High dietary calcium intakes reduce zinc absorption and balance in humans 1–4

Richard J Wood and Jia Ju Zheng

ABSTRACT Optimal calcium intakes of 37.5 mmol (1500 mg)/d have been proposed for elderly people. We investigated the effects of calcium supplementation on zinc absorption and balance in 18 relatively healthy, postmenopausal women aged 59–86 y. All subjects received a standardized basal diet of typical foods supplying 269 μmol (17.6 mg) Zn/d and 22.2 mmol (890 mg) Ca/d during the 36-d study. In two of three experimental periods, an additional 11.7 mmol (468 mg) Ca/d as either milk or an inorganic calcium phosphate supplement was provided. Net zinc absorption and zinc balance were significantly reduced by ∼2 mg/d during both high-calcium treatments. In a second study, conducted in a separate group of men and women aged 21–69 y, a whole-gut lavage, zinc-absorption test was used to investigate the acute effect of a 15-mmol CaCO3 (600 mg Ca) supplement, with and without extra zinc, on zinc absorption from a single test meal supplying 111.7 μmol (7.3 mg) Zn. Zinc absorption was reduced significantly by 50% when the calcium supplement was given with the meal. Inclusion of an extra 119.3 μmol (7.8 mg) Zn as part of a calcium supplement offset the detrimental effect of calcium on zinc absorption. Our findings suggest that high-calcium diets can reduce net zinc absorption and balance and may increase the zinc requirement in adult humans. Am J Clin Nutr 1997;65:1803–9.

KEY WORDS Optimal calcium intake, mineral-mineral interactions, elderly, postmenopausal women, zinc bioavailability, endogenous fecal zinc, breath hydrogen

INTRODUCTION

Estimates of dietary zinc intake in the US population suggest that a low zinc intake is common in many population groups, particularly in elderly women (1). The current recommended dietary allowance (RDA) for zinc in adult women is 12 mg/d (2). However, about one-half of adult women in the United States consume <7.5 mg Zn/d (1). Low dietary zinc intakes in elderly women and age-associated reductions in the efficiency of intestinal zinc absorption (3, 4) put elderly people at increased risk of developing marginal zinc status (5). Moreover, the nutritional status of elderly people may be particularly vulnerable to any changes in dietary habits that affect dietary zinc bioavailability (6). Zinc deficiency has many untoward effects, including loss of appetite, growth retardation, skin changes, and immunologic abnormalities (2).

Dietary surveys indicate that the diets of most women in the United States provide considerably less than the current RDA for calcium of 800 mg/d (7). Considerable public and research attention has been given to the need to increase dietary calcium intakes in women in hopes of preventing age-associated bone loss (8–11). This growing awareness of the need for high amounts of dietary calcium to prevent bone loss has resulted in a significant increase in the sale of calcium supplements and the introduction of many new calcium-fortified foods. In 1994 the National Institutes of Health Consensus Conference on Optimal Calcium Intakes recommended that estrogen-deficient women and elderly people consume 37.5 mmol (1500 mg) Ca/d to minimize bone loss (12). The major food sources of calcium in the US are milk and milk-based products. According to the second National Health and Nutrition Examination Survey (NHANES II), meat and milk contribute ∼60% of the total dietary zinc in the United States (1). Beef or dishes containing beef, such as stews, contribute most of the dietary zinc for all age and sex groups in the United States, except in women aged 65–74 y. In this group of postmenopausal women, milk is the most prevalent source of dietary zinc, accounting for 22% of total zinc intake.

High calcium intakes can reduce zinc absorption and exacerbate the signs of zinc deficiency in animals fed low-zinc diets (13). In humans, several previous studies reported the effects of milk or calcium supplementation on zinc absorption, with variable findings (14–20). However, the nutritional consequences of increased calcium intakes, via consumption of either milk or calcium supplements, on zinc balance in postmenopausal women has not been addressed.

