Calcium Bioavailability and Its Relation to Osteoporosis (43409)

Connie M. Weaver[1]
Department of Foods and Nutrition, Purdue University, West Lafayette, Indiana 47907

Abstract. **The balance of data suggests that calcium intake has a positive influence on bone mass in premenopausal women and has a preventive effect on the rate of bone loss in postmenopausal women. Even small advantages in bone mass provide great reductions in fracture rates. However, the majority of studies have tested the relationship of calcium intake and bone mass using calcium supplements. Few intervention studies have manipulated calcium intake through foods. Calcium is only useful to the skeleton once it is absorbed. Therefore, the bioavailability of dietary calcium becomes important in the prevention and treatment of osteoporosis.**

Isotopic tracer techniques have only recently been employed in the labeling of foods with calcium isotopes for evaluation of calcium absorption. Milk calcium is usually the referent food which is typically absorbed at 20–40% depending on the calcium status of the subject. The absorptive efficiency of most vegetable sources is as good or better than for dairy foods, unless they have high concentrations of oxalic acid (spinach, for example) or phytic acid (wheat bran cereal, for example). Few vegetable sources are concentrated sources of calcium. Therefore, it would be difficult to obtain adequate intakes of calcium to protect against osteoporosis without liberal use of dairy products in the diet. Alternately, calcium supplements provide concentrated amounts of absorbable calcium, but they do not provide other nutrients necessary for skeletal growth and maintenance. [P.S.E.B.M. 1992, Vol 200]

Osteoporosis is a disease characterized by a decreased skeletal mass and increased susceptibility to bone fractures. The average women loses 30–40% of her bone mass by the age of 70 (1). Since the incidence of vertebral fractures is inversely proportional to bone mineral content in Caucasian females over the age of 50 (2), an increase in bone mass at maturity is likely to decrease the incidence of fracture. The age at which maximum bone mass is achieved is not certain, but it is estimated to occur between the ages of 25 and 35. In children, total body calcium increases with age up to age 20, with a sharp increase at puberty (3). In women, bone loss begins prior to menopause, with the loss increasing rapidly for about 5 years following menopause (4). Because calcium as hydroxyapatite is the dominant mineral in bone, adequate calcium intake during formative years and later for skeletal maintenance is hypothesized to influence bone mass and, therefore, vulnerability to fracture.

[1] To whom requests for reprints should be addressed at Department of Foods and Nutrition, Purdue University, West Lafayette, IN 47907

0037-9727/92/2002-0157$3.00/0

The relationship between calcium intake and bone density has been widely studied using cross-sectional designs and, to a large extent, using calcium supplements in intervention protocols. Few investigators have considered the bioavailability of dietary calcium. The importance of bioavailability, if any, will be examined in this overview.

Calcium Intake and Bone Mass

Calcium intakes early in life may influence bone health in later years. Women who reported habitual milk drinking in early life had higher bone densities than those who did not (1).

Cumming (5) tested recently the strength of the literature on calcium intake and bone mass in adult women with a meta-analysis. The inclusion criteria included restriction to studies of adult women and reported bone mass measurements. For intervention studies, assignment of calcium supplemented by the investigators and a control gorup were further requirements. Of the 49 separate studies which met these requirements published between 1986 and 1989 in 37 different papers, seven tested premenopausal women, six tested both pre- and postmenopausal women, and 36 tested postmenopausal women. Of those 36 in postmenopausal women, 12 were intervention studies (nine were randomized trials), eight were longitudinal observational studies, and 16 were cross-sectional studies. Cross-sectional studies showed a small positive correlation between calcium intake and bone mass; the summary mean correlation coefficient was greater for premenopausal women (0.18) than for postmenopausal women (0.04). Although longitudinal studies gave diverse results, intervention studies in women with a mean age in their 50s showed an overall improvement, with calcium intervention of 0.8% bone mass per year. The author speculated from this result that up to half of the women who take calcium supplements might prevent the usual 2% loss in bone per year that occurs with aging. Taken over 10 years, the conservation of bone afforded by calcium supplementation is enough to alter the risk of fractures. Thus, the author concluded that high calcium intake could benefit women in their early postmenopausal years. However, it is difficult to confirm this hypothesis, since estrogen deficiency would outweigh the effect of calcium intake and estrogen replacement therapy during this period would greatly overshadow any protective role of calcium.

