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Physical Fitness, Growth and Appetite of Kenyan School Boys with Hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* Infections Are Improved Four Months After a Single Dose of Albendazole[1,2]

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ABSTRACT We studied physical fitness with the Harvard Step Test, growth, and appetite in primary school boys infected with hookworm (96% baseline prevalence), *Trichuris trichiura* (98% prevalence) and *Ascaris lumbricoides* (41% prevalence) who received a single 600-mg dose of albendazole or an identical placebo. Boys were examined, allocated at random within pairs by descending hookworm egg count to placebo ($n = 26$) or albendazole ($n = 27$) groups, treated, and re-examined 4 mo later. Four months after treatment, the albendazole group showed highly significant improvements in fitness score, resting heart rate, and heart rates at 1, 2, 3 and 4 min after the Harvard Step Test, whereas the placebo group had not changed significantly. The albendazole group also exhibited significantly more rapid growth judged by weight gain (1.0 kg greater than the placebo group, $P < 0.0002$), height increment (0.6 cm more, $P < 0.003$), arm circumference (0.3 cm more, $P < 0.0002$), and triceps and subscapular skinfolds (1.0 mm more, $P < 0.0002$), and showed improved appetite with objective and subjective measures. We conclude that single-dose treatment with albendazole can allow improved physical fitness, growth, and appetite in school-age children in areas where these helminths and poor growth are highly prevalent. J. Nutr. 123: 1036–1046, 1993.

INDEXING KEY WORDS:

- *children* • *growth* • *appetite*
- *geohelminths* • *physical fitness*

In 1990, we reported that Kenyan school boys with relatively high hookworm and *Trichuris trichiura* egg counts and *Ascaris lumbricoides* infection exhibited low physical fitness scores with the Harvard Step Test, but that fitness improved markedly, when compared with a placebo group, 7 wk after receiving a standard 400 mg dose of albendazole (Stephenson et al. 1990). We also found smaller but significant improvements in fitness scores 3 mo after treatment of undernourished Indonesian primary school boys and girls infected mainly with *Ascaris* and *Trichuris*, and with very light loads of hookworm (Totoprajogo 1989). Multivariate analyses showed that decrease in intensity of hookworm and *Ascaris* infections in the Kenyan boys and decrease in intensity of *Ascaris* in the Indonesian children explained much more of the improvements in fitness score than did *Trichuris* egg counts, which did not change significantly in Kenyan boys and decreased in Indonesian children but still left 80% of subjects infected.

It was difficult to determine the precise relationship between the geohelminths and physical fitness, because a single dose of albendazole essentially cures *Ascaris* and hookworm infections and usually produces marked reductions in *Trichuris* egg counts. Both hookworm and *Trichuris* can lower hemoglobin concentrations, which in turn may decrease fitness. We did not understand what mechanisms might explain the decreased fitness and improvements after treatment, because mean hemoglobin concentrations did not rise in subjects in the Kenyan study after treatment. We also did not know how long the beneficial effects of treatment may last in

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children constantly exposed to reinfection. So in 1989–1990 we conducted a follow-up study that employed a single 600-mg dose of albendazole to better treat *Trichuris* infections, as recommended by Ramalingam et al. (1983). We repeated baseline examinations at 4 mo instead of only 7 wk after treatment. We measured changes in hemoglobin concentrations as before, and added two new components: assessment of changes in anthropometry at follow-up and subjective and objective measures of appetite before and 4 mo after treatment.

The primary objectives of the study were to determine the effect of treatment with a single 600-mg dose of albendazole on physical fitness, parasite rates, growth rates, appetite and hemoglobin concentrations in Kenyan primary school boys with hookworm, *Trichuris* and *Ascaris* infections compared with a placebo group, and to examine the relationships between these variables in multivariate analyses. The study was conducted in a community in which our previous work had shown that treatment for these three geohelminths with albendazole improves growth rates in school children over 6 mo (Stephenson et al. 1989).

MATERIALS AND METHODS

Study population, experimental design and treatment. The 60 boys selected for this study were chosen from a group of >300 children (>150 boys) in Mvindeni Primary School in Kwale District, Coast Province, Kenya, who were participating in a large study on the effects of treatment for hookworm, *T. trichiura* and *A. lumbricoides* infections, once or twice per school year, on child growth and parasite rates (Stephenson et al. 1992 and 1993). Details of selection of the larger group of subjects are described elsewhere (Stephenson et al. 1993). The 60 boys were chosen because they had a hemoglobin concentration >80 g/L (for ethical reasons), showed willingness to cooperate in the physical fitness and appetite tests, showed no signs of puberty and were infected with at least one of three geohelminths but had a hookworm egg count <20,000 eggs per gram of feces (epg) (for ethical reasons), had a hookworm or *Trichuris* egg count ≥1000 epg or an *Ascaris* egg count ≥4000 epg. Parental consent for the children's participation was obtained, and all were free to withdraw at any time. The study protocol was reviewed and approved by the Cornell University Committee on Human Subjects and the Kenya Medical Research Institute.