We report the findings from two studies that addressed the effects of a high calcium intake on zinc absorption and balance in adults. In the first study, conducted in postmenopausal

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women confined to a metabolic ward for 36 d, we compared
the effects of a diet providing a high calcium intake, similar to
the intake currently recommended as being optimal for elderly
people (12), with the effects of a diet containing approximately
the current RDA for calcium. In the second study, conducted in
adult men and women (21), we used a single-meal, zinc-
absorption test with the nonisotopic whole-gut lavage, zinc-
absorption method to investigate the acute effects of a calcium
carbonate supplement on zinc absorption from a high-beef
meal.

SUBJECTS AND METHODS

Subjects in both studies completed a medical exam and
medical-history questionnaire as part of a screening procedure
before the study began. Subjects were excluded from the study
if they had evidence of diabetes mellitus or parathyroid or
thyroid gland disorders, or a history of significant cardiac,
renal, or gastrointestinal disease. If subjects took vitamin and
mineral supplements, they were asked to discontinue use 1 mo
before the study began. Procedures used in these studies were
approved by the Human Investigation Review Committee at
Tufts University. Written informed consent was obtained from
all subjects.

Study 1: metabolic-balance study

Subjects

Eighteen healthy, elderly white women aged 59–86 y were
recruited from various parts of the United States to reside in the
Metabolic Research Unit (MRU) of the Jean Mayer US
Department of Agriculture (USDA) Human Nutrition Research
Center (HNRC) on Aging at Tufts University in Boston with
strict control of dietary intake and urine and stool collections
for a 36-d zinc-balance study.

Breath-lactose test

A breath-lactose test was administered before the balance
study to identify any lactose intolerance among postmeno-
pausal subjects. Lactose tolerance was determined by measur-
ing (model 12 Microlyzer; Quintron Instruments, Milwaukee)
the rise in breath-hydrogen concentration for 4 h after the
ingestion of 73 μmol lactose. Lactose intolerance was judged
by a rise in breath-hydrogen concentration of ≥ 20 ppm (22).
The results of the breath-lactose test showed two elderly
women to be lactose intolerant. These two subjects were fed
milk that had most of the lactose removed by incubation with
excess β-galactosidase (LactAid; LactAid Co, Pleasantville,
NJ). We reported previously that milk and lactase-treated milk
had similar effects on zinc absorption in postmenopausal
women (15).

Diet records

The subjects completed a 3-d dietary record before the
metabolic study began. These records were coded for individ-
al food items, and daily mineral intakes were calculated. The
Dietary Assessment Unit of the HNRC analyzed the food
records using version 8709 of the GRAND nutrient database
(USDA/Agricultural Research Service Grand Forks, HNRC,
Grand Forks, ND).

Study design

The zinc-balance study was divided into three 12-d experi-
mental periods. The order of treatment was randomized for
each subject across the three phases of the study. Subjects were
housed at the HNRC MRU during the study and fed a standard
basal metabolic diet consisting of normal foods and 20 g

<table>
<thead>
<tr>
<th>Meal</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
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<tbody>
<tr>
<td>Breakfast</td>
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<tr>
<td>Bran flakes cereal</td>
<td>Wheat cereal</td>
<td>Oatmeal cereal</td>
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<tr>
<td>Stewed prunes</td>
<td>Muffin</td>
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<td>Wheat bread</td>
<td>Butter</td>
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<tr>
<td>Peanut butter</td>
<td>Sugar</td>
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<tr>
<td>Skim milk</td>
<td>Skim milk</td>
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<td>Nondairy creame</td>
<td>Brown sugar</td>
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<td>Cranberry juice</td>
<td>Coffee</td>
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<td>Tuna</td>
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<td>Butter</td>
<td>Ketchup</td>
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<td>Coconut beverage</td>
<td>Coconut beverage</td>
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<tr>
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<td>Beef caserole</td>
<td>Salisbury steak</td>
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<td>Dinner roll</td>
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<td>Pears</td>
<td>Crackers</td>
<td>Skim milk</td>
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<td>Cranberry juice</td>
<td>Orange juice</td>
<td>Apple juice</td>
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<td>Coconut beverage</td>
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<td>Butter</td>
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1 Milk was substituted for the coconut beverage during the milk-
supplemented diet phase.
milk (21%). The distribution of dietary zinc by meal was 36% from breakfast, 29% from lunch, 32% from dinner, and 3% from snacks.

