ABSTRACT A randomized, double-blind, placebo-controlled iron supplementation trial was conducted in Kenya to examine the effect of iron supplements on appetite and growth in 87 primary school children. Sustained-release ferrous sulfate (150 mg) or placebo tablets were provided daily at school for 14 wk. Prior to tablet administration, baseline anthropometry, iron nutritional status (hemoglobin and serum ferritin), parasitic infections and clinical indicators of morbidity were measured. A baseline appetite test was conducted twice on each child by quantitatively measuring the ad libitum consumption of a midmorning snack. In addition, each child was asked for a subjective assessment of his or her appetite. Follow-up exams and appetite tests were identical to those at baseline. Findings indicated that provision of iron supplements resulted in improved growth and improved appetite (in terms of both energy intake of the snack and child report of appetite) as compared with children receiving the placebo. The increased energy intake from the snack was 10% of the daily estimated energy intake for children of this same age group living elsewhere in Kenya. Further research into the underlying physiological mechanisms may shed light on the relationship between iron nutritional status and appetite. J. Nutr. 124: 645-654, 1994.

INDEXING KEY WORDS:
• iron supplementation • growth • appetite
• children • anorexia

Iron deficiency anemia is considered to be the most prevalent nutritional deficiency worldwide (DeMaeyer and Adiels-Tegman 1985). Growing children require large amounts of iron for growth and are therefore vulnerable to iron deficiency, particularly those children whose diets are marginal in iron content and who experience heavy iron losses due to parasitic infections. The provision of iron to iron-deficient children has been shown to improve growth (Aukett et al. 1986, Briend et al. 1990, Chwang et al. 1988, Judisch et al. 1966, Latham et al. 1990a, Stockman and Clark 1984). The mechanism for this improved growth is still uncertain.

One symptom associated with iron deficiency in humans is loss of appetite, sometimes referred to as anorexia (Judisch et al. 1966, Pollitt and Leibel 1976 and Theuer 1974). To date, no well-controlled longitudinal studies have attempted to measure a loss of appetite associated with iron deficiency anemia. However, some authors have speculated that the improved growth observed in children provided with iron supplements might be attributable to a correction of anorexia (Auckett et al. 1986, Chwang et al. 1988, Latham et al. 1990a). Decreased food intake and decreased growth have been reported in iron-deficient piglets (Hannan 1971), rats (Canale and Lanzkowsky 1970, Koivistoimen et al. 1968) and bovines (Reddy et al. 1987).

In tropical Kenya, where parasitic infections and poor dietary intakes coexist, iron deficiency is a
major public health problem. Therefore, to assess whether the provision of iron tablets improves child appetite and growth, we conducted an iron supplementation trial among Digo primary school children in Kenya's Coast Province.

MATERIALS AND METHODS

Sample selection. All children between the ages of 6 and 11 y and attending Standards 1 and 2 in Shamu primary school, located in Shamu village, Coast Province, Kenya, were eligible to enter the study. Each child received a baseline medical exam (Exam 1), which included 1) a determination of initial hemoglobin and serum ferritin as indicators of iron status; 2) anthropometric measurements including weight, height, and triceps and subscapular skinfolds as indicators of nutritional status; 3) a physical exam for morbidity screening; and 4) the collection of fecal samples for determination of the prevalence and intensity of helminthic infections, including Trichuris trichiura, Ascaris lumbricoides and hookworm (predominantly Necator americanus).

One hundred and twelve children were initially recruited; two of these were eliminated because of parental refusal. Another 23 children were eliminated for the following reasons: 1) severe anemia as indicated by hemoglobin <80 g/L \( (n = 3) \); 2) heavy hookworm infection with egg counts >10,000 eggs per gram feces \( (n = 5) \); 3) blood in the urine, which, in this area, is usually indicative of Schistosoma haematobium infection \( (n = 4) \); 4) clinical evidence of other serious illness requiring immediate treatment \( (n = 2) \); 5) difficulty either in blood sampling or in conducting other parts of the physical exam \( (n = 2) \); 6) a self-reported dislike (upon being queried) of uji, the porridge used in the appetite test \( (n = 2) \); or 7) repeated absence of the child when the initial exams were being conducted \( (n = 5) \). The final sample size was 87. Of the 23 children excluded from the study, those needing medical treatment were treated immediately by a physician. There was only one dropout during the study: a child who moved with his family to another village. All analyses presented are on the final complete data set containing 86 children, for whom data were available at both the pre-intervention and post-intervention examinations.

