4. Calcium nutrition and osteoporosis

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Abstract • Résumé

Objective: To recommend appropriate levels of calcium intake in light of the most recent studies.

- **Options:** Dietary calcium intake, calcium supplementation, calcium and vitamin D supplementation; ovarian hormone therapy in postmenopausal women.
- **Outcomes:** Fracture and loss of bone mineral density in osteoporosis; increased bone mass, prevention of fractures and improved quality of life associated with osteoporosis prevention.
- **Evidence:** Relevant clinical studies and reports were examined, in particular those published since the 1988 Osteoporosis Society of Canada position paper on calcium nutrition. Only studies in humans were considered, including controlled, randomized trials and prospective studies, using bone mass and fractures as end-points. Studies in early and later phases of skeletal growth were noted. The analysis was designed to eliminate menopause as a confounding variable.

Values: Preventing osteoporosis and maximizing quality of life were given a high value.

- **Benefits, harms and costs:** Adequate calcium nutrition increases bone mineral density during skeletal growth and prevents bone loss and osteoporotic fractures in the elderly. Risks associated with high dietary calcium intake are low, and a recent study extends this conclusion to the risk of kidney stones. Lactase-deficient patients may substitute yogurt and lactase-treated milk for cow's milk. True milk allergy is probably rare; its promotion of diabetes mellitus in susceptible people is being studied.
- **Recommendations:** Current recommended intakes of calcium are too low. Revised intake guidelines designed to reduce bone loss and protect against osteoporotic fractures are suggested. Canadians should attempt to meet their calcium requirements principally through food sources. Pharmaceutical calcium supplements and a dietician's advice should be considered where dietary preferences or lactase deficiency restrict consumption of dairy foods. Further research is necessary before recommending the general use of calcium supplements by adolescents. Calcium supplementation cannot substitute for hormone therapy in the prevention of postmenopausal bone loss and fractures. Adequate amounts of vitamin D are necessary for optimal calcium absorption and bone health. Elderly people and those who use heavy sun screens should have a dietary intake of 400 to 800 IU of vitamin D per day.
- Validation: These recommendations were developed by the Scientific Advisory Board of the OSC at its 1993 Consensus Conference.
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In the recent past the importance of calcium nutrition for bone health has been controversial. Since the 1930s, when nutritional studies were done in Scottish schoolchildren, it has been generally accepted that adequate amounts of dietary calcium are necessary for normal bone growth and development in children. By the 1970s osteoporosis had become the subject of modern medical research; calcium balance studies¹ demonstrated that calcium requirements increase after menopause in women and this, together with an early epidemiologic study² associating increased hip fracture rates with low calcium intake, strongly suggested the importance of ad-

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equate calcium nutrition with regard to osteoporosis, particularly in postmenopausal women.

In the 1980s, on the other hand, studies³ using new methods of bone densitometry failed to demonstrate effects of dietary calcium intake on spinal bone mass, leading to controversy and confusion and giving rise to the feeling by many that either calcium nutrition does not affect bone mass or fracture rates or, if there is an effect, it is so small in relation to other factors that it is insignificant for practical purposes. Despite this, the Osteoporosis Society of Canada⁴ took the position that "there is general agreement that calcium deficiency could seriously affect bone health and predispose one to osteoporosis" and recommended that Canadians follow the Health and Welfare Canada guidelines with regard to calcium intake.

At its 1993 Consensus Conference, the Scientific Advisory Board of the Osteoporosis Society of Canada reviewed more recent reports on the subject, principally the new evidence that had accumulated since 1988. It found much new evidence in favour of the concept that dietary calcium is important for bone health, both in terms of its positive effects on bone mass and in lowering fracture rates. This led the OSC to take an even firmer position in support of optimal calcium nutrition as an effective preventive measure against osteoporosis. Much of the controversy of recent years may be ascribed to inadequacies of technical approach or study design and, in particular, the failure of many studies to take account of confounding variables.

Recent studies on calcium and bone

Our 1988 consensus was largely based on calcium balance data that were too variable and imprecise to be a basis for firm conclusions, and on largely uncontrolled cross-sectional studies of the effects of dietary calcium on bone mineral content as assessed by dual-photon densitometry (as well as studies using radiogrammetry). During the past 7 years, several controlled, randomized trials and some prospective studies of changes in bone mass and fracture incidence in relation to calcium intake have been conducted. The newer evidence is of higher quality and a much greater degree of certainty in concluding that dietary calcium affects bone health and osteoporosis. At the 1993 consensus conference, only studies involving humans were reviewed.

