase (Faust 1948, Findlay & Whiting 1971, Bittencourt et al. 1979, Guimarães & Souza 1987, Miligan & Burns 1988, Rocha et al. 1995b, Andrade Filho et al. 1998).

Faust (1948) reported several cases of extragenital skin lesions caused by *Schistosoma japonicum* in soldiers who had fought in Asia in World War II. Ramos (1973), working in Mozambique, also found a 4% incidence of extragenital lesions in 100 patients with schistosomiasis.

A patient with several small necrotic lesions on the chest during acute schistosomiasis has been reported (Fig. 14). Skin biopsies did not find ova of *S. mansoni*, but vasculitis was described by a pathologist and was attributed to the deposition of circulating immune complexes. The skin lesions disappeared after treatment with steroids and oxamniquine (Lambertucci et al. 1997).

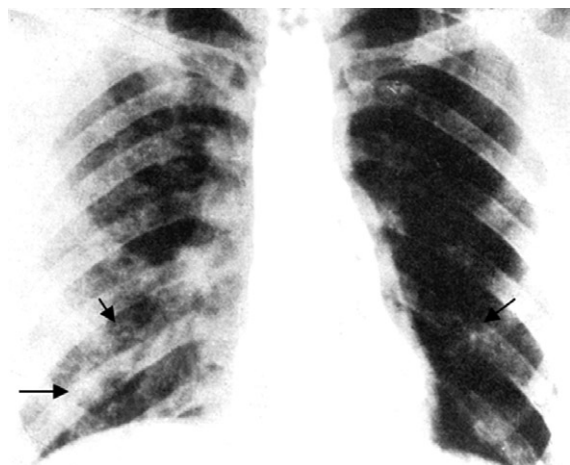


Fig. 10: pulmonary condensations and micronodules probably due to dead schistosomula trapped in the lung. Note the aspect of cotton candy on the right lung (arrow) and micro nodules (short arrows).

In a series of 34 patients with acute schistosomiasis, angioedema and urticaria were described in 16 (47%). The intensity of skin manifestations was mild, with only one case of generalised and lasting urticaria (Rocha et al. 1995a).

*Pyogenic liver abscesses* - Lambertucci et al. (1990) described the cases of two children with skin pustules and acute schistosomiasis who also developed multiple pyogenic liver abscesses caused by *Staphylococcus aureus* (Fig. 15). Liver abscesses were duplicated in a murine model of schistosomiasis when mice were injected with bacteria 60 days after receiving cercariae of *S. mansoni* (Fig. 16). **Other investigators have confirmed and extended our initial findings** (Teixeira et al. 1996, Mahmoud & Awad 2000, Lambertucci et al. 2001, Sánchez-Olmedo et al. 2003, Goldani et al. 2005).

Several mechanisms have been proposed as probable explanations for the association of schistosomiasis with pyogenic abscesses: (i) liver necrosis caused by *S. mansoni* eggs or dead worms may be colonised by bacteria (Ottens & Dickerson 1972) (Fig. 17), (ii) there is transient impairment of cell-mediated immunity in the acute phase of schistosomiasis in animal models and (iii) the literature contains several reports of cases of recurrent infections caused by *S. aureus* in the presence of high serum IgE levels (Buckley et al. 1972, Lambertucci 1996).

To complete the picture, migrating larvae of other parasitic agents have been associated with pyogenic abscesses. Liver abscesses have been described in patients infected with *Toxocara canis* (visceral larva migrans) and intestinal nematodes (Rayes et al. 1999, 2001, Moreira-Silva et al. 2002). Tropical pyomyositis (pyogenic muscle abscesses) caused by *S. aureus* has also been described in association with *T. canis* infection (Rayes et al. 2000). Similar pathogenetic mechanisms may be operating on these cases.

