High Prevalence and Presumptive Treatment of Schistosomiasis and Strongyloidiasis among African Refugees

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(See the editorial commentary by Keystone on pages 1316–8)

Background. Schistosomiasis and strongyloidiasis cause substantial morbidity and mortality among hundreds of millions of infected persons worldwide. In the United States, these infections are most commonly found among international travelers, immigrants, and refugees from areas of endemicity. Refugees resettled to the United States since 2000 include >3800 “Lost Boys and Girls” of Sudan and 8000 Somali Bantu. Many Lost Boys and Girls of Sudan reported chronic abdominal pain only since arrival, and some received diagnoses of schistosomiasis or strongyloidiasis. We assessed seroprevalence of these infections among these refugees and hypothesized an association between infection and abdominal pain.

Methods. We offered a survey assessing chronic abdominal pain and serologic testing for schistosomiasis and strongyloidiasis to all 800 attendees of a Lost Boys and Girls of Sudan reunion in the United States. Serologic testing was performed on preimmigration specimens obtained from 100 United States–bound Somali Bantu refugees.

Results. Of the 462 Sudanese refugees (58%) tested, 44% and 46% were seropositive for schistosomiasis (primarily due to Schistosoma mansoni) and strongyloidiasis, respectively; 24% of those who tested positive for schistosomiasis had S. mansoni antigenemia. Forty-six percent reported chronic abdominal pain only since arrival, and some received diagnoses of schistosomiasis or strongyloidiasis. We assessed seroprevalence of these infections among these refugees and hypothesized an association between infection and abdominal pain.

Conclusions. The high seroprevalence of schistosomiasis and strongyloidiasis among Sudanese Lost Boys and Girls and Somali Bantu refugees supports presumptive treatment for these refugees. Current refugee resettlement policies inadequately address these diseases; our data support consideration of predeparture presumptive therapy for all refugees from areas of endemicity.

More than 200 million people in developing countries are infected with Schistosoma species, and 30–100 million are infected with Strongyloides stercoralis [1–4]. In the United States, these infections are most commonly found among refugees, immigrants, and travelers from areas of endemicity. Both parasites persist for years to decades in the human host and can cause significant morbidity and mortality. Complications of schistosomiasis include intestinal disease, anemia, stunting, organomegaly, portal hypertension, urinary tract dysfunction, and devastating neurologic disease. Complications of strongyloidiasis include chronic intestinal disease and, in immunocompromised hosts, life-threatening dissemination [1–4]. Many persons with schistosomiasis and strongyloidiasis have clinically unrecognized infection and do not receive treatment with the highly effective antihelminthic drugs that are widely available. Diagnosis of these infections has...
traditionally relied on microscopic examination of stool or urine specimens for parasite eggs and larvae, although these means of examination may be insensitive for low-intensity infections [4, 5]. However, serologic tests for these infections have greater sensitivity than examination of stool or urine samples [5, 6].

Refugees are not routinely screened or treated for schistosomiasis and strongyloidiasis and are typically not included in national control programs that deliver chemotherapy for intestinal helminths or schistosomiasis. The United States resettles up to 70,000 refugees annually, ~25,000 of whom are from Africa [7]. In 2000–2001, a total of 3800 “Lost Boys and Girls” of Sudan were resettled from the Kakuma refugee camp in northwestern Kenya; in 2004–2005, ~8000 Somali Bantu refugees were resettled from the same area. The Lost Boys and Girls are a group of Sudanese persons who banded together after being orphaned as children during the Sudanese Civil War in the 1980s and 1990s. After traveling though southern Sudan and Ethiopia, they arrived at Kakuma, and years later, they resettled in the United States; most are now young adults. These Somali Bantu are a persecuted minority who fled the Somali Civil War in the 1990s and also relocated to Kakuma before eventually resettling in the United States.

During 2004, the Centers for Disease Control and Prevention (CDC) received multiple reports of undiagnosed chronic abdominal pain among Lost Boys and Girls of Sudan, including several persons in whom a diagnosis of schistosomiasis or strongyloidiasis had been confirmed. We thus conducted an investigation to determine the prevalence and characteristics of abdominal pain in this group and to assess possible associations with schistosomiasis or strongyloidiasis. The investigation occurred during the national Lost Boys and Girls of Sudan reunion held on 26–29 August 2004, in Phoenix, Arizona. Subsequently, we tested stored serum samples obtained from Somali Bantu refugees to determine the prevalence of schistosomiasis and strongyloidiasis in a different African refugee population.