In the meta-analysis by Cumming (5), the only bone site measured that was not protected by calcium supplementation was the vertebrae. This finding is inconsistent with the retrospective observation that calcium supplements plus Vitamin D decreased the risk of vertebral fractures (6). Interestingly, calcium balance correlates better with changes in the trabecular bone, as in the vertebrae, than with cortical bone (7). We need to better understand the relationship of not only calcium intake, but also absorption on bone development.

Few studies have attempted to determine the effect of the form of calcium ingested on improving bone mass. Dawson-Hughes (8) compared calcium carbonate with calcium citrate/malate on bone mineral density over 2 years in postmenopausal women in a double-blind, placebo-controlled trial. Both calcium supplements were protective in women whose usual dietary intake was less than 400 mg/day than in those whose intake was between 400 and 650 mg/day. Calcium citrate/malate was more effective than calcium carbonate in reducing bone loss. In women on habitually low calcium intakes, calcium citrate/malate significantly reduced bone loss relative to the placebo group for the spine/femoral neck and radius, whereas bone mineral density changes for the calcium carbonate group were only significantly different from the placebo group for the radius.

Only two intervention studies have examined the effects of dairy products on bone density or calcium kinetics in bone (9, 10). Baran *et al.* (9) increased the usual calcium intakes of premenopausal women by an average of 610 mg/day with dairy products for 3 years in a randomized trial. Despite the already high intake of calcium among the controls (892 mg/day), the extra calcium in the dairy supplemented group (1572 mg/day) was able to prevent the vertebral bone loss observed in the controls. Although dairy products were not directly compared with calcium salt supplements, Dawson-Hughes *et al.* (8) did not observe a protective effect of calcium salts when calcium intakes were as high as the intakes in the Baran *et al.* study. However, the difference in response between the two studies may be related more to subject age than to either calcium intake or form of calcium. The subjects in Baran *et al.'s* study were between the ages of 30 and 42. Peak bone mass must have been achieved in many of these subjects given the decrease in bone mass over the 3 years in the control group. Nevertheless, these results are consistent with Cumming's (5) observation that calcium intake is more closely linked with bone mass in pre- than in postmenopausal women.

Recker and Heaney (10) fed 24 oz of milk per day to 13 women and compared their calcium balance and kinetics to nine women who received no intervention. Calcium balance improved from -0.061 ± 0.056 to -0.017 ± 0.073 g/day in the milk-supplemented group. Bone remodeling was suppressed by milk supplementation less than they had observed previously for calcium carbonate. However, given the small sample size of this study, the fact that calcium carbonate and milk were not tested directly in the same subjects, and that we do not know whether suppression of bone turnover is helpful in reducing risk of osteoporosis, it would be premature to draw a conclusion from this study that milk was better than calcium carbonate in maintaining the skeleton. Milk supplementation resulted in the same changes in calcium absorption and excretion as expected from previous calcium carbonate trials, and, thus, any relationship found between intake of calcium carbonate and bone mass should be applicable to milk.

Calcium Absorption and Bone

If the dietary form of calcium is to influence bone mass, it must occur at the site of absorption or at some postabsorptive site. Aside from the influence of dietary protein on increasing calcium excretion by the kidney, there is little evidence to support an effect of dietary factors on postabsorptive calcium metabolism. Thus, the effect of diet on calcium utilization by the skeleton largely occurs in the gut.

