

Schistosoma mansoni infection and nutritional status in schoolchildren: a randomized, double-blind trial in northeastern Brazil¹⁻³

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ABSTRACT Brazilian schoolchildren with mild- to moderate-intensity schistosome infections (<400 *Schistosoma mansoni* eggs/g stool) were randomly allocated to a treatment (oxamniquine) or placebo group in a double-blind fashion. Anthropometric measurements were made at baseline, 6 mo, and 1 y for 353 students. At baseline, the groups were not significantly different with respect to nutritional status or selected socioeconomic and biological characteristics, including anthropometric measures. One year later, significant differences were noted only in the nutritional status of boys treated for schistosome infection. Treated boys had greater measurements for weight, triceps skinfold thickness, midarm circumference, arm muscle area, and body mass index than untreated boys. They also showed significant increases over the year in weight, height, midarm circumference, and body mass index. The rates of improvement in weight and height were more accelerated in the first 6 mo after therapy than the last. These results indicate that, at least in boys, chronic *S. mansoni* infection at any intensity is detrimental to short-term growth and development. *Am J Clin Nutr* 1998;68:1247-53.

KEY WORDS *Schistosoma mansoni*, growth, sex, oxamniquine, morbidity, therapy, anthropometry, parasitic infection, schoolchildren

INTRODUCTION

Chronic infectious diseases, repeated episodes of acute infections, conditions of poverty, and inadequate dietary intakes are all associated with compromised growth and development of children ≤5 y of age in developing countries. In addition to conditions of poverty and deficient dietary intakes, older children in developing countries are frequently subject to infection with helminthic parasites that may further restrict their recovery from infant malnutrition (1). Estimates indicate that one-third of failure to reach optimal growth can be attributed to illness, especially diarrhea and parasitic infections, even when these infections are subclinical (2).

Infections with the parasites *Schistosoma mansoni*, *S. haematobium*, and *S. japonicum* are among the most prevalent and serious in the developing world (3). *S. haematobium* produces urinary obstruction, bladder cancer, and anemia whereas infection with *S. japonicum* can result in portal hypertension, pulmonary

hypertension, and epilepsy. The most widespread schistosome parasite, however, is *S. mansoni*. This parasite is responsible for disease throughout Africa and the Arabian Peninsula and it is the only human schistosome transmitted in the Americas. More people are infected with *S. mansoni* than with any other species. The most common severe pathologies caused by *S. mansoni* are hepatosplenomegaly, portal hypertension, and esophageal bleeding. In Egypt, bleeding from intestinal lesions accounts for some cases of severe anemia. In northeastern Brazil, severe morbidity generally correlates with the intensity of infection in adults (4) and in school-age children (5, 6). Only ≈10% of those infected, however, will develop clinically apparent pathology and will benefit from treatment on this basis. Most people infected carry light- and moderate-intensity infections, the effects of which are thought to be minimal or ill defined.

A few cross-sectional studies indicate that *S. mansoni* is associated with nutritional deficiencies in adults (7) and children (8-10). In a previous cross-sectional study in the northeastern Brazilian town of Nazaré, Bahia (10), we compared anthropometric indexes between infected schoolchildren and those who were uninfected. The nutritional status of the overall population studied showed a deficit relative to the US National Center for Health Statistics (NCHS) reference population. Children infected with *S. mansoni* were significantly more malnourished than children with a negative stool sample for several anthropometric variables. When the groups were analyzed according to sex, only the anthropometric differences between infected and uninfected girls remained significant. According to z scores, boys suffered significantly greater deficits than girls in all measures of growth and body composition, but no differences were observed between infected and uninfected boys except for smaller subscapular skinfold thicknesses in those infected. The failure to observe effects

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of schistosome infection on growth in boys was thought to be due to their relatively greater degree of malnutrition.

Only 2 prospective studies have examined the relation of schistosome infection to nutritional status by comparing growth of infected children randomly assigned to specific treatment or placebo groups. These studies investigated infections with *S. haematobium* (11) and *S. japonicum* (12), parasites that cause disease syndromes distinct from those of *S. mansoni*. No prospective, intervention study has thus far examined the nutritional consequences of *S. mansoni* infection. This study examined how treatment of light and moderate *S. mansoni* infections affected growth in school-age children in a South American population because there is now no clinical, epidemiologic, or ethical basis for not treating heavily infected children to prevent severe morbidity.