Much of the confusion in past studies related to failure to take into account the impact of the menopause on bone loss. It has now been demonstrated that during the first several years after the menopause, calcium supplementation cannot significantly ameliorate the bone loss associated with estrogen deficiency.⁵⁻⁷ Once this variable has been eliminated by careful study design, it is possible to see a significant effect of dietary calcium on bone mass.⁶ The study of Dawson-Hughes and colleagues⁷ indicates that provision of adequate dietary calcium to women over 65 reduces bone loss at all sites in the skeleton by 12% to 25% over 2 years. There is now good evidence from at least three studies⁷⁻⁹ that dietary calcium slows osteoporotic bone loss. The magnitude of the reduction is generally from 1% to 2% annually. Thus, over a number of years, the degree of reduction in bone loss is of sufficient magnitude that it should result in fracture prevention over time. However, all studies using estrogen as a comparison group have shown that calcium supplementation is less effective than estrogen in preventing postmenopausal bone loss. On the other hand, the preventive effect of calcium supplementation against bone loss is particularly evident in women more than 10 years postmenopause.⁷

Several studies of hip fracture¹⁰⁻¹³ incidence have demonstrated that fracture rates are related to calcium intake. In 1988, Holbrook and colleagues¹⁰ reported a prospective study of 957 men and women in southern California aged 50 to 79 years whose dietary history had been taken by 24-hour recall and whose subsequent hip fractures had been counted over 13 years. The findings suggested that an adequate intake of calcium might reduce hip fracture incidence by up to 60%. In addition, two retrospective studies^{11,12} demonstrated a reduction in fracture risk of 50% to 80% associated with high calcium intakes. Thus, the magnitude of the preventive effect of calcium intake appears to be significant from the clinical point of view.

The study of Chapuy and coworkers¹³ focused particularly on older age groups. In this study, 3270 women, aged 69 to 106 years, in French nursing homes were given 1200 mg calcium supplement and 800 IU vitamin D daily. Over 18 months, there was a reduction in hip fractures of about 20%. Although many of these women would have been considered vitamin D deficient by North American standards, hence the positive effect cannot be ascribed to calcium supplementation alone, the study indicates that nutritional measures that affect the amount of calcium absorbed influence fracture rate when examined in a double-blind randomized study design. Furthermore, in view of the age of the women, it is also possible to infer that it is probably never too late to prevent osteoporotic fractures.

In summary, these studies present persuasive new evidence that calcium nutrition is of great importance in the maintenance of bone health and the prevention of osteoporotic fractures. Although not all studies have shown a protective effect of calcium on the skeleton, those that did not can be discounted on the basis of flaws in study design or failure to eliminate important confounding variables. Taken together with the results of nutritional surveys that indicate that a large proportion of our population, women in particular, have diets that are deficient in calcium, these new data call for a re-examination of Canadian dietary recommendations for calcium intake. In addition, several recent studies have shown significant effects of dietary calcium intake on mineral accretion in the growing human skeleton. The 1992 study of Johnston and colleagues¹⁴ is probably the most convincing. It showed that 1000 mg calcium citrate malate per day, when given to one member of each of 70 pairs of identical twins for 3 years, resulted in significantly higher bone density (mean 1.4%) at several sites in the skeleton. Conducting the study in identical twins allowed these investigators to focus on the effects of dietary calcium on bone mass while eliminating the effects of heredity. Other studies in unrelated adolescents also show significant effects of calcium intake on bone mineral density.¹⁵

More detailed study of this issue is required to measure more precisely the magnitude of the effect on skeletal growth, but it seems clear that the period of rapid skeletal growth at and around puberty is one time in life when calcium nutrition is most critical.¹⁶ The effect of calcium nutrition during skeletal growth is a statistically independent predictor of subsequent bone mass, and is noted in all areas of the skeleton.¹⁶ However, more research is probably necessary before recommending general use of dietary calcium supplements by adolescents.¹⁷ In addition, a recent prospective study in college students in the third decade of life demonstrated a significant positive effect of dietary calcium on bone mineral accretion during this later phase of skeletal growth.¹⁸

How much calcium is enough?

