

Community and International Nutrition

School-Based Deworming Program Yields Small Improvement in Growth of Zanzibari School Children after One Year^{1,2,3}

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ABSTRACT Efficacy trials of antihelminthic therapies conducted in Africa have reported improvements in children's growth, but nutritional evaluations of large-scale deworming programs are lacking. We evaluated the first-year effect on growth of a school-based deworming program in Zanzibar, where growth retardation occurs in school children. Children in four primary schools were given thrice-yearly mebendazole (500 mg) and compared with children in four schools that received twice-yearly mebendazole and children in four non-program schools. Evaluation schools were randomly selected and allocated to control, twice-yearly or thrice-yearly deworming. Approximately 1000 children in each program group completed the 1-y follow-up. Children <10 y old gained 0.27 kg more weight ($P < 0.05$) and 0.13 cm more height ($P = 0.20$) in the twice-yearly group, and 0.20 kg more weight ($P = 0.07$) and 0.30 cm more height ($P < 0.01$) in the thrice-yearly group, compared with the control group. Children <10 y old with higher heights-for-age at baseline had higher weight and height gains in response to deworming. In children ≥ 10 y old, overall program effects on height or weight gains were not significant. But in this age range, younger boys had significant improvements in height gain with thrice-yearly deworming, and children with higher heights-for-age had greater improvements in weight gain with deworming. We conclude that the deworming program improved the growth of school children, especially children who were younger and less stunted, but the improvements were small. More effective antihelminthic regimens or additional dietary or disease control interventions may be needed to substantially improve the growth of school children in areas such as Zanzibar. *J. Nutr.* 127: 2187–2193, 1997.

KEY WORDS: • humans • Africa • growth • geohelminths • hookworms

School-based deworming has been advocated as a highly cost-effective public health measure in less-developed countries (World Bank 1993). It is estimated that over 1 billion people are infected with *Ascaris lumbricoides*, 880 million with hookworms, and 770 million with *Trichuris trichiura* (Warren et al. 1993), and school children are the group most heavily infected with these geohelminths (Savioli et al. 1992). The expected benefits from deworming in this age group are improved school participation and performance, growth and iron status (Warren et al. 1993).

Improved growth of primary school children could result in greater adult height, which is associated with greater work capacity in men and women and with improved reproductive

outcomes in women (WHO Expert Committee 1995). We previously published evidence that Zanzibari school children experience significant linear growth retardation compared with international growth references (Stoltzfus et al. 1997a). Because helminth infections are highly prevalent in Zanzibar, the growth of school children might be improved if helminth infections were controlled.

Several efficacy trials of antihelminthic therapies in school children have produced promising results (Kruger et al. 1996, Latham et al. 1990, Stephenson et al. 1989, 1993a and 1993b), especially in coastal East Africa, where helminth infections are prevalent and intense. In these controlled randomized trials, growth, appetite, fitness and iron status improved in children treated with antihelminthic drugs. However, evidence is lacking in the literature on the program effectiveness of large-scale school-based deworming efforts.

We report here the results of an evaluation of a school-based deworming program implemented by the Ministries of Health and Education of Zanzibar on Pemba Island. The evaluation measured the effect of the program on helminth infections, nutritional status and school attendance and compared the effects of two deworming schedules, twice-yearly and

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thrice-yearly. A single 500-mg dose of generic mebendazole was chosen as the anthelmintic treatment because of its simplicity and low cost (US\$0.027 per dose, Albonico et al. 1994). We describe the effect of twice-yearly and thrice-yearly deworming on the height and weight gains of primary school children in Zanzibar.

METHODS

The school-based deworming program. The Zanzibar school-based deworming program began in 1994 on Pemba Island, the smaller of the two islands of Zanzibar, a part of the United Republic of Tanzania. From 1988 to 1992, a school-based "test-and-treat" program was conducted on Pemba Island for the control of urinary schistosomiasis (Renganathan et al. 1995). This program had been implemented by the Pemba Island Helminth Control Team, a unit of the Ministry of Health, in cooperation with the Ministry of Education and local school teachers. Surveys conducted by the Helminth Control Team showed that geohelminth infections were also highly prevalent throughout Pemba (Renganathan et al. 1995). Building on the success of the test-and-treat campaign for schistosomiasis, a school-based deworming program to control intestinal parasites was planned.

On the basis of a trial of anthelmintic drugs conducted in Pemba (Albonico et al. 1994), a single 500-mg dose of generic mebendazole was chosen as the regimen to be used in the program. Although mebendazole did not control hookworm infection as well as albendazole, its effect on *A. lumbricoides* and *T. trichiura* infections was similar to that of albendazole, and the cost of mebendazole was around 10% the cost of albendazole at that time. A thrice-yearly regimen was chosen because of the rapidity of reinfection with helminth infections (Albonico et al. 1995) and the limited efficacy of mebendazole against *T. trichiura* and the hookworms.

