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Epidemiology of iron deficiency anemia in Zanzibari schoolchildren: the importance of hookworms¹⁻³

Rebecca J Stoltzfus, Hababu M Chwaya, James M Tielsch, Kerry J Schulze, Marco Albonico, and Lorenzo Savioli

ABSTRACT Anemia is estimated to affect one-half of school-age children in developing countries. The school years are an opportune time to intervene, and interventions must be based on sound epidemiologic understanding of the problem in this age group. We report on the distribution of iron deficiency and anemia across age, sex, anthropometric indexes, and parasitic infections in a representative sample of 3595 schoolchildren from Pemba Island, Zanzibar. Iron status was assessed by hemoglobin, erythrocyte protoporphyrin (EP), and serum ferritin concentrations from a venous blood sample. Overall, 62.3% of children were anemic (hemoglobin < 110 g/L), and 82.7% of anemia was associated with iron deficiency. The overall prevalence of iron-deficient erythropoiesis (EP > 90 $\mu\text{mol/mol}$ heme) was 48.5%, and the prevalence of exhausted iron stores (serum ferritin < 12 $\mu\text{g/L}$) was 41.3%. In bivariate analyses, iron status was slightly better in girls than in boys, and was better in children aged 7-11 y than in those older or younger. Hemoglobin but not EP or serum ferritin concentrations were lower in stunted children. Infection with malaria, *Trichuris trichiura*, *Ascaris lumbricoides*, and hookworms were all associated with worse iron status; the association with hookworms was strongest by far. In multivariate analyses, hookworm infection intensity was the strongest explanatory variable for hemoglobin, EP, and serum ferritin. Sex, malarial parasitemia, *A. lumbricoides* infection, and stunting were also retained in the multivariate model for hemoglobin. Twenty-five percent of all anemia, 35% of iron deficiency anemia, and 73% of severe anemia were attributable to hookworm infection; < 10% of anemia was attributable to *A. lumbricoides*, malaria infection, or stunting. We conclude that anthelmintic therapy is an essential component of anemia control in schoolchildren in whom hookworms are endemic, and should be complemented with school-based iron supplementation. *Am J Clin Nutr* 1997;65:153-9.

KEY WORDS Humans, iron deficiency, anemia, schoolchildren, geohelminths, hookworms, malaria, schistosomiasis, ascariasis, trichuriasis

INTRODUCTION

Iron deficiency affects more people in the world than any other form of malnutrition, and its control is a global priority in public health. Iron deficiency anemia results from a variety of causes, including inadequate iron intake, high physiologic demands in early childhood and pregnancy, and iron losses from parasitic infections. The relative importance of these causes,

and thus the appropriate strategies for prevention of iron deficiency anemia, differs among populations and age groups.

Iron deficiency anemia is most prevalent and severe in young children and women of reproductive age (1). As a result, these groups have been the focus of most epidemiologic investigations of the problem and its causes. However, iron deficiency anemia is also common among school-age children. In developing regions of the world, the prevalence of anemia in 5-12-y olds is estimated to be 46%, with the highest rates found in Africa (49%) and South Asia (50%) (2). The school-age years are an opportune time to address this problem for several reasons. Iron deficiency impairs children's cognitive abilities, and interventions to prevent and correct iron deficiency may enhance children's learning potential in school (3). Improving the iron status of schoolchildren will also increase their fitness and work capacity (4), and improvements in girls' iron status during the school-age years may help to prevent anemia during their reproductive years. Finally, the school setting offers an ideal distribution system for public health interventions of many types (5), including health education, iron supplementation, and treatment or prevention of parasitic infections.

To develop and target effective interventions to prevent iron deficiency anemia in school-age children, a sound epidemiologic understanding of the problem is needed. As a first step to evaluate a school-based deworming program in Zanzibar, we conducted a baseline survey of iron deficiency anemia and its determinants in schoolchildren. Our objective in this paper was to describe the distribution of iron deficiency and anemia in Zanzibari schoolchildren by age and sex, anthropometric indicators, and parasitic infections. We then used these findings to

¹ From the Center for Human Nutrition and WHO Collaborating Center for Research on Intestinal Parasites and Human Nutrition, Department of International Health, The Johns Hopkins School of Public Health, Baltimore; the Ministry of Health, Zanzibar, United Republic of Tanzania; and the Schistosomiasis and Intestinal Parasites Unit, Division of Control of Tropical Diseases, World Health Organization, Geneva.

