

High Fiber Diets Slow Bone Turnover in Young Men but Have No Effect on Efficiency of Intestinal Calcium Absorption^{1,2,3}

KIMBERLY O. O'BRIEN,⁴ LINDSAY H. ALLEN, PAULA QUATROMONI,*
MEI-LING SUI-CALDERA, NANCY E. VIEIRA,[†] ALBERTO PEREZ,*
MICHAEL F. HOLICK* AND ALFRED L. YERGEY[†]

Department of Nutritional Sciences, University of Connecticut, Storrs, CT 06269-4017;
*General Clinical Research Center, Boston University School of Medicine, Boston, MA
02118; and [†]Section on Metabolic Analysis and Mass Spectrometry, National Institutes of
Health, Bethesda, MD 20892

ABSTRACT Dietary fiber reduces the absorption of dietary calcium from a meal, but its impact on calcium kinetics is unknown. We therefore evaluated the effects of a high fiber diet on calcium balance and kinetics and on calcium-regulating hormones. Seven young men each participated in two 23-d experiments. In the low fiber period the controlled diet provided 6.5 g fiber/d and 530 mg calcium/d. In the high fiber period fiber was increased to 31.3 g/d and calcium to 586 mg/d by substituting high fiber cereal. Measured between d 7 and 12 of each period, the high fiber diet significantly lowered the apparent absorption of calcium (from $60.6 \pm 23.8\%$ to $37.1 \pm 26.5\%$) and reduced calcium balance, although balance remained positive overall. Fiber had no effect on serum total or ultrafiltrable calcium, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D or parathyroid hormone concentrations measured on d 1, 7, 12 and 20. Calcium kinetics was studied between d 17 and 23 by administering oral ⁴⁴Ca and intravenous ⁴²Ca to fasting subjects. Fractional absorption of calcium in the fasting state was unaffected by fiber. However, during the high fiber period, subjects had significantly lower bone accretion, resorption and turnover rates, and calcium flow to bone from the exchangeable pool than during the low fiber period. We conclude that the fiber-induced reduction in calcium absorption slowed down bone calcium turnover but did not increase the efficiency of intestinal absorption. *J. Nutr.* 123: 2122-2128, 1993.

INDEXING KEY WORDS:

- calcium • kinetics • dietary fiber
- vitamin D • humans

When animals or humans consume low calcium diets, this causes well-described changes in calcium-regulating hormones that improve the efficiency of intestinal calcium absorption. Predominant among these changes are increases in serum parathyroid

hormone and in the subsequent synthesis of the active metabolite of vitamin D, 1,25-dihydroxyvitamin D [$1,25(\text{OH})_2\text{D}$]⁵ (Norman 1990).

Through a poorly understood mechanism, reduced calcium absorption may also lead to depletion of 25-hydroxyvitamin D [$25(\text{OH})\text{D}$]. Vieth et al. (1987) observed that plasma $25(\text{OH})\text{D}$ fell to undetectable levels in 4 wk when rats consumed a calcium-deficient diet, even though the diet contained vitamin D. Clements et al. (1987) reported that when the amount of calcium absorbed by rats was severely reduced, either by feeding a low calcium diet or by adding sodium phytate to a normal calcium diet, $25(\text{OH})\text{D}$ was degraded more rapidly with a reduction in half-life from about 15 to 9 d. This phenomenon could not be explained by a faster conversion of $25(\text{OH})\text{D}$ to $1,25(\text{OH})_2\text{D}$ and probably involves a direct effect of $1,25(\text{OH})_2\text{D}$ on $25(\text{OH})\text{D}$ degradation (Clements et al. 1987, Halloran et al. 1986, Lore et al. 1982). In the

¹Funded by the National Dairy Board in cooperation with the National Dairy Council, the Storrs Agricultural Experiment Station, and NIHMOIRR0533.

²Scientific Contribution no. 1482, Storrs Agricultural Experiment Station, Storrs, CT.

³The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 USC section 1734 solely to indicate this fact.

⁴To whom correspondence should be addressed at: National Institutes of Health, 9000 Rockville Pike, Building 10, Room 6C101, Bethesda, MD 20892.