METHODS

Survey and Serologic Testing

Lost Boys and Girls of Sudan. During the Lost Boys and Girls of Sudan reunion, through multiple announcements and posters, all attendees were invited to participate in a written, self-administered survey that addressed abdominal pain and other symptoms. Investigators and translators assisted participants on site. On the survey, chronic abdominal pain was defined as abdominal pain, cramping, or side pain that had been recurrent since resettlement.

Serologic testing was offered to all reunion participants. Serum specimens obtained from each person were tested for antibodies to Schistosoma species using the Falcon assay screening test ELISA (FAST-ELISA), which uses the Schistosoma mansoni adult microsomal antigen [5]. A value of ≥10 U was accepted as a positive result. This assay has ~99% sensitivity for S. mansoni infection and 90% sensitivity for Schistosoma haematobium infection [5, 8, 9].

Subsequently, a random sample of 10% of ELISA-positive serum specimens was tested by Schistosoma enzyme-linked immunoelectrotransfer blot (immunoblot) for species identification; species-specific adult worm microsomal antigens for S. mansoni and S. haematobium were used [5]. These assays have >95% sensitivity and nearly 100% specificity for both species [8, 10]. In addition, capture ELISA testing for S. mansoni circulating cathodic antigen was conducted on all S. mansoni FAST-ELISA–positive specimens and on a 15% random sample of FAST-ELISA–negative specimens [8, 11]. Any detectable antigen (≥0.001 μg/mL) was regarded as a positive result, which is consistent with active S. mansoni infection of at least moderate intensity [8, 11].

EIA testing for Strongyloides antibodies was performed with soluble antigens from S. stercoralis third-stage larvae [6]. A value of ≥9% was accepted as a positive result. Although the sensitivity of this test is ~95% among persons whose stool specimens yield positive results, specificity has not been precisely determined for persons living in areas where other intestinal helminths are prevalent [6]. Because patients typically become negative for antibodies to Strongyloides 1–2 years after cure, and because the immune system is not expected to clear the infection in the absence of treatment [6, 12], the presence of antibodies usually indicates ongoing infection.

All Lost Boys and Girls of Sudan who tested positive for schistosomiasis were offered treatment at the reunion. Schistosomiasis treatment consisted of 2 doses of praziquantel (20 mg/kg) given 6–8 h apart. After the reunion (through collaboration with state and local health departments), persons who tested seropositive for strongyloidiasis were offered albendazole (400 mg twice per day for 3 days), and attempts were made to treat attendees with schistosomiasis who had not received treatment at the reunion. Albendazole was chosen instead of ivermectin because of the possibility of heavy coinfection with Loa loa and the risk of inducing encephalopathy with ivermectin [13]. The relatively short duration of therapy (3 days) was chosen because of concerns about supervision of therapy and adherence. The protocol was approved by the CDC and Arizona Department of Health Services human subjects review boards. All participants provided written informed consent.

Somali Bantu refugees. From a bank of anonymous serum samples that remained after a preimmigration screening of 2000 Somali Bantu, samples from 100 persons were selected by using a random number generator. S. mansoni FAST-ELISA, S. hae-
**RESULTS**

**Lost Boys and Girls of Sudan.** Among 800 reunion attendees, 464 (58%) participated in the survey. The participants were residents of 25 states; 54% were residents of Arizona, 80% were aged 21–30 years, and 96% were male.

Two hundred fourteen participants (46%) reported experiencing chronic abdominal pain since resettlement. No distinct clustering of clinical symptoms was detected. Chronic abdominal pain was reported along with complaints from every body system.

Of the 462 participants who underwent laboratory testing, 203 (44%) had FAST-ELISA results positive for *Schistosoma* antibodies, and 214 (46%) had EIA results positive for *Strongyloides* antibodies (table 1). Among persons who tested positive for *S. mansoni* by FAST-ELISA, 48 (24%) had detectable *S. mansoni* antigenemia. Immunoblot testing of 21 randomly selected persons who tested positive for schistosomiasis by FAST-ELISA revealed a predominance of *S. mansoni* (*S. mansoni* infection alone, 57% of persons; *S. mansoni* and *S. haematobium* coinfection, 19%; *S. haematobium* infection alone, 9%). Overall, 103 persons (22%) were seropositive for both schistosomiasis and strongyloidiasis, and 314 (68%) were seropositive for ≥1 of these infections.