Calcium absorption occurs by both a carrier-mediated, saturable route and a passive, paracellular route. Absorption is greatest in the ileum, where the residence time is greatest despite the reduced efficiency of the active route in this intestinal segment. These two routes are affected differently by dietary and physiological factors. Physiological factors that affect active calcium absorption relate primarily to calcium status relative to calcium demands of the body at a particular stage in the life cycle. The integrated action of vitamin D, parathyroid hormone, and calcitonin maintains serum calcium levels by regulating absorption, excretion, and bone resorption and accretion. In deficient states, calcium intestinal absorption is increased through activation of calcitriol production, which stimulates calcium binding protein production. In the elderly, calcium absorption decreases, partly because of decreased conversion of vitamin D to calcitriol and partly because of the decrease in estrogen with menopause. In aging, bone loss is associated with an increase in bone turnover (11). It is difficult for serum calcium levels to be maintained through diet with an inefficient absorptive mechanism, and, thus, the skeleton is taxed for the needed calcium. The most important dietary factor influencing the amount of absorbed calcium is total calcium intake. Calcium fractional absorption significantly ($P < 0.001$) decreases linearly with logarithmic load (12), but the total amount absorbed passively increases. Calcium absorptive efficiency ranges from <10% to >60% and, despite a tight correlation with intake, only 20% of the intersubject variation in calcium absorption can be explained by intake. Within a subject, calcium absorptive efficiency is highly constant. Approximately 60% of the variance in calcium absorption among individuals can be accounted for by their individual absorptive efficiencies (13). Thus, an elderly woman who absorbs calcium carbonate poorly will also absorb milk calcium poorly (unpublished data). Factors that dictate an individual's absorptive efficiency have not been elucidated, but could relate to a wide variety of nutritional, hormonal, and life-style factors including calcium, vitamin D, and estrogen status, as well as physical activity level, history of fractures, and drug and alcohol consumption.

The chemical nature of the calcium compound and co-ingested constituents also can influence calcium absorption. It is assumed that calcium must be solubilized in the intestinal chyme to be absorbed. This usually means that calcium is freed from its association with ligands in food. Therefore, solubility of a calcium salt or food stuff in water at neutral pH is a poor predictor of its bioavailability (14). However, solubilities of salts at the extremes can influence absorption of calcium. For example, the very soluble calcium citrate/malate is absorbed better than calcium carbonate (15). This may explain the increase in femoral bone density observed in postmenopausal women given calcium citrate/malate as opposed to calcium carbonate (8) as discussed in the previous section. Conversely, calcium oxalate, the least soluble salt of those studied, is poorly absorbed (only 10% compared with 35.8% for milk in the same subjects) (16).

Calcium Bioavailability from Foods

Food sources of calcium may be preferable to calcium supplements in ensuring adequate dietary intakes to reduce fracture risk, not because the calcium from food is better absorbed, but because mineral imbalances can be avoided and because foods can supply nutrients other than calcium necessary for bone development and maintenance. Calcium absorption from various foods has been estimated from balance studies for most of this century. However, calcium absorption from a specific source cannot be distinguished from other sources in a complex diet by this approach. Recently, the use of isotopic tracer techniques to measure calcium absorption from endogenously labeled foods has allowed the measurement of calcium absorption from individual foods to be determined more specifically and accurately than previously possible.

In the last 4 years, calcium absorption from 10 different foods has been determined. Results of this work were reviewed recently (17). Calcium absorption from most foods tested is similar to milk when given at the same load. Absorption of milk calcium averages 25–35% at daily intakes in the range of the current recommended dietary allowance. Even vegetables (18) and grains (19), expected to provide less available calcium than milk due to their fiber and phytic acid content, provided slightly better absorbable calcium than milk. Only when phytic acid was very concentrated, such as in extruded wheat bran cereal (19) or soybeans (20), was calcium absorption reduced compared with milk.

The one food studied thus far with very poor calcium absorption relative to milk was spinach (5.1% for spinach vs 27.6% for milk), a high oxalate-containing vegetable (21). Calcium absorption from this food was even poorer than from calcium oxalate, which provides the least absorbable calcium of any salt studied so far (14).