⁵Abbreviations used: AAS, atomic absorption spectrophotometry; $25(\text{OH})\text{D}$, 25-hydroxyvitamin D, $1,25(\text{OH})_2\text{D}$, 1,25-dihydroxyvitamin D, $1,25(\text{OH})_2\text{D}_3$, 1,25-dihydroxycholecalciferol; PEG, polyethylene glycol; V_0^+ , bone calcium accretion, V_0^- , bone calcium resorption, V_t , total bone turnover.

single existing investigation of how high fiber intake affects vitamin D kinetics in humans, subjects who had 20 g fiber/d added to their usual diet for 30 d had a significantly lower half-life of serum tritiated 25-hydroxycholecalciferol [25(OH)D₃] compared with controls (Batchelor and Compston 1983).

The experiment reported here was the first in a series designed to evaluate the impact of reducing calcium absorption on vitamin D and calcium kinetics in humans. In this report dietary fiber was used to lower the amount of calcium absorbed; high fiber diets have also been reported to reduce the absorption of radioactive calcium consumed in a meal (Knox et al. 1991) and to affect calcium retention adversely (Cummings et al. 1979, Spiller et al. 1986).

There is no information available on how fiber-induced reductions in calcium absorption, or indeed low calcium intakes, affect overall calcium kinetics of humans. Chronic feeding of low calcium diets increased the whole-body retention of an oral dose of radioactive calcium (Dawson-Hughes et al. 1988), but the relative impacts of calcium restriction on calcium absorptive efficiency and bone calcium turnover rates are unknown. This is an important question, given the high prevalence of vitamin D deficiency and osteomalacia in individuals with calcium malabsorption (Driscoll et al. 1982) and those consuming high fiber diets (Gibson et al. 1987).

This report describes the impact of fiber-induced reductions in calcium absorption on calcium kinetics, using dual stable calcium isotopes. These isotopes were administered to fasting subjects to avoid direct effects of fiber on calcium absorption. An alternative approach would have been to administer the isotopes in the presence of a fiber-containing meal, but this strategy would not have permitted us to separate the direct effects of fiber on isotope absorption from any changes in the absorptive efficiency of the subjects.

MATERIALS AND METHODS

Subjects. Seven healthy Caucasian men were recruited at the Boston University School of Medicine between March and October of 1989. The study was approved by the human studies committees of the University of Connecticut and the Boston University School of Medicine and was conducted at the General Clinical Research Center of the latter institution. Before acceptance all subjects were given a routine physical examination, which included a clinical blood chemistry screen and urinalysis. Subjects indicated their willingness to participate by signing a consent form. Individuals were not accepted for study if they were taking any medications known to affect calcium or vitamin D metabolism, or any vitamin or mineral supplements.

The experiment was a randomized cross-over design with each subject participating in one low fiber

TABLE 1

Average daily nutrient intakes of men consuming low and high fiber diets¹

Nutrient	Dietary period	
	Low fiber	High fiber
Energy, <i>Mj</i>	11.24	11.27
Protein, % of energy	13	13
Carbohydrate, % of energy	54	54
Fat, % of energy	33	33
Calcium, mg/d	530	586
Vitamin D, $\mu\text{g/d}$	7.68	6.88
Dietary fiber, g/kg diet	2.78	13.37

¹Nutrient values were calculated using the Autonutritionist III program. Calcium concentration of the diet was determined from duplicate digests of the diet using flame atomic absorption spectrophotometry.

and one high fiber dietary period, each lasting 23 d. Each subject started the second dietary period within 60 d of the first dietary period to reduce the potential for seasonal changes in initial 25(OH)D levels. All subjects applied SPF 15 sunscreen to their exposed skin daily during each 23-d period to avoid endogenous vitamin D synthesis (Holick 1987) and were requested to avoid prolonged exposure to sunlight.

Diet. The basal diet was constant in each study period, with only the dietary fiber level and source varying between periods (Table 1). The diet consisted of normal foods in a 3-d cycling menu with an average energy intake of 11.24 MJ. The nutrient content of the diets was analyzed using the Autonutritionist III program (N-Squared Computing, Silverton, OR). The database was checked for missing nutrient values and was updated with manufacturer's data to ensure completeness. All meals were prepared in the metabolic kitchen of the General Clinical Research Center using standardized methods. All fruits and vegetables were canned items purchased in a single lot at the start of the study and were frozen or stored until needed. Calcium and vitamin D intakes were carefully controlled. Calcium intake averaged 530 mg/d (low fiber period) and 586 mg/d (high fiber period); because of the higher calcium content of the All Bran cereal used, calcium intake was significantly higher from the high fiber diet ($P < 0.001$, Student's *t* test). In the low fiber period, subjects consumed 85 g/d of Special K, a lower fiber cereal that contains trace levels of dietary fiber (defined as < 1 g of dietary fiber per 1-oz serving; Kellogg Co., Battle Creek, MI). In the high fiber period this cereal was replaced by the same weight of All Bran (Kellogg Co.), which contains 1 g of soluble and 8 g of insoluble dietary fiber per 1-oz serving. Mean daily fiber intakes were 6.5 g (low fiber period) and 31.3 g (high fiber period). Duplicate portions of each 3-d menu were digested by wet-ashing