Serologic evidence of schistosomiasis or strongyloidiasis was not related to chronic abdominal pain (table 2). Age was not significantly associated with either infection. No associations were found among other potential indicators (such as diarrhea, hematochezia, hematuria, cough, dyspnea, fever, or rash) of these parasitoses and *Schistosoma* antibody positivity, *S. mansoni* antigenemia, or *Strongyloides* antibody positivity. Multivariate modeling did not identify clinical predictors of either parasitic disease (data not shown).

Of the *Schistosoma*-positive Lost Boys and Girls of Sudan, 191 (94%) received treatment for schistosomiasis (178 received treatment during the reunion, and 13 of the remaining 25 *Schistosoma*-seropositive persons received treatment after the reunion). Of those who tested positive for *Strongyloides* infection, 133 (62%) were treated (all after the reunion).

**Somali Bantu refugees.** The median age of the 100 Somali Bantu refugees whose anonymously stored specimens were tested was 28 years (range, 1–83 years), and 44% were male.

Seventy-three (73%) tested positive for *Schistosoma* antibodies; 255 (92%) tested positive for *S. mansoni* FAST-ELISA and *S. haematobium* immunoblot. The entire cohort showed a predominance of infection with *S. haematobium*. Age was associated with increased risk of infection: adults (age, ≥18 years) were 3 times more likely (95% CI, 1.6–5.6 times more likely) to have schistosomiasis than were children, and persons aged ≥30 years were 2.5 times more likely (95% CI, 1.2–5.3 times more likely) to have strongyloidiasis than were those aged <30 years. Twenty-three subjects (23%) had antibodies to *Strongyloides*, as determined by EIA. Overall, 75 persons (75%) were seropositive for either schistosomiasis

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### Table 1. Results of serologic tests for strongyloidiasis and schistosomiasis for Lost Boys and Girls of Sudan and Somali Bantu refugees who had resettled in the United States, 2004.

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Lost Boys and Girls of Sudan</th>
<th>Somali Bantu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of persons tested</td>
<td>No. (%) of persons with positive results</td>
</tr>
<tr>
<td>Strongyloides antibody&lt;sup&gt;a&lt;/sup&gt;</td>
<td>462</td>
<td>214 (46)</td>
</tr>
<tr>
<td>Schistosoma antibody&lt;sup&gt;b&lt;/sup&gt;</td>
<td>462</td>
<td>203 (44)</td>
</tr>
<tr>
<td>Schistosoma mansoni antigen&lt;sup&gt;c&lt;/sup&gt;</td>
<td>ELISA-positive persons</td>
<td>203</td>
</tr>
<tr>
<td></td>
<td>ELISA-negative persons</td>
<td>34</td>
</tr>
</tbody>
</table>

<sup>a</sup> Tested by EIA.

<sup>b</sup> Lost Boys and Girls of Sudan were tested only by *S. mansoni* Falcon assay screening test ELISA; Somali Bantu refugees were all tested by *S. mansoni* Falcon assay screening test ELISA and *S. haematobium* immunoblots.

<sup>c</sup> Tested by capture ELISA for *S. mansoni* circulating cathodic antigen.

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*matobium* immunoblot, and *Strongyloides* EIA testing, as described above, were performed on all serum specimens. The CDC’s institutional review board approved the protocol.

### Statistical Analysis

Using SAS software, version 8.02e (SAS Institute), we used the χ² test, Fisher’s exact test, and Mantel-Haenszel χ² test for linear trend to compare the characteristics of persons with and without chronic abdominal pain, schistosomiasis, or strongyloidiasis. Cox regression models were used to estimate adjusted prevalence ratios and 95% CIs for variables associated with dependent variables (chronic abdominal pain, schistosomiasis, and strongyloidiasis) [14]. Using a stepped-down model-building approach, all clinically relevant variables associated with dependent variables (P < .05) were examined for inclusion in the models.

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or strongyloidiasis, and 21 persons (21%) were seropositive for both infections.

**DISCUSSION**

We demonstrated high seroprevalences of both schistosomiasis and strongyloidiasis among Lost Boys and Girls of Sudan and Somali Bantu refugees who had been resettled in the United States during the previous 5 years. Although these results are striking, other studies have demonstrated high prevalences of these infections among refugees. Surveys of Southeast Asians resettled in Canada [15] and Australia [16] demonstrated 65% and 24% seroprevalences of strongyloidiasis, respectively; notably, stool specimen examinations for these populations were positive for *Strongyloides* for only 25% and 2% of subjects, respectively. In a recent study from Boston, Massachusetts, asymptomatic refugees with eosinophilia from diverse regions who were evaluated serologically had infection rates of 22% for *Schistosoma* infection and 39% for *Strongyloides* infection [17]. A small series suggested that rates of schistosomiasis and strongyloidiasis of 52% and 12%, respectively, among resettled Lost Boys and Girls of Sudan whose specimens were also tested by CDC serological assays [18]. Other studies have also demonstrated high infection rates among nonrefugee immigrant populations, underscoring the global importance of these infections [19].