Design of the program evaluation. Because the deworming program was planned to be extended to Zanzibar Island and sustained for the indefinite future, a controlled evaluation of its effect was justified, even though this meant delaying the start of the program in a small number of schools. Also, a twice-yearly deworming regimen was evaluated along with the thrice-yearly regimen of choice, to provide evidence to the Ministry of Health as to whether a twice-yearly regimen would be adequate to improve nutrition outcomes and school attendance. The evaluation was planned before the start of the deworming program in any school so that an optimal research design could be implemented.

Of the 72 public primary schools on Pemba Island, 12 schools were randomly selected for evaluation (Fig. 1). Pemba is divided into four districts of roughly equal size, and the selection of schools was stratified by district, so that three schools in each district were chosen. Within districts, the schools were randomly allocated to the control, twice-yearly or thrice-yearly group. All children within a school received the same program regimen. For logistical reasons, only morning classes were selected for the survey. Although the deworming program was administered to all classes of grades 1–5, only classes of grades 1–4 were included in the evaluation of nutritional effect, because malnutrition was expected to be of greatest importance in younger children. Grades 1 and 2 were deliberately overrepresented for the same reason.

Baseline, 6-mo and 12-mo follow-up nutrition and parasitology surveys were conducted in March–May 1994, October–November 1994 and March–May 1995, respectively. The design was based on the comparison of within-individual changes in children's nutritional status from baseline to 12 mo in each treated group vs. the placebo group, and these are the analyses presented in this article. The 6-mo follow-up survey was planned to provide an interim measure of program effect for evaluation of whether a nontreated group could be maintained ethically. The full battery of assessments was not completed at 6 mo, and those data are not presented here. A sample size of 1000 children per group was estimated to be sufficient to compare the twice-yearly and thrice-yearly program groups with the control group, accounting for the design effect of randomizing at the school level and planning for subgroup analyses.

Before the study began, meetings were held at each school to inform parents of the deworming regimen that would be implemented

in their school, the purpose of the evaluation, its risks and benefits, and alternatives to participation in the surveys. All children present in school on survey days were invited to participate in each survey. Children found to have hemoglobin <70 g/L (3.5% of children) were treated with mebendazole and oral iron supplements. Inclusion or exclusion of these children did not affect the growth results, and they are included in the analyses presented here. Overall, 91% of children listed on teachers' class registers participated in the baseline survey, and 85% of those children were assessed again at the 12-mo follow-up, in the following school year (Fig. 1). Compared with children who completed the study, those lost to follow-up were similar in all measured characteristics except that they were more likely to be boys (60.0% vs. 50.3%, $P < 0.001$) and less likely to be stunted (height-for-age Z-score < -2, 42.1 vs. 48.6%, $P < 0.005$). Both of these characteristics were associated with greater growth effect from deworming (see Results); thus, any bias caused by loss to follow-up would act to diminish the effect that we measured. The study was approved by the institutional review boards of The Johns Hopkins University, the World Health Organization and the Ministry of Health of Zanzibar.

Nutritional and parasitologic assessments. Nutritional assessment methods have been described in greater detail elsewhere (Stoltzfus et al. 1997a and 1997b) but are briefly reported here. Children's weights were measured to the nearest 0.1 kg using a battery-powered digital scale (Seca Inc., Columbia, MD), and heights were measured to the nearest 0.1 cm using a wooden stadiometer (Shorr Productions Inc., Olney, MD). Children were lightly clothed and shoes were removed. Age was calculated from the birth date on school records. When this was missing, the child's self-reported age was used. A venous blood sample was drawn to assess micronutrient status. Hemoglobin was determined using the HemoCue method (HemoCue AB, Angelholm, Sweden), and erythrocyte protoporphyrin was determined using a fluorometer (Aviv Biomedical, Lakewood, NJ). Serum ferritin was determined using an immunoassay (DELFI System by Wallac Inc., Gaithersburg, MD).

Parasitological methods are described in greater detail elsewhere (Stoltzfus et al. 1997b), and are briefly recounted here. Stool containers were given to children on the day before the survey, and they were instructed to bring a sample of their stool to school the next day. About 95% of children returned stool samples in each survey. Quantitative counts of helminth eggs in feces were determined by the Kato-Katz method (WHO 1994). Urine samples were collected from 100% of children. Microhematuria was determined using Hemastix test strips (Ames Laboratories, Elkhart, IN) and was used as a proxy indicator of urinary schistosomiasis (Savioli et al. 1990). Thick and thin blood films were stained with giemsa, and malaria parasites were counted against leukocytes using standard methods (WHO 1991).