Study design. Following the baseline examination (Exam 1), children were stratified by gender and initial hemoglobin values. The stratification was conducted by creating separate lists for boys and girls in order of increasing initial hemoglobin value. Going down the lists, the children were then randomly assigned to either the iron-treated or placebo group using a random-number table (Snedecor and Cochran 1980). This procedure ensured that the iron-treated and placebo groups were comparable in gender ratio and mean baseline hemoglobin values.

A double-blind, placebo-controlled iron supplementation trial was then initiated. Supplements in the form of 150 mg of sustained-release ferrous sulfate and identical-appearing placebo capsules (FEOSPAN spansule capsules, Smith Kline & French Laboratories Ltd, Hertfordshire, England) were provided daily at school early in the morning (between 0800 and 1000 h) by field workers unaware of which capsules contained the iron. The sustained-release spansules were chosen rather than ordinary ferrous sulfate tablets because they are administered only once a day rather than three times a day and because the slow-release iron results in fewer side effects than do ordinary ferrous sulfate tablets \( (n = 5) \). Compliance was ensured on weekdays by having the field assistants observe each child ingest the capsule.

An appetite test was administered twice to each child before and again twice after the 14-wk trial. At the end of the supplementation period, a second set of examinations was conducted (Exam 2, similar to Exam 1), after which all of the children were treated as needed for anemia and/or helminthic infections.

The protocol for this research was approved by the Cornell University Committee on Human Subjects and received both scientific approval and ethical human subjects clearance from the Kenya Medical Research Institute, Nairobi, Kenya.

Physical examination methods. The 86 children participating in the supplementation trial were examined twice: at baseline (Exam 1) in March 1990 and 14 wk later (Exam 2) in July 1990. The following components were included in both exams, unless otherwise specified:

1) Pretreatment questionnaire. Background information was obtained from each subject, including child’s name, parents’ names, ethnic group, age, sex, school grade, number of siblings, and other relevant information (Exam 1 only)

2) Anthropometry. Anthropometric measurements used to assess growth were performed at both exams by the same examiner (the second author, MCL) according to the methods of Jelliffe \( (n = 4) \). This procedure ensured that the iron-treated and placebo groups were comparable in gender ratio and mean baseline hemoglobin values.

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from the Fels Research Institute and U.S. Health Examination Surveys. These constitute the international growth reference curves recommended by the World Health Organization (WHO).

3) Parasitology. Fecal specimens were collected at both Exam 1 and Exam 2 for quantitative determination of hookworm, Trichuris trichiura, and Ascaris lumbricoides eggs (eggs per gram feces) following a modified Kato technique (Peters et al. 1980) using 50-μg templates and a glycerine-malachite green solution (WHO-UNICEF 1981). This provides qualitative data (presence or absence) as well as quantitative data (eggs per gram of feces) on intestinal nematode prevalence and intensity. Thick and thin blood smears were collected and prepared using Field’s and Giemsa’s stains (Manson-Bahr and Afted 1982), respectively, and examined for malaria parasite prevalence, intensity, and species by an experienced technologist (Exam 2 only). Giemsa’s stain was diluted 1:10 and buffered to a pH of 7.0.

4) Clinical examination. A clinical exam was conducted by a physician for signs of nutrient deficiencies and other diseases. Spleen size was estimated and rated using the Hackett scale (Bruce-Chwatt 1980). Liver enlargement was recorded as centimeters below the right costal margin and the mid-sternum. Blood in the urine was determined by a positive test (++ or greater) on urinary reagent strips (Ames N-Multistiks; Ames Company, Elkhart, IN). Morbidity data were obtained by child recall of illnesses during the week previous to the physical examination, with specific questions concerning the presence of cough or diarrhea.

