Clinical Medicine 2011, Vol 11, No 5: 479–82

CME Tropical medicine

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Schistosomiasis

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For most helminth infections, morbidity is concentrated in endemic settings and associated with heavy exposure. Helminths, with the notable exception of Strongyloides, cannot complete their life cycle in man so worm burden is related to the extent of environmental exposure. Global morbidity related to schistosomiasis is predominantly restricted to rural and semi-urban communities where freshwater exposure is a feature of daily life, affording the parasite repeated opportunities for infection and thus generating a cumulative worm burden in the human host. Manifestations of such heavy schistosome infections are occasionally seen in non-endemic settings among migrants from these communities. Diagnosis is usually straightforward.

Light infections, particularly in travellers, are sometimes medically important. Disease pathogenesis in this patient group is related to hypersensitivity in previously unexposed individuals or to ectopic worm migration to the central nervous system (CNS). Prompt recognition and treatment requires a good travel history, a high index of suspicion and an appreciation of the relevance of a peripheral blood eosinophilia.

The parasite and its life cycle

Schistosomes are trematodes (flukes) whose intermediate hosts are aquatic snail species. Free swimming cercariae released from snails into freshwater penetrate exposed intact human skin or mucous membranes, develop into schistosomula in the tissues and migrate through the circulation to the lungs. After further development, they migrate through the systemic circulation to their final destination in the mesenteric or vesical veins where adult male and female worms pair. The females lay eggs which are shed into the tissues, provoking a granulomatous response which aids excretion of the eggs across the mucosa into the lumen of the bowel or bladder. Defecation/urination into the same freshwater sources allows snail reinfection and completion of the cycle.

The most prevalent species are:

- *Schistosoma haematobium*, which lives in the venous plexus around the bladder and deposits eggs into bladder mucosa.
- *S. mansoni*, which lives in the mesenteric and hepatic portal veins and deposits eggs into the bowel mucosa.

Other important species infecting humans are *S. japonicum, S. mekongi and S. intercalatum*, the adults of which are found, like *S. mansoni*, in the portal circulation.

Epidemiology in endemic and non-endemic settings

Schistosomiasis is endemic in 76 countries, with 85% of those infected living on the African continent. Peak prevalence and infection intensities are seen in older children and young adults.

- *S. haematobium*: almost completely restricted to sub-Saharan Africa and the Nile delta
- *S. mansoni*: the same regions, but also in Brazil and the southern Caribbean
- *S. intercalatum*: West and Central Africa
- *S. japonicum* (China, Indonesia and the Philippines) and *S. mekongi* (Laos and Cambodia) have more restricted foci.

Since 1998, 99% of patients diagnosed with schistosomiasis at the Hospital for Tropical Diseases (HTD) in London acquired their infection in Africa. The median age was 28 years, with fewer than 5% under 18 and 10% aged over 45 (unpublished data).

Pathogenesis of chronic disease

Retention of eggs within tissues, with resultant granulomatous inflammation, is the hallmark of disease pathogenesis. This is followed by fibrosis, leading to obstructive uropathy and squamous cell carcinoma in the bladder. *S. haematobium, S. mansoni* and other schistosome species cause portal hypertension (resulting from hepatic fibrosis) due to egg deposition around the portal tracts by adult worms residing in the hepatic sinusoids. Disease severity is proportional to the egg burden, which is in turn associated with adult worm burden.[1]

Diagnosis

Diagnosis can usually be made by finding ova in the urine or stool of infected patients, or by seeing ova in biopsies of bladder or bowel mucosa. Serology, based on finding antibodies to egg antigens, is of limited use in endemic countries but helpful in the diagnosis of low intensity infections in migrants or returning travellers in non-endemic settings.