Data analysis. The study was designed to detect differences in the twice-yearly or thrice-yearly treated group compared with the placebo group; however, our sample size was not designed to detect differences in effect between twice-yearly and thrice-yearly deworming. Thus we present statistical tests of these two comparisons, rather than comparisons among the three groups.

First, baseline characteristics of the treatment groups and the placebo group were compared using simple linear regression. Characteristics that differed to a potentially biologically important degree were controlled for in subsequent tests of program effect.

The measures of program effect on growth were the 12-mo weight and height increments for each child. All analyses were performed at the individual level and were adjusted for within-school correlations using the generalized estimating equations approach (Diggle et al.). Some baseline characteristics of children in the three program groups differed at baseline (Table 1). Thus, the overall 1-y program effects on weight and height increments of children in twice-yearly and thrice-yearly dewormed schools were compared with those in control schools, using multiple linear regression to adjust for characteristics that differed at baseline.

Given the heterogeneity of school children, we expected that some subgroups of children would benefit more from deworming than others. Multiple linear regression models with program group interaction terms were used to test whether program effects were greater in children with certain baseline characteristics. Baseline characteristics

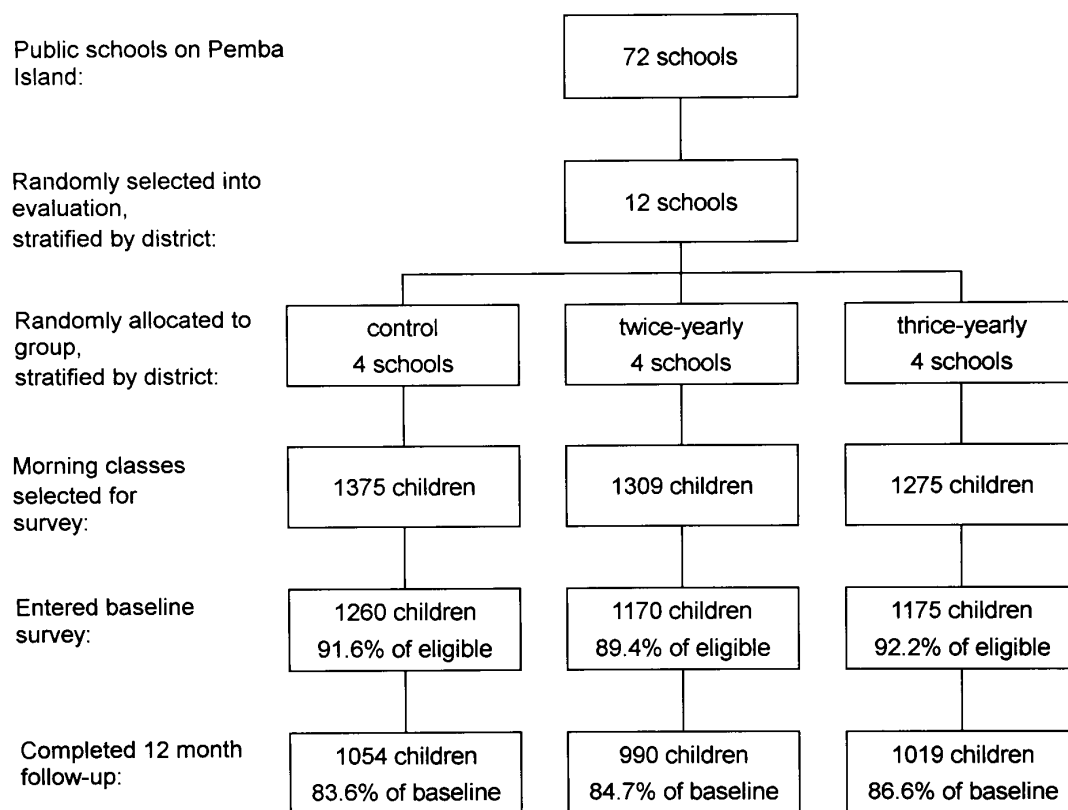


FIGURE 1 Schema of research design, including numbers of children in each program group at each step of the evaluation.

associated with greater benefit from the program are termed predictors of benefit. Interactions with program group were considered potentially important if they were significant at P levels <0.15 and if they were consistent in both program groups.