5) Hematology. Hemoglobin determinations were performed within 6 h of blood collection on duplicate specimens of finger prick capillary blood analyzed using the cyanmethemoglobin method on a Spec- tronic20 spectrophotometer. Plasma ferritins were determined using an enzyme immunoassay (EIA) kit (Ferrizyme™; Abbott Laboratories, Chicago, IL) on finger prick plasma collected in two heparinized capillary tubes measuring 75 × 1 mm (Fisher Scientific, Pittsburgh, PA; Pootrakul et al. 1983). All of the samples collected during both Exams 1 and 2 were analyzed for ferritin at the end of the supplementation trial. The Ferrizyme assay was conducted a total of seven times, with each assay containing approximately equal numbers of samples collected from children in the iron-treated and placebo groups. A WHO International Standard for human liver ferritin (1st International Standard, 1984, Reagent #80/602; National Institute for Biological Standards and Control, London, England), reconstituted and diluted to 97.0 and/or 9.70 ng/mL, was included in each assay. A more detailed description of the methods employed was presented by Lawless (1993).

Appetite determination. A previous search of the literature for a quantitative measure of appetite has revealed no reliable method appropriate for a field study [Latham et al. 1990b, Stephenson et al. 1993]. Appetite itself is difficult to quantify. Because to nutritionists the most important outcome of appetite is food intake, Latham et al. (1990b) devised a method of using a culturally appropriate food to which the children had free access as a snack during mid-morning, with ad libitum consumption of the snack then becoming a quantitative proxy for appetite. The food offered was uji, a thin maize porridge that the children liked and which was a common component of their diet. Later we discovered that uji was one of the most frequent foods offered by concerned caregivers to children exhibiting anorexia in this culture in an attempt to encourage these children to eat [Lawless, unpublished data]. Because of the liquid consistency of uji, the volume ingested by each child was easy to measure. The constituents of 1 L of uji are: 100 g maize meal, 50 mL whole milk, 62.5 g sugar, and enough water added to make 1 L. Based on these constituents, the energy content of uji is 2709 kJ/L [Latham et al. 1990b].

The steps used for appetite determination were as follows:

1) Approximately 12 children were tested at one session, each sitting at a table in the school room.
2) Uji was offered to each child in a 1-L measuring jug, together with a mug and spoon, for ad libitum consumption at ~1100 h.
3) Each child was encouraged to consume as much as desired; if the entire liter was consumed, the jug was refilled with another 0.5 L and the child was allowed to continue eating.
4) When the child was “satisfied,” the amount of uji consumed (in mL) was determined and recorded.

On the day the uji test was administered, a food recall was conducted on each child to assess the amount of food already eaten that morning. Actual food samples and culture-specific measures (such as tin cups and plates) were used in conducting the recall. A field assistant acted as translator, probing the children to identify all of the foods eaten and to estimate portion size. The energy value of the morning food intakes was then computed using nutrient values reported for local Kenyan foods [USDHEW 1972 as calculated by Kurz 1985; Murphy et al. 1991]. Neither the children nor their mothers were informed of which days they would be receiving the uji at school.

In addition to the food recall, each child was asked (in Kidigo, their native language) for a subjective assessment of his or her appetite in the following manner: “Do you consider your appetite in the last few days to be: very poor, poor, average, good, or very good?” Responses were coded as an appetite score ranging from 1 to 5, with 1 = very poor and 5 = very good.

Statistical analyses. Data were analyzed using DataDesk™ software [v. 3.0, DataDescription, Ithaca,
ny). Student's t tests were used to test for differences between group means in the iron-supplemented and placebo groups; one-way ANOVA was used for testing differences among more than two means. Paired sample Student's t tests were employed when examining changes within groups between Exams 1 and 2. Variables exhibiting a log-normal distribution (plasma ferritins, parasite egg counts) were log-transformed to approximate normality for inclusion in certain analyses; results presented are specified as either the arithmetic or geometric means. Chi-square analyses were conducted on group comparisons of prevalence rates of anemia, cough, diarrhea, splenomegaly and malaria. Multiple linear regression analyses (OLS regression) using the all variables method were performed to determine the most significant predictors of the most important outcomes of the supplementation trial (changes in growth, appetite and ferritins; Neter et al. 1990). The paired Wilcoxon signed rank test was used to assess differences between baseline and follow-up qualitative appetite scores derived from the appetite self-perception question asked on the day of the iii test administration [Snedecor and Cochran 1980]. A P value of <0.05 was considered significant in all statistical tests.

