Effect of calcium supplementation on bone mineral accretion in Gambian children accustomed to a low-calcium diet[1–3]

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ABSTRACT

Background: Rural Gambian children have poor growth, delayed puberty, a low bone mineral content, and a low calcium intake.

Objective: We investigated the effect of a calcium supplement on bone mineral accretion in rural Gambian children.

Design: A randomized, double-blind, placebo-controlled study was conducted in 160 children (80 boys, 80 girls) aged 8.3–11.9 y. Bone mineral content (BMC), bone mineral density (BMD), and BMC adjusted for bone width, body weight, and height (size-adjusted BMC) were measured at the midshaft and distal radius. Each child received either 1000 mg Ca/d (as calcium carbonate) or a placebo 5 d/wk for 12 mo. Supplementation increased calcium intake from 342 to 1056 mg/d (8.6 to 26.4 mmol/d).

Results: Calcium supplementation resulted in a higher BMC, BMD, and size-adjusted BMC ($\bar{x}$ difference ± SE): midshaft radius—BMC (3.0 ± 1.4%; $P = 0.034$), BMD (4.5 ± 0.9%; $P \leq 0.0001$), and size-adjusted BMC (4.6 ± 0.9%; $P \leq 0.0001$); distal radius—BMC (8.4 ± 3.2%; $P = 0.009$), BMD (7.0 ± 2.7%; $P = 0.011$), and size-adjusted BMC (5.5 ± 2.7%; $P = 0.042$). Supplementation had no significant effect on height, weight, or bone width at the midshaft radius or distal radius. At the end of the study, the calcium group had a significantly lower mean plasma osteocalcin concentration than the placebo group after adjustment for baseline concentration, sex, and pubertal status (−21.9 ± 6.5%; $P = 0.001$).

Conclusions: Increased calcium intake resulted in increased bone mineral status, possibly in association with a decreased bone remodeling space. Further studies are needed to determine whether an increased calcium intake has long-term benefits in Gambian children. *Am J Clin Nutr* 2000;71:544–9.

KEY WORDS Bone mineral accretion, calcium, children, Gambia, osteocalcin, single-photon absorptiometry

INTRODUCTION

How much calcium a growing child needs to support optimal growth and to maximize peak bone mass in later life is still a subject of considerable debate. There are concerns that calcium intake in many children and adolescents may be insufficient to maximize bone mineral accretion, resulting in calls for changes to current recommendations (1). Recent calcium supplementation studies have shown a beneficial effect of calcium supplementation on bone mineral acquisition in children (2–7). However, few studies have investigated the response in relation to customary calcium intake, although a recent study indicated that the effect of a calcium supplement appeared to be greatest in children with a calcium intake <880 mg/d (22 mmol/d) (8). This suggests that bone mineral accretion may be limited by calcium supply and raises questions about the adequacy of the diet for children accustomed to a low calcium intake.

The mean dietary calcium intake of Gambian children is ≈300 mg/d (9), about one-fourth to one-third of US (10) and British (11) recommendations. Children in rural areas of The Gambia have poor growth, delayed puberty, and a low bone mineral status compared with British and American children (9, 12). An intake of 300 mg Ca/d is close to the theoretical peak rate for bone mineral accretion during childhood and adolescence, even without accounting for incomplete absorption (9). Therefore, it is plausible that the low calcium supply in Gambian children may contribute to their poor growth performance and bone mineralization.

The aim of this study was to examine whether an increase in calcium intake to close to recommended amounts would improve bone mineral acquisition in 8–12-y-old Gambian children. This age group was chosen because most would not have reached puberty and some studies have indicated that the effect of calcium supplementation is confined to prepubertal children, although this finding is not universal (2–4, 6, 7). Bone width and body size were monitored and plasma osteocalcin concentrations, a marker of bone formation rate, were quantified to provide an insight into the mechanism of action and to investigate whether calcium supplementation would decrease bone remodeling space, resulting in a reversible increase in bone mineral at skeletal surfaces, rather than promote bone growth (2, 13–15).