Analyses were conducted separately for children <10 y and ≥ 10 y of age, to separate the effects on pre-pubertal and pubertal growth. Sexual maturation was not assessed. Height-for-age Z-scores were determined using the anthropometric subroutines of EpiInfo, version 6 (Centers for Disease Control and Prevention, Atlanta, GA). Weight-for-height Z-scores and body mass index [BMI, weight (kg)/height² (m²)] percentiles were considered as indicators of thinness. Body mass index is presented here because it is recommended for assessing children >10 y of age, whereas weight-for-height Z-score is not (WHO Expert Committee 1995), and there are no recommendations for assessing thinness in children 6–10 y old. The BMI percentiles were defined by the sex and race-specific tables of Must et al. (1991a and 1991b). Analyses were performed using Systat (SPSS, Chicago, IL) and SAS (SAS Institute, Carey, NC) statistical software.

RESULTS

Baseline characteristics of the study sample. The study sample was composed about equally of boys and girls, whose average age was 10 y (Table 1). Helminth infections were nearly universal. Around 95% of children were infected with hookworms and *T. trichiura*, and about two-thirds were infected with *A. lumbricoides*. Around 60% had circulating malaria parasites and about one-third had microhematuria, an indication of urinary schistosomiasis. Stunting and low BMI were common and increased with age. The iron status of the population was very poor. The prevalence of anemia (hemoglobin <110 g/L) was 62.3%, and 82.7% of anemia was associated with iron deficiency (protoporphyrin >90 $\mu\text{mol/mol}$ heme or serum ferritin <18 $\mu\text{g/L}$) (Stoltzfus et al. 1997b).

There were several significant differences among the three program groups at baseline (Table 1). This is not surprising, because only 12 schools were randomly allocated. Both program groups had more hookworm and *T. trichiura* infection than the control group, but the twice-yearly group had less *A. lumbricoides* infection than the other groups. In terms of anthropometry, the twice-yearly group was less stunted than the other two groups at baseline.

Program effect on helminth infections. There was a clear dose response with frequency of deworming on all three helminths (Table 2). Ascariasis was effectively controlled, but hookworms and *T. trichiura* were controlled less well. These deworming regimens reduced the intensity of *T. trichiura* and hookworm infections but had little effect on the prevalence of infection.

Overall program effect on growth. Adjusted for baseline characteristics, the 12-mo weight gains were ~ 2 kg for children <10 y old and 3 kg for children ≥ 10 y old (Table 3). In children <10 y old, the twice-yearly group had weight gains 0.27 kg greater than those of the control group ($P < 0.05$). The thrice-yearly group had weight gains 0.20 kg greater than those of the control group, but this difference was not significant ($P = 0.07$). There were no significant program effects on weight gains in children ≥ 10 y of age. In children <10 y old, the 12-mo height gains in the thrice-yearly group were 0.30 cm greater than in the control group ($P < 0.01$). In children ≥ 10 y of age, there was no significant program effect on height.

Predictors of benefit. As expected, children with certain characteristics had a greater growth response to deworming. Among children <10 y old, the degree of stunting was the only predictor of benefit (Fig. 2). Children who had higher height-for-age Z-scores at baseline benefited more from deworming. On the basis of the multiple regression model with

TABLE 1

Baseline characteristics of study children by program group¹

Characteristic	Program group		
	Control	Twice-yearly deworming	Thrice-yearly deworming
	(n = 1054)	(n = 990)	(n = 1019)
Male sex, %	51.2	50.4	49.4
Age, y	10.5 ± 1.8	10.7 ± 1.8*	10.5 ± 1.8
Hookworms			
Infected, %	91.2	94.5*	95.8*
Eggs/g feces	332 (48, 2304)	505 (73, 3458)*	601 (86, 4204)*
<i>T. trichiuria</i>			
Infected, %	94.7	96.7*	97.3*
Eggs/g feces	531 (95, 2949)	577 (104, 3186)	625 (115, 3398)
<i>A. lumbricoides</i>			
Infected, %	73.0	66.5*	76.4
Eggs/g feces	239 (7, 8642)	149 (4, 5307)*	335 (9, 11,959)
Malaria parasitemia, %	57.3	57.0	65.6*
<i>S. haematobium</i> , %	31.9	21.3*	39.5*
Age <10 y	(n = 473)	(n = 442)	(n = 476)
HAZ	-1.44 ± 1.30	-1.21 ± 1.30*	-1.44 ± 1.31
HAZ < -2, %	30.7	26.0	36.1
BMI	14.4 ± 1.2	14.3 ± 1.2	14.4 ± 1.2
BMI < 5th centile, %	22.6	22.1	21.9
Age ≥10 y	(n = 581)	(n = 548)	(n = 543)
HAZ	-2.33 ± 1.25	-2.24 ± 1.24	-2.44 ± 1.24
HAZ, < -2, %	64.0	59.6	66.3
BMI	14.8 ± 1.4	15.1 ± 1.4*	15.0 ± 1.4
BMI < 5th centile, %	48.9	48.4	43.5