After the baseline examination in September-October 1989 (Exam 1) boys were allocated at random by descending hookworm egg count to albendazole or placebo groups and treated; 53 of 60 completed all follow-up tests 4 mo later in January–February 1990 (Exam 2). The albendazole group received a single dose of 600 mg of albendazole (3 × 200 mg tablets, SmithKline Beecham, Brentford, Middlesex, U.K.) at Exam 1, and the placebo group received identical placebos. All doses of albendazole and placebos were consumed in the presence of project staff. For ethical reasons, the few boys with heavy hookworm egg counts (>20,000 epg) at Exam 1 or 2 were immediately given 600 mg albendazole and a 6-wk course of $FeSO_4$ (200 mg/d) and did not participate in the randomization or, if found at Exam 2, were reassigned to the heavily infected treated group and followed. At the end of the study, all subjects in the placebo and albendazole groups received a single dose of albendazole, and any boys with heavy hookworm infection received albendazole and a 6-wk course of $FeSO_4$.

Parasitology. Both examinations were conducted by the same team, each doing the same procedures, and were done in a blind fashion. On the same day that fecal specimens were passed, examinations for parasite eggs were done using a modified Kato technique recommended by WHO (1991), using templates to measure ~50 mg of stool and a cellophane coverslip soaked in glycerine-malachite green solution. Hookworm eggs were counted 30–60 min after smear preparation (Martin and Beaver 1968). Egg counts, as estimates of worm burden or intensity of infection, were expressed as epg. Percentage of egg reduction rates from Exam 1 to Exam 2 were also calculated from the arithmetic and geometric mean egg counts with the formula: % egg reduction = [(initial epg − final epg) ÷ initial epg] × 100. The percentage of reduction in arithmetic mean counts refers to the population of all subjects' worms, but because egg counts follow a negative binomial distribution, the percentage of reduction in the geometric mean counts better reflects the decrease in the average subject.

Anthropometry and hemoglobin concentrations. Anthropometric measurements were performed using the methods described by Jelliffe and Jelliffe (1989) and included weight (to the nearest 0.1 kg on a portable Seka model 770 balance, Seka, Columbia, MD), standing height (to the nearest 0.1 cm with a Microtoise portable anthropometer, Mabo, France), mid upper arm circumference (to the nearest 0.1 cm on the left arm) and triceps and subscapular skinfold thicknesses (in triplicate, to the nearest 0.5 mm with Lange calipers, Cambridge Scientific Industries, Cambridge, MD). Raw anthropometric values were converted to percent of the median for age with the National Center for Health Statistics (NCHS) growth references (Hamill et al. 1977, Johnson et al. 1981). Our previous work has shown the similarities in attained growth between the NCHS references and privileged East African Bantu children and the appropriateness of the NCHS references for this population (Stephenson et al. 1983). Changes in measurements between Exams 1 and 2 for each boy were adjusted to 123 d (4.04 mo), the mean number of days for all boys between treatment and follow-up, and were calculated assuming linear growth between exams. Hemoglobin determinations were done in duplicate on fingerprick blood with the cyanmethemoglobin method (Interdepartmental Committee on Nutrition for National Defense 1963) on a Spectronic 20 spectrophotometer (Bausch & Lomb, Rochester, NY).

Physical fitness. Physical fitness was assessed with the Harvard Step Test modified to measure submaximal performance in children (Gallagher and Brouha 1943). This involved each boy stepping up and down on a step adjusted in height for his leg length, 30 times per min for 5 min while wearing a backpack containing bags of sand equal to 20% of his body weight, as previously described (Stephenson et al. 1985). Each boy had his heart rate measured at rest, then performed the standardized exercise for 5 min, then the heart rate was measured at 1, 2, 3 and 4 min following the exercise. Heart rates of children who are physically fit returned to normal more rapidly than those who are less fit. A physical fitness score was calculated as follows: fitness score = duration of test (300) × 100 + sum of heart rates per min taken at 1, 2 and 3 min after test completion (Basta et al. 1979).

Appetite. To assess appetite, we used a test we had developed for this series of studies that would be appropriate for the culture, age group and educational level of the subjects and that could be easily and inexpensively administered in a field setting (Latham et al. 1990a). We chose a bland, commonly consumed local food (corn meal porridge, or uji) that would be acceptable to all subjects, and then used the most commonly preferred recipe, which contained 100 g of corn meal, 50 mL of whole milk, 62.5 g of sugar, and enough water added to yield 1 L of porridge. The porridge was thin enough to be drunk from a cup and to measure in milliliters. It contained 2709 kJ/L. It was freely available as a late-morning snack before and again 4 mo after treatment. To determine whether food eaten at home on the morning of the porridge test influenced porridge consumption, the boys were asked to report quantities of all food and drink consumed between the time they got up that day and the administration of the porridge test. The energy content of their breakfasts was calculated by a nutritionist experienced in the nutrient content of local foods. Before the porridge test was administered, the boys were also asked to rate their own appetites on a 5-point scale as very poor, poor, average, good or very good.

Statistical analysis. Data were analyzed on a Compaq Portable III computer with SPSS-PC+ version 3.0 (SPSS, Chicago, IL). Statistical tests used were Chi-square tests for association, McNemar's test for changes in prevalence, group and paired t tests, Wilcoxon's Signed Rank and Rank Sum tests, Pearson correlation coefficients and stepwise multiple regression analysis. Heteroscedastic or negative binomial distributions (egg counts) were transformed to common logarithms with the $n + 1$ transformation before applying parametric tests (Sokal and Rohlf 1969). Values presented are means ± SEM.