*Neuroschistosomiasis* - As in other organs affected by schistosomal infection, the periovular granulomatous

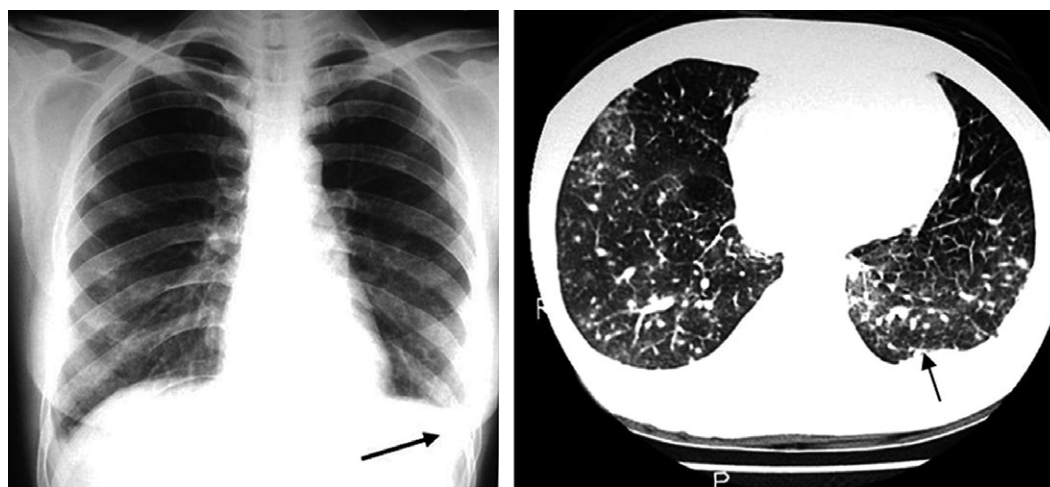


Fig. 11: a 26-year-old female patient with pleural effusion (arrow) on the left and micronodules on the right lung. A computerised tomography scan of the chest on the right with micro nodules and pleural effusion (arrow).



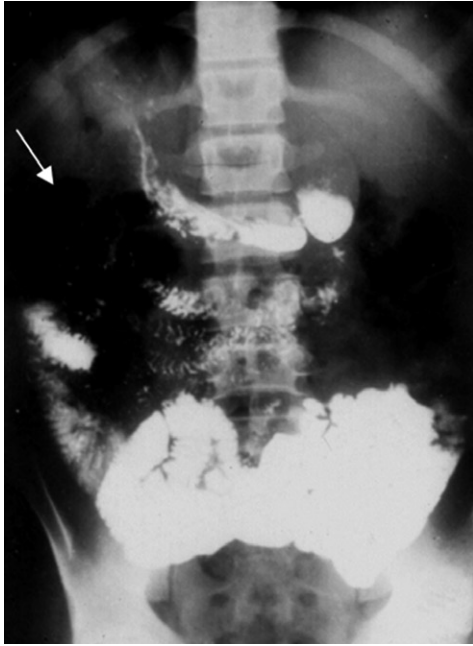


Fig. 12: a contrasted x-ray of the intestine showing a jejunal area without contrast fixation (arrow) in acute schistosomiasis mansoni. A biopsy of this area showed an intense inflammatory reaction around *Schistosoma mansoni* eggs.



Fig. 14: an officer of the Brazilian Army who developed small necrotic lesions on the trunk and abdomen during acute schistosomiasis mansoni. Biopsy revealed vasculitis.



Fig. 13: an adult patient with zosteriform lesion on the trunk. Biopsy of one lesion revealed the presence of *Schistosoma mansoni* eggs.

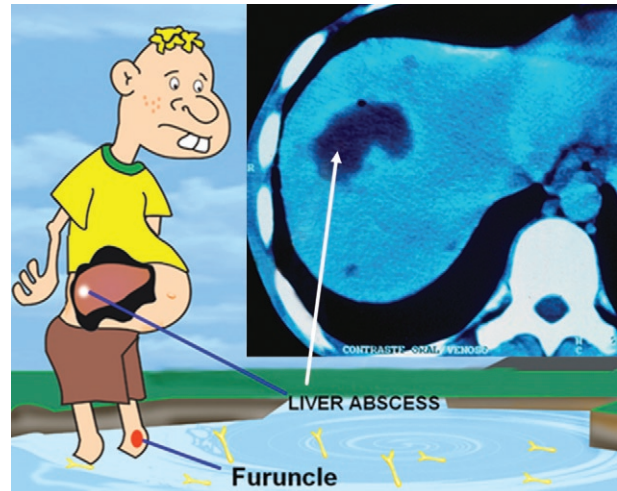


Fig. 15: cercarial dermatitis, pruritus, scratching, furuncle, bacteremia, liver with necrotic-exudative granuloma, abscess formation (computerised tomography scan of a liver abscess in the insert).

reaction in the central nervous system comprises three stages: necrotic-exudative, productive and a stage of healing by fibrosis. These stages represent a modulation of the immune response to parasite antigens as the disease evolves from the acute to the chronic stage (Pitella 1991). Perivascular inflammatory infiltration and vascular lesions (vasculitis) have been reported in patients with neuroschistosomiasis (Jauréguiberry et al. 2007).