¹ Values are means ± SD. For measures of eggs per gram of feces, values are geometric means (-1 SD, +1 SD); zero values were included, with log-transformed values defined as zero. * Significantly different from corresponding value for the control group ($P < 0.05$). HAZ = height-for-age Z-score, BMI = body mass index (kg/m²).

height-for-age Z-score as a continuous variable, children with height-for-age $Z = 0$ gained 0.44 kg and 0.39 cm more in the twice-yearly group and 0.46 kg and 0.51 cm more in the thrice-yearly group than children in the control group (all comparisons to control group, $P < 0.005$). In children with height-for-age $Z = -2$, the only benefit was 0.23 cm greater height

gain in the thrice-yearly group compared with the control group ($P < 0.05$).

Among children ≥ 10 y old, shortness-for-age again predicted weight gain from deworming (Fig. 3). Children who were less stunted (higher height-for-age Z-score) at baseline gained more weight in response to deworming. Also, in this age group, age and sex predicted height gain from deworming. Girls grew less than boys in response to deworming, and the growth response was greatest in younger boys. Ten-year-old boys gained 0.31 cm more in the twice-yearly group ($P < 0.020$) and 0.49 cm more in the thrice-yearly group ($P < 0.025$) compared with the control group.

The presence or intensity of the three geohelminth infections at baseline did not predict benefit from the deworming program for either weight or height gain, nor did iron deficiency or anemia.

TABLE 2

Prevalence and intensity of helminth infections by program group at 12-mo follow-up survey

	Program group ¹		
	Control	Twice-yearly deworming	Thrice-yearly deworming
<i>A. lumbricoides</i>			
Prevalence, %	84	58	38
Eggs/g feces	653 (25, 17,367)	54 (2, 1433)	10 (0, 289)
<i>T. trichiura</i>			
Prevalence, %	97	92	85
Eggs/g feces	788 (96, 6449)	340 (41, 2633)	147 (19, 1256)
Hookworms			
Prevalence, %	96	89	88
Eggs/g feces	778 (94, 6728)	329 (41, 2826)	262 (30, 2044)

¹ Samples sizes per group given in Figure 1. All values for twice-yearly and thrice-yearly groups differ significantly from corresponding values for the control group ($P < 0.05$). For measures of eggs per gram of feces, values are geometric means (+1 SD, -1 SD); zero values were included, with log-transformed values defined as zero.

DISCUSSION

This evaluation provides strong evidence that the school-based deworming program improved the growth of school children. The pre-post design of the evaluation, the comparison between randomly allocated program and control schools, and statistical adjustment for the differences in baseline characteristics among groups enable us to conclude that periodic anti-helminthic treatment caused greater height and weight gains among children participating in the deworming program.

The fact that control of helminth infections improved the linear growth of children <10 y old also provides support for our previous inference that Zanzibari children experience lin-

TABLE 3

Overall adjusted 12-mo growth increments in children in control, twice-yearly or thrice-yearly deworming program schools

	Program group ¹		
	Control	Twice-yearly deworming	Thrice-yearly deworming
Weight gain, kg			
Age <10 y ²	2.11 ± 0.08	2.38 ± 0.08*	2.31 ± 0.08
Age ≥10 y ³	3.01 ± 0.11	3.20 ± 0.12	3.04 ± 0.12
Height gain, cm			
Age <10 y ⁴	4.29 ± 0.07	4.42 ± 0.07	4.59 ± 0.07**
Age ≥10 y ³	4.74 ± 0.08	4.67 ± 0.08	4.81 ± 0.08

¹ Samples sizes per group are given in Figure 1. Values are means ± SEM. * Significantly different from corresponding value for the control group ($P < 0.05$). ** Significantly different from corresponding value for the control group ($P < 0.01$).

² Adjusted for district, sex, age, and height-for-age Z-score.

³ Adjusted for district, sex, age, height-for-age Z-score, and low body mass index.

⁴ Adjusted for district, sex, height-for-age Z-score and low body mass index.

ear growth retardation during their early school years (Stoltzfus et al. 1997a). If these children were achieving their genetic potential for linear growth in the absence of intervention, then antihelminthic treatment would not have increased their rate of linear growth.