RESULTS

Baseline data and results of treatment. The albendazole ($n = 27$ completing study) and placebo ($n = 26$ completing study) groups were comparable before treatment and did not differ significantly in age (9.6 ± 0.28 y for the albendazole group, 9.6 ± 0.33 y for the placebo group, range = 7–13 y for both groups), presence of signs of puberty (negative in both groups at both exams), baseline prevalence and intensity of geohelminth infections (**Table 1**) or baseline anthropometry and hemoglobin concentrations (**Table 2**). Anthropometry and hemoglobin concentrations showed that at least half of the boys exhibited poor growth or were anemic: 53% were below 80% weight-for-age, 62% were below 95% height-for-age and 32% had a weight-for-height below 90%. Also, 47% had a hemoglobin concentration <120 g/L, the cut-off point recommended by WHO (1968) as suggestive of anemia in this age group. The two groups also did not differ significantly before treatment in Harvard Step Test scores, heart rates before or after the baseline test or appetite assessed by intake of corn meal porridge, breakfast recall on day of the porridge test or direct questioning about appetite (**Tables 3** and **4**, **Fig. 1**).

Four months after treatment, the albendazole group exhibited highly significant reductions in the prevalence and intensity of hookworm and *Ascaris* infections and the intensity of *Trichuris* infection, but the placebo group showed no significant changes in prevalence or intensity for any of the three geohelminths (Table 1). The albendazole group showed an 81% reduction in the arithmetic mean hookworm egg count, compared with a 31% increase in the placebo group, a 99% reduction in *Ascaris* egg count, compared with a 27% increase in the placebo group, and a 39% reduction in *Trichuris* egg count, compared with a 1% increase in the placebo group. At follow-up, 44% of the albendazole group still had or had reacquired patent hookworm infection, 85% had *Trichuris*, and 18% had *Ascaris*, but the intensity of infection for hookworm and *Ascaris* was very low.

As expected, the albendazole group had grown much faster over the 4-mo period than the placebo group; they gained a mean of 1.0 kg more or 167% more in weight than the placebo group, and 22% (6 of 27) gained more than 2.0 kg whereas none of the

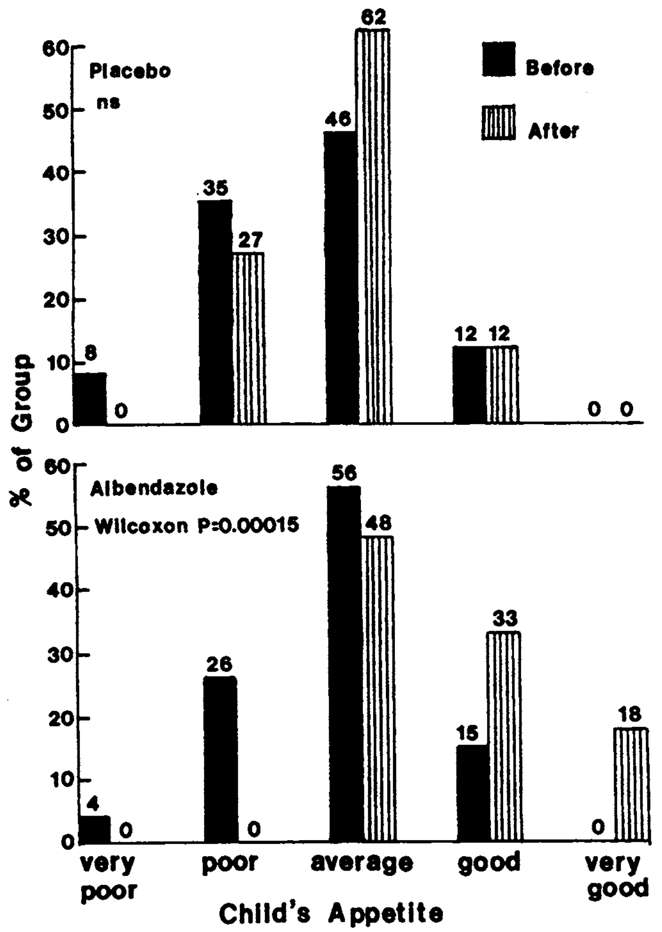

FIGURE 1 Boys' own ratings of their appetites in albendazole and placebo groups before and 4 mo after treatment. No significant differences between groups before treatment with Wilcoxon Rank Sum Test. After treatment, albendazole group increased significantly (Wilcoxon Signed Rank Test $P = 0.00015$), placebo group nonsignificant (ns).

placebo group did (Fig. 2). The albendazole group also increased more in height, height-for-age, weight-for-height, and arm circumference and both triceps and subscapular skinfold thicknesses (Table 2). In addition, the albendazole group increased significantly in weight-for-age, weight-for-height, and triceps and subscapular skinfold thicknesses-for-age, whereas the placebo group decreased significantly in weight-for-age, height-for-age, weight-for-height and arm circumference-for-age. Hemoglobin concentrations dropped significantly by 6 ± 1.0 g/L in the placebo group, to 114 ± 2.0 g/L, whereas they showed a nonsignificant decrease of 2 ± 1.2 g/L in the albendazole group. The difference between groups of 4 g/L was statistically significant but was relatively small and not likely to be of much biological or functional importance, especially when compared with the differences in growth rates.