Conclusive data are not available on how much calcium is required. Estimates from different studies vary widely and are influenced by the method used to estimate calcium requirements. Evidence indicates that calcium is a threshold nutrient;^{7,19} that is, intakes below a certain threshold level will result in calcium deficiency, but increasing calcium intake significantly above the threshold value does not result in increased skeletal protection or benefit. Because calcium requirements vary throughout life, the OSC recommendations are listed according to age (Table 1).

Age, yr	Recommended intake, mg/d
7–9	700
10–12 (boys)	900
10–12 (girls)*	1200-1400
13–16	1200–1400
17–18	1200
19–49	1000
≥ 50	1000-1500+

*Girls go through their adolescent growth spurt 2 years earlier than boys on average.

A minimum of 1000 mg is recommended, but a higher intake may be advisable if the risk of osteoporosis is high.

What are the risks of excess calcium?

The risks associated with high intake of dietary calcium are few. In the past it has been customary to caution people at risk for kidney stones to keep their calcium intake low, as it has been thought that high dietary calcium increases the risk of stones. A recent study²⁰ has reversed medical opinion on this point. This large, thorough study has shown that high intakes of dietary calcium actually decrease the risk of kidney stones significantly in most people.

Some Canadians suffer from intolerance of milk and dairy foods due to lactase deficiency. These people may experience upset stomach or diarrhea after ingestion of milk. These symptoms can be avoided by using lactasetreated milk or by substituting yogurt for milk as a calcium source. True milk allergy is probably uncommon. The possibility has been raised that milk may, through an allergic mechanism, promote the development of diabetes mellitus in susceptible people.²¹ More research is necessary to measure this risk in the general population.

The OSC believes that ensuring adequate dietary calcium through food sources or pharmaceutical supplements does not engender significant risks for the vast majority of people and is essential to maintain bone health.

In what form should calcium be taken?

Food sources

There is general agreement that the best form of calcium is food sources, simply because bone, like other tissues, requires balanced nutrition. In particular, milk is the best food source of vitamin D, a nutrient essential for normal calcium absorption and bone health. Milk and dairy products, such as cheese, yogurt and ice cream, contain the highest levels of calcium. Although many people tend to avoid milk because of its fat content, which might predispose them to heart disease, especially those with hypercholesterolemia, low-fat dairy products such as skim and 1% milk are safe and contain high levels of calcium. Nondairy food sources of calcium generally contain much lower levels, but significant amounts occur in canned salmon and sardines when the bones are also eaten. Some green vegetables (such as kale, broccoli and spinach) as well as legumes (such as soybeans and common beans) either contain much less calcium than dairy products or the calcium is poorly absorbed by the body, or both.22 Vegetarians who do not consume milk products should take special care to ensure that they are receiving adequate amounts of calcium in their diets. Some Canadians will find it difficult to obtain the recommended amounts of dietary calcium through diet alone; for many, a combination of food sources and pharmaceutical supplements is a good compromise.

Pharmaceutical supplements

In general, absorption does not vary significantly among various supplements and is roughly equivalent to absorption from milk. Care should be taken when reading labels to ensure that the amount of calcium is stated as elemental calcium. The amount of elemental calcium in different calcium salts varies widely. The recommended intakes in Table 1 refer to amounts of elemental calcium.

A wide range of supplements is available, with variations in size of pill, type of preparation (tablets, chewable forms, dissolvable tablets or liquid preparations) and price. The most expensive preparations are not necessarily the best. Some authors have found that some calcium preparations will not dissolve easily in water and have suggested that these cannot be used effectively by the body. On the other hand, supplements may dissolve more easily in the acid environment of the stomach and also may be absorbed in the intestine, below the stomach; therefore, solubility may not be a major concern.²³ In addition, some supplements, particularly bone meal and dolomite, have been found to contain lead as a contaminant;²⁴ thus, calcium supplements should be of pharmaceutical grade.

It has been suggested that very large intakes of supplemental calcium may interfere with absorption of other minerals, especially iron, but recent data suggest this may not be a significant concern.²⁵ Calcium supplements are better absorbed when taken with food and may be better absorbed when taken in divided doses rather than all at once.

Modifying factors

Calcium requirements are increased in postmenopausal women or women who have had ovariectomy or premature ovarian failure. Caffeine has been shown to affect calcium retention, but is probably not of major concern at the level of two cups of coffee per day²⁶ as long as at least one glass of milk is consumed per day for most of the adult years.²⁷ High-fibre diets may decrease calcium absorption; with very high dietary intakes of fibre, calcium intake may need to be increased over recommended levels.