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[2] Shire Pharmaceuticals and Nycomed Pharma donated the calcium and placebo tablets.

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SUBJECTS AND METHODS

Subjects

Children aged 8.3–11.99 y in the rural village of Keneba, West Kiang, The Gambia were eligible to take part in the study. Parents were approached and their children selected in descending age order until the target numbers of 80 boys and 80 girls were achieved. A total of 162 children were approached but 2 did not participate because they moved from the village early in the study period. The children were mainly from the Mandinka tribe and lived in Keneba at the time of the study. The subjects were healthy children with no history of any medical condition known to affect calcium or bone metabolism. None of the subjects had had a recent fracture; were consumers of alcohol, antacids, calcium, or other nutritional supplements; or were smokers. None of the girls were taking contraceptive pills. The study was approved by the MRC/Gambian Government Ethics Committee, and informed consent was obtained from all children and their parents.

Calcium supplementation

Subjects were stratified by sex and randomly assigned to receive a calcium supplement or placebo. The randomization procedure was conducted by a member of the staff in Cambridge who was otherwise not involved in the study. The subjects and the field and laboratory staff remained unaware of the assignments throughout the study. Four children started the study each week to allow recruitment to be spread over one calendar year. All measurements in each subject were completed within a 7-d period. Assignment to group was by a randomized permuted block of 4 to ensure that an equal number of subjects was allocated to the calcium and placebo groups each week, to minimize the potential for seasonal confounding.

The calcium supplement consisted of 2 chewable calcium carbonate tablets (Calcichew; Shire Pharmaceuticals Ltd, Andover, United Kingdom and Nycomed Pharma AS, Oslo) containing 500 mg (12.5 mmol) elemental Ca/tablet. The placebo consisted of 2 tablets of similar shape, taste, and texture, produced by the manufacturer of the calcium tablets. Each subject received either the calcium supplement or the placebo for 5 d each week for 12 mo, starting the week after baseline measurements were taken. The tablets were dispensed to the subjects at a centrally located building in the village and were consumed under strict supervision. To achieve regular attendance, a youth club was organized every weekday evening. For children who were unable to attend the youth club for any reason, tablets were dispensed at the children's homes by the fieldworkers on the same day.

The supplement was consumed in the early evening, between 1700 and 1900. This allowed the tablets to be administered between lunch (generally between 1400 and 1500) and dinner (≈2030) to minimize possible interference with absorption of other minerals, such as iron and zinc. During the fasting month of Ramadan, tablets were consumed later in the evening, immediately after the subjects had broken fast but before the main meal was eaten. Tablets that were missed because of illness or absence from the village were consumed on weekends; the dose remained at 1000 mg/d. The tablets were well accepted, there were no reports of adverse side effects, and the overall compliance for each child was 100%. Thus, by the end of the 12-mo supplementation period, every child had consumed all the tablets that had been assigned to him or her at the start of the study.

Bone mineral status

Measurements of bone mineral content (BMC; g/cm), bone width (BW; cm), and bone mineral density (BMD; g/cm^2) at the midshaft and distal radius of the left arm were made by using single-photon absorptiometry (Lunar SP2 scanner; Lunar Radiation Corporation, Madison, WI). Baseline measurements were conducted during the week before supplementation began. Outcome measurements were made after ≈12 mo ($\bar{x}$ ± SD: 385 ± 41 d), during the week before the supplement was withdrawn. The duration of this period was similar in the 2 groups (calcium group: 387 ± 28 d; placebo group: 388 ± 28 d).

The midshaft radius on the ulna was located by measuring the distance between the midpoint of the ulnar styloid process and the proximal edge of the olecranon and marking the position that was one-third of this length from the ulnar styloid process. Three transverse scans were made at the same position and the mean was recorded. The wrist measurement was made at the 5-mm distal site, defined as the site where the distance between the radius and ulna is 5 mm. This site was located by performing a rectilinear scan with a step distance of 1.5 mm and using the value for which the interosseous distance was closest to 5 mm but between 4 and 6 mm.