Although the *S. mansoni* FAST-ELISA result remains positive for many years after cure of infection and cannot differentiate active from past infection [5], it is likely that many of the Lost Boys and Girls of Sudan and Somali Bantu who were seropositive for schistosomiasis had active infection. One-quarter of *Schistosoma* antibody–positive Lost Boys and Girls of Sudan had circulating antigen for *S. mansoni*—a marker of active infection of at least moderate intensity. Because the antigen assay does not detect low-intensity *S. mansoni* infection or *S. haematobium* infection, the actual percentage of persons with active infection is likely higher [11]. Moreover, it is unlikely that any of the refugees had previously received treatment for schistosomiasis, and the life expectancy of adult schistosomes often exceeds 5 years—the maximum period of time since the refugee’s resettlement. Similarly, strongyloidiasis-seropositive persons presumably had active infection. Typically, untreated strongyloidiasis persists for the host’s life, because of its autoinfection cycle [1, 2], and the *Strongyloides* EIA result becomes negative only 1–2 years after receipt of successful treatment [6, 12].

In our study of Lost Boys and Girls of Sudan, abdominal symptoms were not associated with either infection, and the high prevalence of chronic abdominal pain probably resulted, at least in part, from other conditions. We did not investigate the presence of other infections, such as *Helicobacter pylori* infection or viral hepatitis, or physical and psychiatric conditions known to be associated with chronic abdominal pain that are common among refugees [20, 21].

The high rates of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan and Somali Bantu refugees are not surprising, given the high likelihood of environmental exposure in or after departure from their home countries and the general lack of access to appropriate therapy, including in refugee camps. Moreover, the current policy for United States–bound African refugees (i.e., presumptive treatment with a single 600-mg dose of albendazole) is not effective for treatment of schistosomiasis or most *Strongyloides* infections. This policy is based on the results of previous studies of African refugees that demonstrated the cost-effectiveness of presumptive pre-departure treatment for intestinal parasitic infections among migrants [22–25]. Upon arrival in the United States, refugees may undergo stool examinations to detect parasites, but these examinations lack sufficient sensitivity. Serologic testing is not widely available, and infection cannot be predicted solely on clinical grounds. Moreover, many physicians in the United States are not familiar with the clinical consequences of these infections or with diagnosis and treatment. Thus, infected refugees often harbor the parasites for years and remain at risk for serious complications [26]. Because the number of refugees resettling in the United States from countries where these infections are endemic is large (there were 109,338 resettled individuals during 2000–2004 [7]), there is a need for a standardized approach for managing these infections in refugees.

**Treatment guidelines for Lost Boys and Girls of Sudan and Somali Bantu refugees.** On the basis of the experience reported here, the CDC has issued presumptive treatment guidelines for the Lost Boys and Girls of Sudan and Somali Bantu refugee groups [27, 28]. All refugees in these groups should receive presumptive treatment for schistosomiasis and strongyloidiasis. Both groups should be treated for schistosomiasis with praziquantel (40 mg/kg divided in 2 doses administered 6–8 h apart). For the Lost Boys and Girls of Sudan, strongyloidiasis should be treated with albendazole (400 mg twice per day for 7 days). Somali Bantu refugees should be treated for strongyloidiasis with ivermectin (200 µg/kg per day on 2 consecutive days). The recommendations for the treatment courses