Physical fitness tests. Physical fitness assessed by the Harvard Step Test was generally poor before treatment, with only 15% (8 of 53) of boys achieving scores over 80, which have been judged to indicate good to excellent fitness (Basta et al. 1979), even though the boys understood and performed the test properly. Four months later, heart rates in the albendazole group at 1, 2, 3 and 4 min after test completion were significantly lower than in the placebo group, which indicated improved fitness (Table 3). The mean Harvard Step Test score had not changed significantly in the placebo group but had improved significantly in the albendazole group (77 vs. 82) (Table 4). All but one (96%, 26 of 27) of the boys in the albendazole group improved their Harvard Step Test score 4 mo after treatment, whereas only 50% (13 of 26) of boys

TABLE 1

Parasite prevalence and intensity in placebo (PL) and albendazole (A) groups before and 4 mo after treatment[1]

Parasite	Group	Positive Pre	Positive Post	Change (McNemar's test) P	Arithmetic mean epg Pre	Arithmetic mean epg Post	Egg reduction	Geometric mean epg Pre	Geometric mean epg Post	Egg reduction	Paired t test P
		%					%			%	
Hookworm	PL	96	100	ns	3693	4854	–31	1384	2054	–48	ns
	A	96	44	0.00005 D	3023	575	81	1704	14	99	<0.0002 D
Trichuris trichiura	PL	100	100	ns	6281	6352	–1	3577	3373	6	ns
	A	96	85	ns	6136	3716	39	2687	476	82	<0.0005 D
Ascaris lumbricoides	PL	38	38	ns	16,657	21,180	–27	42	44	–5	ns
	A	44	18	0.0196 D	18,177	90	99	82	1	99	<0.0005 D

[1] t tests were performed on logs of egg counts. Means are for all cases per group; $n = 26$ for PL group, 27 for A group. McNemar's tests and paired t tests were two-tailed for PL group and one-tailed for A group (hypothesize decrease). No significant differences between PL and AL groups in pre-treatment prevalence or geometric means of egg counts. After treatment, hookworm prevalence ($P < 0.0001$) and eggs per gram of feces (epg) ($P < 0.0002$), *Trichuris* prevalence ($P = 0.022$) and epg ($P < 0.0025$) and *Ascaris* epg ($P < 0.005$) significantly lower in the A group. D = decrease; ns = not statistically significant ($P > 0.05$).

TABLE 2

***Anthropometric measurements and hemoglobin concentrations in albendazole (A) and placebo (PL) groups before and 4 mo after treatment*[1]**

Variable	Group	Before	After	Paired t test P[2]	Increase (after-before)	Group t test P	Growth greater than placebo by
Weight, *kg*	PL	24.9 ± 0.72	25.4 ± 0.75	0.0002 I	0.6 ± 0.08	0.0002	
	A	25.8 ± 0.86	27.4 ± 0.96	0.0002 I	1.6 ± 0.15		1.0 kg 167%
Weight/age, %	PL	78.7 ± 1.62	76.7 ± 1.58	0.002 D	−2.0 ± 0.24	0.0002	
	A	81.5 ± 1.85	82.6 ± 2.14	0.0105 I	1.0 ± 0.42		3.0% points
Height, *cm*	PL	129.7 ± 1.58	131.2 ± 1.60	0.0002 I	1.4 ± 0.08	0.003	
	A	130.9 ± 1.68	133.0 ± 1.76	0.0002 I	2.0 ± 0.19		0.6 cm 43%
Height/age, %	PL	94.5 ± 0.66	93.9 ± 0.64	0.0002 D	−0.6 ± 0.06	0.0015	
	A	95.4 ± 0.92	95.3 ± 0.93	ns	−0.1 ± 0.13		0.5% points
Weight/height, %	PL	92.3 ± 1.18	91.7 ± 1.08	0.0245 D	−0.6 ± 0.28	0.0002	
	A	93.6 ± 1.24	95.1 ± 1.42	0.002 I	1.6 ± 0.49		2.2% points
Arm circumference, *cm*	PL	16.2 ± 0.20	16.2 ± 0.21	ns	−0.0 ± 0.05	0.0002	
	A	16.8 ± 0.26	17.1 ± 0.25	0.0002 I	0.3 ± 0.06		0.3 cm
Arm circumference for age, %	PL	81.2 ± 1.16	79.7 ± 1.24	0.0002 D	−1.5 ± 0.23	0.0005	
	A	83.7 ± 1.10	83.7 ± 1.08	ns	−0.0 ± 0.33		1.5% points
Triceps skinfold, *mm*	PL	6.0 ± 0.26	6.0 ± 0.28	ns	−0.0 ± 0.10	0.0002	
	A	5.7 ± 0.24	6.7 ± 0.25	0.0002 I	1.0 ± 0.09		1.0 mm
Triceps skinfold/age, %	PL	68.7 ± 2.84	67.4 ± 3.10	ns	−1.4 ± 1.19	0.0002	
	A	64.9 ± 2.57	75.1 ± 2.73	0.0002 I	10.2 ± 1.04		11.6% points
Subscapular skinfold, *mm*	PL	4.3 ± 0.24	4.3 ± 0.22	ns	0.0 ± 0.07	0.0002	
	A	4.2 ± 0.15	5.2 ± 0.18	0.0002 I	1.0 ± 0.09		1.0 mm
Subscapular skinfold/age, %	PL	83.8 ± 4.12	82.8 ± 3.86	ns	−1.0 ± 1.36	0.0002	
	A	83.5 ± 2.44	100.6 ± 2.66	0.0002 I	17.1 ± 1.67		18.1% points
Hemoglobin, *g/L*	PL	120 ± 2.0	114 ± 2.0	0.0004 D	−6 ± 1.0	0.002	
	A	121 ± 1.8	119 ± 2.0	ns	−2 ± 1.2		4 g/L