RESULTS

Baseline characteristics. Table 1 summarizes the baseline description of subjects. There were no significant differences between the groups in any of the measured variables shown here. Children were comparable in age and gender distribution. Mean initial hemoglobin was 112.3 g/L in the placebo group and 110.4 g/L in the iron-treated group. Ferritin values were comparable in the two groups (geometric means of 20.4 vs. 17.1 µg/L, placebo vs. iron-treated). Virtually all of the children were infected with hookworm, and approximately half of the children in each group had splenomegaly.

Prevalence of anemia in the sample. The prevalence of anemia at the baseline exam was determined in the placebo and iron-treated groups using the WHO hemoglobin cutoff of 120 g/L. Both groups exhibited a high prevalence of anemia (71.4% in the placebo group compared with 79.5% in the iron-treated group, not significantly different; Table 1). Combining groups, the prevalence of anemia among the Shamu schoolchildren aged 6–11 y was 75.6%.

Baseline helminthic infections. Table 2 summarizes the baseline (Exam 1) prevalence and intensity of the three helminth infections (Necator americanus, Trichuris trichiura and Ascaris lumbricoides) in Shamu children in their iron-treated and placebo groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>Iron-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>[n = 42]</td>
<td>[n = 44]</td>
</tr>
<tr>
<td>Age, y</td>
<td>8.9 ± 1.3</td>
<td>8.6 ± 1.3</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>22:20</td>
<td>23:21</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>112.3 ± 11.1</td>
<td>110.4 ± 9.7</td>
</tr>
<tr>
<td>Ferritin, µg/L</td>
<td>20.4</td>
<td>17.1</td>
</tr>
<tr>
<td>Hookworm</td>
<td>92.9%</td>
<td>97.7%</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>52.4%</td>
<td>45.5%</td>
</tr>
<tr>
<td>Anemic</td>
<td>71.4%</td>
<td>79.5%</td>
</tr>
</tbody>
</table>

1Values are means ± SD.
2Values are geometric means.
3Values are percent positive.

Hematological and clinical changes between Exams 1 and 2. Table 3 summarizes the hematological measurements and clinical findings in the supplemented group: 52.4% in the placebo group compared with 29.5% in the iron-treated group (x², P < 0.05).

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>Iron-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
<td>[n = 44]</td>
<td>[n = 42]</td>
</tr>
<tr>
<td>Hookworm</td>
<td>% prevalence</td>
<td></td>
</tr>
<tr>
<td>Arithmetic mean</td>
<td>2515 ± 2505</td>
<td>2067 ± 2192</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>1231</td>
<td>745</td>
</tr>
<tr>
<td>Trichuris</td>
<td>% prevalence</td>
<td></td>
</tr>
<tr>
<td>Arithmetic mean</td>
<td>5269 ± 6662</td>
<td>3957 ± 6832</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>1155</td>
<td>1050</td>
</tr>
<tr>
<td>Ascaris</td>
<td>% prevalence</td>
<td></td>
</tr>
<tr>
<td>Arithmetic mean</td>
<td>4924 ± 12,947</td>
<td>7649 ± 15,906</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>14.3b</td>
<td>97.2</td>
</tr>
</tbody>
</table>

1Values are means ± SD for arithmetic means and means for geometric means. Arithmetic and geometric means are derived from number of worm eggs per gram of feces. 2Significantly different (P < 0.05) from placebo children, x² between group test.
3Significantly different (P < 0.05) from placebo children, group t test.
placebo and iron-supplemented groups both before (Exam 1) and after (Exam 2) supplementation. Mean hemoglobin levels fell 2.4 g/L in the placebo group and rose 3.2 g/L in the iron-supplemented children (mean change significantly different, group t test, P < 0.005). Serum ferritin concentrations in the iron-treated group increased significantly compared with those of the placebo group (16.5 compared with 0.3 µg/L, respectively; P < 0.001). Clinical examination showed no significant difference between the two groups of children in prevalence of splenomegaly or child report of diarrhea or cough during the week prior to each exam. The results for prevalence of malaria at Exam 2 indicated no difference between the two groups; prevalence among the children receiving the placebo capsules was 68%, whereas among the iron-supplemented children it was 66%.