SUBJECTS AND METHODS

Study design and population sample

A randomized, placebo-controlled trial was conducted in schoolchildren (7–14 y old) from the town of Nazaré, state of Bahia, in northeastern Brazil. According to census data, the population of Nazaré was $\approx 25\,000$ in 1991, of whom 27% were aged 7–14 y (13). A campaign for the control of schistosomiasis by mass chemotherapy was conducted in 1988 when the prevalence of infection was $\approx 30\%$. Since then there have been no further mass treatments for this parasite. *S. mansoni* infection has been hyperendemic in the region around Nazaré for decades (14).

The study population was described in detail in an earlier publication (10). Exclusion criteria were as follows: 1) >400 *S. mansoni* eggs/g stool, 2) hematocrit <0.33 , 3) weight-for-age <-3 SDs of the NCHS standards, or 4) a history of convulsions. Children excluded under any of these criteria were not enrolled in the study but were referred to local health authorities for evaluation and treatment. In addition, those for whom a date of birth could not be confirmed were also excluded. The study period extended from November 1992 to December 1993. The protocol for this study was approved by the human research committees of the Federal University of Bahia School of Medicine and Case Western Reserve University School of Medicine. After hearing an oral presentation by the investigators on the etiology and health implications of *S. mansoni* infection as well as the objectives of the study, each parent or guardian was asked to allow his or her children to participate, and, if they agreed, to sign or mark an informed consent form.

Parasitologic examination

Capped plastic containers were labeled, numbered, and distributed to the schoolchildren by officials of the National Health Foundation (NHF). The NHF provided instruction on stool collection, collected the samples, and performed the parasitologic examinations. The Kato-Katz technique (15) was used to count the number of *S. mansoni* eggs/g stool and to identify the presence of other helminth eggs (principally *Ascaris lumbricoides* and *Trichuris trichiura*). Those children who were found to have *S. mansoni* eggs in their first stool sample were asked for 2 additional stool samples to confirm the intensity of infection. The identification of parasites and counting of *S. mansoni* eggs were checked in a sample of 10% of the slides by 2 senior laboratory technicians not involved with the study.

Randomization and treatment

All eligible children infected with *S. mansoni* were randomly assigned to treatment (oxamniquine) or placebo groups. Each child in the oxamniquine group received the medication in the form of a syrup (20 mg/kg). The placebo, prepared by a local pharmacist, consisted of a glucose-based syrup used in pharmaceutical preparations to which coloring had been added to mimic the color and consistency of the oxamniquine preparation. The placebo was placed in thoroughly washed bottles identical to those used for oxamniquine and both series of bottles were labeled with single letters by an individual not involved in the study. The placebo was administered in the same amounts as the oxamniquine. As is customary, the drug was distributed by officials of the NHF. None of the NHF officials, the investigators, or the children knew the identity of the treatments until the code was revealed at the end of the study. At the end of the 1-y follow-up, all infected children received a therapeutic dose of oxamniquine.

Anthropometric evaluation

The anthropometric measurements were carried out according to Weiner and Lourie (16), except that arm measurements were made on the right arm rather than the left because reference data are based on the right arm (17). All measurements were made at baseline and 6 and 12 mo after treatment. Measurements were taken in duplicate and the mean of 2 measurements was analyzed.

Weight was measured with electric scales (Filizola ID-1500 digital battery/electric scale; Indústria Filizola S/A, São Paulo, Brazil) donated by the National Institute of Nutrition of Brazil with 150-kg capacities, accurate to 100 g. All children were weighed in a standard hospital gown whose weight (200 g) was subtracted for the final net value. For measurement of height, a stadiometer (Ross Laboratories, Columbus, OH) was taped to a wall at the same location for each measurement. Triceps and subscapular skinfold-thickness measurements were obtained with Lange calipers (Beta Technology, Cambridge, MA). Midupper arm circumference was taken with a nonexpandable tape measure (Ross Laboratories). Scales and calipers were professionally calibrated before each measurement period.

Measurement technique was standardized to evaluate inter- and intraexaminer precision and reliability (18). Each examiner made 2 sets of measurements of 10 children who were not part of the study population. For the second set of measurements, the examiner was blind to the result from the first set and sufficient time had lapsed so that the second measurement was not influenced by the first. These 2 sets of measurements were compared for reproducibility. For reference, the measurements made by the examiners were compared against the measurements made by one of the authors (IP). The measurement precision ranged from 80% for triceps skinfold thickness to 100% for weight before data collection and 80% for triceps skinfold thickness to 98% for midupper arm circumference at the end of data collection. The measurements by the examiners were highly correlated; coefficients of correlation (r) ranged from 0.94 to 1.00 before data collection and from 0.80 to 1.00 after.