[1]Values are means ± SEM; $n = 26$ for PL group, 27 for A group. No significant differences between groups before treatment with group t tests. Paired t tests on anthropometry were one-tailed for PL group (raw-hypothesize increase, percents-hypothesize decrease, based on previous studies) and one-tailed for A group (hypothesize increase). Paired t tests on hemoglobin concentrations were two-tailed for both groups. Group t tests on increases were one-tailed (hypothesize A group greater).

[2]D = decrease; I = increase; ns = not statistically significant ($P < 0.05$).

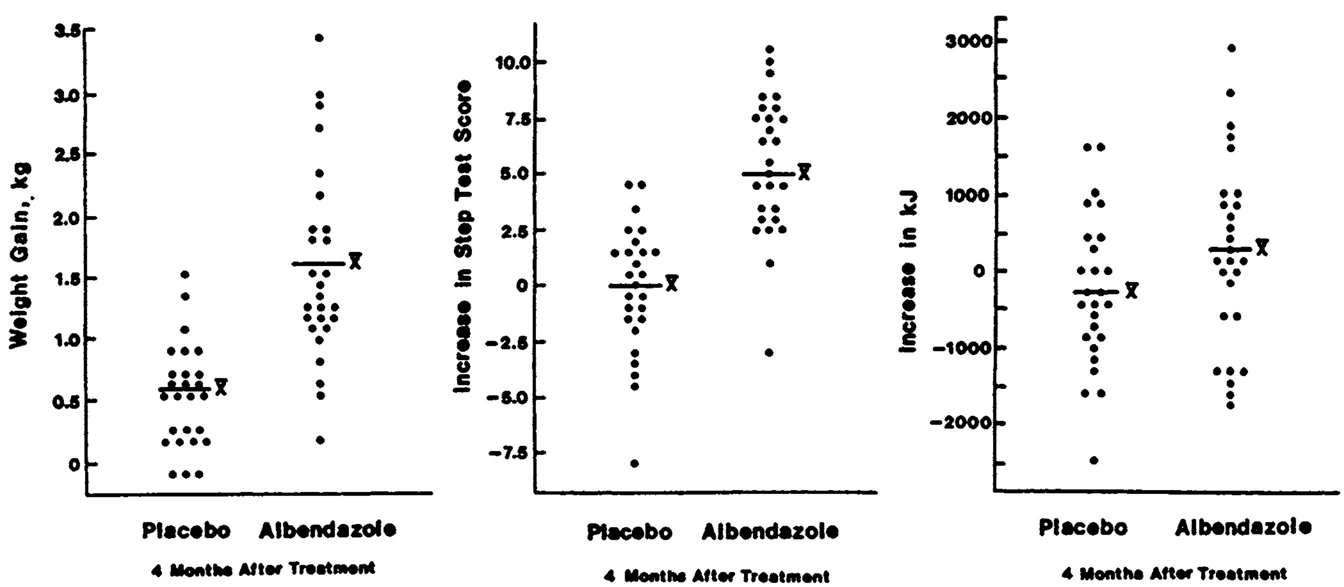

FIGURE 2 Weight gain and increases in fitness score on Harvard Step Test and breakfast + porridge energy intakes in albendazole and placebo groups 4 mo after treatment. The means for the albendazole group are significantly higher than placebo (weight gain $P < 0.0002$, fitness score $P < 0.0002$, energy intake $P < 0.05$).

in the placebo group did so (Fig. 2). Resting heart rates had also decreased after treatment, indicating improved fitness (similar to that found in trained athletes), whereas they had not changed in the placebo group (−2.8 ± 0.78 beats/min in the albendazole group, vs. +0.4 ± 0.76 beats/min in the placebo group) (Table 4).

Appetite tests. Appetite before treatment was generally good in both groups, with boys reporting consumption of 1155–1512 kJ for breakfast and consuming an average of ~880 mL of corn meal porridge, equivalent to ~2415 kJ, as a late morning snack during our ad libitum porridge test (Table 4). This is undoubtedly a high energy snack, but we expect that this is a better measure of desire for food than consumption measured at home might be, because the latter is affected in the morning by shortage of time before school and, at all meals, by the need to share food with siblings and parents and by observer influence and error.

At Exam 2, 4 mo after receiving a single treatment for geohelminth infections, the albendazole group boys reported consuming a mean of 386 kJ more than the placebo group for breakfast, and they also drank a mean of 122 kJ more porridge, so overall they were eating ~525 kJ more food per morning than the placebo group ($P < 0.05$, Table 4). These are not huge differences, but we did not expect huge differences in energy intakes per day in chronic infections that last for years, as intestinal worm infections do. The range of changes in energy intakes after treatment was large in both groups, as was expected with dietary intake data, which typically show great inter-subject variation. However, 41% (11 of 27) of the albendazole group boys increased their energy intakes by at least 420 kJ after treatment, whereas only 19% (5 of 26) of the placebo group boys did (Fig. 2).