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³ Address reprint requests to RJ Stoltzfus, Center for Human Nutrition, Department of International Health, The Johns Hopkins School of Public Health, 615 North Wolfe Street, Baltimore, MD 21205. E-mail: RSTOLTZF@PHNET.SPH.JHU.EDU.

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discuss the most promising strategies for control of iron deficiency anemia in schoolchildren of coastal east Africa.

SUBJECTS AND METHODS

Study population

The study was conducted on Pemba Island, the smaller of the two islands of Zanzibar, just off the east coast of mainland Tanzania. The population is predominantly rural, with agricultural activities devoted to subsistence crops and cloves, an exported cash crop. Typical of coastal East Africa, Pemba Island is characterized by intense transmission of *Plasmodium falciparum* malaria, *Schistosoma haematobium*, and geohelminths. Both species of hookworms (*Necator americanus* and *Ancylostoma duodenale*) are endemic, with *N. americanus* predominating (6). The iron bioavailability of the Pembian diet is low. The primary staple food is cassava, with rice being more desired but less affordable. These foods are usually eaten with vegetable sauces and small fish. Meat is always a luxury item, and there are seasonal shortages of vegetables and fish.

The study population comprised first- through fourth-grade schoolchildren of Pemba Island, Zanzibar. This survey was conducted between March and May 1994, and was reviewed and approved by the institutional review boards of The Johns Hopkins University, the Ministry of Health of Zanzibar, and the World Health Organization. To form the study sample, we randomly selected 12 primary schools from the 72 schools on Pemba Island. From these schools, 76 morning classes of standards 1-4 were invited to participate in the survey. A total of 3605 children were enrolled in the survey, constituting 90% of children registered in those classes and $\approx 11\%$ of the total schoolchild population on Pemba Island. Data were collected in the school classrooms by specially trained local staff of the Ministry of Health. Age and sex data were obtained from 3595 children (99.7% of the sample), and these children were used in the present analyses.

Assessment of nutrition and health status

Children's weight was measured to the nearest 0.1 kg with a battery-powered digital scale (Seca, Inc, Columbia, MD). Height was measured to the nearest millimeter with a wooden stadiometer (Shorr Productions, Inc, Olney, MD). Age was calculated from the birth date on school records, which are based on birth certificates. When the school had no record of age, the child's self-reported age was used.

Iron status and anemia were assessed by hemoglobin, erythrocyte protoporphyrin (EP), and serum ferritin (SF) concentrations. Assessing the iron status of malaria-endemic populations has been a subject of controversy; however, we found that these indicators assessed iron status reliably in this population (7). Blood samples were collected by venipuncture from 100% of children surveyed. The hemoglobin concentration was determined by using the HemoCue hemoglobinometer (HemoCue, AB, Angelholm, Sweden), and the EP concentration was measured with a hematofluorometer (Aviv Biomedical Inc, Lakewood, NJ). An aliquot of blood was centrifuged at $1000 \times g$ for 20 min at room temperature and serum was collected. Sera were stored at -10°C for ≤ 10 wk, transported on liquid nitrogen to Baltimore, and stored at -70°C for ≤ 6 mo. SF was determined by using a fluorescence-linked immu-

noassay (DELFA System by Wallac, Inc, Gaithersburg, MD) on 3309 serum samples, 91.8% of the total enrollment. Missing data for SF were the result of losses of samples from mishandling or mislabeling in transport to Baltimore, or the result of laboratory error.

Thick and thin blood smears were fixed and stained with Giemsa, and malaria parasites were counted against leukocytes. Typically, 200 leukocytes were counted; if < 10 parasites were seen, the microscopist continued counting up to 500 leukocytes. Parasite counts were converted to parasite densities on the basis of 8×10^9 leukocytes/L blood (8). Malaria species were identified from the thin smear. All infections were *P. falciparum*; in $< 5\%$ of slides, *P. malariae* was also identified. A random 10% subsample of slides were reread by the Malaria Team leader. Agreement between readers was excellent for the presence of malaria parasitemia ($\kappa = 0.93$, 95% CI: 0.89, 0.98), and parasite density measures were also highly reliable with an intraclass correlation of 0.85.