Using magnetic resonance (MRI) of the brain, it is possible to demonstrate the presence of a conglomerate

of nodules with well-defined limits (Scrimgeour & Gajdusek 1985, Lambertucci et al. 2008a, b) (Fig. 18).

Neurological symptoms over the course of acute schistosomiasis are frequently accompanied by fever and eosinophilia (Wood et al. 1976, Urban et al. 1996). Patients may become confused, develop focal or generalised seizures or become stuporose. Diagnosis is usually confirmed by surgical brain biopsy because differential diagnosis with brain tumour, based on clinical and imaging aspects, is difficult.



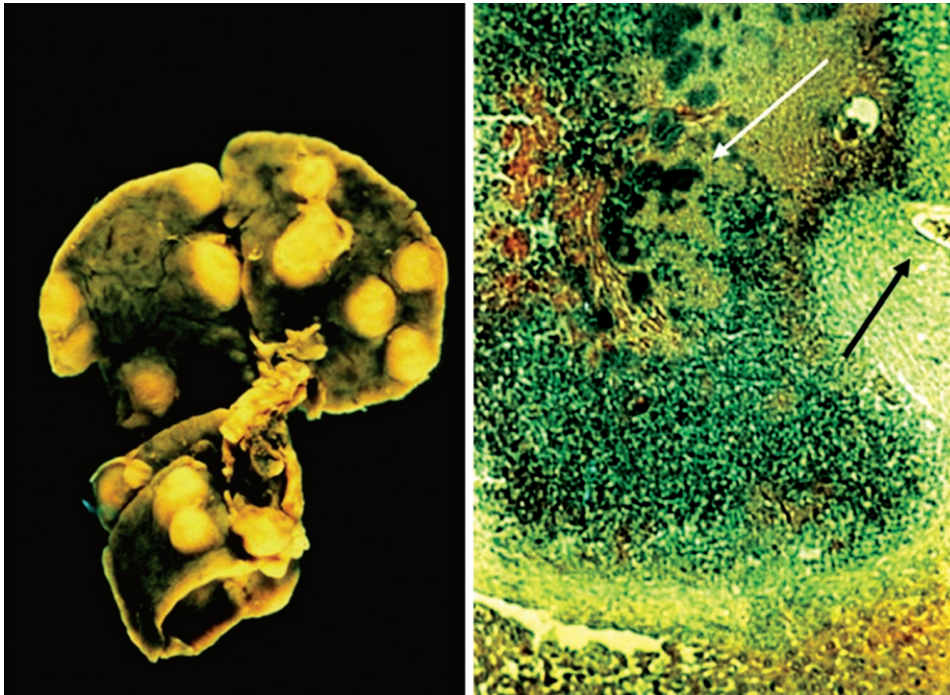


Fig. 16: liver of a mouse with multiple abscesses on the left. On the right, microscopy shows eggs of *Schistosoma mansoni* (black arrow) and colonies of *Staphylococcus aureus* (white arrow).

TABLE V

Treatment of acute schistosomiasis mansoni
Treat for strongyloidiasis (ivermectin 12 mg, single oral dose for adults)
Prednisone (1 mg/kg, body weight, single dose for 7 days, 0.5 mg/kg for 7 days and 0.25 mg/kg for 7 days)
Praziquantel (60 mg/kg, body weight, single oral dose)
Oxamniquine (15 mg/kg, body weight, single oral dose)
Stool examinations 2-3 months later