The albendazole group boys also reported improved appetites after treatment. No boy reported a very good appetite before treatment (Fig. 1). Four months later, 18% of albendazole group boys reported a very good appetite, whereas no placebo boys did, and more than twice as many boys in the albendazole group rated their appetites as good (33 vs. 12%, Fig. 1). No treated boys rated their appetites as poor or very poor after treatment, whereas 27% of boys in the placebo group did. The improvements in reported appetite in the albendazole group were highly significant ($P < 0.00015$) and not significant in the placebo group.

Multivariate analysis. Stepwise multiple regression analyses were done to determine which of the variables measured were significant predictors of improvements in growth rate, physical fitness and energy intake after treatment, and predictors of how the improvements were interrelated (**Table 5**). Weight gain was highest in boys who had larger decreases in intensity of hookworm infection (judged by decreases in logs of egg counts), who reported greater improvements in appetite, and who exhibited larger increases in hemoglobin concentration (R^2 for equation = 0.37). Similarly, increases in triceps skinfold were higher in boys who had larger decreases in intensity of hookworm infection, who had lighter loads of *Ascaris* left at follow-up, and who reported greater improvements in appetite (R^2 for equation = 0.43). Increase in fitness score on the Harvard Step Test was the most successful equation, with an R^2 of 0.59. Again, decrease in intensity of hookworm infection was the most important predictor, followed by weight gain after treatment and increase in energy intake after treatment. As expected, increase in morning energy intake was the most difficult variable to explain, but we could explain 18% of the variation in its increase with two geohelminths: decrease in intensity of *Trichuris* infection, and presence of hookworm at Exam 2, after treatment. So of the three geohelminths, hookworm infection had the greatest explanatory power, but treatment for all three parasites was related statistically to the improvements found in growth, fitness and appetite. Weight gain was related also to increase in hemoglobin concentration

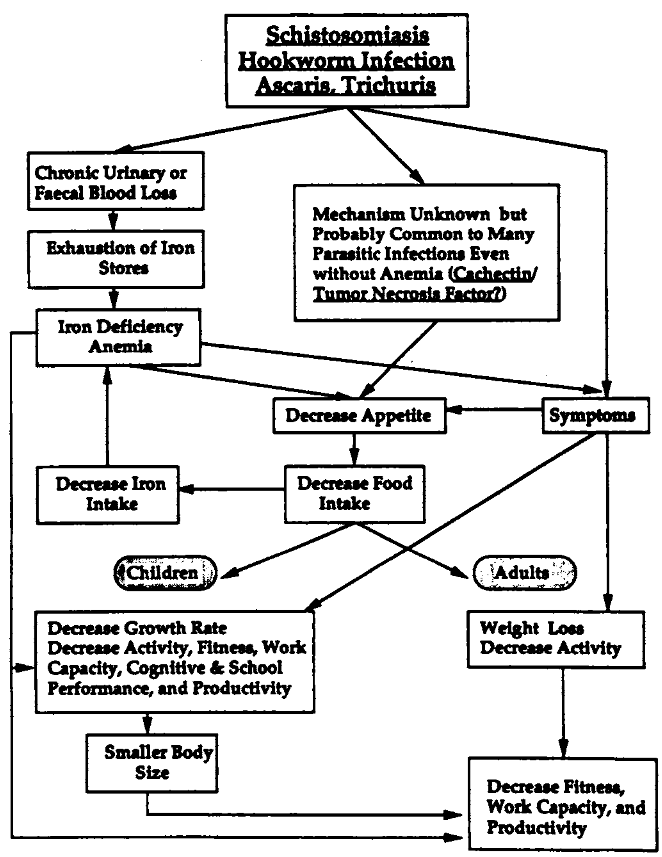

FIGURE 3 Mechanisms by which intestinal helminths and schistosomiasis may decrease appetite, growth, physical fitness and productivity in undernourished populations.

TABLE 3

Harvard Step Test-heart rates in albendazole (A) and placebo (PL) groups before and 4 mo after treatment[1]

Group	Heart rate: Resting	+ 1 min	+ 2 min	+ 3 min	+ 4 min
	beats/min				
Before					
PL	84 ± 1.2	154 ± 1.4	127 ± 1.3	111 ± 1.4	96 ± 1.1
A	84 ± 1.5	154 ± 1.0	126 ± 1.1	109 ± 1.0	98 ± 0.9
P	ns	ns	ns	ns	ns
After					
PL	85 ± 1.2	156 ± 1.0	127 ± 1.3	111 ± 1.6	95 ± 1.2
A	81 ± 1.0	147 ± 1.0	117 ± 1.3	100 ± 1.3	90 ± 1.0
P	0.0115	<0.0002	<0.0002	<0.0002	<0.0005

[1]Values are means ± SEM, $n = 26$ for PL group, 27 for A group. ns = not statistically significant ($P > 0.05$). Significance determined by group *t* test, two-tailed before and one-tailed after treatment.

as well as to decrease in hookworm egg count, even though changes in hemoglobin concentrations were not large.