Socioeconomic survey

Source of drinking water, sewage and garbage disposal, and the possession of selected appliances were used as indicators of socioeconomic status for the study population. The socioeconomic survey was conducted on a subsample of 44.4% of schoolchildren selected randomly. The information was obtained



by observation or interview of the child's parent or guardian during a home visit by the authors.

Data analysis

Only the results from children with a complete data set were used for all analyses. In this study, the anthropometric variables of interest were the measurements of weight (kg), height (cm), triceps and subscapular skinfold thicknesses (mm), and midupper arm circumference (cm). In addition to these direct measurements, the following indexes were calculated: height-for-age (expressed as a *z* score), body mass index (weight/height²), arm muscle area calculated as recommended by the World Health Organization (19), and body fat reserves using the sum of both skinfold-thickness measurements. The computed anthropometric indexes were compared with those of the NCHS reference population (20).

Because the working hypothesis presumed a positive effect of treatment, a one-tailed *P* value ≤ 0.05 was used to determine statistical significance. For the terms of interaction and determination of significant differences between groups, a two-tailed *P* value was used. Sex-specific analyses of variance (ANOVAs) controlling for age were performed to compare the age-adjusted means of anthropometric variables. A nonparametric Mann-Whitney *U* test was used in cases in which the variances were not homogeneous. The anthropometric indexes were constructed by using EPINFO (21) and a program developed by one of the authors (IP) to calculate weight-for-height percentiles and *z* scores for children > 10 y of age. The other analyses were performed by using SPSS/PC+ (22).

To assess the magnitude and duration of the effects of treatment for the time periods from 0 to 6 mo and from 7 to 12 mo, the percentage increase for a given measure was calculated as follows:

$$100 \times \frac{(\text{mean measurement at time A} - \text{mean measurement at time B})}{\text{mean measurement at time B}} \quad (1)$$

where A is greater than B. The magnitude of change was calculated only for measurements that were found to differ significantly between treatment and placebo groups.

RESULTS

The results of the parasitologic examination of the whole community were reviewed in detail elsewhere (10). Baseline anthropometric measurements were obtained for 539 infected children. There were 50 (9.3%) children excluded from the randomization. Forty-nine had egg counts >400/g stool and one had a history of convulsions. No children were excluded because of a hematocrit value <0.33 or weight-for-age <-3 SDs of the NCHS standard. Thus, 489 infected schoolchildren were randomly assigned to treatment or placebo groups, and complete measurements at baseline, 6 mo, and 1 y were obtained for 353 (168 boys and 185 girls). Subjects were lost mainly because of migration to more economically advanced urban centers.

At the start of the study, the oxamniquine and placebo groups were not significantly different with respect to several socioeconomic characteristics as well as mean number of *S. mansoni* eggs/g stool and the presence of *A. lumbricoides* and *T. trichiura* eggs in stool (Table 1). They were also not significantly different with respect to anthropometric measurements and indexes. Despite losses during follow-up periods, all the socioeconomic

TABLE 1
Biological and socioeconomic characteristics of *Schistosoma mansoni*-infected children by treatment group¹

Characteristic	Oxamniquine (n = 168)	Placebo (n = 185)
Age (y) ²		
7-9	31	26
10-14	69	74
Sex		
Male	50	45
Female	50	55
Mean schistosome egg count ³	98 ³	87
<i>Tricharis trichiura</i> -infected children	79	77
<i>Ascaris lumbricoides</i> -infected children	77	77
Number of household members		
2-5	36	34
6-9	52	56
>9	12	10
Present in the household		
Electricity	96	95
Stove	92	92
Refrigerator	63	57
Television	71	68
Indoor toilet	80	77
Sewage disposal		
Public system	24	23
Pit	58	54
None	20	23
Water source		
Piped	51	38
Cistern	41	55
Other	9	8

¹There were no significant differences between the groups by chi-square test.

²Mean age of both groups was 11.2 y.

³Geometric mean number of eggs/g stool.

variables remained similar between the groups at 1 y. They differed significantly, however, with respect to prevalence and intensity of *S. mansoni* infection and anthropometric measurements. At 1 y after treatment, 62% of the oxamniquine group was negative for *S. mansoni* as compared with 30% of the placebo group. Of those infected, geometric mean egg counts were 93.7 ± 2.8 and 90.7 ± 2.8 /g stool, respectively, for those in the oxamniquine group and those receiving placebo.