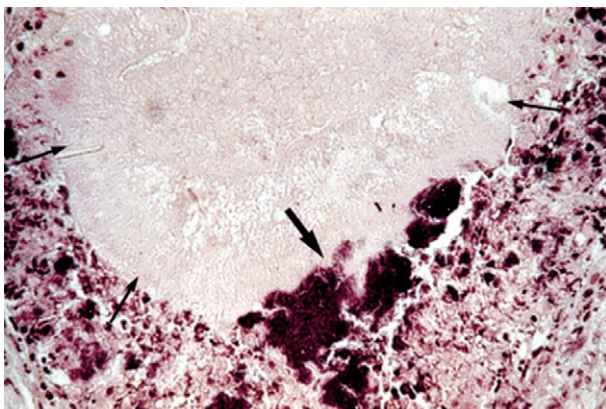


Fig. 17: a dead *Schistosoma mansoni* worm in the liver (thin arrows) of a mouse surrounded by colonies of *Staphylococcus aureus* (thick arrow).

Schistosomal myeloradiculopathy (SMR) is caused by the inflammatory reaction accompanying the deposition of eggs in the venules located in and around the spinal cord. Analysis of the cerebral spinal fluid of SMR patients reveals slight to moderate increases in protein content, lymphocytosis and eosinophils (Neves et al. 1973, Braga et al. 2003, Silva et al. 2002, 2004, Souza-Pereira et al. 2006, Lambertucci et al. 2007b).

Characteristically, the illness starts with a burning pain in the lumbar region that radiates to the lower limbs, followed by weakness, flaccid paralysis and sensory loss. The pain usually subsides with the onset of paraplegia (Silva et al. 2002, Ahmed et al. 2008). Tendon reflexes in the legs usually cannot be elicited and dysfunction of the bladder and rectal sphincters are common. Men become impotent (Lambertucci et al. 2005, 2007b).

MRI reveals abnormalities in the spinal cord in almost all SMR cases (Fig. 19). Following treatment with schistosomicides and corticosteroids, the alterations observed by MRI disappear as the clinical condition of the patient improves (Silva et al. 2004). Occasionally, the neurological symptoms may return after stopping treatment, but as soon as treatment is re-started, the signs and symptoms of SMR disappear.

#### Acute over chronic infection

Katayama syndrome caused by *S. japonicum* infections also occurs in people living in endemic areas with a history of previous infection. At least two cases of re-infection have been reported in Brazil (Katz & Bitencourt 1965, Neves & Raso 1965).