Although many lay publications recommend that magnesium be taken to aid calcium utilization, there is no good evidence to support a requirement for magnesium in healthy people consuming a balanced diet. Adequate amounts of dietary magnesium are provided in most diets from animal and vegetable sources.

Animal protein has been suggested as a risk factor for osteoporosis, because it may increase calcium losses in the urine, primarily as a result of the metabolism of sulfur-containing amino acids. However, conclusive evidence of a significant risk is lacking; as much or more High intakes of dietary phosphorus or sodium have also been incriminated as risk factors for osteoporosis in some publications, but there is not sufficient evidence to support these claims.

The greatest impact of these various dietary factors on calcium metabolism is likely to be in those already at risk because of inadequate calcium intakes relative to their physiological needs²⁸ or in those with other significant nondietary risk factors for osteoporosis. Some medications such as glucocorticosteroids (e.g., Prednisone), and large amounts of magnesium-containing antacids have been shown to interfere with calcium absorption. People taking these medications should ensure that they obtain adequate amounts of dietary calcium.

Requirements for vitamin D

Vitamin D deficiency has long been recognized as a cause of bone disease in humans, rickets in children, and osteomalacia in adults. However, vitamin D deficiency can also contribute to the low bone mineral mass and fractures seen in patients with osteoporosis.^{13,29} The vitamin is normally obtained either in the diet (fish oils, liver, milk) or from sunlight, which induces the production of vitamin D in the skin. With the advent of artificial fortification of milk with vitamin D, the incidence of vitamin D deficiency rickets virtually disappeared in children. However, it is apparent that vitamin D deficiency does occur in Canadians, particularly among housebound elderly people, and that it is more prevalent during the winter months³⁰ and in people who use sun screens continuously.³¹ Vitamin D deficiency can be diagnosed easily by measuring the level of 25-hydroxyvitamin D in blood. The current recommended daily nutrient intake for vitamin D, 200 IU for adults, is probably too low;³² 400 to 800 IU is a more reliable level of intake to prevent fractures,^{13,32} particularly in people not exposed to sunlight.

Conclusions

- To ensure optimal bone health, Canadians should consume adequate amounts of calcium throughout life. Recent evidence suggests that current recommended intakes of calcium are too low. Intakes recommended by the OSC are listed in Table 1. Based on current evidence, these levels should reduce bone loss and protect against osteoporotic fractures.
- Canadians should attempt to meet their calcium requirements principally through food sources. However, if this is not possible, either because of intoler-

ance of dairy foods or because of dietary preferences, the use of calcium supplements should be considered, either in addition to food sources or as the major source of calcium.

- Strict vegetarians who do not consume milk products should take special care to ensure that they are receiving adequate amounts of calcium; if necessary, they should seek professional advice from a qualified dietician. A calcium supplement may be required.
- Further research is necessary before recommending the general use of calcium supplements by adolescents.
- Calcium supplementation cannot substitute for ovarian hormone therapy in the prevention of postmenopausal bone loss and fractures. Although it does have a preventive effect of its own, other preventive strategies such as hormone therapy in menopausal women and a physically active lifestyle are also of major, independent importance in prevention of osteoporotic fractures.
- Adequate amounts of vitamin D are also necessary for optimal calcium absorption and bone health. Although many Canadians obtain sufficient vitamin D through the effects of sunlight, adequate dietary sources of vitamin D are particularly important for elderly people or for those who use sun screen preparations continuously. A dietary intake of 400 to 800 IU/d is recommended for such people.

References

- Heaney RP, Recker RR, Saville PD. Menopausal changes in calcium balance performance. *J Lab Clin Med* 1978;92:953-63.
- Matkovic V, Kostial K, Simonovic I, et al. Bone status and fracture rates in two regions of Yugoslavia. Am J Clin Nutr 1979;32:540-9.
- Riggs BL, Wahner HW, Melton LJ III, et al. Dietary calcium intake and rates of bone loss in women. J Clin Invest 1987;80:979-82.
- Murray TM. The importance of calcium in osteoporosis prevention. Official position of the Osteoporosis Society of Canada. Osteoporosis Society of Canada Bulletin for Physicians 1988;1:2-6.
- Riis B, Thomsen K, Christiansen C. Does calcium supplementation prevent postmenopausal bone loss? A double-blind, controlled clinical study. N Engl J Med 1987;316:173-7.
- Ettinger B, Genant HK, Cann CE. Postmenopausal bone loss is prevented by treatment with low-dosage estrogen with calcium. Ann Intern Med 1987;106:40-5.
- Dawson-Hughes B, Dallal GE, Krall EA, et al. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. N Engl J Med 1990;323:878-83.
- Prince RL, Smith M, Dick IM, et al. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. N Engl J Med 1991;325:1189-95.
- Reid IR, Ames RW, Evans MC, et al. Effect of calcium supplementation on bone loss in postmenopausal women. N Engl J Med 1993;328:460-4, and erratum N Engl J Med 1993;329:1281.