A strong interaction was identified between treatment group and sex for several anthropometric indexes: triceps skinfold thickness ($P = 0.01$), subscapular skinfold thickness ($P = 0.01$), arm muscle area ($P = 0.01$), and body fat reserve ($P = 0.01$). Thus, the analyses of changes in growth were stratified by sex. Girls, who at the start of the study showed higher mean values than boys for most anthropometric indexes (10), did not show treatment-related differences in growth.

Within each sex, there were no significant differences in anthropometric measurements between the placebo and treatment groups at baseline (Table 2). After 1 y, the treated boys had greater measurements for weight ($P = 0.02$), triceps skinfold thickness ($P = 0.04$), midupper arm circumference ($P = 0.01$), arm muscle area ($P = 0.05$), and body mass index ($P = 0.02$) than the untreated boys. Furthermore, the 1-y increases in weight ($P < 0.01$), height ($P = 0.05$), midupper arm circumference ($P = 0.05$), and body mass index ($P = 0.02$) were significantly greater for the treated boys.

TABLE 2Changes in age-adjusted growth variables in schoolchildren treated and untreated for *Schistosoma mansoni* infection

Variable	Baseline		1 y		<i>P</i> ¹	1-y increment		<i>P</i>
	Treated	Placebo	Treated	Placebo		Treated	Placebo	
Weight (kg)								
Boys	30.6 ± 7.9 ²	30.1 ± 7.5 ³	34.2 ± 8.7	33.0 ± 8.4	0.02	3.7 ± 3.7	3.0 ± 1.9	<0.01
Girls	30.8 ± 7.8 ⁴	30.4 ± 7.9 ⁵	35.0 ± 9.1	34.6 ± 9.1	0.40	4.3 ± 2.3	4.2 ± 2.0	0.47
Height (cm)								
Boys	137.0 ± 12.9	136.5 ± 11.7	142.4 ± 13.6	141.4 ± 12.2	0.07	5.4 ± 1.9	5.0 ± 1.7	0.05 ⁶
Girls	136.1 ± 12.3	136.5 ± 11.3	141.7 ± 12.0	142.0 ± 11.0	0.28	5.6 ± 2.2	5.6 ± 2.0	0.44
Triceps skinfold thickness (mm)								
Boys	6.8 ± 1.7	6.5 ± 1.6	7.3 ± 2.3	6.8 ± 2.0	0.04	0.6 ± 1.3	0.3 ± 1.1	0.07
Girls	8.5 ± 2.3	8.3 ± 2.1	9.9 ± 3.3	9.7 ± 2.9	0.33	1.4 ± 1.9	1.4 ± 1.8	0.44
Subscapular skinfold thickness (mm)								
Boys	5.2 ± 1.1	5.1 ± 1.13	5.4 ± 1.0	5.4 ± 1.3	0.36	0.3 ± 0.7	0.3 ± 0.7	0.25
Girls	6.3 ± 1.8	6.1 ± 1.83	7.2 ± 2.5	6.9 ± 2.5	0.26	0.8 ± 1.3	0.8 ± 1.3	0.46
Midupper arm circumference (mm)								
Boys	19.1 ± 2.0	18.8 ± 2.0	20.0 ± 2.2	19.3 ± 3.0	0.01	0.9 ± 0.9	0.5 ± 0.7	0.05
Girls	19.3 ± 2.2	19.1 ± 2.1	20.5 ± 2.6	20.1 ± 2.5	0.12	1.2 ± 0.8	1.1 ± 0.7	0.11
Body fat reserve (mm)								
Boys	11.9 ± 2.6	11.5 ± 2.5	12.8 ± 3.0	12.2 ± 3.0	0.08	0.8 ± 1.8	0.6 ± 1.5	0.22
Girls	14.8 ± 3.8	14.4 ± 3.6	17.0 ± 5.6	16.6 ± 5.1	0.29	2.2 ± 2.9	2.2 ± 2.8	0.48
Arm muscle area (cm ²)								
Boys	23.2 ± 5.7	22.8 ± 5.5	25.2 ± 6.4	24.3 ± 7.1	0.05	1.9 ± 2.8	1.5 ± 3.1	0.10 ⁶
Girls	22.4 ± 5.0	21.9 ± 4.8	24.4 ± 5.4	23.6 ± 5.6	0.12	2.1 ± 2.0	1.7 ± 1.9	0.09
Body mass index (kg/m ²)								
Boys	16.1 ± 1.8	15.9 ± 1.5	16.6 ± 1.5	16.2 ± 1.7	0.02	0.6 ± 0.6	0.3 ± 0.6	0.02 ⁶
Girls	16.3 ± 1.8	16.0 ± 2.1	17.1 ± 2.3	16.9 ± 2.5	0.22	0.8 ± 0.9	0.8 ± 0.8	0.42 ⁶

¹ANOVA.² $\bar{x} \pm SD$; *n* = 89.³*n* = 79.⁴*n* = 89.⁵*n* = 96.⁶Mann-Whitney nonparametric *U* test.