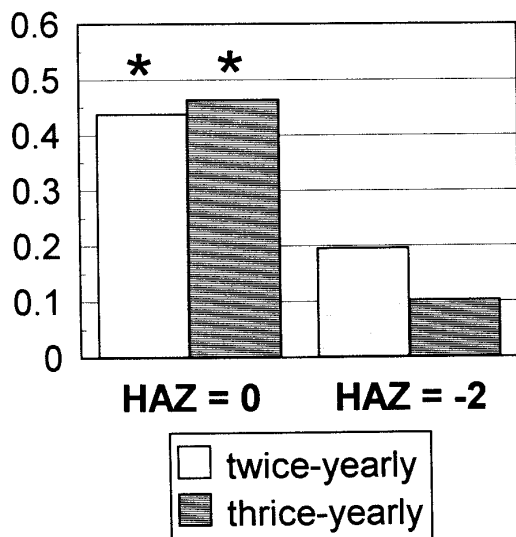
However, the magnitude of the growth response to deworming was small. This can be illustrated in several ways. In children <10 y of age, the growth responses in the thrice-yearly program group were 0.2 kg/y and 0.3 cm/y. Compared with the control group gains, these represent improvements of 10%

in weight and 7% in height. The largest height responses to deworming, seen in less stunted children receiving thrice-yearly deworming, were around 0.5 cm/y, or 12% of control height gains. These gains do not bring the growth of Zanzibari school children in line with the international growth reference. An average 9-y-old child tracking at the median of the WHO reference for height would gain 3.7 kg/y and 5.7 cm/y (average of values for boys and girls, from WHO 1983).

Because Zanzibari children will benefit from the school-based deworming program throughout their primary school years, the effect on growth has a long period of time to accumulate. If children gained an extra 0.3 cm/y from the thrice-yearly deworming program, over a 5-y period they might accumulate a height benefit of 1.5 cm. For an 11-y-old boy, this represents an improvement in height-for-age of 0.22 Z-scores (WHO 1983). Even the largest height benefit we observed in a subgroup, 0.5 cm/y, would mean an improvement of only 0.37 Z-scores if sustained over a 5-y period.

A series of smaller randomized placebo-controlled efficacy trials conducted in Kenya, where the epidemiology of geohelminths is very similar to that in Zanzibar, found larger growth responses to antihelminthic treatment than we did. A single 400-mg dose of albendazole improved height gains by 0.6 cm and weight gains by 1.3 kg in a 6-mo trial in 150 first and second graders (Stephenson et al. 1989). Treatment with mebendazole (which treats both hookworms and *S. haematobium*) or praziquantel (which treats only *S. haematobium*) improved height gains by 0.2 cm in a 5-wk trial in 48 pre-pubescent boys infected with both parasites (Latham et al. 1990). A single 600-mg dose of albendazole improved height gains by 0.6 cm and weight gains by 1.0 kg in 53 boys after 4 mo (Stephenson et al. 1993b). However, those boys were part of a larger trial comparing one dose of albendazole in a 8-mo period to two 4-mo doses in 284 boys and girls (Stephenson et al. 1993a). In the larger and longer trial, weight gains improved by 1.0 kg, but there was no effect on height gains.

Additional weight gain (kg)



Additional height gain (cm)

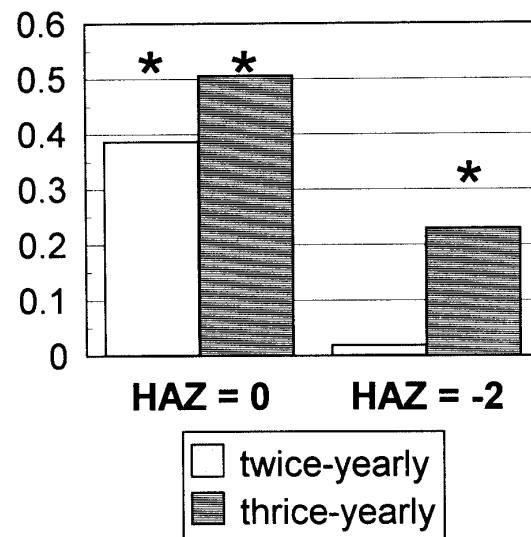
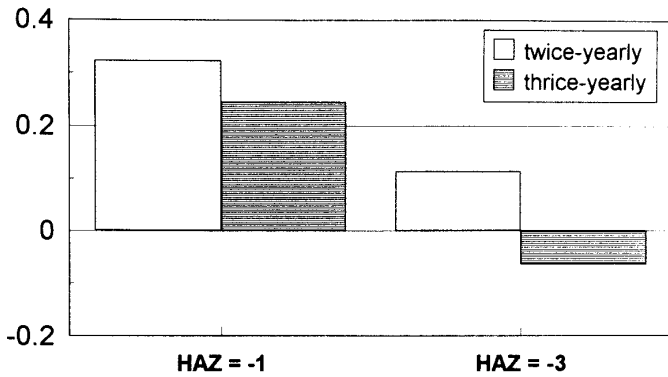