Pathogenesis and disease burden in lightly exposed migrants

Haematuria and haematospermia

Frank haematuria is a common presentation of *S. haematobium* in lightly infected travellers, as well as in heavily

infected migrants where it is the norm in endemic communities. Haematospermia is often described in infected travellers.[2] Terminal urine microscopy is helpful as serology may be negative early in infection. In all patients it is important to ensure that haematuria resolves after treatment (praziquantel 40 mg/kg as a single dose). The drug is well tolerated, with side effects usually associated with a higher worm burden. In the heavily exposed migrant, squamous cell carcinomatous transformation may already have occurred before diagnosis. A low threshold for cystoscopy is advisable.

Ectopic worms

Migration of adult male and female pairs to other sites within the host may result in pathology, as may haematogenous spread of eggs from other sites. Of particular concern are ectopic worms in the CNS, which may cause a myelopathy leading to paralysis or cerebral infection with focal neurological deficits. Egg deposition within the CNS is not an uncommon finding in autopsy studies, usually without significant local inflammation. Travellers may be especially prone to these sequelae due to a more intense immune response generated in the previously unexposed host. Schistosomiasis should be considered in the young traveller with a neurological presentation and a history of freshwater exposure in Africa. Clues to the diagnosis include eosinophilia, present in the majority of patients. As stated above, serology is often negative at first presentation. Characteristic nodular, enhancing lesions may be seen on magnetic resonance imaging.[3]

Treatment. Focus on the immune response is most important in the treatment of ectopic worms – somewhat akin to the management of neurocysticercosis. Praziquantel acts by punching holes in the worm tegument, thus exposing previously hidden antigens to the schistosomicidal effects of the host immune response. Thus, treatment may exacerbate the pathology, and should be preceded by corticosteroids.[4] Many specialists give a prolonged course (eg praziquantel 40 mg/kg on three consecutive days), but there is no evidence base for this practice.

Acute schistosomiasis

As in neurological schistosomiasis, with which disease does not necessitate a high worm burden, another characteristic presentation of imported disease is Katayama fever. Oviposition (occurring usually 2–8 weeks after infection) exposes egg antigens to a previously unexposed host, generating strong type 2 cytokine responses with eosinophilia. Clinical manifestations are non-specific: fever is usual, while myalgia, headache, diarrhoea and cough are not uncommon. The well-described widespread urticarial rash (Fig 1) is seen in only a minority of patients,[5] splenomegaly is present in some cases and neuroschistosomiasis may occur simultaneously.

Microscopy for eggs (in urine or stool) is usually negative at this early stage in