**Anthropometric changes between Exams 1 and 2.**

The anthropometry data are presented in Table 4. All

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Exam 1</th>
<th>Exam 2</th>
<th>Paired t test</th>
<th>X Change [Exam 2 - Exam 1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>PL</td>
<td>22.9 ± 3.8</td>
<td>23.6 ± 3.8</td>
<td>(P &lt; 0.0000)</td>
<td>0.7 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>22.1 ± 3.1</td>
<td>23.6 ± 3.3</td>
<td>(P &lt; 0.0000)</td>
<td>1.6 ± 0.5³</td>
</tr>
<tr>
<td>Height, cm</td>
<td>PL</td>
<td>124.3 ± 7.5</td>
<td>125.4 ± 7.5</td>
<td>(P &lt; 0.0000)</td>
<td>1.1 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>122.9 ± 6.5</td>
<td>124.3 ± 6.5</td>
<td>(P &lt; 0.0000)</td>
<td>1.4 ± 0.5²</td>
</tr>
<tr>
<td>Weight-for-age Z-score²</td>
<td>PL</td>
<td>-1.32 ± 0.81</td>
<td>-1.32 ± 0.79</td>
<td>NS</td>
<td>0.00 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>-1.30 ± 0.89</td>
<td>-1.08 ± 0.91</td>
<td>(P &lt; 0.01)</td>
<td>0.22 ± 0.12²</td>
</tr>
<tr>
<td>Height-for-age Z-score²</td>
<td>PL</td>
<td>-1.26 ± 1.08</td>
<td>-1.34 ± 1.06</td>
<td>(P &lt; 0.05)</td>
<td>-0.08 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>-1.20 ± 1.06</td>
<td>-1.24 ± 1.06</td>
<td>NS</td>
<td>-0.04 ± 0.09²</td>
</tr>
<tr>
<td>Weight-for-height Z-score²</td>
<td>PL</td>
<td>-0.65 ± 0.75</td>
<td>-0.55 ± 0.72</td>
<td>(P &lt; 0.05)</td>
<td>0.10 ± 0.21</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>-0.74 ± 0.79</td>
<td>-0.31 ± 0.80</td>
<td>(P &lt; 0.001)</td>
<td>0.43 ± 0.22²</td>
</tr>
</tbody>
</table>

¹Values are means ± SD, n = 42 in the PL group and n = 44 in the FE group. NS = not significant. ²FE significantly different from PL group t test (P < 0.01). ³FE significantly different from PL group t test (P < 0.001). ⁴FE significantly different from PL group t test (P < 0.05).

²See Materials and Methods for description of derivation.
children increased in weight and height between Exams 1 and 2, but the mean changes in weight and height were significantly greater for children receiving iron capsules than for those receiving placebo (group t test, $P < 0.01$). The mean change in growth represented by Z-scores for both weight-for-age and weight-for-height increased significantly in the iron-treated children compared with the placebo group (group $t$ test, $P < 0.001$). Although mean change in height-for-age was also significantly different for iron-treated children compared with controls ($P < 0.05$; Table 4), both groups of children displayed overall mean decreases in height-for-age, indicating that, on average, children from both groups were lagging in linear growth and failed to track the NCHS growth curve for heights.

Figures 1 and 2 present graphic illustrations of changes in anthropometric indicators between Exams 1 and 2 for the two groups. Figure 1a illustrates how the mean changes in Z-score indicators for weight-for-age and weight-for-height were significantly greater in iron-treated children than in controls ($P < 0.001$), whereas height-for-age between Exams 1 and 2 actually decreased for children in both experimental groups. Figure 1b presents mean changes in arm circumference, triceps skinfolds and subscapular skinfolds between Exams 1 and 2 for children in the iron-treated and placebo groups. The iron-treated children exhibited significantly greater increases in all three indicators than did children in the placebo group (group $t$ test, $P < 0.001$).

Figure 2 presents frequency distribution curves of children in the iron-treated and placebo groups plotted separately for both their change in weight-for-age and their change in weight-for-height Z-scores.