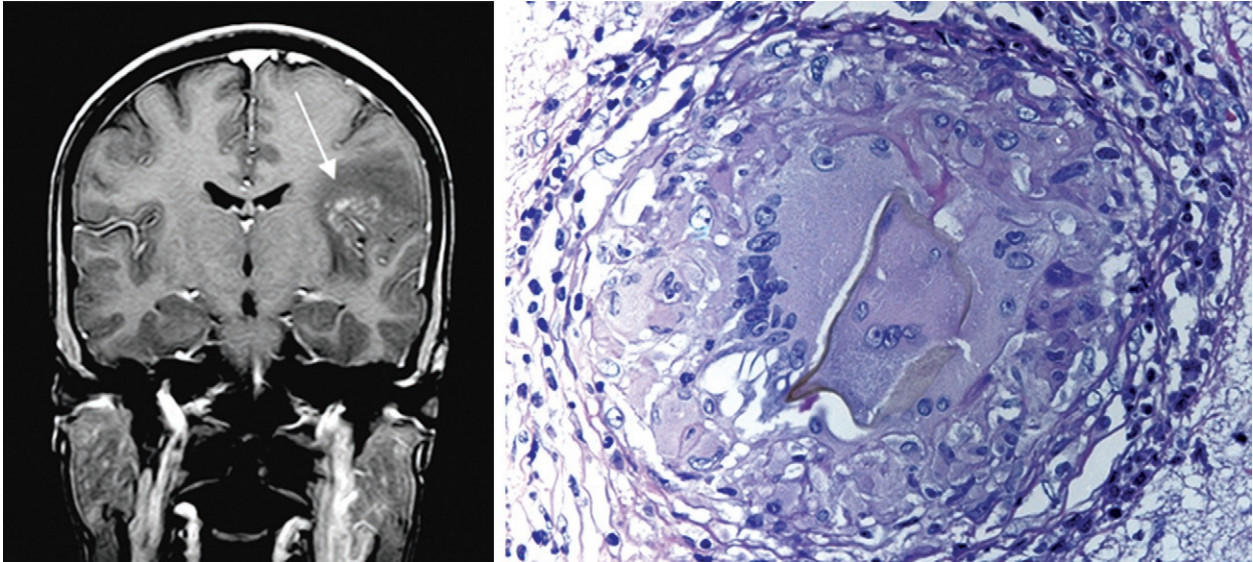


Fig. 18: this is the case of a 23-year-old female who presented seizures and headache two months after bathing in a endemic area for schistosomiasis in Brazil. Magnetic resonance image showed a conglomerate of nodules enhanced by contrast (arrow). On the right, a brain biopsy revealed a well formed granuloma around a *Schistosoma mansoni* egg.

We recently examined two male patients (18 and 19 years old) with chronic schistosomiasis who were re-infected in the stream waters of a gold mine near Belo Horizonte (unpublished observations). They were admitted to different hospitals for investigation of an FUI and both presented fever, diarrhoea and emaciation. One patient died and autopsy showed a liver with typical Symmers fibrosis but with a miliary distribution of ova of *S. mansoni*, as has been described in acute schistosomiasis; however, there was an interesting difference: no granulomas had a necrotic-exudative appearance (Fig. 20). The other patient, treated with steroids and oxamniquine, survived. In a fragment of his liver obtained by percutaneous ultrasound-guided biopsy, similar microscopic findings were described. Both patients probably had severe re-infection with dissemination of ova facilitated by the presence of portal hypertension and portosystemic shunts.

#### Serology for diagnosing acute schistosomiasis

The most common technique used in antibody detection is the enzyme-linked immunosorbent assay (ELISA). Soluble egg antigen, worm antigen and the cathionic fraction 6 display high sensitivity but low specificity. An ELISA test using keyhole limpet haemocyanin as the antigen has been shown to be efficient in differentiating acute from chronic schistosomiasis in patients living in endemic areas of Egypt and Brazil (Rabello 1995). While these tests may be useful for diagnosing patients from non-endemic areas visiting endemic areas, in general, antibody-based methods suffer from low specificity, persistence after chemotherapy, cross-reactivity and the need for reference centre to perform them.

**Antigen detection** - The sensitivity of antigen detection varies from 55-100%, being low in patients with

low worm burdens and thus this technique offers no advantage over stool examination. Antigen capture with monoclonal antibodies is expensive and reproducibility of the method is not good.

#### Treatment

Two main approaches have been proposed for the treatment of acute schistosomiasis:

**Schistosomicides alone** - Oxamniquine and praziquantel are potent schistosomicides against mature *S. mansoni* worms (Lambertucci et al. 1982). However, they present low efficacy against immature worms both in man and in experimentally infected mice (Lambertucci et al. 1980, 1989a, 2000). A cure rate of 40-50% may be expected in acute schistosomiasis. Schistosomicides may be used alone in asymptomatic patients. Treatment should be repeated 2-3 months later in patients still passing eggs in the stools. A deterioration or exacerbation of the clinical picture after treatment has been reported (Chou et al. 1963, Lambertucci et al. 1982, Harries & Cook 1987, Grandière-Perez et al. 2006, Jauréguiberry et al. 2007). Asymptomatic patients may become symptomatic, emboli of dead worms may end up in the liver or lungs with rebound liver pain, pulmonary symptoms and radiological alterations and antigens liberated by dead worms may form immune complexes and cause vasculitis or urticaria. The efficacy of schistosomicides is also immune-dependent (Doenhoff et al. 1988, 1991, Lambertucci et al. 1989a).

**Association of steroids and schistosomicides** - Clinical and experimental evidence indicate that steroids act synergistically with schistosomicides in the treatment of acute schistosomiasis (Lambertucci et al. 1989a,





Fig. 19: magnetic resonance of the spinal cord shows thickening of the *conus medullaris* (arrows: a sagittal section on the left and an axial on the right) with enhancement after contrast injection in a patient with acute schistosomiasis mansoni.