FIGURE 2 Effects of twice-yearly or thrice-yearly deworming on 12-mo weight and height gains of children <10 y of age, according to height-for-age Z-score (HAZ) at baseline. The y-axis represents the average additional height or weight gain associated with being in the twice-yearly or thrice-yearly dewormed groups compared with the control group, adjusted for sex, age and district. Asterisks indicate weight or height gains that are significantly different ($P < 0.05$) from control group gains at the indicated HAZ value. Interaction between HAZ and program group on weight was significant at $P = 0.047$ for twice-yearly deworming and at $P = 0.005$ for thrice-yearly deworming. Interaction between HAZ and program group on height was significant at $P = 0.008$ for twice-yearly deworming and at $P = 0.041$ for thrice-yearly deworming. Sample sizes per group are given in Figure 1.

Additional weight gain (kg)



Additional height gain (cm)

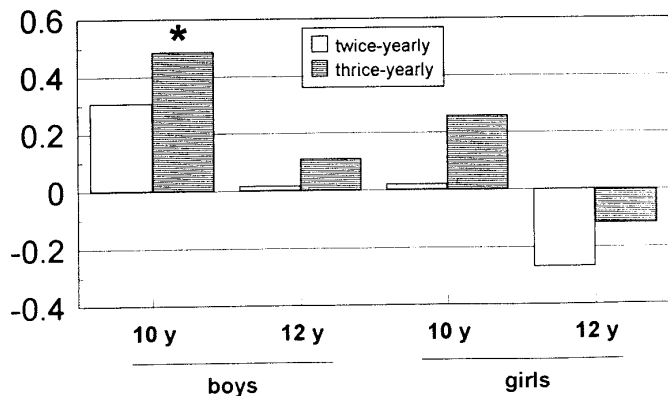


FIGURE 3 Effect of twice-yearly or thrice-yearly deworming on 12-mo weight and height gains of children ≥ 10 y of age, by baseline characteristics. The y-axis represents the average additional height or weight gain associated with being in the twice-yearly or thrice-yearly dewormed groups compared with the control group, adjusted for sex, age and district. Asterisks indicate weight or height gains that are significantly different ($P < 0.05$) from control group gains at the values indicated on the x-axis. HAZ = height-for-age Z-score. Interaction between HAZ and program group on weight was significant at $P = 0.02$ for twice-yearly deworming and at $P = 0.12$ for thrice-yearly deworming. Interaction between age and program group on height was significant at $P = 0.0001$ for twice-yearly deworming and at $P = 0.002$ for thrice-yearly deworming. Interaction between sex and program group on height was significant at $P = 0.11$ for twice-yearly deworming and was not significant ($P = 0.30$) for thrice-yearly deworming. Samples sizes per group are given in Figure 1.

There are several possible reasons why the growth effect we observed was small. First, there might be other factors limiting the growth of these children in addition to helminth infections, i.e., helminth control is necessary but not sufficient to improve substantially the growth of Zanzibari school children. This explanation is supported by the consistent finding that less stunted children had the greatest growth response to deworming. This effect modification was apparent in both program groups for height and weight gains of children < 10 y of age and for weight gains of children ≥ 10 y of age. If helminth infection were the only factor holding back the linear growth of children, then we would expect to see the most stunted children having the greatest growth response to antihelminthic treatment. We found the op-

posite to be true, which is consistent with the idea that something in addition to geohelminth infections is slowing the growth of stunted children.

Under conditions found in areas such as Zanzibar, additional zinc or iron may be needed for children to achieve normal growth. A potential role of vitamin A deficiency can be ruled out, because the serum retinol distribution of first-graders in this sample was nearly identical to that of children in the United States (data not shown). These children were significantly iron deficient (Stoltzfus et al. 1997b), and iron supplementation improved the growth of Kenyan school children (Lawless et al. 1994). We have not evaluated zinc status in this population, but zinc deficiency has been reported in other parts of sub-Saharan Africa (Ferguson et al. 1993). In addition to geohelminths, chronic malarial infection or strongyloidiasis might limit the growth of school children. An effective bednet program improved the growth of preschool children in an area of mainland Tanzania with malaria epidemiology similar to that in Zanzibar (Shiff et al. 1996). The prevalence of *Strongyloides stercoralis* infection in a subsample of this study cohort at baseline was 41.2% (Albonico, M., and Cancrini, G., unpublished data), but the nutritional consequences of this infection are largely unknown (Stephenson 1987).