DISCUSSION

This study showed that treatment of undernourished, geohelminth-infected Kenyan school boys with a single dose of albendazole resulted in marked reductions in helminth loads and also in significant improvements over 4 mo in growth, physical fitness, resting heart rates and perceived appetite, and small but significant improvements in measured appetite and hemoglobin concentrations compared with the placebo group as well, despite continual exposure to reinfection and some incomplete cures. A follow-up study in a different group of 56 young children in the same school also showed increased spontaneous physical activity during school play periods along with improved growth 9 wk after treatment with albendazole (Adams et al. 1991). These two studies, our previous studies over 17 y in children and adult males in this part of Kenya and research in several

TABLE 4

Fitness scores on Harvard Step Test, resting heart rates, and breakfast and porridge intakes in albendazole (A) and placebo (PL) groups before and 4 mo after treatment[1]

	Group	Before	After	Paired *t* test *P*	Increase	Group *t* test *P*	Greater than placebo by
Fitness score	PL	76 ± 0.7	76 ± 0.7	ns	0 ± 0.6	<0.0002	
	A	77 ± 0.5	82 ± 0.7	<0.0002 I	5 ± 0.6		+5
	t test *P*	ns	<0.0002				
Resting heart rate, *beats/min*	PL	84 ± 1.2	85 ± 1.2	ns	+0.4 ± 0.76	0.0025	
	A	84 ± 1.5	81 ± 1.0	<0.0005 D	−2.8 ± 0.78		−3.2
	t test *P*	ns	0.0115				
Breakfast intake, *kJ*	PL	1445 ± 133.6	1172 ± 197.8	—	−273 ± 181.0		
	A	1394 ± 133.6	1508 ± 213.4	—	113 ± 218.0	0.09	386
Porridge intake, *kJ*	PL	2465 ± 135.2	2470 ± 164.6	—	4 ± 163.4		
	A	2293 ± 141.5	2419 ± 153.7	—	126 ± 121.4	ns	122
Breakfast + porridge, *kJ*	PL	3914 ± 191.5	3641 ± 238.1	—	−273 ± 201.2		
	A	3688 ± 206.6	3944 ± 191.5	—	256 ± 239.0	0.05	529

[1]Values are means ± SEM; $n = 26$ for PL group, 27 for A group. No significant differences between groups before treatment with group *t* tests. Paired *t* tests were two-tailed for PL group and one-tailed for A group (fitness and intakes, hypothesize increase; resting heart rate, hypothesize decrease; based on previous studies). Group *t* tests on increases were one-tailed (hypothesize A group greater). Porridge contains 2.71 MJ/L or consumption of about 880 mL per child per morning. Adjustment per kg body weight yields same statistical conclusions. D = decrease; I = increase; ns = not statistically significant.

TABLE 5

Multiple regression analyses of weight gain and increases in triceps skinfold thickness, fitness score on Harvard Step Test and breakfast + porridge energy intakes in albendazole and placebo groups 4 mo after treatment[1]

Independent variables	Beta	B	SE of B	*t*	*P*
Dependent variable: weight gain, *kg*					
Hookworm epg decrease,					
log Exam 1 – log Exam 2	0.30	0.15355	0.06169	2.49	0.016
Increase in appetite score	0.28	0.28	0.12	2.38	0.021
Increase in hemoglobin, *g/L*	0.27	0.0342	0.01552	2.20	0.032
Constant (A)	—	0.901	0.150	6.02	0.0001
$F = 9.72$ ($P < 0.0001$); $R^2 = 0.37$; adjusted $R^2 = 0.34$.					
Dependent variable: increase in % triceps skinfold thickness for age					
Hookworm epg decrease,					
log Exam 1 – log Exam 2	0.34	1.7801	0.60038	2.96	0.0047
Ascaris epg, *log Exam 2*	–0.33	–1.5284	0.51547	–2.96	0.0047
Increase in appetite score	0.31	3.03	1.10	2.75	0.0084
Constant (A)	—	2.63	1.30	2.02	0.048
$F = 12.4$ ($P < 0.0001$); $R^2 = 0.43$; adjusted $R^2 = 0.40$.					
Dependent variable: increase in fitness score					
Hookworm epg decrease,					
log Exam 1 – log Exam 2	0.55	1.4376	0.27003	5.32	0.0001
Weight gain, *kg*	0.24	1.25	0.523	2.38	0.021
Increase in energy intake					
(breakfast + porridge), *kJ*	0.20	0.000715	0.000335	2.14	0.038
Constant (A)	—	–0.013	0.632	–0.02	0.98
$F = 23.9$ ($P < 0.0001$); $R^2 = 0.59$; adjusted $R^2 = 0.57$.					
Dependent variable: increase in breakfast + porridge intake, *kJ*					
Trichuris epg decrease,					
Exam 1 – Exam 2	0.29	0.05699	0.0254818	2.24	0.030
Hookworms present Exam 2					
(0 = neg, 1 = pos)	–0.24	–620.8	335.6	–1.85	0.07 bord
Constant (A)	—	373.4	289.4	1.29	0.20
$F = 5.35$ ($P = 0.0078$); $R^2 = 0.18$; adjusted $R^2 = 0.14$.					