Each subject's body weight was measured weekly. Small adjustments in the energy content of the diet were made to maintain a stable body weight when necessary. To maintain an equivalent energy intake among all treatment phases, the subjects received a high-energy beverage during the two phases of the study when they were not receiving the milk supplement. Precautions were maintained during the study to reduce extraneous zinc contamination. Foods were prepared in stainless steel cookware or acid-washed glassware, and food was eaten with plastic utensils. Only distilled water was consumed during the study. Subjects were trained by a research dietitian to scrape and rinse their plates. Meals were eaten at the HNRC MRU under supervision. Occasionally, some food was left uneaten. In these cases, the food was weighed and small adjustments in the calculated zinc intake of the subject were made according to the analyzed zinc content of the uneaten food items.

Zinc absorption and zinc balance

Complete collections of all urine and fecal samples were made during all three metabolic periods to determine net zinc absorption (zinc intake — fecal zinc) and apparent zinc balance (net zinc absorption — urine zinc). Subjects were given a radioactive nonabsorbable fecal marker (51Cr) at the beginning of each treatment phase and at the end of the study. Throughout the study, each fecal sample was measured for 51Cr with a whole-body counter at the HNRC to demarcate the appropriate fecal pools for each treatment period. A sharp peak that represented the bulk of the fecal marker invariably appeared in a single fecal sample (data not shown), thus allowing for easy pooling of the samples. To ensure that the full fecal collection was made for the last treatment period that ended on day 36, subjects remained in the MRU until the last radioactive marker appeared in a stool sample.

Individual stool samples were collected in acid-washed containers and were lyophilized and weighed. Appropriate fecal pools were dry homogenized in a food processor with a plastic blade. For each treatment period, the 51Cr-marked fecal samples and all subsequent samples before the appearance of the 51Cr marker from the next treatment period were included in a fecal pool. Samples of diet and feces were acid wet-ashed in vented polytetrafluoroethylene vessels by using a microwave digestion unit (model MDS-81D; CEM Corporation, Mathews, NC). Samples were appropriately diluted and zinc was determined by direct-current plasma (DCP) emission spectrometry (Beckman Instruments, Inc, Palo Alto, CA) (23). Certified liver samples obtained from the National Institute of Standards and Technology (Gaithersburg, MD) were digested and analyzed as a standard quality-control reference material for zinc in each batch of asheod samples. The average value for liver zinc was within 1 SD of the certified value, and the interassay CV for 36 replicated ashed liver samples was 6%.

Complete 24-h urine samples were collected in acidified (3% by vol, Ultrace-brand hydrochloric acid; JT Baker Chemical Co, Phillipsburg, NJ) plastic trace element–free collection jugs during all three experimental periods. These samples were measured for volume and then were separated and pooled (10% of volume/d) for analysis of urinary zinc by DCP emission spectrometry and creatinine by a standard automated clinical chemical method.

Serum assays

Blood was collected after an overnight fast at the start and end of each treatment period in trace element–free syringes and allowed to clot at room temperature. Serum zinc was measured by atomic-absorption spectroscopy by using a fivefold dilution of serum and aqueous zinc standards prepared in a diluted glycerol matrix (24). The interassay precision of this method in our laboratory is 3%. We also measured serum 25-hydroxycholecalciferol (calcidiol) (25), 1,25-dihydroxycholecalciferol (calcitriol) (26), and intact parathyroid hormone (PTH) (27).

Study 2: whole-gut lavage, zinc-absorption test

Subjects

Ten healthy adult subjects (five men and five women) were recruited from the greater Boston area. Subjects ranged in age from 21 to 69 y (mean: 47 y). Each subject resided for 1 d at the HNRC MRU on three occasions, separated each time by 1 wk, and their zinc absorption from a standard test meal was measured by a whole-gut lavage, zinc-absorption technique, as described previously (21).