**Appetite changes between Exams 1 and 2.** The results of the appetite test in terms of both the volume consumed and mean energy content of the maize porridge consumed by the iron-treated group as compared with the placebo group both before (Exam 0

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**FIGURE 1** a) Mean change in Z-scores for the three anthropometric indicators [weight-for-age (Wt/Age), height-for-age (Ht/Age), and weight-for-height (Wt/Ht)] for children in the iron-treated (FE) and placebo (PL) groups (Exam 2 – Exam 1). b) Mean change in arm circumference (AC), triceps skinfold (TSS) and subscapular skinfold (SSS) in children in the iron-treated (FE) and placebo (PL) groups (Exam 2 – Exam 1). Values are means ± SD, $n = 44$ in the FE group and $n = 42$ in the PL group.

**FIGURE 2** Frequency distribution curves of change in weight-for-age Z-scores and change in weight-for-height Z-scores for children in the iron-treated (FE) and placebo (PL) groups plotted separately, $n = 44$ in the FE group and $n = 42$ in the PL group.
TABLE 5

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Exam 1</th>
<th>Exam 2</th>
<th>Paired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uji, kJ</td>
<td>PL</td>
<td>1688 ± 769</td>
<td>1894 ± 659</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>1684 ± 718</td>
<td>2373 ± 718</td>
<td>(P &lt; 0.001)</td>
</tr>
<tr>
<td>Uji, mL</td>
<td>PL</td>
<td>623 ± 283</td>
<td>699 ± 243</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>FE</td>
<td>621 ± 265</td>
<td>876 ± 264</td>
<td>(P &lt; 0.001)</td>
</tr>
</tbody>
</table>

1Values are means ± SD, n = 42 in the PL group and n = 44 in the FE group. NS = not significant. 

The results indicate a significantly greater mean volume and energy intake (2373 ± 718 kJ compared with 1894 ± 659 kJ; mean ± SD, group t test, P < 0.01) of the porridge in the iron-treated group as compared with the placebo group after the 3-mo supplementation period.

The recalls conducted to establish the morning food intakes for both groups prior to administering the appetite test showed no significant difference between children in the two groups in terms of total breakfast energy intake (Exam 1: 565 ± 260 vs. 649 ± 214 kJ; Exam 2: 708 ± 225 vs. 741 ± 311 kJ; mean ± SD, placebo vs. iron-treated group, respectively.)

The results for self-perception of appetite are presented in Table 6. Children in the iron-treated group reported a better appetite at Exam 2 than at Exam 1 (paired Wilcoxon signed rank test, P < 0.05), whereas there was no significant difference in perceived appetite in the placebo group.

**Multivariate models and analyses.** Multiple regression models for some of the most important outcome variables [including change in uji (porridge) intake (energy consumed), change in weight-for-height Z-score, and change in ferritin (µg/L)] were developed, but only the best model for explaining the variability in change in porridge intake between Exams 1 and 2 is presented here (Table 7). The other models will be discussed in brief where appropriate in the Discussion section (see Lawless 1993 for more details).

After controlling for age and gender, the model constructed for change in porridge intake between Exams 1 and 2 shows that group (iron tablets), change in ferritin, and change in self-reported child appetite score all exhibited a significant positive linear effect on the outcome [R² (adj) = 38.9%; Table 7]. Predictors exhibiting a significant negative effect on change in porridge intake included initial hemoglobin value and presence or absence of diarrhea during the week prior to Exam 1. In addition, a significant interaction between gender and group entered the model, with girls exhibiting a significantly greater change in intake of porridge than did boys.

**DISCUSSION**

The overall prevalence of anemia at Exam 1 in both groups of children combined was 75.6% when calculated using the WHO hemoglobin cutoff of 120 g/L. In comparison, in the recently published findings from the Collaborative Research Support Project (Murphy et al. 1992), prevalence of anemia using the WHO cutoff (adjusted for altitude) was reported to be 74.3% among Kenyan children inhabiting the Embu District.

In addition to iron deficiency and parasitic infections, there are other potential causes of anemia in the study children. These include other nutrient deficiencies (folate, vitamin B-12 and protein), chronic infections or inflammatory diseases (although ferritin...
values do not indicate that these were a major problem among this population, and hemoglobinopathies such as sickle cell anemia or thalassemia (but the latter are unlikely to have influenced the hemoglobins to the degree reported here).

As shown in Table 4, at baseline the children were relatively but not severely stunted (as indicated by weight-for-age and height-for-age Z-scores) with some wasting (as indicated by weight-for-height Z-score). The intervention improved both the weight-for-height and the weight-for-age Z-scores significantly. Height did not change much, nor is this surprising given that the intervention lasted for only 14 wk.