with Ultrex nitric and perchloric acids (J. T. Baker, Phillipsburg, NJ). The calcium content of the digests was determined using flame atomic absorption spectrophotometry (AAS) (model 2380, Perkin Elmer, Norwalk, CT). Vitamin D levels were estimated using the Autonutritionist III program.

Subjects consumed breakfast and lunch in the General Clinical Research Center under the supervision of the dietetic staff. Each person was given a bottle of distilled water and plate scraper with each meal and was instructed to rinse and scrape all plates and glasses, and to drink the rinses. The cereal intake was divided between the morning and mid-day meal so that its consumption could be observed. The evening meal and snack were packaged to take out, allowing the subjects more freedom in the evening. In addition, distilled water was provided but no other food or drink was permitted. The caffeine intake from coffee and soda was kept constant within each subject between dietary periods. If necessary, additional sugar and soft drinks were used to maintain the subject's weight to within ± 1 kg during the experimental periods. The heaviest individual refused these extra foods and lost an average of 4.5 kg per period.

Calcium balance. During the first 12 d of each period, polyethylene glycol 3350 (PEG, Union Carbide, Moorestown, NJ) was administered to correct for differences in fecal transit time. Subjects consumed 1 g dissolved in distilled water with each meal of the day for a total of 3 g/d. After subjects consumed each diet for 1 wk, a calcium balance was performed from d 7 to 12 to confirm an inhibitory effect of fiber on calcium absorption. During this time all urine and stool samples were collected. Urine was collected in acid-washed plastic collection containers. The total volume was measured, and aliquots were stored in polyethylene containers and frozen at -70°C until analyzed. Urinary calcium was determined by AAS. Fecal samples were collected into plastic buckets lined with plastic bags. All voids from each 24-h period were combined into a single pool. Daily fecal samples were homogenized with deionized water and wet acid digested using Ultrex nitric and perchloric acids. Acid digests were then analyzed for calcium content using AAS.

Polyethylene glycol in fecal samples was measured using a modified version of our published method. To 1 g of PEG standard or sample, 10 mL of distilled water, 1 mL of 150 g/L BaCl_2 , 2 mL of 47.3 g/L $\text{Ba}(\text{OH})_2$ and 2 mL of 300 g/L $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ solution (Annino 1964) were added sequentially. These samples were then shaken and allowed to stand 10 min before further treatment as detailed previously (Allen et al. 1979). The mean recovery of known amounts of PEG added to stool samples was $106.9 \pm 3.4\%$ ($n = 12$). The inter-assay CV for a test sample was 1.78% ($n = 9$). Daily recovery of PEG was used to correct for fecal calcium content (Allen et al. 1979).

Serum hormones. On d 1, 7, 12 and 20 of each dietary period, serum calcium and related hormones were measured. Intact serum parathyroid hormone, 25(OH)D, and 1,25(OH) $_2$ D were analyzed with commercial kits (Nichols Diagnostics, San Juan Capistrano, CA). Ultrafiltrable serum calcium was obtained by centrifugation through MPS-filters (Amicon, Danvers, MA), and ultrafiltrable and total calcium were measured by AAS.

Calcium fractional absorption. From d 17 to 23 a calcium kinetic study was performed. Stable calcium isotopes were obtained from Oak Ridge National Laboratory (Oak Ridge, TN), and sterile solutions of these were prepared for intravenous administration by the Pharmaceutical Development Branch at the National Institutes of Health. Isotopes were administered to fasting subjects to avoid direct meal interference with calcium absorption. On the morning of d 17, ^{44}Ca was given orally (0.5 mg/kg) and ^{42}Ca intravenously (0.2 mg/kg). The oral isotope was added to orange juice and allowed to equilibrate for at least 12 h prior to administration. Breakfast was consumed 2 h after isotope administration. Serum was collected at 5, 10, 15, 30 and 45 min and at 1, 2, 4, 8, 12, 24, 48, 72 and 144 h after dosing. All urine was collected into acid-washed polyethylene containers in nine 8-h pools. Calcium was extracted from the urine and serum using ammonium oxalate precipitation (Yergey et al. 1980).