The instrument was calibrated daily, and long-term stability was assessed regularly by using phantoms. The CVs over the study period for BMC, BW, and BMD were 1.11%, 0.94%, and 0.82%, respectively, for the small phantom (BMC = 0.374 g/cm) and 0.52%, 0.41%, and 0.53%, respectively, for the large phantom (BMC = 1.196 g/cm), indicating satisfactory instrument stability with no sign of drift.

Dietary calcium intake

Dietary calcium intake was measured during the week of baseline measurements. The assessment was made by using a direct-weighing method over 2 d (16). Each subject was visited by a fieldworker before and after each meal and on several other occasions during the measurement period. All food items consumed and any leftovers were weighed and recipes for all dishes were recorded. Consumption of snacks during and between meals was determined by recall at the next visit. Computation of nutrient intakes was carried out using GAMBIAN DIDO and MW1N4 software programs (17) based on McCance and Widdowson's food composition data (18), supplemented by information on the composition of Gambian foods (19). This additional information had been obtained by analyzing raw ingredients and cooked dishes and accounting for food items that were rich in calcium but were either eaten in small quantities or infrequently, such as certain vegetables and small fish bones (19). Calcium from drinking water was not quantified because the calcium concentration of Keneba water is low (< 0.25 mmol/L, or < 10 mg/L) (19).

The diet in Keneba is based on groundnuts, cereals, fish, and vegetables and is known to be deficient in many nutrients (9, 20). There were no significant differences in dietary patterns or nutrient intakes between the calcium and placebo groups.

Anthropometry and pubertal status

Anthropometry and pubertal stage assessments were conducted at the beginning and end of the study. Each subject was weighed to the nearest 0.1 kg while wearing light clothing and no shoes. Standing height of subjects without shoes was recorded to the nearest 0.1 cm. Pubertal status was assessed according to Tanner staging (21). The pubertal status of the girls

was based on breast and pubic hair development and the assessment was conducted by a female pediatric consultant physician (EMEP). The pubertal status of the boys was assessed by the principal investigator (BD) and was based on genital and pubic hair development.

Plasma osteocalcin

Blood was collected after an overnight fast in the week before and 12 mo after supplementation began, before the supplement was withdrawn. The sample was anticoagulated with lithium heparin, kept cool, separated, frozen within 45 min, and transported on dry ice to Cambridge. An unavoidable delay during transportation resulted in the thawing of samples from 62 subjects, precluding their analysis. Results are presented here only for those subjects who had osteocalcin measurements made at both baseline and at the end of the 12-mo supplementation period (n = 49 in the calcium group and n = 49 in the placebo group). Intact osteocalcin was quantified by using an immunoradiometric assay (N-TACT Osteocalcin; INCStar Corporation, Stillwater, MN) that had a between-run precision of 6% during the study period for a control sample, measured in duplicate, with a concentration of 26 μg/L. The vitamin D status of all subjects was within the normal range, as indicated by a plasma 25-hydroxyvitamin D concentration >25 nmol/L.

Statistical analysis

Descriptive statistics are reported as means ± SDs and differences ± SEs for all variables, unless otherwise stated. Statistical analysis was performed by using analysis of variance, analysis of covariance, and multiple regression analysis (LINEAR MODEL SOFTWARE, DATADESK 4.1; Data Description Inc, Ithaca, NY). All continuous variables were converted to natural logarithms to facilitate examination of power relations between continuous variables and to investigate proportional effects of discrete variables (22, 23). In all cases, the distribution of the logged variables approximated normality. When the dependent variable is expressed as a natural logarithm, the regression coefficient for a discrete variable corresponds closely to the percentage effect: (difference/mean) × 100 (22, 23).