Mean changes for the Z-scores of the three indicators (weight-for-age, height-for-age and weight-for-height) and mean changes in arm circumference, triceps skinfold and subscapular skinfold were significantly greater in the iron-treated group than in the placebo group (Figure 1a,b). These findings support previous studies in Kenya and elsewhere that reported accelerated growth of anemic children treated with iron supplements (Auckett et al. 1986, Briend et al. 1990, Chwang et al. 1988, Judisch et al. 1966, Latham et al. 1990a, Stockman and Clark 1984). The frequency distribution curves for the iron-treated children were shifted to the right of that for the controls for both changes in weight-for-age and changes in weight-for-height Z-score units (Fig. 2), confirming that the group differences in mean change for these indicators is due not to a large change among a few children but to a shift of the entire population of treated children.

The physiological mechanism for the improved growth observed in the iron-supplemented children compared with children in the placebo group is not known. Multivariate analyses examining appetite as an intermediary outcome and growth as a final outcome did not yield useful findings. However, reduced food intake due to poor appetite among anemic children may be a factor. In a recent analysis (Becker et al. 1991) that examined weight gain determinants in Bangladeshi children 5–18 mo of age, inadequate food intake was the most important determinant of growth faltering (as compared with diarrhea, fever or other illnesses). Although growth patterns and determinants seen in very young children may not necessarily apply to those seen in children of primary school age, the Bangladeshi findings do suggest that this factor (food intake) be considered among older children.

The mean energy content of the porridge consumed per child per sitting in the iron-treated and placebo groups at baseline was 1686 kJ (Table 5). This is &gt;25% of the mean daily intake (6510 kJ/d) for both boys and girls combined from this same age group and during this same season (March through June in 1984 and 1985) in Embu District, Kenya (CRSP 1987). If we assume that the mean daily intakes of the Kenyan Digo children in our study are about the same as for the Embu children, then following supplementation, the mean porridge consumption increased in the iron-treated group by an additional 10.6% of their mean daily energy intakes (689 kJ), whereas porridge consumption increased by only 3.2% in the placebo group (206 kJ). Such an increase in food intake at a single sitting brings the iron-supplemented children closer to the Recommended Dietary Allowance (RDA) for energy intakes for American children of the same age group (8232 kJ; NRC 1989); such increases, if observed at every meal, would contribute significantly to overall food intakes.

An increase in intake of 10.6% (689 kJ) in the iron-treated children can be compared with the reported average reduction in most nutrient intakes of ~10% during febrile illnesses among children 5 to 30 mo of age in Bangladesh (Brown et al. 1985), and an average reduction in food intake of almost 20% (equal to 735 kJ in absolute figures) due to the anorexic effect of selected common illnesses in rural Guatemalan children aged 15–60 mo (Martorell et al. 1980). Our 10% estimated increase in intake related to the provision of iron supplements may be an underestimation. Again we understand that these other data are based on children younger than those in our study and that determinants of nutrient intakes may be different.

The increase in porridge intake observed in our study correlated strongly with the improved iron nutritional status (as measured by changes in hemoglobin and ferritin concentrations) of the supplemented children. In addition, the children’s perceptions of their own appetite improved in the iron-treated group but not in the placebo group (Table 6).

A multiple regression model for explaining the variability in change in porridge intake between Exams 1 and 2 for all children, after controlling for age and sex, showed significant positive and negative predictors of the changes (Table 7). The significant positive predictors were variables associated with provision of the iron tablets; including: 1) children in the iron-treated group, who, with all other factors being equal, exhibited a 139 kJ greater change in porridge energy intake than children in the placebo group; 2) increase in self-reported child appetite score, which for each unit change resulted in a 197 kJ greater change in snack intake; and 3) rise in ferritin, which for each 1 µg/L rise resulted in a 6 kJ greater change in porridge energy intake (among iron-supplemented children as compared with children receiving placebo, the ferritin predictor would translate into a group difference of 99 kJ due to the ferritin rise alone).