At 6 mo, the boys treated with oxamniquine had greater increments for most of the anthropometric indicators than boys given placebo, but the differences were not significant. To determine how the improvement in growth was distributed over the 12-mo period, increases in weight, height, and midupper arm circumference were compared for the intervals from 0 to 6 mo and from 7 to 12 mo. For weight and height in the treated group, the magnitude of growth during the first 6 mo represented 64% and 62%, respectively, of the total net growth in 1 y (Figure 1). The magnitude of growth was nearly equal in the placebo group for the first and last 6 mo of the year. For midupper arm circumference

there was little change in the percentage increase in the treatment group, whereas the placebo group showed 66% of the net 12-mo increase in the first 6 mo.

DISCUSSION

This study is the first to show by means of a double-blind, placebo-controlled trial that *S. mansoni* infection contributes to the high prevalence of malnutrition in children in the developing world. In addition, the results presented here show that treatment of light- to moderate-intensity *S. mansoni* infection has a posi-

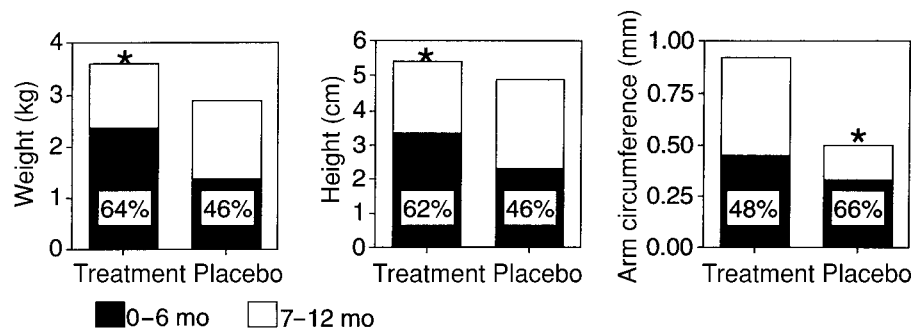


FIGURE 1. Age-adjusted increment in boys' growth during the first and second 6-mo interval after oxamniquine treatment for schistosome infection (*n* = 89) or placebo (*n* = 79). The percentage of total growth attained in the first 6 mo is shown. *Significant difference between the first and second 6-mo increment in growth, *P* = 0.04 (ANOVA).

tive effect on weight, height, midupper arm circumference, and body mass index in school-age boys. Thus, the infection is itself an obstacle to optimal growth. The improvement in nutritional status due to treatment occurred in 1 y. Because schistosome infection is chronic, its effect on growth is likely to be much greater when extended over what is often a 10-y period from infection to maturity.

Clear sex differences in the response to treatment were observed. In the previous cross-sectional study of the same population, a correlation between nutritional status and intensity of *S. mansoni* infection was observed for girls but not for boys (10). In contrast, treatment exerted a more pronounced effect on the growth of boys than girls. This finding may be related to the initially poorer nutritional status of boys compared with girls in this population. In a similar study on the relation of *S. haematobium* infection to growth, Stephenson et al (11) reported a more positive effect of treatment on those Kenyan students whose initial nutritional status was most compromised. A more rapid recovery of those most malnourished in response to improved economic or environmental conditions has also been observed in other settings (23, 24).

We did not measure an effect of treatment on height for the 2 groups of boys at 1 y ($P = 0.07$), although the increment in height was greater for the treatment group ($P = 0.05$). By contrast, both the mean weight and the 1-y increase were greater in the treatment group ($P = 0.02$ and < 0.01 , respectively). The better response of weight than height to treatment that we observed is consistent with the findings of Stephenson et al (11) after treatment of *S. haematobium* infection. Although these authors found that treatment produced significant improvement in various anthropometric measurements of subjects compared with the placebo group, no effect was observed for height. This may suggest the following:

- 1) It is physiologically more demanding to recover height (25), and these children consumed diets with low energy densities (MS Prado, unpublished observations, 1997).
- 2) Recovery of height depends on a prerequisite, adequate weight-for-age, as suggested by Golden (25).
- 3) Recovery of height is dependent on other risk factors not analyzed here, such as adequate intake of vitamin A (26, 27), zinc (28), or iron (29, 30).