### Table 2. Crude prevalence ratios of chronic abdominal pain according to schistosomiasis and strongyloidiasis test results, Lost Boys and Girls of Sudan, 2004.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Prevalence ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Schistosomiasis</td>
<td>0.97 (0.80–1.19)</td>
</tr>
<tr>
<td>Strongyloidias</td>
<td>0.98 (0.80–1.19)</td>
</tr>
<tr>
<td><em>Schistosoma</em> and <em>Strongyloides</em> coinfection</td>
<td>0.93 (0.73–1.19)</td>
</tr>
<tr>
<td>Either <em>Schistosoma</em> or <em>Strongyloides</em> infection</td>
<td>1.00 (0.81–1.24)</td>
</tr>
</tbody>
</table>
of albendazole and ivermectin represent increases in the duration of therapy from our original treatment recommendations; these changes are based on discussions with experts and published literature [29]. Ivermectin is preferred over albendazole for presumptive strongyloidiasis treatment in refugees in whom the diagnosis of L. loa can be excluded parasitologically or on the grounds of a lack of exposure. Because the Lost Boys and Girls of Sudan are at risk for L. loa infection, albendazole is the recommended therapy for presumptive treatment of strongyloidiasis in these individuals, unless blood smears examined in a reliable laboratory demonstrate an absence of L. loa microfilaraemia. The Somali Bantu refugees should also receive a single 600-mg dose of albendazole to treat intestinal helminths, such as hookworm, that are poorly responsive to ivermectin.

We recommend presumptive treatment rather than diagnostic testing before treatment, because of the high rates of active infection in these groups, the expense and limited availability of serologic tests, and the poor sensitivity of microscopic examination of stool and urine samples. These recommended treatment regimens are safe and relatively inexpensive. Physicians should be aware that these regimens may not cure all patients with these infections, and the possibility of persistent strongyloidiasis should be considered before administration of immunosuppressive therapy. In addition, when these regimens are administered, symptomatic reactions to dying schistosomes or to dying microfilariae may occur in persons who are coinfected with Onchocerca volvulus and other filariae [30].

Change in refugee policy. Expansion of this policy to include all refugees who are from, have traveled through, or are living in countries where schistosomiasis or strongyloidiasis is endemic should be considered. We recommend presumptive treatment before resettlement, given the logistics and cost of caring for refugees once they have dispersed in their new country. Indeed, our experience with the Lost Boys and Girls of Sudan demonstrated such difficulties: although we obtained contact information from each participant, after the reunion, we were able to locate only approximately one-half of those needing treatment. Consideration of this type of strategy has previously been suggested by other refugee health experts [31]. Although our study focused on refugees, nonrefugee immigrants from areas of endemicity with poor living conditions or other risk factors for Schistosoma or Strongyloides infection have much in common with refugees and would likely benefit from similar strategies.

Our presumptive treatment strategy seems to be cost-effective. In an analysis of approaches to intestinal nematode infections among immigrants, presumptive treatment with albendazole was more cost-effective than were watchful waiting or stool screening and treatment of infected persons [23]. The same cost-effectiveness model predicted superiority of presumptive treatment of Strongyloides infection when the prevalence exceeded 16%, even if the prevalence of all other intestinal helminths combined was 0%. A more recent study found that, if the prevalence of Strongyloides infection exceeds 2%, a presumptive treatment strategy is cost-effective [24]. Although these models examined different treatment and testing strategies than were used in our study and did not address schistosomiasis, they would support presumptive treatment on the basis of data from our study.

Limitations. There are limitations to our study. In addition to overestimates of the prevalence of schistosomiasis associated with the persistence of specific antibodies in persons who have had past infection, the prevalence of S. haematobium infection may have been underestimated in our investigation of the Lost Boys and Girls of Sudan, because, although the S. mansoni FAST-ELISA is 99% sensitive for S. mansoni infection, it is only 90% sensitive for S. haematobium infection [8, 9]. In contrast, all Somali Bantu refugees were tested with the S. mansoni FAST-ELISA and the S. haematobium immunoblot (sensitivity, 97%; specificity, 100% [10]), and the seroprevalence of 73% is a reasonable estimate of infection.

The Strongyloides EIA may have overestimated the prevalence of infection. Although the tests used in this investigation have demonstrated a sensitivity of 95% among stool-positive persons [6], evaluation of specificity indicated reactivity of serum specimens obtained from patients from areas of endemicity in whom a parasitological diagnosis of strongyloidiasis was not confirmed but infection with hookworm, Trichuris, Clonorchis, Paragonimus, or Filaria species was detected. In these cases, occult strongyloidiasis (i.e., infection without detectable larvae in stool samples) could not be ruled out; in fact, serum samples obtained from healthy control subjects from the United States have been found to be nonreactive by Strongyloides EIA (CDC, unpublished data).

Conclusions. In conclusion, a high percentage of Lost Boys and Girls of Sudan and Somali Bantu may harbor schistosomes and Strongyloides species after resettlement in the developed world. These groups should receive presumptive therapy to prevent future morbidity. Policies concerning refugees from other areas where schistosomiasis and strongyloidiasis are endemic should be reevaluated, with consideration toward implementing a presumptive treatment strategy.

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