For the assessment of helminth infections, containers were distributed to each class and the children were asked to bring a sample of their feces to school the next day. More than 95% of children surveyed returned a fecal sample. These samples were stained the same day and examined within 1 h of staining by using the Kato-Katz method (9). Hookworm, *Trichuris trichiura*, and *Ascaris lumbricoides* eggs were counted. If $> 10\,000$ eggs per gram feces (epg) were found for any helminth, the sample was diluted by using a modified Stoll technique (10) and was reexamined. A random 10% subsample of fecal smears was reexamined by the most skilled technician for quality control. Intraclass correlations between staff and quality-control readings were 0.88 for *A. lumbricoides* epg, 0.79 for *T. trichiura* epg, and 0.89 for hookworm epg.

As an indicator of *S. haematobium* infection, urine samples were collected on the day of the survey to test for microhematuria with Hemastix test strips (Ames Laboratories, Elkhart, IN). This procedure screens for urinary schistosomiasis with 69% sensitivity and 89% specificity (11).

Data analysis

Stunting was defined as a height-for-age Z score < -2 . These Z scores were calculated by using EpiInfo (Centers for Disease Control and Prevention, Atlanta). An appropriate indicator for wasting in primary school-aged children is not well defined. For children aged > 10 y, the 5th centile of body mass index [BMI, weight (kg)/height squared (m^2)] is recommended whereas for children aged 5-10 y, there is no accepted recommendation (12). We used a BMI less than the 5th centile according to the sex- and race-specific tables of Must et al (13, 14) to define wasting. The relation of iron deficiency and anemia to stunting and wasting was examined separately for children younger than and older than 10 y, to separate prepubertal and pubertal growth patterns.

Anemia was defined as a hemoglobin value < 110 g/L. This anemia cutoff value is lower than the WHO-recommended cutoff for this age group, but a race-specific anemia criterion (10 g/L lower for blacks) optimizes the screening performance of this indicator to detect iron deficiency (15). Distributions of EP and SF were skewed to high values so geometric means are presented. Iron deficiency anemia was defined as anemia with a SF concentration < 18 $\mu\text{g/L}$ or an EP concentration > 90

$\mu\text{mol/mol}$ heme. Severe anemia was defined as a hemoglobin value < 70 g/L.

The categorizations of age and parasitic infections in Tables 1-3 were based on relations observed in exploratory analyses of those variables and iron-status indicators. For example, malaria parasitemia was considered as a dichotomous variable because there was no evidence of an empirical relation of parasite density to the iron-status indicators. Because hookworm and *T. trichiura* egg counts were linearly related to iron-status indicators, increasing categories of 2000 epg were used in subsequent analyses (Table 2).

Means of continuous variables were compared by using Student's *t* test, proportions were compared by using the chi-square test, and linear trends in mean values and proportions were tested by linear regression. Multivariate-linear-regression models of hemoglobin, EP, and SF were built in a forward, stepwise fashion. Variables were entered into the model in the order of their strength of association in the bivariate tables, and those that did not remain significant at a probability level of 5% were not retained. Interaction terms were considered for age, but none were retained using a probability level of 15% as criterion for significance.

To assess which risk factors were associated with the greatest proportion of the anemia in this population, we estimated the attributable fraction of anemia for each risk factor. This is analogous to attributable risk, except that anemia prevalence was used in place of incidence. The equation for attributable risk and its variance were taken from Kahn (16).

Data were entered by using EpiInfo software and were managed and analyzed by using SYSTAT statistical software (SYSTAT Inc, Evanston, IL).

RESULTS

The sample comprised approximately equal numbers of boys and girls, mostly between the ages of 7 and 13 y (Table 4). Parasitic infections were extremely prevalent. The prevalences

of hookworm, *T. trichiura*, and *A. lumbricoides* infections were 94%, 96%, and 72%, respectively, and 99% of children were infected with at least one of these helminths. Of the 3361 children with complete parasitologic data, only one child was negative for all three helminths, malaria, and hematuria. Growth retardation was also highly prevalent.

The iron status of the children was very poor (Table 1). Overall, 62.3% of children were anemic and 51.5% had iron deficiency anemia by our definition. The overall prevalence of iron-deficient erythropoiesis (EP > 90 $\mu\text{mol/mol}$ heme) was 59.7%, and the prevalence of exhausted iron stores (SF < 12 $\mu\text{g/L}$) was 41.3%.

By all indicators, the iron status of boys was slightly worse than that of girls (Table 1). The EP and SF values supported the fact that iron status was best in 7-10-y olds, slightly worse in children 11 y and older, and notably the worst in the small group of children younger than 7 y. In contrast, hemoglobin concentration and anemia prevalence improved with age, with no trend toward worsening values in children 11 y and older.