Calcium isotopes were measured in urine samples at the University of Connecticut using a Finnigan 3000 mass spectrometer (Finnigan MAT, San Jose, CA) modified for single filament thermal ionization mass spectrometry (Yergey et al. 1980). Isotopic ratios were recorded using a programmable multiple ion monitor (Davco, San Jose, CA) and a three-pen chart recorder (Kipp and Zonen, Bohemia, NY). Approximately 15 μg of extracted calcium was dried onto the rhenium filament. Ratios between each administered isotope and naturally occurring ^{48}Ca were calculated to increase measurement precision. Triplicate ratios were obtained from each filament, and multiple filaments were analyzed until the mean ratios differed from one another by $<5\%$. The relative accuracy and SD of the natural abundance isotopic ratios were 1.09 and 3.55% for $^{42}\text{Ca}:^{48}\text{Ca}$ and 0.5 and 4.0% for $^{44}\text{Ca}:^{48}\text{Ca}$. The cumulative excretion of calcium isotopes in the first three urine pools was used to calculate the fractional absorption of calcium, using equations described previously (Yergey et al. 1987).

Calcium kinetic model. Isotopic ratios in serum samples were measured at the National Institutes of Health using a Finnigan MAT Thermoquad (Bremen, Germany) mass spectrometer. Relative accuracy and precision of natural abundance ratios for this instrument are 1.3 and 0.5% for $^{42}\text{Ca}:^{48}\text{Ca}$ and 0.7 and 0.3% for $^{44}\text{Ca}:^{48}\text{Ca}$.

Kinetic parameters were determined from a non-compartmental model fit to the isotopic dilution data

using the SAAM program (Berman and Weiss 1978). A linear least squares fit was made from d 17–23 serum data (Neer et al. 1967, Yergey et al. 1990). Variables determined from the intravenous tracer disappearance were the total exchangeable calcium pool size, system mean residence time, bone calcium accretion rate (V_o^+), bone resorption rate (V_o^-) and rate of total bone turnover (V_t), using previously described equations (Abrams et al. 1992, Covell et al. 1984). Endogenous calcium secretion was estimated to be 2 mg/(kg·d), based on earlier studies undertaken in men of this age consuming self-selected diets, in whom endogenous calcium secretion was found to be only minimally related to dietary calcium intake (Heaney and Skillman 1964, Neer et al. 1967). Data from one subject in this study were excluded due to a problem in the administration of the intravenous tracer.

Statistical analysis. The data were analyzed using Student's *t* test. Values are expressed as means \pm SD. Paired *t* tests were used to test for differences in calcium kinetic parameters between the low and high fiber periods. Each subject served as his own control. A *P* value of <0.05 was considered to be significant in all analyses.

RESULTS

The mean age, height and weight of the subjects were 26.9 ± 3.7 y [range 21–33], 172.72 ± 8.35 cm [167.64–182.88] and 74.5 ± 13.2 kg [52.5–94.3], respectively.

Effect of fiber on calcium balance. Recovery of PEG did not differ significantly between the low and high fiber dietary periods (87.5 and 97.9%, respectively). Subjects were assumed to be equilibrated to the diet (i.e., their intestinal contents were unaffected by pre-experimental diet) when day-to-day PEG

TABLE 2

Calcium intake and absorption in men consuming low and high fiber diets¹

	Dietary period	
	Low fiber	High fiber
Calcium intake, mg/d	530	586***
Urinary calcium, mg/d	157.3 \pm 44.0	164.5 \pm 111.5
% of intake	29.7 \pm 8.3	28.1 \pm 19.0
Fecal calcium, mg/d	209 \pm 126.0	368 \pm 155.5**
% of intake	39.4 \pm 23.8	62.9 \pm 26.5*
Apparent absorption, %	60.6 \pm 23.8	37.1 \pm 26.5*
Balance, mg/d	163.8 \pm 159.2	52.9 \pm 173.0***

¹Values are means \pm SD, *n* = 7. Values that are significantly different from the low fiber period are indicated: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

TABLE 3

Gastrointestinal function in men consuming low and high fiber diets¹

	Dietary period	
	Low fiber	High fiber
Fecal wet weight, g	80.1 \pm 45.2	152.9 \pm 48.8
Fecal dry weight, g	26.41 \pm 14.7	46.1 \pm 12.8**
Laxation rate, no./6 d	4.3 \pm 1.8	6.6 \pm 2.6*

¹Values are means \pm SD, *n* = 7 per dietary treatment. Values that are significantly different from the low fiber period are indicated: **P* < 0.005, ***P* < 0.001.

values did not differ by more than 10%. All of the subjects in the high fiber period and six of those in the low fiber period were equilibrated to the diet.