Study design

This study was designed to see whether calcium alone, as a calcium carbonate supplement, could acutely affect zinc absorption from beef, an important dietary source of zinc. We also wanted to determine whether the addition of supplemental zinc in the same meal could offset the negative effects of calcium on zinc absorption. Thus, zinc and calcium absorption were measured during three different conditions in each subject: 1) test meal alone, containing 11 mmol (7.3 mg) Zn; 2) test meal plus 15 mmol (600 mg) Ca as a commercial calcium carbonate tablet (Caltrate 600; Lederle Consumer Health, Pearl River, NY); and 3) test meal plus a commercial supplement tablet from the same manufacturer (Caltrate Plus Minerals) supplying 15 mmol Ca as calcium carbonate, 0.12 mmol (7.8 mg) Zn as zinc oxide, and small amounts of additional minerals. The analyzed zinc content of Caltrate 600 was negligible, 0.1 μmol.

Test meal

The test meal used in the single-meal absorption test consisted of 140 g ground beef, 100 g French-fried potatoes, and 0.250 L distilled water. This meal supplied 455 kcal, 33 g protein, 19 g fat, and 38 g carbohydrate; 29% of energy was from protein, 38% was from fat, and 33% was from carbohydrate.

Statistical analysis

The statistical significance of treatment effects was evaluated by one-way analysis of variance (ANOVA) with repeated measures by using SYSTAT (version 6; Systat Inc, Evanston, IL). If a significant F test was found by ANOVA, then post hoc comparisons of calcium treatment means with the control treatment means were done by Dunnett's test at P < 0.05. Data are expressed as means ± SEMs.
RESULTS

Metabolic-balance study

Prestudy diet

On the basis of a 3-d diet record, the estimated free-living dietary zinc intake for this group of postmenopausal women was 122.5 \(\mu\text{mol/}(8\ \text{mg/d})\) (range: 60–169 \(\mu\text{mol/d}\), or 3.9–11 mg/d). Dietary calcium and phosphorus intakes were 18.75 mmol (752 mg/d) (range: 7.35–32.58 mmol, or 295–1306 mg/d) and 34.48 mmol (1068 mg/d) (range: 16.29–43.93 mmol/d, or 505–1761 mg/d), respectively.

Body weight change, baseline blood measurements, and urinary creatinine

No significant changes were observed in body weight during the study. The average body weight of the group was 71.0 \(\pm\) 3.1 kg at the beginning of the study and 70.3 \(\pm\) 3.1 kg at the end. Baseline values for serum minerals, calcidiol, calcitriol, and PTH were within our normal laboratory ranges and are shown in Table 2. No significant changes in these blood measurements were observed as a result of calcium treatment (data not shown). Urinary creatinine was constant (\(\approx\) 8.84 mmol/d, or 1 g/d) in all three metabolic periods.

Net zinc absorption

Zinc intake, fecal zinc, and calculated net zinc absorption (zinc intake − fecal zinc) during the three metabolic periods are shown in Table 3. By design, no significant differences in zinc intake were observed among the three dietary treatments. We did observe that additional calcium added to the diet as either milk or an inorganic calcium supplement increased fecal zinc losses, resulting in significantly reduced net zinc absorption. No significant differences in zinc absorption were seen between the milk- and calcium phosphate–supplemented diets. Net zinc absorption efficiency as a percentage of dietary zinc intake decreased significantly (\(P < 0.05\)) during the calcium-supplementation periods. Fractional zinc absorption was 13 \(\pm\) 3% during the basal diet period compared with 2 \(\pm\) 3% and 1 \(\pm\) 3% during the calcium phosphate– and milk-supplementation periods, respectively.

### Table 2
Baseline characteristics of subjects in the zinc-balance study

<table>
<thead>
<tr>
<th>Value</th>
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<tbody>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
</tr>
<tr>
<td>Height (cm)</td>
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<tr>
<td>Serum zinc ((\mu\text{mol/L}))</td>
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<tr>
<td>Serum ionized calcium (mmol/L)</td>
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<tr>
<td>Serum magnesium (mmol/L)</td>
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<tr>
<td>Serum phosphorus (mmol/L)</td>
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<tr>
<td>Serum parathyroid hormone (pmol/L)</td>
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<tr>
<td>Calcidiol (nmol/L)</td>
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<tr>
<td>Calcitriol (pmol/L)</td>
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<tr>
<td>Prestudy zinc intake ((\mu\text{mol/d}))</td>
</tr>
</tbody>
</table>

\(^1\) \(x\) range in parentheses, \(n = 18\).
\(^2\) \(x \pm \text{SEM}; n = 18\).