The percentage increase in weight, height, and arm circumference over time indicates a major benefit of treatment for boys in the first 6 mo and a smaller degree of improvement thereafter. For weight and height, 64% and 62%, respectively, of the net increase at 1 y occurred in the first 6 mo after treatment (Figure 1). The placebo group obtained 46% of their total increase in weight and height in the first 6 mo. It is likely that the decline in the rate of improvement in part represents an accumulation of the confounding effects of reinfection on the treatment group. Although we were not able to examine the children's stools a few weeks after treatment, it is well documented that oxamniquine has a cure rate of 85% in Brazil (31). The 1-y reinfection rate, therefore, can be estimated at 15–20%. The absence of an adequate sewage system, the presence of susceptible snail species, and the use of contaminated bodies of water for fishing, recreation, and domestic activities produce high rates of reinfection (32) and would tend to decrease the effect of treatment over the 1-y follow-up period.

For midupper arm circumference, the increment at 1 y was greater for boys receiving treatment than for those receiving

placebo. In a comparison of the magnitudes of change over time, it appears that although the treatment group was maintaining their level of growth in arm circumference, the rate of increase for the placebo group actually declined. When differences in composition that influence arm circumference were compared, both measurements of fat (triceps skinfold thickness) and protein (arm muscle area) were significant at 1 y. Improvement in these independent factors with treatment may explain the difference in the rate and magnitude of increase in arm circumference over time compared with measurements of weight and height.

Note that the population studied here differed in several respects from those examined prospectively for the nutritional impact of *S. haematobium* (11) and *S. japonicum* infections (12). The Brazilian population in this region is a mixture of descendants of African, European, and indigenous peoples. Additionally, the study population contained only lightly and moderately infected children, unlike the study by McGarvey et al (12) in which some heavily infected children were included. At baseline, the Brazilian population had greater deficits in height-for-age (21%) and weight-for-age (13%), but had normal weight-for-height, indicating predominantly linear stunting due to chronic malnutrition. Anthropometric indexes for height and weight as well as gross measurements of midupper arm circumference and subscapular skinfold thickness were significantly lower for boys than for girls (10).

The severe forms of morbidity in schistosomiasis mansoni (eg, hepatic fibrosis and portal hypertension) result from the host's response to increasing numbers of eggs that lodge in tissues over a period of months or years. Therefore, the numbers of eggs in tissue (intensity of infection) and duration of infection generally correlate with severity of disease. For this reason, there is no consensus that all schistosome infections should be treated. One acceptable strategy for schistosomiasis control is to treat only the most heavily infected children, because they are responsible for most of the morbidity as well as transmission in a community, and to ignore light infections (33, 34). There are increasing indications, however, that even low- to moderate-intensity infections have deleterious effects on childhood nutritional status (9, 10, 35).


These early studies, however, were all based on a cross-sectional design. Double-blind, placebo-controlled treatment intervention allows the establishment of a cause and effect relation between infection and nutritional status (36). Stephenson et al (11) used this approach to show a causal relation between mild *S. haematobium* infection and impaired growth in Kenyan schoolchildren. Anthropometric measurements were compared between groups of school-age children 8 mo after they were randomly assigned to receive specific therapy or a placebo. The treatment group showed a 4% increase in the indexes of weight-for-age and weight-for-height, a 13% increase in percentage triceps skinfold thickness per age, and a 20% increase in subscapular skinfold thickness per age. A similar design was used by McGarvey et al (12) to show a link between malnutrition and *S. japonicum* infection. In the treated group, they found a greater improvement in hemoglobin concentrations and in the sum of the skinfold thicknesses. There has been no similar study for *S. mansoni* infection.

Praziquantel is the drug of choice for the treatment of *S. mansoni*, although its efficacy does not differ from that of oxamniquine in Brazil (37, 38). Treatment in this study was with oxamniquine because it is the drug used by the Brazilian Min-



istry of Health, and the results with oxamniquine were those typically expected. An advantage of oxamniquine for this study was that it does not affect parasites other than *S. mansoni* (39, 40). Because praziquantel has become cheaper than oxamniquine, the Brazilian government is now considering using praziquantel in their schistosome control program (ML Barreto, personal communication, 1997).