Hemoglobin concentration and anemia prevalence were significantly worse in stunted children, in both children younger than and older than 10 y. Overall, the hemoglobin concentration ($\bar{x} \pm \text{SD}$) was 102 ± 16 g/L in children with a height-for-age Z score < -2 , and 105 ± 16 g/L in children with Z scores ≥ -2 ($P < 0.001$). The prevalences of anemia and iron deficiency anemia were also higher in stunted children than in nonstunted children (66.3% compared with 58.6% for anemia, 54.7% compared with 48.6% for iron deficiency anemia; $P < 0.001$ for both comparisons). However, iron status as assessed by EP and SF was not worse in stunted children. Wasting was not associated with iron status by any indicator.

By far the most dramatic relation to iron status was that of hookworm infection (Table 2). This intensity-dependent relation was strongly apparent in every indicator. For example, hemoglobin concentration decreased by ≈ 50 g/L for each 2000 hookworm epg. Particularly noteworthy is the relation of hookworm infection to severe anemia. Among children with ≥ 6000

TABLE 1
Iron-status indicators by sex and age

	Hemoglobin	Protoporphyrin	Serum ferritin	Anemia ¹	Severe anemia ²	Iron deficiency anemia ³
	g/L	$\mu\text{mol/mol}$ heme	$\mu\text{g/L}$	%	%	%
Sex						
Boys ($n = 1864$)	$103 \pm 16^{4,5}$	99 (56, 174) ^{5,6}	13.4 (6.9, 25.9) ^{5,6}	65.6 ⁵	4.1 ⁵	55.7 ⁵
Girls ($n = 1731$)	106 ± 15	95 (55, 163)	14.8 (7.5, 29.0)	58.8	2.8	47.2
Age (y)						
< 7 ($n = 46$)	92 ± 16^7	128 (75, 217) ⁷	11.7 (6.1, 22.5) ⁷	73.9	19.6 ⁷	67.4
7.0-8.9 ($n = 734$)	103 ± 16	94 (54, 161)	14.5 (7.4, 28.4)	63.0	4.4	50.8
9.0-10.9 ($n = 1585$)	104 ± 16	94 (54, 164)	14.4 (7.3, 28.3)	62.8	2.6	50.6
11.0-12.9 ($n = 935$)	104 ± 16	100 (58, 174) ⁷	13.7 (7.0, 26.9) ⁷	61.7	3.5	53.3
≥ 13 ($n = 295$)	105 ± 16	104 (61, 178) ⁷	12.7 (6.6, 24.6) ⁷	57.6	2.7	50.2
All children ($n = 3595$)	104 ± 16	97 (56, 166)	14.0 (7.2, 27.3)	62.3	3.5	51.5

¹ Hemoglobin < 110 g/L.

² Hemoglobin < 70 g/L.

³ Anemia with protoporphyrin > 90 $\mu\text{mol/mol}$ heme or ferritin < 18 $\mu\text{g/L}$.

⁴ $\bar{x} \pm \text{SD}$.

⁵ Significantly different from girls, $P < 0.05$.

⁶ Geometric mean (-1 SD, $+1$ SD).

⁷ Significantly different from children aged 7.0-10.9 y, $P < 0.05$ (chi-square test).