### Table 3
Zinc intake, fecal excretion, urinary excretion, and apparent zinc absorption during three 12-d metabolic-balance periods in 18 postmenopausal women fed either a basal diet or the basal diet supplemented with additional calcium as either milk or a calcium phosphate tablet

<table>
<thead>
<tr>
<th>Dietary treatment</th>
<th>Basal diet</th>
<th>Basal diet + calcium phosphate</th>
<th>Basal diet + milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc intake</td>
<td>268.6 ± 2.0</td>
<td>269.5 ± 2.8</td>
<td>265.2 ± 1.9</td>
</tr>
<tr>
<td>Fecal zinc</td>
<td>233.5 ± 7.5</td>
<td>263.5 ± 8.2(^2)</td>
<td>262.7 ± 8.9(^2)</td>
</tr>
<tr>
<td>Urinary zinc</td>
<td>6.9 ± 0.8</td>
<td>6.7 ± 0.8</td>
<td>7.0 ± 0.9</td>
</tr>
<tr>
<td>Apparent zinc absorption</td>
<td>35.1 ± 7.8</td>
<td>6.1 ± 8.6(^2)</td>
<td>2.6 ± 9(^2)</td>
</tr>
</tbody>
</table>

\(^1\) \(x \pm \text{SEM}.\)
\(^2\) Significantly different from the basal diet, \(P < 0.05\) (Dunnett’s test).

Zinc balance

Urinary zinc was not affected by dietary treatment and did not reflect changes in zinc absorption (Table 3). As shown in Figure 1, zinc balance decreased significantly (\(P < 0.05\)) during consumption of the high-calcium diets compared with the basal diet. The mean (\(\pm\) SEM) zinc balance was 28.2 \(\pm\) 7.6 \(\mu\text{mol/d}\) (1.8 \(\pm\) 0.5 mg/d) during the basal diet, −0.8 \(\pm\) 8.8 \(\mu\text{mol/d}\) (−0.1 \(\pm\) 0.6 mg/d) during the calcium-phosphate–supplemented diet, and −4.5 \(\pm\) 9.1 \(\mu\text{mol/d}\) (−0.3 \(\pm\) 0.6 mg/d) during the milk-supplemented diet. The mean reduction in zinc balance between the basal diet and the milk-supplemented diet was 32.6 \(\mu\text{mol/}(2.13\ \text{mg/d})\). More subjects were in negative zinc balance when they consumed the calcium-supplemented diets, which supplied amounts of calcium similar to those recommended as being optimal for elderly people, than when
they consumed the basal diet, which provided close to the current RDA for calcium. Two of the 18 postmenopausal women were in negative zinc balance when they consumed the basal diet, whereas 10 of the 18 women were in negative balance when they consumed the milk-supplemented, high-calcium diet. Of these 10 subjects in negative zinc balance during the milk-supplemented diet, 4 lost between 0.1 and 0.9 mg Zn/d (−1.5 to −13.8 µmol Zn/d), 3 lost between 1.0 and 1.9 mg Zn/d (−15.3 to −29.1 µmol Zn/d), 1 lost between 2.0 and 2.9 mg Zn/d (−30.6 to −44.4 µmol Zn/d), and 2 lost between 3.0 and 5.4 mg Zn/d (−45.9 to −82.6 µmol Zn/d).