Urinary calcium did not differ between dietary periods (Table 2). However, consumption of the high fiber diet resulted in significantly higher fecal calcium, wet and dry weights, and laxation rate (Table 2 and Table 3). Each additional gram of fiber in the diet increased stool calcium and fecal wet weight by an average of 6.4 mg and 4.1 g, respectively.

The apparent absorption of calcium (intake minus fecal loss) was significantly lower during consumption of the high fiber diet (Table 2). Mean calcium balances were 52.9 ± 173 and 164 ± 159 mg/d during the high and low fiber periods, respectively. The high fiber diet lowered calcium balance by an average of 111 ± 28.9 mg/d (*P* < 0.009), despite its significantly higher calcium content due to the higher calcium level in the high fiber cereal. Although balance was significantly lower during the high fiber period, on average calcium balance remained positive in both dietary periods.

Serum calcium and related hormones. No differences in concentration were observed for any of the calcium-related hormones between periods. The mean values for each of the measured variables are presented in Table 4.

Calcium fractional absorption and kinetics. Fractional calcium absorption, assessed by administering stable calcium isotopes to fasting subjects, did not differ significantly between dietary treatments (Table 5). Significant differences were observed in other calcium kinetic variables between the two periods. During consumption of the high fiber diet the rate of bone turnover was significantly lower, by 2.88 mg/(kg·d). The high fiber diet also caused significantly lower rates of bone accretion [by 3.35 mg/(kg·d)] and bone resorption [by 2.54 mg/(kg·d)]. The parameter K_o^+ (defined as the ratio of V_o^+ to the total exchangeable calcium pool) serves as a measure of calcium flow to bone from the exchangeable pool (Abrams et al. 1992). This value was significantly

TABLE 4

Concentrations of calcium and its regulating hormones in serum of men consuming low and high fiber diets¹

	Dietary period	
	Low fiber	High fiber
25-Hydroxyvitamin D, $\mu\text{g/L}$	30.8 \pm 14.6	31.2 \pm 15.4
1,25-Dihydroxyvitamin D, ng/L	41.1 \pm 7.6	42.9 \pm 14.2
Intact serum parathyroid hormone, pmol/L	2.88 \pm 0.62	3.41 \pm 1.57
Total Ca, mmol/L	2.27 \pm 0.12	2.26 \pm 0.17
Ultrafiltrable Ca, mmol/L	1.12 \pm 0.07	1.08 \pm 0.11

¹Values are means \pm SD, $n = 7$.

lower when the high fiber diet was consumed (-0.04). No difference in the total exchangeable pool size could be attributed to the treatment period. The average time a calcium atom remained in the system (mean residence time) tended to be longer (by 21.4 min) during the high fiber period ($P < 0.06$).

Despite the significantly lower V_{O}^+ and V_{O}^- during the high fiber period, the ratio of these two variables ($V_{\text{O}}^-:V_{\text{O}}^+$) was similar in both periods. The ratio constant E (defined as the ratio of $V_{\text{O}}^-:V_{\text{t}}$) is an indicator of the rapidly miscible calcium pool turnover rate due to osteolysis. This ratio was unaffected by dietary treatment.