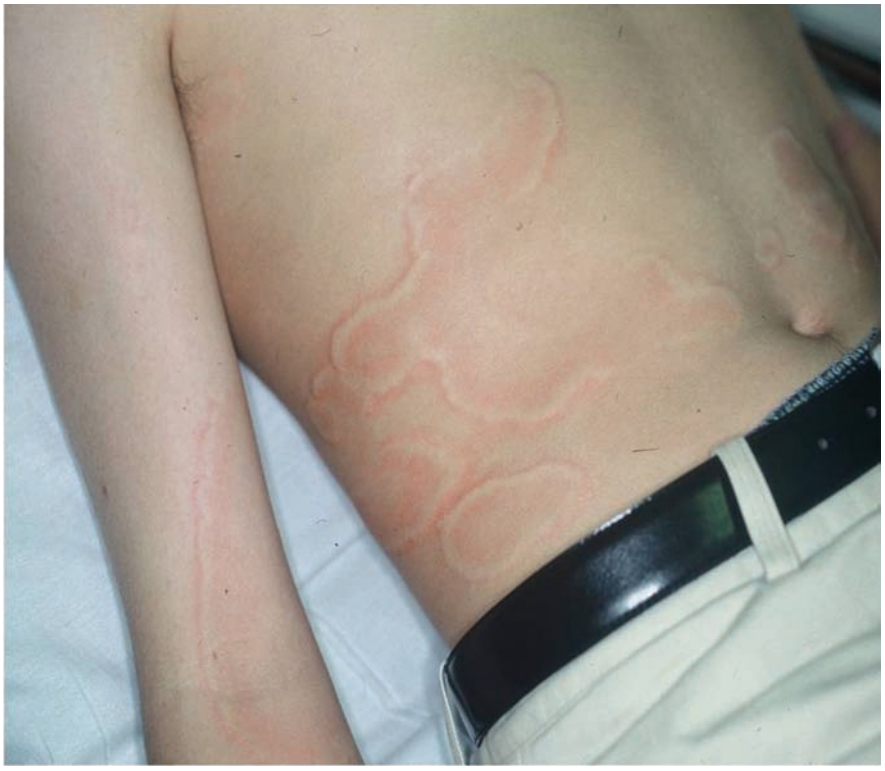

Fig 1. Urticarial rash in a young man with Katayama fever following a trip to Lake Malawi. Reproduced with permission of Oxford University Press.[6]

Key points

Schistosomiasis is predominantly an African disease; infection may persist for years after leaving endemic settings

Acute manifestations of schistosomiasis in non-endemic settings are predominantly related to ectopic worm migration (such as neurological schistosomiasis) or hypersensitive immune responses (such as Katayama fever)

The diagnosis, which is often clinical, should rarely be missed if a travel history is performed and attention paid to the absolute eosinophil count

Treatment with praziquantel, sometimes preceded by corticosteroids, is effective

KEY WORDS: eosinophilia, returning traveller, schistosomiasis

egg production, and the egg antigen-specific antibody response detected by most serological assays is usually insufficient at first presentation, maturing during the following days.

Diagnosis is therefore clinical. The hallmark of this type of presentation is the recent exposure history and the presence of a peripheral eosinophilia (although this may be absent).[7] Katayama fever can be treated with corticosteroids, followed by praziquantel 40 mg/kg, repeated at least 2–4 weeks later (see below).

Identifying and treating the asymptomatic patient

Most travellers who become infected incidentally with schistosomiasis have a very low worm burden and remain asymptomatic – hence routine investigation of exposed travellers is of limited benefit. Instead, investigation should be reserved for those with symptoms, with an eosinophilia or migrants from endemic countries who may have a heavy worm burden. Worms live for an average of 5–10 years, but there is evidence that they may survive for decades and hence persist long after migration from endemic countries. Although morbidity is uncommon in non-endemic settings where heavy infection is rarely seen, undiagnosed schistosomiasis in migrants may have consequences which are preventable by early recognition and treatment. Often the only manifestation of helminth infections is a peripheral absolute eosinophilia.

Recently published recommendations (Fig 2) provide a simple strategy for exclusion of medically important helminths in patients with an eosinophilia and a history of travel to the tropics.[8] These recommendations are based in part on studies which found schistosomiasis to be the most prevalent helminth infection among patients referred to the HTD with eosinophilia,[9] and that infection was asymptomatic in 50% of patients diagnosed with schistosomiasis.[10] Eosinophilia is not always present: 56% of schistosome-infected patients in this cohort had a normal absolute eosinophil count. Because of the 'window' between infection and egg production (alluded to previously), post-travel screening of travellers, including stool and urine microscopy and serology, should be delayed for at least three months after exposure.[11] Furthermore, praziquantel has low efficacy against immature worms – hence the need for repeated treatment in those with acute schistosomiasis.[12]