**Acute effect of calcium carbonate supplementation on zinc absorption from a test meal**

The beef-based test meal contained 111.7 µmol (7.3 mg) Zn. Absorption of zinc from this standard test meal was 22.5 ± 3.6 µmol (1.47 ± 0.23 mg). As shown in **Figure 2**, consumption of the calcium supplement (15 mmol Ca as calcium carbonate) along with the test meal significantly (P < 0.01) reduced zinc absorption from the meal to 11.5 ± 3.1 µmol (0.75 ± 0.2 mg). However, zinc absorption from the test meal with a calcium carbonate supplement that supplied an additional 119.3 µmol (7.8 mg) Zn restored zinc absorption to 24.5 ± 5.7 µmol (1.61 ± 0.37 mg), a value similar to that observed from the test meal alone. Calcium absorption was measured in these subjects after each calcium-supplemented test meal and was found to be 20% from both calcium carbonate–containing supplements.

[FIGURE 2. Effect of calcium carbonate supplementation (15 mmol, or 600 mg), with and without additional zinc, on zinc absorption in adult men and women (n = 10) from a single high-beef test meal containing 111.7 µmol (7.3 mg) Zn. Zinc absorption was measured nonisotopically with a whole-gut lavage, zinc-absorption test. Mean zinc absorption was significantly reduced by the calcium supplement alone (Dunnett’s test, P < 0.05). Zinc absorption after treatment with calcium plus added zinc (119.3 µmol, or 7.8 mg) was not significantly different from zinc absorption after the control test meal.]

**DISCUSSION**

Our findings clearly suggest that consumption of a high-calcium diet can significantly reduce net zinc absorption and zinc balance in postmenopausal women and increase the risk of developing negative zinc balance. Moreover, about one-half of our subjects were in negative zinc balance when consuming the high-calcium diet. This observation was surprising because the zinc intake during the study was relatively high (18 mg/d) and exceeded the current RDA for zinc for elderly women by 50%. This high zinc intake during the metabolic study was twice the usual reported zinc intake of this group. The low reported zinc intakes of the older women in our study group were typical, however, for this age group and were consistent with those from national diet surveys. In NHANES II, the mean zinc intake for elderly women was 8.6 mg/d and the median intake was 6.3 mg/d (1). Thus, about one-half of older women in the United States consume less than one-half of the current RDA for zinc. This observation suggests that elderly women may be particularly vulnerable to factors that can alter zinc bioavailability or the requirement for zinc, such as a high-calcium diet as shown here (6).

The zinc needs of elderly people are poorly defined (5). There are few studies in which zinc balance has been measured in elderly women. These studies have been conducted under a variety of experimental conditions and frequently report aggregate data for both men and women. For example, Bunker et al (28) performed a 5-d zinc-balance study in 24 elderly people (11 men and 13 women) aged 70–86 y living in their homes in the United Kingdom and consuming their usual diets. The mean zinc intake for the group was 137 µmol (9 mg)/d (range: 46–210 µmol/d, or 3.0–13.7 mg/d). Net zinc absorption was 6 µmol (0.4 mg)/d (range: −41 to 37 µmol/d, or −2.6 to 2.4 mg/d). Zinc balance for the group was 1 µmol (0.1 mg)/d (range: −47 to 31 µmol/d, or −3.1 to 2.0 mg/d).

In another study, Burke et al (29) measured zinc balance in two small groups of elderly subjects aged 56–83 y from the United States. Subjects ate breakfast and dinner at a metabolic unit but were provided with lunch for consumption at home. The subjects were fed a basal diet containing 91.8 µmol (6 mg) Zn/d. A zinc sulfate supplement also was provided so that the total zinc intake was either 119.3 µmol (7.9 mg)/d or 355.8 µmol (23.26 mg)/d. Five subjects received the low-zinc diet and six subjects received the high-zinc diet for 30 d. These investigators found that zinc intake did not influence zinc retention. Three of the six subjects fed the high-zinc diet were in net negative zinc balance. The mean (± SD) zinc retention was −5.2 ± 22.3 µmol/d (−0.34 ± 1.46 mg/d) with the low-zinc diet and −3.5 ± 25.7 µmol/d (−0.23 ± 1.68 mg/d) with the high-zinc diet. Additional research is needed to more precisely define the zinc requirement of older women.