TABLE 5

Calcium kinetics in men consuming low and high fiber diets^{1,2}

	Dietary period	
	Low fiber	High fiber
TEP, mg/kg	81.6 \pm 19.3	80.5 \pm 5.6
α , %	51.9 \pm 9.3	45.6 \pm 9.8
V_{t} , $\text{mg}/(\text{kg}\cdot\text{d})$	17.0 \pm 3.0	14.1 \pm 2.3**
V_{O}^+ , $\text{mg}/(\text{kg}\cdot\text{d})$	12.9 \pm 3.0	9.6 \pm 2.4*
V_{O}^- , $\text{mg}/(\text{kg}\cdot\text{d})$	13.0 \pm 2.9	10.4 \pm 2.5*
$V_{\text{O}}^-/V_{\text{O}}^+$	1.010 \pm 0.03	1.106 \pm 0.09
K_{O}^+ ($V_{\text{O}}^+/\text{TEP}$)	0.160 \pm 0.01	0.120 \pm 0.01*
E ($V_{\text{O}}^-/V_{\text{t}}$)	0.761 \pm 0.02	0.733 \pm 0.03
MRT_{Syst} , min	108.4 \pm 12.9	129.8 \pm 17.4

¹Values are means \pm SD, $n = 6$. Values that are significantly different from the low fiber period are indicated: * $P < 0.05$, ** $P < 0.01$.

²Abbreviations used: TEP, total exchangeable calcium pool; α , fractional calcium absorption; V_{t} , bone calcium turnover rate; V_{O}^+ , bone calcium accretion rate; V_{O}^- , bone resorption rate; K_{O}^+ , calcium flow to bone from exchangeable pool; E, turnover rate of miscible calcium pool due to bone resorption; MRT_{Syst} , average time a calcium atom remained in the system.

DISCUSSION

Several investigators have demonstrated a negative effect of fiber on calcium balance (Andersson et al. 1983, Kelsay et al. 1979) and on absorption of labeled calcium added to a single meal (Weaver et al. 1991). The magnitude of this effect depends on the duration of the study and the type and level of dietary fiber consumed (Eastwood and Morris 1992, Jenkins et al. 1987). Under our study conditions, dietary fiber significantly increased fecal calcium losses and reduced calcium balance. This effect can probably be explained by the phytate portion of the fiber forming insoluble, unabsorbable calcium complexes that prevent intestinal absorption (Andersson et al. 1993).

In the lower fiber period two of the seven subjects were in negative calcium balance. When the fiber (and calcium) intake was increased, these same two individuals remained in negative calcium balance, and balance in another individual changed from positive to negative. The rest of the subjects maintained a positive calcium balance despite the limited calcium and high fiber intakes. It is common for wide variations in calcium balance to occur even among humans consuming diets similar in calcium content (Spencer et al. 1984).

For the fractional calcium absorption measurements, isotopes were administered to fasting subjects to avoid acute effects of the diet on absorption. This approach was used intentionally because it measures the potential for subjects to absorb calcium without dietary interferences and better reflects fiber's effect on the intrinsic ability of the individuals to actively absorb dietary calcium. It was not intended to measure the effects of fiber on calcium absorption from the high and low fiber diets. We recognize that this approach limits our ability to calculate V_{bal} and V_{O}^- with confidence. However, because the same design was used in each subject we could detect relative differences in fractional calcium absorption and kinetic parameters due to the presence of fiber in the diet. Because the study design did not result in an overall negative calcium balance, and because no changes were observed in total levels of calcium-related hormones, the lack of any difference in fractional calcium absorption in fasting subjects was not unexpected.

Because calcium intake was restricted, isotopes were administered in a calcium carrier that contained only 20.2 mg of calcium. This, coupled with the administration of the isotopes to subjects who had been fasting for at least 12 h, led to fractional absorption values higher than those normally reported from studies in which isotope is administered with a meal containing a calcium content of ≥ 100 mg (Eastell et al. 1989).

Fiber significantly increased fecal calcium losses and lowered calcium balance despite the higher

calcium content of the high fiber diet. To obtain more detailed information on fiber-induced changes in calcium metabolism, stable calcium isotopes were used to obtain kinetic determinations of bone flow rates and pool sizes, comparing paired measurements on the same individual. This revealed significant differences in the bone flow rates between dietary treatments. Consumption of the high fiber diet significantly decreased the rate of bone turnover, accretion and resorption and the ratio of bone accretion to the total exchangeable pool (K_0^+). No hormonal stimulus for the alterations in the rates of bone flow was identified. The only significantly different variable between the dietary periods was the lower calcium balance during consumption of the high fiber diet. Bronner et al. (1963) found bone formation and calcium absorption, and also bone formation and resorption, to be linearly related in healthy adult women and in women with scoliosis and post-menopausal osteoporosis. However, no information was obtained on which variable was the independent parameter or whether these relationships were functions of a third independent factor (Bronner et al. 1963). Dawson-Hughes et al. (1988) measured the fractional whole-body retention of oral ^{47}Ca in women with low (300 mg/d) and high (2,000 mg/d) calcium intakes for up to 8 wk. Fractional whole-body retention of the isotope was increased after 1 wk of the low calcium diet even though serum $1,25(\text{OH})_2\text{D}_3$ concentrations declined after this time. These results were interpreted as showing that calcium absorption increased with the low calcium diet, but by a mechanism independent of $1,25(\text{OH})_2\text{D}_3$ stimulation. An alternative interpretation suggested by the present data is that isotope retention is apparently increased, consistent with a lower turnover rate. We might speculate that in the face of lower dietary calcium inputs, bone accretion rate is diminished and calcium is maintained in more readily accessible pools for purposes of homeostatic maintenance. System mean residence time was calculated to be greater during the high fiber diet periods at a level approaching significance.