TABLE 2
Iron-status indicators by parasitic infections

Parasitic infection	Hemoglobin	Protoporphyrin	Serum ferritin	Anemia ¹	Severe anemia ²	Iron deficiency anemia ³
	g/L	$\mu\text{mol/mol heme}$	$\mu\text{g/L}$	%	%	%
Malaria parasitemia						
Negative ($n = 1406$)	105 \pm 16 ^{4,5}	93 (55, 156) ^{5,6}	14.1 (7.2, 27.9) ⁵	58.6 ⁵	3.0 ⁵	46.3 ⁵
Positive ($n = 2164$)	103 \pm 16	99 (57, 174)	13.9 (7.1, 27.2)	64.8	3.8	55.1
Microhematuria⁷						
Negative ($n = 2469$)	104 \pm 16	97 (56, 169)	14.0 (7.3, 27.2)	62.9	3.4	52.4
Positive ($n = 1096$)	104 \pm 16	96 (56, 163)	14.1 (7.3, 27.2)	60.9	3.5	49.5
Hookworms						
0 epg ($n = 215$)	110 \pm 13 ⁸	84 (49, 142) ⁸	18.3 (9.6, 34.6) ⁸	46.5 ⁸	0.9 ⁸	33.5 ⁸
1-1999 epg ($n = 2562$)	105 \pm 15	93 (56, 155)	14.8 (7.9, 27.9)	60.0	2.5	48.7
2000-3999 epg ($n = 456$)	100 \pm 17	107 (63, 183)	11.5 (6.0, 21.7)	73.7	5.9	64.7
4000-5999 epg ($n = 128$)	96 \pm 19	127 (75, 216)	9.9 (5.2, 18.7)	79.7	10.2	71.1
≥ 6000 epg ($n = 67$)	93 \pm 23	152 (90, 259)	8.1 (4.3, 15.4)	77.6	14.9	74.6
<i>Trichuris trichiura</i>						
0 epg ($n = 137$)	106 \pm 16	97 (56, 166)	15.4 (8.0, 29.8) ⁸	60.6	2.2	52.6
1-1999 epg ($n = 2642$)	104 \pm 16	96 (54, 170)	14.3 (7.2, 28.5)	61.7	3.4	50.4
2000-3999 epg ($n = 428$)	104 \pm 16	97 (56, 166)	13.4 (6.9, 25.8)	63.3	3.5	54.4
4000-5999 epg ($n = 124$)	103 \pm 16	99 (58, 169)	13.1 (6.8, 25.3)	66.9	4.0	55.7
≥ 6000 epg ($n = 96$)	103 \pm 16	98 (58, 166)	12.1 (6.2, 23.4)	62.5	4.2	50.0
<i>Ascaris lumbricoides</i>						
Negative ($n = 961$)	106 \pm 16 ⁵	96 (56, 162)	14.6 (7.4, 28.6)	56.5 ⁵	3.1	46.3 ⁵
Positive ($n = 2466$)	104 \pm 16	97 (56, 167)	14.0 (7.2, 27.2)	64.2	3.5	53.1

¹ Hemoglobin < 110 g/L.

² Hemoglobin < 70 g/L.

³ Anemia with protoporphyrin > 90 $\mu\text{mol/mol heme}$ or ferritin < 18 $\mu\text{g/L}$.

⁴ $\bar{x} \pm \text{SD}$.

⁵ Significantly different from positive, $P < 0.05$.

⁶ Geometric mean (-1 SD, +1 SD).

⁷ An indicator of urinary schistosomiasis.

⁸ Significant linear trend with increasing intensity of infection, $P < 0.05$.

hookworm epg, the prevalence of severe anemia was nearly 15%. Children with circulating malaria parasites had hemoglobin and EP concentrations slightly but significantly worse than children without parasitemia; however, SF concentrations were not different. *T. trichuris* infection was associated with lower SF, and this relation was intensity-dependent, but no other indicator of iron status was related to *T. trichuris*. *A. lumbricoides* infection was associated with lower hemoglobin concentrations, but not with EP or SF. Hematuria was not related to iron status.

When demographic, anthropometric, and parasitologic variables were considered jointly in multivariate models, hookworm remained the strongest explanatory variable for hemoglobin, EP, and SF. For SF, the only variables retained in the multivariate model were hookworm infection and age > 11 y. For EP, hookworm infection, age < 7 y, and stunting were retained. The final multivariate model for hemoglobin concentration was more complex. Hookworm infection, sex, age < 7 y, *A. lumbricoides* infection, malaria parasitemia, and stunting were significant and all appeared to have independent associations with hemoglobin because the regression coefficients from the multivariate model were practically identical to the bivariate differences shown in Tables 1 and 2. Wasting and age > 11 y were not retained in the final hemoglobin model.

To assess the importance of parasitic infections as causes of anemia in this population, we estimated the attributable fraction of the three forms of anemia associated with the parasites

(Table 3). We also calculated an attributable fraction for stunting because it may be considered an indicator of a chronically poor diet. Sex and age, although significantly associated with anemia prevalence, were not considered because they are not preventable. About one-fourth of all anemia, one-third of iron deficiency anemia, and three-fourths of severe anemia were attributable to hookworm infection in this population of schoolchildren. Eleven percent or less of anemia and iron deficiency anemia were attributable to malaria, *A. lumbricoides* infection, or stunting.