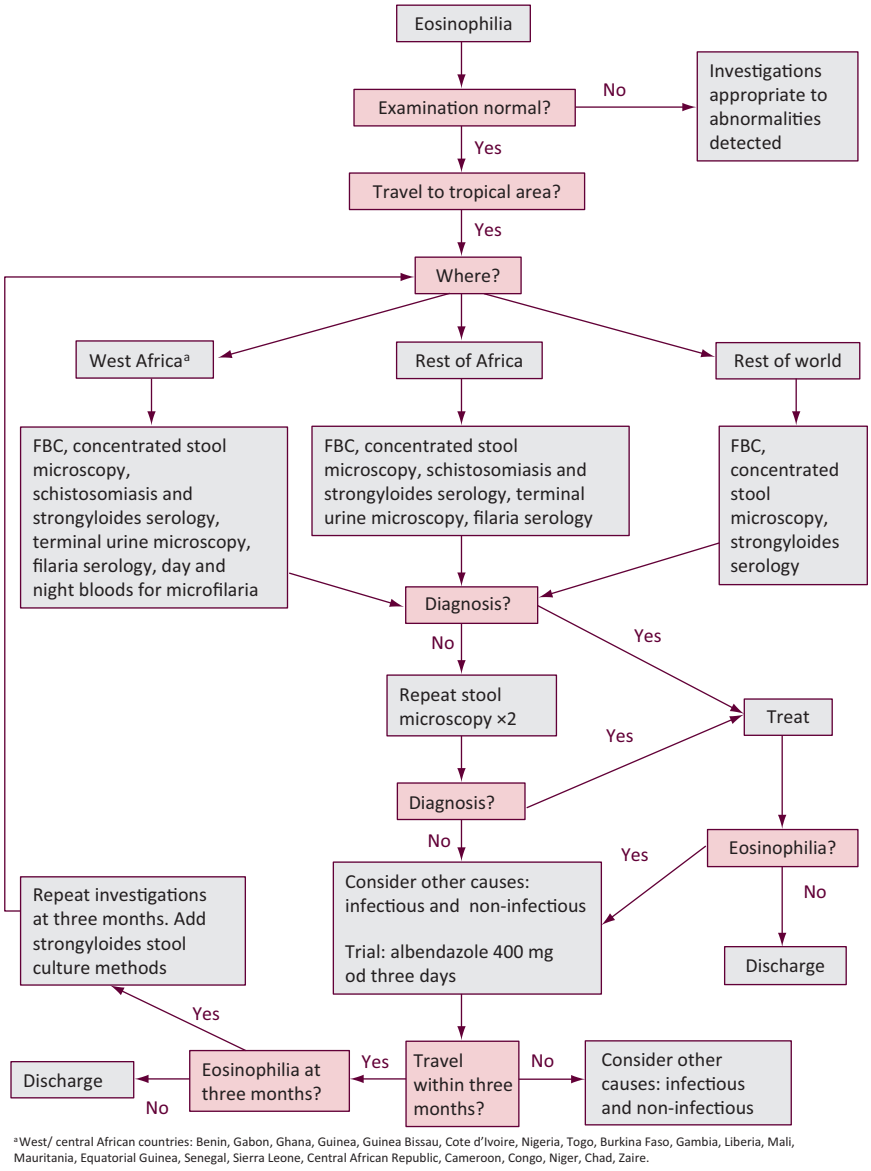

Fig 2. Investigation of asymptomatic eosinophilia based on geographical exposure. FBC = full blood count Reproduced with permission from Elsevier.[8]

Recent developments

Large-scale mass treatment programmes in endemic countries are demonstrating success in reducing disease burden.[13] The direct association between worm burden and pathology means that regular anti-helminthic therapy will reduce the endemic disease burden, but sustained global, political and financial commitment will be required to reduce community transmission sufficiently to eradicate the infection. The impact of schistosome infection on other pathogens, such as tuberculosis, malaria and HIV, has also been the subject of recent and ongoing study. Potential downregulation of protective immune responses to

unrelated antigens by helminth infection provides a rationale for exploring this question in properly conducted randomised controlled trials.[14]

Recent studies have demonstrated the efficacy of the antimalarial drugs (artemisinins, mefloquine and sulfadoxine-pyrimethamine) against schistosomes, in particular against immature parasites. There is so far insufficient evidence to recommend these in preventing or treating infection. Two drug combinations have been shown to be effective in small randomised open-label trials in West African children.[15,16]

Acknowledgements

I am grateful to Anastasia Chew and Christopher Whitty for data from a recent audit on patients with schistosomiasis at HTD.

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