- Holbrook TL, Barrett-Connor E, Wingard DL. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 1988;2(8619):1046-9.
- 11. Lau E, Donnan S, Barker JP, Cooper C. Physical activity and calcium intake in fracture of the proximal femur in Hong Kong. *BMJ* 1988;297:1441-3.
- Cooper C, Barker DJP, Wickham C. Physical activity, muscle strength, and calcium intake in fracture of the proximal femur in Britain. BMJ 1988;297:1443-6.
- 13. Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D, and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992;327:1637-42.
- Johnston CC Jr, Miller JZ, Slemenda CW, et al. Calcium supplementation and increases in bone mineral density in children. N Engl J Med 1992;327:82-7.
- Grimston SK, Morrison K, Harder JA, Hanley DA. Bone mineral density and calcium intake in children during puberty. In: *Nutritional Aspects of Osteoporosis* (Serono Symposium vol 85). New York: Raven Press, 1991:77-89.
- Murphy S, Khaw KT, May H, Compston JE. Milk consumption and bone mineral density in middle aged and elderly women. BM7 1994;308:939-41.
- Matkovic V. Calcium intake and peak bone mass [editorial; comment]. N Engl J Med 1992;327:119-20.
- Recker RR, Davies KM, Hinders SM, et al. Bone gain in young adult women. *JAMA* 1992;268:2403-8.
- Matkovic V, Heaney RP. Calcium balance during human growth: evidence for threshold behaviour. Am J Clin Nutr 1992;55:992-6.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 1993;328:833-8.
- Virtanen SM, Saukkonen T, Savilahti E, et al. Diet, cow's milk protein antibodies and the risk of IDDM in Finnish children. *Diabetologia* 1994;37:381-7.
- 22. Weaver CM, Plawecki KL. Dietary calcium: adequacy of a vegetarian diet. Am J Clin Nutr 1994;59(suppl 5):S1238-41.
- Heaney RP, Recker RR, Weaver CM. Absorbability of calcium sources: the limited role of solubility. *Calcif Tissue Int* 1990;46:300-4.
- Bourgoin BP, Boomer D, Powell MJ, et al. Instrumental comparison for the determination of cadmium and lead in calcium supplements and other calcium-rich matrices. *Analyst* 1992;117:19-22.
- Matkovic V, Ilich JZ, Hsieh L, et al. Calcium, magnesium, and zinc balances in females during early puberty [abstract 144]. *J Bone Miner Res* 1993;8(suppl 1):S152.
- Barger-Lux MJ, Heaney RP, Stegman MR. Effects of moderate caffeine intake on the calcium economy of premenopausal women. Am J Clin Nutr 1990;52:722-5, and erratum Am J Clin Nutr 1991;53:182.
- Barrett-Connor E, Chang JC, Edelstein SL. Coffee-associated osteoporosis offset by daily milk consumption. *JAMA* 1994;271:280-3.
- Massey LK. Dietary factors influencing calcium and bone metabolism: introduction. J Nutr 1993;123:1609-10.
- Yendt ER. Vitamin D and osteoporosis. Osteoporosis Society of Canada Bulletin for Physicians 1994;2(4).
- Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D₃: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D₃ synthesis in human skin. J Clin Endocrinol Metab 1988;67:373-8.
- Matsuoka LY, Ide L, Wortsman J, et al. Sunscreens suppress cutaneous vitamin D, synthesis. *J Clin Endocrinol Metab* 1987;64:1165-8.
- Gloth FM III, Tobin JD, Sherman SS, Hollis BW. Is the recommended daily allowance for vitamin D too low for the homebound elderly? *J Am Geriatr Soc* 1991;39:137-41.