In 1994 the National Institutes of Health Consensus Development Conference on Optimal Calcium Intakes (12) recommended that all elderly people (aged > 65 y) and younger estrogen-deficient adult females consume 37.5 mmol (1500 mg) Ca/d to reduce the rate of bone loss and decrease the risk of osteoporotic bone fractures. Even though elderly women are an important target population for calcium supplementation (8–11), we are not aware of any study that has addressed the effects of calcium supplementation on zinc absorption and balance in older women. Although the possible negative effects
of a high-calcium diet on zinc homeostasis in animals has been appreciated for > 30 y (13, 30), the mechanism underlying the calcium-zinc interaction is still uncertain. Animal-feeding studies have led to the suggestion that a three-way calcium-zinc-phytate interaction is necessary to reduce intestinal zinc absorption (13). Given that our metabolic diet contained both phytate and added dietary fiber, as cellulose, this interaction could be evident in our metabolic study. However, for several reasons we believe that it is unlikely that an interaction between fiber and calcium-zinc-phytate can adequately explain our findings. First, Turnlund et al (31) reported that 30–40 g cellulose had no effect on dietary zinc absorption. Second, we observed an effect of calcium on net zinc absorption when dietary fiber and phytate intakes were low in our single-meal study, in which subjects were fed only beef and French-fried potatoes. Third, Castillo-Duran and Solomons (20) found that calcium supplementation caused a lower rise in plasma zinc concentrations after consumption of a beef meal.

High-calcium diets apparently do not affect true zinc absorption. Several reports have been published in which the effect of a calcium supplement on true zinc absorption in humans was assessed from a single meal with an extrinsic $^{65}$Zn tag method (14, 16, 32). These studies found that extra calcium had no effect on $^{65}$Zn absorption. We reported previously, however, that zinc absorption from $^{65}$Zn-labeled milk was significantly reduced compared with $^{65}$Zn absorption from water alone in postmenopausal women (15). In retrospect, we now believe that this apparent inhibitory effect of milk on true $^{65}$Zn absorption was probably an experimental artifact caused by a non-specific effect of food (milk) and not a specific calcium effect on true $^{65}$Zn absorption. This notion is consistent with our subsequent finding that a milk supplement had no effect on $^{65}$Zn absorption from a typical breakfast (16).

The findings from our metabolic study in postmenopausal women suggest that the mechanism by which high-calcium diets impair zinc balance is attributable to a reduction in net zinc absorption, measured as the difference between zinc intake and fecal zinc recovery. This is consistent with our observation in younger men and women that administration of 15 mmol (600 mg) Ca as calcium carbonate with a beef-based test meal caused a significant reduction in zinc absorption, as determined by the whole-gut lavage absorption method. With use of this nonisotopic absorption method, the difference between zinc intake and fecal zinc excretion is determined after the consumption of a single meal (21). Our finding of an apparent acute meal-based effect of calcium on zinc absorption is consistent with the finding of Castillo-Duran and Solomons (20), who noted a significantly lower postprandial plasma zinc response to a beef meal when calcium carbonate or milk was fed with the test meal.