Most food and supplement sources provide calcium that is comparable in absorption to milk. However, few foods have calcium in sufficient concentrations or can be tolerated in sufficient quantities in the diet to replace dairy products for most people.

This work was supported in part by the National Institutes of Health Grants AR 39560, AR 40553, and AR 39221.

1. Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schram MM, Banesi ML, Kriska AM. Postmenopausal bone density and milk consumption in childhood and adolescence. Am J Clin Nutr **42**:270–274, 1985.
2. Smith DM, Khairi MRA, Johnston CC Jr. The loss of bone mineral content with aging and its relationship to risk of fracture. J Clin Invest **56**:311–318, 1975.
3. Christiansen C, Rodbro P, Nielsen CT. Bone mineral content

and estimated total body calcium in normal children and adolescents. Scand J Clin Lab Invest **35**:507–510, 1975.
4. Smith EL. Exercise for prevention of osteoporosis: A review. Physician Sports Med **10**:72–83, 1982.
5. Cumming RG. Calcium intake and bone mass: A quantitative review of the evidence. Calcif Tissue Int **47**:194–201, 1990.
6. Riggs BL, Seeman E, Hodgson SF, Taves DR, O'Fallon WM. Effect of the fluoride/calcium regimen on vertebral fracture occurrence in postmenopausal osteoporosis. N Engl J Med **306**:446–450, 1982.
7. Hesp R, Deacon AC, Hulme P, Reeve J. Trends in trabecular and cortical bone in the radius compared with whole body calcium balance in osteoporosis. Clin Sci **66**:109–112, 1984.
8. Dawson-Hughes B, Dallai GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. N Engl J Med **323**:878–883, 1990.
9. Baran D, Sorensen A, Grimes J, Lew R, Karellas A, Johnson B, Roche J. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. J Clin Endocrinol Metab **70**:264–270, 1990.
10. Recker RR, Heaney RP. The effect of milk supplements on calcium metabolism, bone metabolism and calcium balance. Am J Clin Nutr **41**:254–263, 1985.
11. Delmas PD, Stenner D, Wahner HW, Mann KG, Riggs BL. Increase in serum bone γ-carboxyglutamic acid protein with aging in women. J Clin Invest **71**:1316–1321, 1983.
12. Heaney RP, Weaver CM, Fitzsimmons ML. Influence of calcium load on absorption fraction. J Bone Miner Res **5**:1135–1138, 1990.
13. Heaney RP, Weaver CM. Oxalate: Effect on calcium absorbability. Am J Clin Nutr **50**:830–832, 1989.
14. Heaney RP, Recker RR, Weaver CM. Absorbability of calcium sources: The limited role of solubility. Calcif Tissue Int **46**:300–304, 1990.
15. Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. Am J Clin Nutr **48**:1291–1294, 1988.
16. Heaney RP, Weaver CM, Fitzsimmons ML, Recker RR. Calcium absorptive consistency. J Bone Miner Res **5**:1139–1142, 1990.
17. Weaver CM, Martin BR, Heaney RP. Calcium absorption from foods. In: Burkhart P, Heaney RP, Eds. Nutritional Aspects of Osteoporosis. New York: Raven Press, **85**: pp133–139, 1991.
18. Heaney RP, Weaver CM. Calcium absorption from kale. Am J Clin Nutr **51**:656–657, 1990.
19. Weaver CM, Heaney RP, Martin BR, Fitzsimmons ML. Human calcium absorption from whole wheat products. J Nutr **121**:1769–1775, 1991.
20. Heaney RP, Weaver CM, Fitzsimmons ML. Soybean phytate content: Effect on calcium absorption. Am J Clin Nutr **53**:745–747, 1991.
21. Heaney RP, Weaver CM, Recker RR. Calcium absorbability from spinach. Am J Clin Nutr **47**:707–709, 1988.