In summary, higher dietary fiber intake resulted in significantly higher fecal calcium losses and slower bone flow rates. A homeostatic mechanism apparently exists that is capable of decreasing rates of total bone turnover and the calcium flow to bone from the exchangeable pool (K_0^+) when calcium availability is limited. This down-regulation seems to be controlled such that the ratio of bone accretion to bone resorption is maintained at a constant level. It is not known how long these changes would be maintained or how they would affect long-term calcium homeostasis, especially in conditions in which calcium balance is negative. However, under the conditions of this experiment, adaptations in bone turnover were responsive to the chronic decrease in

calcium absorption, whereas responses in the efficiency of intestinal calcium absorption were not.

LITERATURE CITED

- Abrams, S. A., Esteban, N. V., Vieira, N. E., Sidbury, J. B., Specker, B. L. & Yergey, A. L. (1992) Developmental changes in calcium kinetics in children assessed using stable isotopes. *J. Bone Miner. Res.* 7: 289-295.
- Allen, L. H., Reynolds, W. L. & Margen, S. (1979) Polyethylene glycol as a quantitative fecal marker in human nutrition experiments. *Am. J. Clin. Nutr.* 32: 427-440.
- Andersson, H., Navert, B., Bingham, S. A., Englyst, H. N. & Cummings, J. H. (1983) The effects of breads containing similar amounts of phytate but different amounts of wheat bran on calcium, zinc, and iron balance in man. *Br. J. Nutr.* 50: 503-510.
- Annino, J. S. (1964) *Clinical Chemistry: Principles and Procedures*, pp. 135-136. Little Brown and Co., Boston, MA.
- Batchelor, A. J. & Compston, J. E. (1983) Reduced plasma half-life of radio-labelled 25-hydroxyvitamin D_3 in subjects receiving a high fiber diet. *Br. J. Nutr.* 49: 213-216.
- Berman, M. & Weiss, M. (1978) SAAM Manual. U.S. DHEW publication no. (NIH) 78-180, Department of Health and Human Services, Washington, DC.
- Bronner, F., Richelle, L., Saville, P., Nicholas, A. & Cobb, J. (1963) Quantitation of calcium metabolism in postmenopausal osteoporosis and in scoliosis. *J. Clin. Invest.* 42: 898-905.
- Clements, M. R., Johnson, L. & Fraser, D. R. (1987) A new mechanism for induced vitamin D deficiency in calcium deprivation. *Nature (Lond.)* 325: 62-65.
- Covell, D. G., Berman, M. & Delisi, C. (1984) Mean residence time—theoretical development, experimental determination, and practical use in tracer analysis. *Math. Biosci.* 72: 213-244.
- Cummings, J. H., Hill, M. J., Houston, H., Branch, W. J. & Southgate, D.J.A. (1979) Effect of meat protein and dietary fiber on colonic function and metabolism. I. Changes in bowel habits, bile acid excretion and calcium absorption. *Am. J. Clin. Nutr.* 32: 2086-2093.
- Dawson-Hughes, B., Stern, D. T., Shipp, C. C. & Rasmussen, H. M. (1988) Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J. Clin. Endocrinol. & Metab.* 67: 62-68.
- Driscoll, R. H., Meredith, S. C., Sitrin, M. & Rosenberg, I. H. (1982) Vitamin D deficiency and bone disease in patients with Crohn's disease. *Gastroenterology* 83: 1252-1258.
- Eastell, R., Vieira, N., Yergey, A. & Riggs, L. (1989) One-day test using stable isotopes to measure true fractional calcium absorption. *J. Bone Miner. Res.* 4: 463-468.
- Eastwood, M. & Morris, E. (1992) Physical properties of dietary fiber that influence physiological function: a model for polymers along the gastrointestinal tract. *Am. J. Clin. Nutr.* 55: 436-442.
- Gibson, R. S., Bindra, G. S., Nizan, P. & Draper, H. H. (1987) The vitamin D status of East Indian Punjabi immigrants to Canada. *Br. J. Nutr.* 58: 23-29.
- Halloran, B., Bickle, D., Levens, M., Castro, M., Globus, R. & Holton, E. (1986) Chronic $1,25$ -dihydroxyvitamin D_3 administration in the rat reduces the serum concentration of 25-hydroxyvitamin D by increasing metabolic clearance rate. *J. Clin. Invest.* 78: 622-628.
- Heaney, R. P. & Skillman, T. G. (1964) Secretion and excretion of calcium by the human gastrointestinal tract. *J. Lab. Clin. Med.* 64: 29-41.
- Holick, M. F. (1987) Photosynthesis of vitamin D in the skin: effect of environmental and life-style variables. *Fed. Proc.* 46: 1876-1882.
- Jenkins, D. J., Peterson, D., Thorne, M. J. & Ferguson, P. W. (1987) Wheat fiber and laxation: dose response and equilibration time. *Am. J. Gastroenterol.* 82: 1259-1263.

