A recent analysis of the North American AIDS Cohort Collaboration on Research and Design study found that there was a 70% reduction in mortality among patients starting antiretroviral therapy with a CD4 cell count of 350–500 cells/μL, compared with those deferring therapy [2]. It will take years for the Strategic Timing of Antiretroviral Treatment (START) study results to be known, and there are ongoing questions about such a study. For example, given current available data, will providers and patients agree to being a part of the randomization process? While awaiting further information, clinicians need to discuss currently available data with patients starting antiretroviral therapy and to make a reasonable, informed, and individualized decision on when to initiate antiretroviral therapy.

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References


Difficulties in the Diagnosis and Treatment of Acute Schistosomiasis

To the Editor—We read with interest the recent clinical description of an outbreak of acute schistosomiasis by Leshem et al. in Clinical Infectious Diseases [1]. We have some comments regarding the diagnosis and treatment of acute schistosomiasis in nonimmune travelers.

Making a diagnosis of acute schistosomiasis is difficult. In this outbreak, diagnosis relied on positive serologic test results in 15 (68%) of the 22 exposed patients and on the combination of clinical symptoms and eosinophilia in 6 patients. Neither method of diagnosis is sensitive enough. Serologic test results are usually negative at the onset of clinical signs, and tests must be repeated to identify seroconversion, which may appear up to 3 weeks after the onset of symptoms and ~6 weeks after exposure [2, 3]. At the first encounter with a clinician, serologic test results are positive in ≤65% of cases [2, 4]. Eosinophilia may also be lacking at the onset of symptoms of acute schistosomiasis; it is only present in 27% of symptomatic patients and may appear up to 3 weeks after onset of fever [2, 5]. In addition, the serologic tests cannot identify the causal species of acute schistosomiasis. For example, reactivity against Schistosoma haematobium was identified in a subset of 3 patients, whereas 1 patient formally received a diagnosis of Schistosoma mansoni infection [1]. In addition, Charcot Leyden crystals were detected in 18% of tested patients, which also points to an intestinal helminthic infection, such as that caused by S. mansoni.

Treatment of acute schistosomiasis poses a real challenge. In this outbreak, the prolonged duration of symptoms and the persistence of eosinophilia in a subset of patients may have explanations other than those discussed by Leshem et al. [1]. First, praziquantel was prescribed at an unknown dosage. The recommended dosage for the treatment of chronic S. haematobium and S. mansoni infection is usually 40 mg/kg once daily. Praziquantel is not effective during acute schistosomiasis and is sometimes associated with severe adverse reactions [6, 7]. Moreover, praziquantel is ineffective against schistosomulae and does not prevent the chronic phase of the disease [2, 5]. Second, treatment was initiated 3 months after exposure. Leshem et al. argued that “>12 weeks after infection, the persistence of nonresponsive schistosomulae was highly unlikely” [1, p. 1504]. Nonetheless, this is a controversial issue. At month 3 after exposure, patients may still be in the invasive phase of acute schistosomiasis, which is before the chronic phase of the disease when the treatment is effective. According to other reports of outbreaks, seroconversion or ova production may appear up to 6 months and 330 days after exposure, respectively [2, 8]. Furthermore, relapses of acute schistosomiasis have been described elsewhere [4]. To our knowledge, the duration of time necessary to complete the parasite cycle (from infection to ova deposition) is unknown, but it is certainly >12 weeks. Finally, corticosteroids were prescribed with praziquantel in 42% of the patients. Corticosteroids decrease the plasma level of praziquantel by 50% [9]. There are many factors that may have contributed to the burden of acute schistosomiasis in this and other outbreaks [1, 2,
On the basis of our experience treating travelers with acute schistosomiasis, we now believe that the use of corticosteroids should be restricted to patients with systemic complications, and praziquantel should only be initiated when ova are detected in stool or urine samples, depending on the species causing infection [7].

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**Reply to Jauréguiberry et al.**

To the Editor—We appreciate the valuable comments of Jaureguiberry et al. [1] regarding our description of an outbreak of acute schistosomiasis in a group of travelers [2]. Jaureguiberry et al. [1] comment on 2 areas in the management of acute schistosomiasis: diagnosis and treatment. Both issues were extensively discussed in a previous report [3].

The diagnosis of acute schistosomiasis during the initial symptomatic period is based on clinical and epidemiologic grounds. Serologic evidence may support the diagnosis. However, because seroconversion often occurs after the onset of symptoms, initial diagnosis often relies solely on clinical evidence. In suspected cases, serologic tests should be repeated if initial results are negative, and acute schistosomiasis should only be ruled out if serologic test results remain negative ≥3 months after exposure. This principle was demonstrated by 2 patients in the described group who presented with symptoms compatible with acute schistosomiasis but were initially seronegative (at weeks 5 and 8 after exposure). Repeated serologic testing revealed seroconversion in both patients (at weeks 7 and 10 after exposure, respectively). In addition, 8 of the 27 exposed travelers in the outbreak did not experience acute schistosomiasis symptoms or eosinophilia [2]. Serologic testing performed ≥3 months after exposure (range, 94-186 days after exposure) revealed that 3 of the 8 were seropositive, and those 3 subsequently received a diagnosis of asymptomatic infection. Only the remaining 5 patients, who were seronegative long after exposure (a minimum of 3 months), were regarded to be not infected. We are unaware of any reports of very late seroconversions that occur even 6 months after exposure, which were mentioned by Jauréguiberry et al. [1]. There are very few case reports that describe patients who were repeatedly seronegative and subsequently received a diagnosis by use of ova detection [4, 5]. These few cases possibly illustrate the different sensitivities of various serologic tests or the pitfalls associated with use of locally produced worm antigen [6].

Ova detection methods are largely insensitive during acute schistosomiasis (sensitivity, 22%-25%) [3, 4]. In our group, only 2 (18%) of 11 stool samples tested had *Schistosoma mansoni* ova detected. This is explained by the fact that acute schistosomiasis symptoms may occur weeks before oviposition. Therefore, the role of ova detection in the diagnosis of acute schistosomiasis, especially during the first few weeks after exposure, is negligible.

All patients who received a diagnosis of acute schistosomiasis in our group were treated with praziquantel (60 mg/kg divided in 2 doses). This high dose was used because of recent reports of praziquantel resistance in travelers [7]. Because praziquantel is less effective against the juvenile forms of schistosoma [3, 8], our policy is to administer it ≥3 months after the last exposure. For 2 of our patients who received concomitant steroid and praziquantel treatment during the acute phase of disease, repeated praziquantel treatment was given 3 months after exposure. No treatment failures were observed during follow-up.

Various treatment options for acute schistosomiasis were never evaluated systematically. The approach that Jaureguiberry et al. [1] suggested of treating acute schistosomiasis with steroids when systemic complications occur and with praziquantel only when ova are detected seems to be a reasonable option. However, because the initiation of oviposition does not preclude the existence of maturing schistosomulae that are insensitive to the drug, repeated praziquantel treatment is needed ≥3 months after exposure.

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