To examine the influence of the calcium supplement and other variables on bone mineral status independently of bone and body size, BMC was adjusted for BW, body weight, and height by using simultaneous multiple regression analysis with backwards elimination (22). A similar approach was used to adjust plasma osteocalcin for sex and pubertal status. The baseline value was entered as an independent variable in all regression analyses to minimize regression toward the mean. The basic model used to examine the effect of the calcium supplement was as follows:

$$\ln(\text{value at the end of the study}) = k + a \times \ln(\text{value at baseline}) + b \times (\text{group}) \quad (1)$$

where k is a constant and a is the slope of the relation between ln (BMC) and ln (value at baseline); the calcium group was coded as 1 and the placebo group was coded as 0. The coefficient b, after multiplying by 100, is either the percentage difference between the calcium and placebo groups at the end of the study after adjustment for baseline values or the difference between the 2 groups in the percentage change from baseline to the end of the study after adjustment for baseline values. These are equivalent interpretations. Fuller models, set up to investigate the effect of the supplement after adjustment for bone width, weight, and height, used the mean and difference of these variables at baseline and at the end of the study, after conversion to natural logarithms (23). The possibility that the response to supplementation was influenced by age, sex, pubertal status, or dietary calcium intake was tested by including appropriate interaction terms in the regression models.

Subject characteristics and bone variables were similar in boys and girls at baseline, except that girls had significantly greater triceps skinfold thickness [by 1.6 ± 0.3 mm ($\bar{x}$ ± SE); $P \leq 0.0001$]. Similar results were obtained when the analyses were conducted in boys and girls separately. Consequently, the characteristics of the 2 groups and the effect of the calcium supplement were examined with the sexes combined.

RESULTS

There were no significant differences at baseline in subject characteristics, anthropometry, or bone variables between the calcium and placebo groups (**Tables 1** and **2**). The children in both groups were small for their age and puberty was delayed compared with British reference children (21, 24). The mean (±SD) z scores of the whole group relative to the British reference were as follows: height-for-age z score = −1.17 ± 0.86 and weight-for-age z score = −1.76 ± 0.85. Most subjects were pre-

TABLE 1
Comparison of subject characteristics and anthropometry between the calcium-supplemented and placebo groups[1]

	Baseline		Outcome	
	Calcium group (n = 80)	Placebo group (n = 80)	Calcium group (n = 80)	Placebo group (n = 80)
Age (y)	10.3 ± 1.0	10.3 ± 1.0	11.3 ± 1.0	11.3 ± 1.0
Weight (kg)	25.5 ± 4.0	24.9 ± 4.1	27.7 ± 4.8	26.8 ± 4.6
Height (cm)	132.5 ± 6.9	131.6 ± 7.6	137.7 ± 7.1	136.8 ± 7.7
MUAC (cm)	18.2 ± 1.6	18.0 ± 1.6	19.3 ± 1.7	18.9 ± 1.6
Triceps skinfold thickness (mm)	8.0 ± 1.7	7.9 ± 1.9	8.6 ± 2.3	8.6 ± 2.8
Grip (kg)	11.1 ± 3.0	10.7 ± 2.7	15.1 ± 3.2	14.7 ± 3.3
Percentage at Tanner stage 1 (%)				
Boys	90	80	68	68
Girls	72	82	70	72

[1] $\bar{x}$ ± SD. MUAC, midupper arm circumference. There were no significant differences between the groups in any of the variables at either baseline or outcome (two-tailed Student's t test or chi-square test).