Predictors exhibiting a significant negative effect on change in porridge intake included 1) initial hemoglobin concentration (after controlling for age, sex and group, for every 1 g/L initial difference in hemoglobin value, there was a decrease in porridge energy intake
of 191 kJ) and 2) presence or absence of diarrhea during the week prior to Exam 1 (among those children having diarrhea at Exam 1, there was a 376 kJ decrease in porridge energy intake between Exams 1 and 2). Because diarrhea is often associated with loss of appetite in children, those infected would be expected to exhibit a smaller change in porridge intake, and it is plausible that those children infected at Exam 1 experienced bouts of diarrhea repeatedly throughout the intervention that repeatedly caused a poor appetite. In addition, it is also plausible that other factors associated with the diarrhea, such as poor hygienic conditions and lower socioeconomic status, would predict higher incidences of other illnesses as well, which in turn would explain the poor appetite.

The negative predictor of initial hemoglobin level on change in energy intakes might be explained as follows: the lower the initial hemoglobin value, the greater the response to iron therapy and therefore the greater the change in porridge intake. Other analyses examining the relationship between initial hemoglobin and change in appetite indicate that this is a plausible explanation (Lawless 1993).

In addition to these predictors, there was also a significant interaction between gender and group, with iron-supplemented girls exhibiting a greater increase in porridge consumption than did boys. It is not known why this occurred.

Despite randomization of children to either the iron-treated or placebo group, baseline prevalence and intensity of Ascaris infections were significantly greater in the placebo group than in the iron-treated group (Table 2). Among all of the variables measured, these variables were the only ones to differ between the two groups at baseline. However, Ascaris infections are considered to be the least important of the three helminth infections in this region, and despite these differences in Ascaris infections at baseline, there were no differences in baseline porridge intakes between the two groups. Further multiple regression analyses examining parasite prevalences, intensities, or changes in parasite intensities between Exams 1 and 2 as predictor variables for changes in porridge intake revealed that none of these parasite predictor variables were significant (data not shown).

The incomplete hemoglobin response to iron therapy (Table 3) in these children is an enigma, although such responses to iron therapy in supplementation trials in the tropics are almost the rule rather than the exception (Chwang et al. 1988, Harvey et al. 1989, Latham et al. 1990a). The Coast Province of Kenya is holoendemic for malaria, and at Exam 2, 67% of the children had Plasmodia parasites identified in their blood films, and more than half of the children in the sample had enlarged spleens (Table 3). Spleen enlargement occurs during acute malaria attacks and is said to be palpable within 2 wk after onset of the malaria (Markell et al. 1986). The increase in numbers of palpable spleens in both groups between exams can be explained by the increase in transmission of malaria occurring during the rainy season. Hence, it is very possible that transmission of malaria accounts in part for the lack of a complete hemoglobin response to the treatment.

Interestingly, in an iron supplementation trial conducted in Papua New Guinea in which school children were given 16 wk of therapy (400 mg of oral ferrous sulfate/d), the rise in hemoglobin was on the same order of magnitude as in the study reported here (+4.0 g/L in the iron-treated group compared with −2.0 g/L in the placebo group; Harvey et al. 1989). These authors attribute the poor response to iron in their school children to the genetic trait alphathalassemia, which may exist in the Papua New Guinean population. We do not have data on this trait in our study sample.

We conclude from this research that provision of iron supplements to anemic Kenyan primary school children resulted in improved growth and improved appetite as compared with children receiving placebo capsules. Whether the improved growth resulted from the improvement in appetite cannot be conclusively determined from this clinical trial. But it is plausible, and likely, that provision of iron tablets to anemic children results in improved appetite, which in turn results in improved growth. Further research into the underlying physiological mechanisms may shed more light on the relationship between iron nutritional status and appetite.

ACKNOWLEDGMENTS

The authors would like to thank Davy Koech, Director of the Kenya Medical Research Institute (KEMRI), and Melani Katsivo, Acting Director of the KEMRI Medical Research Centre in 1990, for permission and encouragement to conduct this research. In addition, we are indebted to the excellent field assistance provided by Hassan Juma Mwamanzu and Zeinabu Omari Mwamlola, and to the Shamu primary school students and teachers for their cooperation. The first author would like also to express her gratitude to the minor members of her special graduate committee for their contributions to the successful completion of this study: Daphne Roe, Dennis Miller and Gertrude Fraser.

LITERATURE CITED