- Kelsay, J. L., Behall, K. M. & Prather, E. S. (1979) Effects of fiber from fruits and vegetables on metabolic responses of human subjects. II. Ca, Mg, Fe, and silicon balances. *Am. J. Clin. Nutr.* 32: 1876-1880.
- Knox, T. A., Kassarjian, Z., Dawson-Hughes, B., Golner, B. B., Dallal, G. E., Arora, S. & Russell, R. M. (1991) Calcium absorption in elderly subjects on high- and low-fiber diets: effect of gastric acidity. *Am. J. Clin. Nutr.* 53: 1480-1486.
- Lore, G., DiCairano, G., Periti, P. & Caniggia, A. (1982) Effect of the administration of 1,25-dihydroxyvitamin D₃ on serum levels of 25-hydroxyvitamin D in postmenopausal osteoporosis. *Calcif. Tissue Int.* 34: 539-541.
- Neer, R., Berman, M., Fisher, F. & Rosenberg, L. E. (1967) Multicompartmental analysis of calcium kinetics in normal adult males. *J. Clin. Invest.* 46: 1364-1378.
- Norman, A. W. (1990) Intestinal calcium absorption: a vitamin D-hormone-mediated adaptive response. *Am. J. Clin. Nutr.* 51: 290-300.
- Spencer, H., Kramer, L., Lesniak, M., De Bartolo, M., Norris, C. & Osis, D. (1984) Calcium requirements in humans: report of original data and a review. *Clin. Orthop. Relat. Res.* 184: 270-280.
- Spiller, G. A., Story, J. A., Wong, L. G., Nunes, J. D., Alton, M., Petro, M. S., Furumoto, E. J., Whittam, J. H. & Scala, J. (1986) Effect of increasing levels of hard wheat fiber on fecal weight, minerals, and steroids and gastrointestinal transit time in healthy young women. *J. Nutr.* 116: 778-785.
- Vieth, R., Fraser, D. & Kooh, S. W. (1987) Low dietary calcium reduces 25-hydroxycholecalciferol in plasma of rats. *J. Nutr.* 117: 914-918.
- Weaver, C. M., Heaney, R. P., Martin, B. R. & Fitzsimmons, M. L. (1991) Human calcium absorption from whole-wheat products. *J. Nutr.* 121: 1769-1775.
- Yergey, A. L., Abrams, S. A., Vieira, N. E., Eastell, R., Hillman, L. S. & Covell, D. G. (1990) Recent studies of human calcium metabolism using stable isotopic tracers. *Can. J. Physiol. Pharmacol.* 68: 973-976.
- Yergey, A. L., Vieira, N. E. & Covell, D. G. (1987) Direct measurement of dietary fractional absorption using calcium isotopic tracers. *Biomed. Mass Spectrom.* 14: 603-607.
- Yergey, A. L., Vieira, N. E. & Hansen, J. W. (1980) Isotope ratio measurements of urinary calcium with a thermal ionization probe in a quadrupole mass spectrometer. *Anal. Chem.* 52: 1811-1814.