A second possible reason for the small growth effect is that anthelmintic treatment might cause a temporary growth spurt that is not sustained. These school children may have multiple "gates", growth inhibitors or missing growth factors, that limit their rate of growth. Geohelminths may be one such growth inhibitor, but when this burden is alleviated the child can grow at a normal rate only until bumping into the next gate. Thus, when evaluated over a 1-y period, the growth effect we observed seems relatively small compared with results from shorter trials.

This explanation is supported by two trials in the literature. First is that of Stephenson et al. (1993a), in which results after 4 mo showed significant height and weight gains; however, when the 8-mo trial was completed, the weight gain had not increased further and the height gain had disappeared (Stephenson et al. 1993b). However, it should be noted that the 4-mo results were reported on a subgroup of boys who may have responded differently from the total group of boys and girls combined. A recent trial conducted north of Cape Town, South Africa (Kruger et al. 1996) also suggests that the effect of deworming on growth velocity abates over time. Iron-deficient 6- to 8-y-old children who received two 200-mg doses of albendazole 4 mo apart had height gains about 0.6 cm greater after 5 mo than children receiving placebo. After 11 mo, the relative height gain remained around 0.6 cm. This study must be interpreted with caution in this context, because the children were also given iron-fortified soup in a factorial design with deworming, and only 73 children composed the iron-deficient subsample.

To explore this possibility in our own data, we compared the observed growth effect using the 6-mo follow-up data to the 12-mo effects. In children < 10 y of age, the weight effects (difference between weight increments in the treated vs. control group) after 6 mo were 0.32 kg ($P < 0.01$) in the twice-yearly group and 0.18 kg ($P = 0.12$) in the thrice-yearly group. These values are similar to the effects observed after 12 mo (see Table 2). The 6-mo height effects from deworming were -0.15 cm ($P = 0.23$) in the twice-yearly group and 0.19 cm ($P = 0.48$) in the thrice-yearly group, values that rather support the assumption that the height effect observed in the thrice-yearly deworming group was gradual throughout the year. These comparisons provide some supporting evidence that deworming causes an immediate increase in weight gain that is not sustained beyond 6 mo. The same does not seem to be true for height. In children ≥ 10 y of age, the 6-mo

weight and height effects were trivial, and none was statistically significant.

A third possible explanation is that mebendazole controlled hookworms and *T. trichiura* too poorly to induce a large growth response. Neither of the benzimidazole antihelminthic drugs is very effective against *T. trichiura* (Albonico et al. 1994). However, the trials conducted by Latham and Stephenson and colleagues in Kenya (Latham et al. 1990, Stephenson et al. 1989, 1993a and 1993b) used antihelminthic treatments that are more effective against hookworms, and larger reductions in the prevalence and intensity of hookworm infection were attained. This explanation is supported by the dose response in the effect of twice-yearly and thrice-yearly deworming on height gains. The height gains of children <10 y of age increased with frequency of deworming, both in terms of the overall group effects (Table 2) and the subgroup analyses (Fig. 2 and 3). However, a similar dose response was not seen in weight gains.

If poor control of helminth burdens is the reason for the small growth effects, then hookworms or *T. trichiura* rather than *A. lumbricoides* must be mainly responsible, given that ascariasis was controlled quite effectively by mebendazole. The lack of effect of *A. lumbricoides* on growth is also suggested by the finding that the growth response to antihelminthic treatment did not differ between children with and without *A. lumbricoides* infection at baseline (i.e., ascariasis was not a predictor of benefit from deworming). Over 30% of children did not have ascariasis at baseline; thus we had reasonable statistical power to observe this effect if it existed. This is in contrast to the hookworms and *T. trichiura*, which infected the vast majority of children at baseline.

Finally, the small effect we observed might be due to chance in the particular sample that we used. It is possible that the growth response in this sample of children was at the lower end of effects that will usually result from school-based deworming programs or that the large growth response in the Kenyan trials represents the upper expectation and will probably not be repeated. Additional evaluations of the growth effect of deworming programs are needed to provide reliable expectations of effect for program planners.

In summary, controlling *A. lumbricoides* infection and reducing the intensity of *T. trichiura* and hookworm infections in Zanzibari school children brought about small improvements in weight and height gains, particularly in children <10 y of age and in children who were less stunted. The public health relevance of the growth effect we observed is questionable. It is possible that helminth control is necessary but not sufficient to substantially improve the growth of school children in areas such as Zanzibar, and additional interventions or combinations of interventions should be tested. Antihelminthic regimens that are more effective against hookworms should be evaluated in programmatic settings and over time frames of at least 1 y. Improved growth is only one potential benefit from school-based deworming programs, and a final appraisal of the worth of such programs must also consider school participation, educational performance and effect on iron status.

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