TABLE 2
Comparison of bone variables and plasma osteocalcin concentrations between the calcium-supplemented and placebo groups[1]

	Baseline		Outcome	
	Calcium group (n = 80)	Placebo group (n = 80)	Calcium group (n = 80)	Placebo group (n = 80)
Midshaft radius				
BMC (g/cm)	0.452 ± 0.087	0.434 ± 0.085	0.493 ± 0.078[2]	0.467 ± 0.090[2]
BW (cm)	0.976 ± 0.117	0.960 ± 0.114	0.988 ± 0.106	0.991 ± 0.118[2]
BMD (g/cm^2)	0.461 ± 0.058	0.451 ± 0.062	0.498 ± 0.050[2]	0.470 ± 0.060[2]
Distal radius				
BMC (g/cm)	0.419 ± 0.096	0.388 ± 0.103	0.487 ± 0.132[2]	0.423 ± 0.111[3]
BW (cm)	1.828 ± 0.183	1.777 ± 0.198	1.903 ± 0.199[2]	1.827 ± 0.190[4]
BMD (g/cm^2)	0.227 ± 0.040	0.217 ± 0.044	0.253 ± 0.050[2]	0.231 ± 0.050[5]
Plasma osteocalcin (μg/L)	24.8 ± 12.1	24.3 ± 7.9	17.9 ± 7.3[2]	23.2 ± 9.5

[1] $\bar{x}$ ± SD. BMC, bone mineral content; BW, bone width, BMD; bone mineral density.
[2–5] Significantly different from baseline (paired t test): [2]$P \leq 0.0001$,[3]$P = 0.0022$, [4]$P = 0.0012$, [5]$P = 0.0123$.

pubertal throughout the study (Table 1). No girl had reached menarche at the start of the study and 2 started menstruating during the intervention. The number of children who had entered puberty at the start or who moved into Tanner stages 2–5 during the study did not differ significantly between the 2 groups. Dietary calcium intake averaged 338 ± 142 mg/d (8.45 ± 3.55 mmol/d) and was not significantly different between the 2 groups (calcium group: 342 ± 129 mg/d, or 8.55 ± 3.28 mmol/d; placebo group: 334 ± 153 mg/d, or 8.35 ± 3.83 mmol/d). Calcium supplementation raised the calcium intake of the children in the calcium group by 714 mg/d (17.85 mmol/d), to a total intake of 1056 mg/d (26.4 mmol/d).

Both groups of children experienced increases in all anthropometric variables and in BMC, BW, and BMD at the midshaft and distal radius over the 12-mo study period (Tables 1 and 2). The incremental gains in BMC and BMD at both the midshaft and distal radius were greater in the calcium than in the placebo group, significantly so after adjustment for baseline values (**Table 3**). These incremental gains were not correlated with age, sex, pubertal status, or dietary calcium intake, and no significant interactions with the supplement group were observed, indicating that the response to the supplement was not influenced by any of these variables. The significant differences in BMC at the midshaft and distal radius at the end of the study between the calcium and placebo groups remained after further adjustment for BW, weight, and height by using regression analysis. There was a trend toward a smaller BW at the midshaft radius in the calcium group at the end of the study, after adjustment for baseline values, but it was not significant. There were no significant effects of the calcium supplement on weight, height, or distal radius BW.

The plasma osteocalcin concentration was not significantly different between the 2 groups at baseline (Table 2). At the end of the study, the calcium group had experienced a decrease in plasma osteocalcin during the 12-mo study period and had significantly lower concentrations than the placebo group (Table 3). The plasma osteocalcin concentration of the placebo group at the end of the study was not significantly different from that at baseline (Table 3). After adjustment for the baseline value, plasma osteocalcin concentrations at the end of the study were not influenced by age but were significantly greater in girls than in boys ($\bar{x}$ difference ± SE 17.8 ± 7.1%; P = 0.015) and in those who were at Tanner stages 2–5 (n = 39) than in those at Tanner stage 1 (n = 59): by 15.8 ± 7.2% (P = 0.031). After adjustment for the baseline value, sex, and pubertal status, the calcium group had significantly lower plasma osteocalcin concentrations than the placebo group (22%; Table 3). There was no evidence of any interaction between the supplement effect on plasma osteocalcin and age, sex, pubertal status, or dietary calcium intake.