DISCUSSION

Evidence of iron deficiency anemia

Our findings confirm that iron deficiency anemia is an urgent problem among schoolchildren in coastal East Africa. In the context of sub-Saharan Africa, Pemba Island is underdeveloped with regard to health and nutrition status, but it is not unique in the prevalence of iron deficiency or parasitic infections. Similarly, poor iron status of schoolchildren has been reported in other studies from both west (17) and east (18, 19) Africa. Given the relative feasibility of addressing parasitic infections and iron deficiency through school health programs, public health actions should be carefully considered.

The pattern of EP and SF concentrations by age remained significant in multivariate models and are biologically plausi-

TABLE 3
Attributable fractions of anemia associated with preventable risk factors¹

Form of anemia and risk factor	Prevalence of risk factor %	Prevalence ratio ²	Attributable fraction ² %
All anemia			
Hookworm infection	94	1.36 (1.17, 1.57)	25 (15, 35)
Ascaris infection	72	1.14 (1.07, 1.21)	9 (5, 13)
Malarial infection	61	1.11 (1.05, 1.17)	6 (3, 9)
Stunting	48	1.13 (1.08, 1.19)	6 (3, 8)
Iron deficiency anemia			
Hookworm infection	94	1.56 (1.29, 1.89)	35 (23, 47)
Ascaris infection	72	1.15 (1.06, 1.24)	10 (5, 15)
Malarial infection	61	1.19 (1.11, 1.27)	10 (7, 14)
Stunting	48	1.15 (1.06, 1.20)	6 (3, 9)
Severe anemia			
Hookworm infection	94	3.81 (0.95, 15.33)	73 (110, 35)

¹ All anemia defined as a hemoglobin concentration < 110 g/L; iron-deficiency anemia defined as anemia with protoporphyrin > 90 μmol/mol heme or ferritin < 18 μg/L; severe anemia defined as a hemoglobin concentration < 70 g/L.

² 95% CIs associated with risk factor in parentheses.

ble. The youngest children (< 7 y) would have most recently experienced the high iron demands of early childhood, whereas children aged ≥ 11 y may have been experiencing the pubertal growth spurt. Boys had EP and SF values indicative of greater iron deficiency compared with girls, but this sex difference did not remain significant in multivariate analyses. Because boys tended to have more intense hookworm infections than girls, the sex difference disappeared when we controlled for hookworm infection intensity. Other studies of iron status of schoolchildren have also found no important sex differences in SF until the later teenage years (20–22).

Evidence for non-iron deficiency anemia

Anemia can stem from a variety of causes, and it is apparent in this population that iron deficiency does not account for all the anemia observed. Whereas EP rose and SF declined at ages > 11 y, hemoglobin did not change significantly. Also, stunting was associated with a lower hemoglobin concentration but was not associated with EP or SF. Lastly, *A. lumbricoides* infection and malarial parasitemia remained significant in the multivariate model for hemoglobin, but were not retained in the models of EP and SF after hookworms were controlled for. These findings suggest that factors other than poor iron status contribute to the low hemoglobin concentrations in this population. It is possible that one or more other nutrient deficiencies link stunting, ascariasis, or malaria to erythropoiesis.

The negative association of hemoglobin to *A. lumbricoides* (23) and malaria (24–26) infections has been reported by others as well. Hemoglobin may be lowered in a nonspecific way during infection—the so-called anemia of chronic disease (27–29). However, it is unlikely that the acute-phase response to infection with malaria or *A. lumbricoides* would influence hemoglobin more than EP or SF. As we described in greater detail elsewhere (7), there was no decreasing trend in hemoglobin concentration as malarial parasitemia increased in this population. We hypothesize that this is because Zanzibari children are exposed to *P. falciparum* repeatedly in their preschool years, and by school age they have developed significant

TABLE 4
Characteristics of the study sample¹

	Frequency %
Age (y)	
< 7	1.3
7.0–8.9	20.4
9.0–10.9	44.1
11.0–12.9	26.0
≥ 13	8.2
Sex (boys)	51.8
Malaria parasitemia	60.6
Hookworm infection	
Negative (0 epg)	6.3
Light (1–1999 epg)	55.5
Moderate (2000–4999 epg)	34.9
Heavy (≥ 5000 epg)	3.3
<i>Trichuris trichiura</i> infection	
Negative (0 epg)	4.0
Light (1–1999 epg)	77.1
Moderate (2000–9999 epg)	17.9
Heavy (≥ 10 000 epg)	1.0
<i>Ascaris lumbricoides</i> infection	
Negative (0 epg)	28.0
Light (1–9999 epg)	61.7
Moderate (10 000–49 999 epg)	10.3
Heavy (≥ 50 000 epg)	0.1
Microhematuria ²	
Negative	69.2
Positive	30.8
Stunted ³	47.6
Wasted ⁴	35.3

¹ epg, eggs per gram feces.