The effects of high-calcium diets on net zinc absorption have been addressed in young and elderly men (18, 19). Spencer et al (18) measured the effects of various amounts of dietary calcium on net zinc absorption and balance in eight men aged 49–64 y who were confined to a hospital metabolic ward for 36–42 d. Net fractional zinc absorption was reduced significantly from 15% to 1% when dietary calcium was increased from 5.4 mmol(216 mg)/d to 50.7 mmol(2028 mg)/d. Zinc balance in these men fed 198.9 μmol(13 mg)Zn/d was 21.4 μmol(1.4 mg)/d after the lowest calcium intake and −7.6 μmol(−0.5 mg)/d after the highest calcium intake, similar to our observation in postmenopausal women (Figure 1). However, Spencer et al (18) found that this difference in zinc balance was not significant, which may reflect the small sample size. In another study described by Spencer et al (18), net fractional dietary zinc absorption decreased, although not significantly, from 24% to 12% to −3% in three groups of men (n = 5–8 subjects per group) as the dietary calcium intake increased from 5.8 mmol(231 mg)/d to 21.5 mmol(859 mg)/d to 50 mmol(2001 mg)/d. We observed a similar change in fractional zinc absorption in our elderly women, in whom a decrease in absorption from 13% to 1% was observed when dietary calcium increased from 890 to 1358 mg/d. However, the effects of a high-calcium diet on zinc homeostasis in younger men is uncertain. Snedeker et al (19) studied net zinc absorption and balance in nine young men aged 24 y who were fed as outpatients controlled diets that contained various amounts of calcium and phosphorus. The metabolic diet supplied 10 mg Zn/d, which resulted in negative zinc balance in all subjects regardless of their calcium or phosphorus intake. These investigators found that calcium intakes as high as 2400 mg/d had no effect on net zinc absorption or zinc balance. The reason for the apparent lack of an effect of a high calcium intake on zinc balance in young men is uncertain. However, several differences in study design, besides the age of the subjects, were evident. Given the increased popularity of calcium supplementation and a general trend toward recommending increased calcium intake for most of the population (12), additional study of the effects of high-calcium diets on zinc balance in various groups, especially in growing girls and young adult females, appears to be warranted. Moreover, note that high-calcium diets also are known to have a negative influence on the absorption of other trace elements, such as manganese (33) and iron (34).

The mechanism through which high-calcium diets influence net zinc absorption is poorly understood. Net zinc absorption measured by the balance-study approach is influenced by both the degree of true zinc absorption and the amount of endogenous fecal zinc losses. As mentioned above, several studies have investigated the effects of calcium on true $^{65}$Zn absorption and found no effect (14, 16, 32). Because net zinc absorption is decreased by a high-calcium diet but true zinc absorption is apparently not affected, we speculate that the effect of a high-calcium diet on net zinc absorption, and thereby zinc balance, may be dependent on increased endogenous fecal zinc losses. Unfortunately, we did not measure endogenous fecal zinc losses directly in our zinc-balance study. Thus, this suspicion will need to be tested by directly measuring the effects of a high-calcium diet on endogenous zinc losses before a firm conclusion can be drawn. If confirmed, however, augmentation of net endogenous zinc losses by a high-calcium diet would represent a unique mechanism of mineral-mineral interactions that could significantly influence zinc requirements.

An important implication of this study is that the zinc requirement of elderly women may actually increase when they consume the amount of dietary calcium considered to be optimal for their age group. Because our zinc-balance periods were only 12 d long, it is possible that our observations represented a marked but merely short-term change in zinc balance that was obscured within the 2-wk metabolic period. To partially address this possibility, we examined zinc-balance data from a subset of our subjects (n = 9) who by chance received a high-calcium diet for two consecutive metabolic periods. We observed no significant difference in zinc balance between the two high-calcium dietary periods, suggesting that the effect of
a high-calcium diet persists for ≥ 24 d, and thus does not represent a short-term change in zinc homeostasis.

An important question that could not be addressed in our study was whether consumption of a high-calcium diet impairs zinc status. It will be important for future studies to determine the long-term effects of calcium supplementation on zinc status and function. We speculate that if the effect of calcium on zinc losses is persistent and if it occurs with low dietary zinc intakes, then a significant depletion of zinc stores and alterations of zinc status may occur in vulnerable population groups such as elderly people, which could lead to compromised function and health. More data on the zinc status of populations consuming high-calcium diets are needed. However, the lack of applicable sensitive tools to assess zinc status in epidemiologic investigations may limit the ability to show this interaction in a large population survey (2).

Given that we observed in our single-meal absorption study that additional dietary zinc can ablate the acute negative effects of calcium supplementation, it seems prudent that vulnerable groups, such as elderly people with low zinc intakes, should increase their zinc intake if they increase their calcium intake substantially. The amount of additional zinc needed to counteract the effects of a high-calcium diet on zinc balance have not been shown experimentally. However, on the basis of the limited amount of data available from our studies and assuming a typical efficiency of intestinal zinc absorption of 20% (2), it appears that an increase of dietary zinc of as much as 10 mg/d (ie, 2 mg extra zinc loss due to the high-calcium diet/20% absorption efficiency) may be needed.

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