DISCUSSION

The results of this study showed that an increase in calcium consumption over a 12-mo period by Gambian children accustomed to a low calcium intake resulted in an increased acquisition of skeletal mineral. The magnitude of the calcium supplement effect was substantial, with an increase in BMD of 4.5% at the midshaft radius and of 7.0% at the distal radius and an increase in size-adjusted BMC of ≈5% at both sites. This represents a shift of ≈0.3–0.4 of the population SD for this age group, which in adults would represent a significant reduction in fracture risk (25). Therefore, the study supports the findings of calcium supplementation studies in other groups of children, which suggest that an increase in calcium intake, if sustained throughout childhood, can positively modify peak bone mass and, thereby, reduce osteoporotic fracture risk in later life (2–7). The results of the present study were necessarily limited by the use of single-photon absorptiometry, which was able to monitor the effects of calcium supplementation only on the bones of the forearm and not at other skeletal sites. However, at the time of the study, there were no facilities for dual-energy X-ray absorptiometry in The Gambia and more comprehensive measurements of bone mineral status were not possible.

The observed increases in bone mineral were similar whether expressed as BMC, BMD, or size-adjusted BMC. In contrast, there was no evidence of a positive effect of the supplement on the size of the growing skeleton, either in terms of increased statural height or in bone width, in fact, there was a trend toward a smaller increase in bone width at the midshaft radius in the calcium group. This suggests that the effect of the higher calcium intake was to increase the amount of mineral present within a given bone volume rather than to promote bone growth. Other intervention studies using calcium salts have shown similar effects, with an increase in bone mineral but no effect on size (2, 3, 5, 6). This contrasts with the results of studies using milk and dairy products (26) or calcium salts extracted from milk (8), in which anabolic effects on the skeleton were also

TABLE 3
Effect of calcium supplementation on height, weight, and bone measures and plasma osteocalcin concentrations[1]

	Absolute change (outcome − baseline)		Percentage difference in change (calcium − placebo)	
	Calcium group (n = 80)	Placebo group (n = 80)	Unadjusted (P)	Adjusted[2] (P)
			%	%
Height (cm)	5.1 ± 0.2	5.2 ± 0.2	−0.1 ± 0.2 (0.7)	−0.0 ± 0.0 (0.9)
Weight (kg)	2.2 ± 0.2	1.9 ± 0.2	0.8 ± 0.8 (0.3)	0.8 ± 0.8 (0.3)
Midshaft radius				
BMC (g/cm)	0.041 ± 0.005	0.033 ± 0.005	2.1 ± 1.6 (0.2)	3.0 ± 1.4 (0.03)
Size-adjusted BMC[3]				4.6 ± 0.9 (≤0.0001)
BW (cm)	0.012 ± 0.007	0.031 ± 0.006	−1.8 ± 0.9 (0.05)	−1.6 ± 0.9 (0.06)
BMD (g/cm^2)	0.037 ± 0.003	0.019 ± 0.003	3.9 ± 1.0 (0.0002)	4.5 ± 0.9 (≤0.0001)
Distal radius				
BMC (g/cm)	0.068 ± 0.011	0.035 ± 0.011	5.5 ± 3.4 (0.1)	8.4 ± 3.2 (0.009)
Size-adjusted BMC[3]				5.5 ± 2.7 (0.04)
BW (cm)	0.075 ± 0.017	0.049 ± 0.015	1.2 ± 1.2 (0.3)	2.0 ± 1.2 (0.09)
BMD (g/cm^2)	0.026 ± 0.005	0.014 ± 0.005	4.8 ± 3.0 (0.1)	7.0 ± 2.7 (0.01)
Plasma osteocalcin (μg/L)[4]	−5.96 ± 1.08	−0.69 ± 1.28	−22.5 ± 8.2 (0.007)	−21.9 ± 6.5 (0.001)

[1] $\bar{x}$ difference ± SE. BMC, bone mineral content; BW, bone width; BMD, bone mineral density.
[2] Adjusted for baseline (*see* text for details).
[3] Adjusted for baseline BMC, bone width, weight, and height (*see* text for details).
[4] n = 49 for both groups (*see* Methods).

indicated. The lack of an effect on height in this group of growth-retarded children also parallels the results of earlier studies in which an increase in height velocity in older children from disadvantaged backgrounds was observed in studies using milk but not in those using calcium salts (9, 27–29). It is possible, however, that deficiencies of other nutrients in the diet of the Gambian children may have limited any potential effect of the calcium supplement on growth.