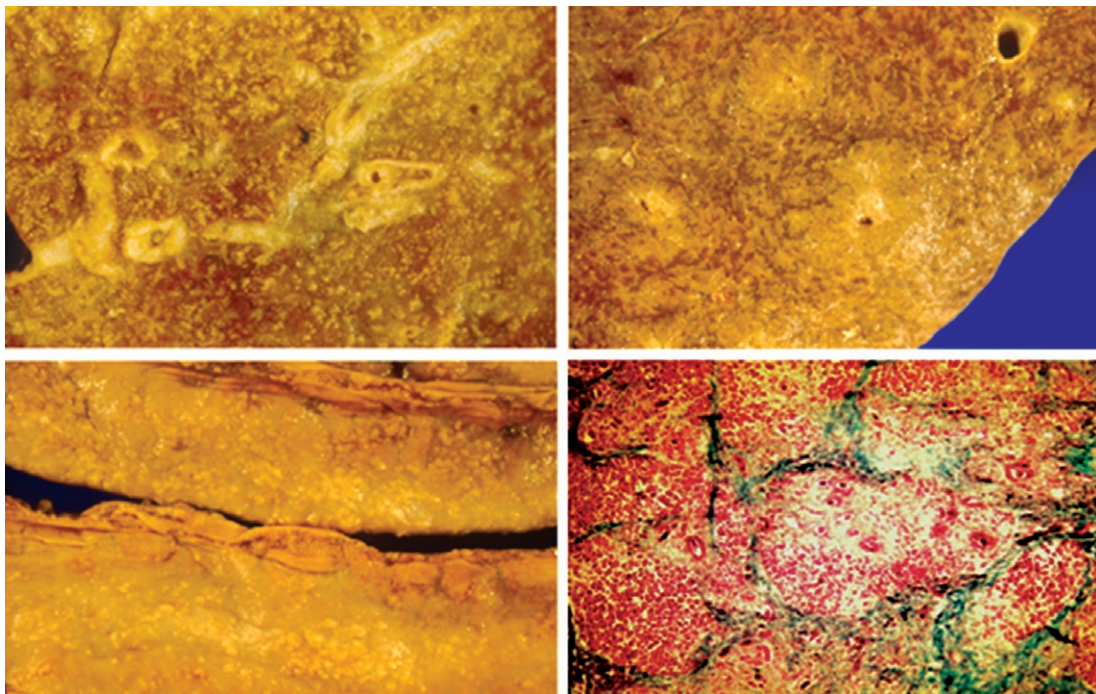


Fig. 20: a 19-year-old male patient who died after *Schistosoma mansoni* re-infection in Brazil. Figures lined on the top show a liver with Symmers fibrosis and a rough granulation on the cut surface. Figures lined below show, on the left, the same granulomatous appearance in the serosa of the intestines. On the right, there are eggs and areas of fibrosis (green).

Lambertucci 1993a, b). We usually give prednisone followed by oxamniquine or praziquantel (Table V). The association of steroids and schistosomicides in the treatment of symptomatic patients augments the cure rate, speeds the recovery time, prevents the recurrence of symptoms and improves the quality of medical care. Before starting steroids, however, it is good medical practice to treat patients for strongyloidiasis with ivermectin (200  $\mu\text{m}/\text{kg}$ , single dose) or albendazole to prevent the development of fatal strongyloides' sepsis triggered by prednisone.

### Artemisinin derivatives

These compounds are active against immature worms of all major human schistosome species (Xiao & Catto 1989). Artemisinins by themselves have been successfully used as antischistosomes in some special circumstances (e.g., in people exposed to the infection at a defined time because of a flood), but they cannot be considered as possible alternatives to other schistosomicides due to their limited activity against adult worms. Artemether seems to be a promising treatment for acute schistosomiasis because it is active against

juvenile worms. Nevertheless, in humans, the efficacy against *Schistosoma haematobium* seems to be moderate (N'Goran et al. 2003).

### CONCLUSION

There is a broad spectrum of clinical manifestations of acute schistosomiasis in humans. Physicians of different medical specialties, including neurology, lung diseases, dermatology, internal medicine and gastroenterology, must be trained to recognise acute schistosomiasis. Groups at risk for acquiring it (tourists, military personnel, religious congregations and people practicing water sports) must be alerted and advised about the disease and its complications. Additionally, physicians of endemic and non-endemic countries are not aware of the importance of acute schistosomiasis and of its multiform clinical presentation.

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