The analysis of the prevalence of the geohelminths *A. lumbricoides* and *T. trichiura* and their relation to nutritional status in this population was reported as part of a cross-sectional study (10). In this study, 67% of the population had *A. lumbricoides* infection, 64% had *T. trichiura* infection, and 79% had one infection or the other on examination of a single stool sample. A two-way ANOVA analyzing the effect of geohelminth infection on nutritional status showed that these infections were not independently associated with malnutrition. Although these geohelminths have been associated with growth deficits, recent studies have indicated no effect (41) or improved growth after treatment only in children <10 y of age (42). These findings are consistent with our previous observations in children aged 7–14 y. In this study, there were no significant differences in the prevalence of geohelminths between the groups after random assignment, and oxamniquine does not affect these parasites. No children were excluded for anemia; therefore, hookworm infections were not likely to be important in this population.

Achieving optimal growth is a worthwhile objective because growth serves as an accessible marker for the optimal development of multiple systems in the body. A failure to reach optimal growth is taken as an indicator of the presence of some stress on the organism and the potential for functional, behavioral, or biological impairment (43, 44). The findings in this study indicate that *S. mansoni* infection in schoolchildren even at low and moderate levels contributes to the burden of disease and is an obstacle to full development. 

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REFERENCES

1. The World Bank. World development report 1993: investing in health. New York: Oxford University Press, 1993.
2. Allen LH. Nutritional influences on linear growth: a general review. *Eur J Clin Nutr* 1994;48(suppl):S75–89.
3. WHO. Major parasitic infections: a global review. *World Health Stat Q* 1986;39:145–60.
4. Lehman JS, Mott KE, Morrow RH, Muniz TM, Boyer MH. The intensity and effects of infection with *Schistosoma mansoni* in a rural community in Northeast Brazil. *Am J Trop Med Hyg* 1976;25:285–94.
5. Barreto ML, Loureiro S. The effect of *Schistosoma mansoni* infection on child morbidity in the state of Bahia, Brazil. I. Analysis at the ecological level. *Rev Inst Med Trop Sao Paulo* 1984;26:230–5.
6. Barreto ML, Loureiro S, Melo AS, Anjos CFD. The effect of *Schistosoma mansoni* infection on child morbidity in the state of Bahia, Brazil. II. Analysis at the individual level. *Rev Inst Med Trop Sao Paulo* 1985;27:167–71.
7. Mikhail MM, Mansour MM. Complications of human schistosomiasis and their effect on levels of plasma copper, zinc and serum vitamin A. *Hum Nutr Clin Nutr* 1982;36C:289–96.
8. de Lima e Costa MF, Leite ML, Rocha RS, de Almeida Magalhães MH, Katz N. Anthropometric measures in relation to schistosomiasis mansoni and socioeconomic variables. *Int J Epidemiol* 1988;17:880–6.
9. Corbett EL, Butterworth AE, Fulford AJC, Ouma JH, Sturrock RF. Nutritional status of children with schistosomiasis mansoni in two different areas of Machakos district, Kenya. *Trans R Soc Trop Med Hyg* 1992;86:266–73.
10. Parraga IM, Assis AMO, Prado MS, et al. Gender differences in growth of school-aged children with schistosomiasis and geohelminth infection. *Am J Trop Med Hyg* 1996;55:150–6.
11. Stephenson LS, Latham MC, Kurz KM, Kinoti SN. Single dose metrifonate or praziquantel treatment in Kenyan children. II. Effects on growth in relation to *Schistosoma haematobium* and hookworm egg counts. *Am J Trop Med Hyg* 1989;41:445–53.
12. McGarvey ST, Aligui G, Graham KK, Peters P, Olds GR, Olveda R. Schistosomiasis japonica and childhood nutritional status in north-eastern Leyte, the Philippines: a randomized trial of praziquantel versus placebo. *Am J Trop Med Hyg* 1996;54:498–502.
13. FIBGE. Censo Demográfico-Bahia. (Demographic Census-Bahia.) Rio de Janeiro: Fundação Instituto Brasileiro de Geografia e Estatística, 1991 (in Portuguese).
14. Pellon AB, Teixeira I. Distribuição da esquistossomose mansônica no Brasil. (Distribution of schistosomiasis mansoni in Brazil.) Rio de Janeiro: Organização Sanitária, 1950 (in Portuguese).
15. Katz N, Chaves A, Pellegrino J. A simple device for quantitative determination of *S. mansoni* eggs in faeces examined by the thick-smear technique. *Rev Inst Med Trop Sao Paulo* 1972;14:397–400.
16. Weiner JS, Lourie JA. Human biology. A guide to field methods. Philadelphia: FA Davis Co, 1969.
17. Frisancho RA. Anthropometric standards for the assessment of growth and nutritional status. Ann Arbor, MI: The University of Michigan Press, 1993.
18. Lohman TG, Roche AF. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books, 1988.
19. WHO. Physical status: the use and interpretation of anthropometry. *World Health Organ Tech Rep Ser* 1996;452.
20. Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. *Am J Clin Nutr* 1979;32:607–29.
21. CDC. EPINFO. Anthropometric software package. 6.0 ed. Stone Mountain, GA: Centers for Disease Control, Division of Nutrition, CCDPHP, 1995.
22. Norusis MJ. SPSS-PC for the IBM PC/XT/AT. Chicago: SPSS, Inc, 1986.
23. Bielicki T, Charzewski J. Sex difference in the magnitude of statural gains of offspring over parents. *Hum Biol* 1977;49:265–77.
24. Bielicki T. Growth and economic well-being: 20th century. Human growth: a comprehensive treatise. New York: Plenum Press, 1986.
25. Golden MHN. Is complete catch-up possible for stunted malnourished children? *Eur J Clin Nutr* 1994;48:S58–71.
26. Assis AMO. Suplementação com vitamina A e crescimento pondó-estatural em crianças. (Vitamin A and morbidity in NE Brazil). PhD thesis. Federal University of Bahia, Salvador, Brazil, 1996 (in Portuguese).
27. Sommer A, West KP. Vitamin A deficiency: health, survival and vision. New York: Oxford University Press, 1996.
28. Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lönnerdal B, Stekel A. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 1992; 56:491–8.
29. Chwang LC, Soemantri AG, Pollitt E. Iron supplementation and physical growth of rural Indonesian children. *Am J Clin Nutr* 1988; 47:496–501.
30. Latham MC, Stephenson LS, Kinoti SN. Improvements in growth following iron supplementation in young Kenyan school children. *Nutrition* 1990;6:159–65.