[1] *n* = 53. epg = eggs per gram of feces; bord = borderline ($P < 0.10$).

countries by other scientists, especially research dating back 85 y on hookworm infection, show that children and adults grow and feel better, are healthier, and can be more physically and mentally active and productive after treatment for helminth infections or anemia. They also show that degree of improvement correlates with larger decreases in helminth egg counts or larger increases in hemoglobin concentrations following treatment with anthelminthics or oral $FeSO_4$ (see data and reviews in Crompton and Stephenson 1990, Latham 1983 and 1989, Latham et al. 1990a, 1990b and 1991, Lawless et al. 1991, Pollitt 1989, Pollitt et al. 1991, Stephenson 1989, Stephenson et al. 1990, 1992 and 1993, Totoprajogo 1989).

The more recent studies are important because older descriptive studies, particularly on hookworm anemia from 1915 to 1935, did not employ randomized designs, placebo groups or differential statistics, nor did they use or have methods to adequately measure nutritional status, nutrient intakes, functional capacity or physical fitness and activity levels. Newer studies, especially in combination with the precise, holistic descriptions of worm-infested persons in the older literature, provide insights into the mechanisms by which helminth infections (and anemia) are likely to influence growth and physical and cognitive abilities. The conceptual framework that our and others' studies have led us to develop is shown in **Figure 3**. It seems likely that worm infections depress growth, physical fitness, physical activity and cognitive performance via two pathways, both of which have depressed appetite as a central feature. One mechanism (a minor one for this study, given the small changes in hemoglobin concentrations) involves iron deficiency anemia and the resulting poor appetite, poor growth and decreased activity (Aukett et al. 1986, Chwang et al. 1988, Judisch et al. 1966, Latham et al. 1990b and 1991, Lawless et al. 1991). The other, most likely, major pathway for studies using direct treatment of worms themselves with anthelminthics involves cachectin-tumor necrosis factor alpha (TNFα), and possibly such other cytokines as interleukin-1, which are produced by the human body in response to parasitic infestation. These cytokines can act directly on the brain to depress appetite and are known to increase metabolic rate, decrease activity, and produce cachexia and fat and protein catabolism (Pearson et al. 1990, Plata-Salaman et al. 1988, Rothwell and Grimble 1992, Tracey and Cerami 1989). Elevated serum levels of cachectin-TNFα before treatment and decreased levels 3–6 mo after treatment have been documented in humans with *Schistosoma mansoni* (Zwingenberger et al. 1990), but evidence is lacking for human geohelminth infection. Assays sensitive enough to detect the low serum levels of cachectin-TNFα that may be continually produced in chronic geohelminth infections have become available in the last few years and will enable testing of this hypothesis in the near future. We have not as yet studied this likely mechanism.

Decreased appetite leads to decreased food intake, which in turn decreases growth rate, physical fitness, physical activity and cognitive performance. These effects eventually lead to decreased fitness and productivity of the adult population, partly by decreasing body size (Spurr et al. 1983). This chain of events is clearly undesirable in communities in developing countries in which most children and adults need to be physically fit and to perform heavy manual labor in order to grow their own food or earn money to buy food.

The most important new finding in this study is the significant improvement in perceived and measured appetite that accompanied improved growth and fitness in typical worm-infested school-age children a full 4 mo after treatment. This reminds us that in prevention and control of malnutrition and its functional sequelae, it is often just as important to improve children's desire to eat as it is to improve parents' ability to grow or buy food. Children or adults who consume too little food and energy for all of the physical activities they desire, including those whose appetite and food intake are inhibited by illness, can achieve energy balance and avoid becoming severely undernourished only by decreasing their physical activities (Latham 1989). The children in this and our previous studies were undernourished and were not physically fit, partly because of intestinal worm or schistosome infections. Studies of malnourished preschool children in Guatemala and Kenya have shown that acute symptoms and infections (diarrhea, apathy, fever, respiratory infections) can reduce total daily energy intakes by a mean of 630–735 kJ per day of illness (Martorell et al. 1980, Neumann et al. 1988). These figures are of the same order of magnitude as in the present study (525 kJ/morning greater than for the placebo group) and in our previous work in which boys were treated for *Schistosoma haematobium* and hookworm and their appetites measured 5 wk after treatment (357 kJ/morning greater than the placebo group) (Latham et al. 1990a). We know of no other randomized placebo-controlled study that demonstrates improved appetite or food intake following treatment for geohelminths in free-living school-age children, and only one study in Indonesian preschoolers treated for *Ascaris* has successfully documented this phenomenon (Jalal 1991). Measuring changes in 24-h food, nutrient and energy consumption in children treated for geohelminths is labor-intensive, expensive and time-consuming, but our results imply that such an effort would be worthwhile and that we will not be able to understand fully the magnitude of the effects of geohelminths on nutrition or energy balance without such studies.

We conclude that treatment for hookworm, *Trichuris* and *Ascaris*, with a single dose of albendazole may improve growth, physical fitness, resting heart rate and appetite of school-age children in areas where these helminths and poor growth are common. We agree with WHO (1992) that "school children harbour some of the most intense helminth infections with adverse effects on health, growth and school performance" and that "treatment without prior individual screening of the whole population is recommended where surveys of school-age children indicate that the prevalence of intestinal helminths or schistosome infection exceeds 50%." We also recommend further research to determine the specific roles of these three helminths in interfering with functional capacity, including studies on physical fitness, appetite, food intake, symptomatology, quantity and quality of activity, and cognitive and school performance. Cost-effectiveness of large-scale treatment programs will increase with more knowledge about the extent and duration of these improvements following treatment with differing regimens in various age groups and in communities with different degrees of malnutrition and parasitism.

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