² An indicator of urinary schistosomiasis.

³ Height-for-age Z score < -2.

⁴ Body mass index below the 5th centile of reference population.

resistance to this infection (7). The difference in hemoglobin concentration between children with and without these infections was significant but small (20 g/L for both malaria and ascariasis).

Risk factors for iron deficiency anemia

The most impressive finding in this study was the contribution of hookworms to the burden of iron deficiency and anemia. The strength of the association we observed is explained by the range of hookworm infection intensities in the population, and the lack of storage iron that would buffer the effect of hookworm-related blood loss on iron status (30). Our data confirm the findings of Stephenson et al (18, 31) in coastal Kenya, in which the hemoglobin deficit associated with hookworm infection was greater than that of either schistosomiasis or malaria among schoolchildren.

Although we did not assess dietary iron intake, it is also clear from our data that dietary iron intakes were seriously inadequate. Even among children with no hookworm infection, the prevalence of anemia was 46.5%, and the average values for hemoglobin, EP, and SF only bordered on adequacy. Although anemia was prevalent in children without hookworm, severe anemia was rare (< 1%). If one imagines a normal hemoglobin distribution, it appears that dietary deficiency shifts the distribution significantly to the left, driving many children into a

state of mild iron deficiency anemia. The addition of hookworms pulls the center of the distribution even farther left, and dramatically pulls down the left tail.

The intensity-dependent association between *T. trichiura* infection and SF concentration is likely explained by their common association with hookworm, because *T. trichiura* infection did not remain significant in the multivariate model of SF. The presence and intensity of *T. trichiura* infection was significantly associated with hookworm-infection intensity, despite the different routes of transmission of these two helminths. One clinical study found intestinal blood loss associated with *T. trichiura* infection (32), but another did not (33). We studied intestinal iron loss in this population and found no association between fecal hemoglobin concentration and *T. trichiura* infection after hookworm infection was controlled for (34). Thus, we conclude that the cross-sectional association between iron-status indicators and *T. trichiura* infection observed by us and others (35) was probably not caused by *T. trichiura*-associated blood loss.

Other investigators have found a strong association between urinary schistosomiasis and iron status in sub-Saharan Africa (18, 31, 36). The lack of association in our study may be due to several reasons. Most probably, it is because a highly effective test-and-treat campaign for schistosomiasis was conducted on Pemba Island from 1988 to 1992 (37). Thus, children with a positive indication of schistosomiasis in our study may have had the disease for only a short duration. Also, hookworm infection was significantly less common in children with schistosomiasis in this sample. Finally, hematuria is an excellent field tool but an imperfect diagnostic indicator of schistosomiasis (11), and misclassification would attenuate a true association. Use of quantitative egg counts in urine would be a more powerful way to examine this relation.

Implications for control of iron deficiency anemia

The most important application of these findings is to guide development of appropriate interventions to control iron deficiency anemia in African schoolchildren. Our results provide a strong basis for hookworm control as a strategy to control iron deficiency in this population group. If hookworms could be eradicated, anemia might be reduced by as much as 25%, iron deficiency anemia by 35%, and severe anemia by 73%. Because of the intensity-dependent relation of hookworm infection to intestinal iron loss and iron status, reducing hookworm burdens (rather than eradicating infection) is the most rational short- to medium-term goal (38). Anthelmintic drugs are safe and inexpensive (\approx US\$0.025-0.20 per treatment), and periodic delivery of them through the school system is a highly feasible public health intervention (39). Our findings indicate that hookworm control will have the greatest effect on the lower tail of the hemoglobin distribution, ie, preventing relatively severe anemia.

Stopping the leakage of iron from children's bodies will not replenish their stores however, and thus hookworm control alone will not solve the problem. Additional intake of iron will be needed. In Zanzibar and many other parts of sub-Saharan Africa, iron fortification of foods is not yet feasible. School-based iron supplementation could be an opportunity to make up the iron deficit that many children bring with them from the preschool years, and to build stores to carry them into adult-

hood. Applied research is needed to find the most effective dosing regimens to achieve these goals.

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