31. Katz N, Rocha RS, de Souza CP, et al. Efficacy of alternating therapy with oxamniquine and praziquantel to treat *Schistosoma mansoni* in children following failure of first treatment. *Am J Trop Med Hyg* 1991;44:509–12.
32. Barreto ML. Geographical and socioeconomic factors associated with the distribution of *Schistosoma mansoni* in an urban area in north-east Brazil. *Bull World Health Organ* 1991;69:93–102.
33. Klotzel K. “Selective” chemotherapy for schistosomiasis mansoni. *Trans R Soc Trop Med Hyg* 1974;69:344.
34. Mahmoud AAF, Wahab MFA. Schistosomiasis. Tropical and geographical medicine. 2nd ed. New York: McGraw-Hill, 1990.
35. McGarvey ST, Aligui G, Daniel BL, Peters P, Olveda R, Olds GR. Child growth and schistosomiasis japonica in northeastern Leyte, the Philippines: cross-sectional results. *Am J Trop Med Hyg* 1992;46:571–81.
36. Margetts BM, Rouse IL. Experimental studies. Design concepts in nutritional epidemiology. Oxford, United Kingdom: Oxford University Press, 1991.
37. Cioli D, Pica-Mattocchia L, Archer S. Antischistosomal drugs: past, present...and future? *Pharmacol Ther* 1995;68:35–85.
38. Stelma FF, Sall S, Daff B, Sow S, Niang M, Gryseels B. Oxamniquine cures *Schistosoma mansoni* infection in a focus in which cure rates with praziquantel are unusually low. *J Infect Dis* 1997;176:304–7.
39. Webster LT. Update on chemotherapy of schistosomiasis. In: Mahmoud AAF, ed. Baillière’s clinical tropical medicine and communicable diseases. Schistosomiasis. Vol 2. London: Baillière Tindall, 1987:435–47.
40. Taddese K, Zein ZA. Comparison between the efficacy of oxamniquine and praziquantel in the treatment of *Schistosoma mansoni* infections on a sugar estate in Ethiopia. *Ann Trop Med Parasitol* 1988;82:175–80.
41. Kightlinger LK, Seed JR, Kightlinger MB. *Ascaris lumbricoides* aggregation in relation to child growth status, delayed cutaneous hypersensitivity, and plant anthelmintic use in Madagascar. *J Parasitol* 1996;82:25–33.
42. Stolfus RJ, Albonico M, Tielsch JM, Chwaya HM, Savioli L. School-based deworming program yields small improvement in growth of Zanzibari school children after one year. *J Nutr* 1997;127:2187–93.
43. Matorell R, Rivera J, Kaplowitz H, Pollitt E. Long-term consequences of growth retardation during early childhood. Human growth: basic and clinical aspects. Amsterdam: Elsevier Science Publishers, 1992.
44. Waterlow JC. Protein energy malnutrition. London: Edward Arnold, 1992.