The increased bone mineral in the calcium group was accompanied by a marked decrease in plasma osteocalcin concentration, a marker of bone formation rate. Interestingly, the one other study using calcium salts that investigated alterations in plasma osteocalcin also showed a decrease in plasma osteocalcin concentrations in the group of children who responded to the supplement (2). This contrasts with the lack of an effect on the bone formation marker in children supplemented with milk (26), suggesting that the mechanism of action of these 2 sources of calcium on the skeleton may differ.

The decrease in plasma osteocalcin observed in this study suggests that the effect of the supplement on bone mineral status may have been due to a phenomenon known as the bone remodeling transient (30–32), in which an increase in calcium supply leads to a decrease in the activation frequency of osteoclasts at the start of the remodeling process. This produces a decrease in bone resorption and, because of coupling within each bone remodeling cycle, ultimately reduces the bone formation rate. This decreases the proportion of skeletal surfaces that are actively undergoing bone remodeling at any one time, resulting in an increase in the mineral present per unit volume of bone. The increase in bone mineral reaches an upper threshold with the completion of resorption cycles initiated before the change in calcium supply and is reversed if the calcium supply returns to its original level. These alterations in bone mineral can be sufficiently large to be detected by absorptiometry (33). The phenomenon of the bone remodeling transient is well recognized in adults and is the basis for the antiresorptive action of calcium used as a therapy for postmenopausal bone loss (33). However, whether a reduced rate of skeletal remodeling, or specifically of bone formation, represents a benefit for the growing skeleton is unknown and requires further study. Although it has been suggested that the lower rates of bone remodeling observed in American black children than in white children may underpin the differences in peak bone mass and osteoporotic fracture rates between these ethnic groups (14), more research is required to determine the long-term outcome of a reduction in the bone formation rate in growing individuals as a result of dietary manipulation.

The children in the present study had a low customary calcium intake, averaging ≈350 mg/d, which increased ≈3-fold with the calcium supplement. Despite this, the magnitude of the observed calcium effect was similar to the 2–6% increase reported from studies in children with a considerably higher customary calcium intake or in which lower amounts of supplemental calcium were used (2, 3, 5, 6). Our study, therefore, provides no evidence to support the possibility that children with a very low calcium intake have a greater response to calcium supplementation than do children with high intakes (8). Therefore, it is difficult to equate the results in these Gambian children with a correction of calcium deficiency because analogous effects have been noted in children with a customary calcium intake before supplementation similar to that of the Gambian children after receiving extra calcium (2–4, 7). Instead, our results suggest that the bone remodeling space decreases with increasing calcium intake in an approximately linear fashion over a wide range of intakes. This parallels the findings from the mathematical modeling of data from balance studies in children in which calcium retention appeared to rise with increasing calcium intakes up to a maximum threshold at high intakes (10). If this interpretation proves correct, it raises questions about the relation of the bone remodeling rate to bone health and about what level of bone remodeling should be regarded as optimal for the growing skeleton.

In summary, this randomized, controlled study in The Gambia showed that supplementation with calcium carbonate increased bone mineral status, decreased the bone formation rate, but did not alter growth in prepubertal and peripubertal children with a low customary calcium intake and who were lighter, shorter, and less mature than reference children of the same age. Calcium supplementation may benefit Gambian children by increasing bone mineralization and, ultimately, peak bone mass. Alternatively, these results may indicate an alteration in bone remodeling, the consequences of which for bone health are unknown. Follow-up studies of the Gambian children are currently in progress to resolve some of these issues.

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