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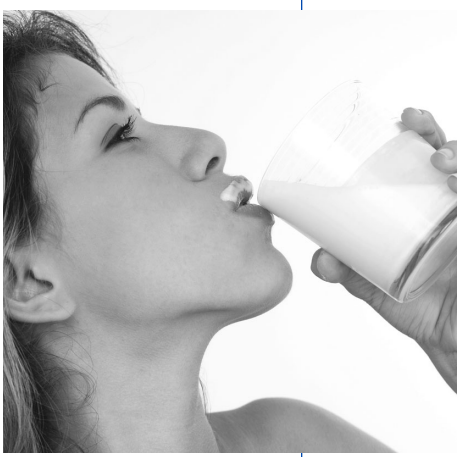
A NEW APPRECIATION FOR VITAMIN D

SUMMARY

In the last decade, vitamin D has become a focus of renewed interest. This attention stems from the unexpected finding of widespread vitamin D deficiency in children and adults, emerging evidence of an expanding beneficial role for vitamin D in health, and growing support for increasing dietary recommendations for this fat-soluble vitamin.

Vitamin D is unique because, given adequate exposure to sunlight, the body can synthesize all the vitamin D it needs. However, because people have variable and in many cases limited exposure to sunlight, vitamin D is considered an essential nutrient. In the body, vitamin D is metabolized to a specific circulating form called calcidiol and to a physiologically active hormonal form called calcitriol. Vitamin D not only regulates blood calcium levels, but identification of vitamin D receptors in most cells and tissues of the body suggests other regulatory functions.

In addition to exposure to sunlight, vitamin D is obtained from foods (unfortified and fortified) and dietary supplements. Only a few foods such as oily marine fish (e.g., salmon) naturally contain vitamin D. In the U.S., milk and some other dairy foods (e.g., some yogurts, cheese), as well as some breakfast cereals among other foods, are fortified with vitamin D. While optional, nearly all cow's milk sold in the U.S. is fortified with vitamin D to obtain a standardized amount of 400 IU/quart.



Dietary recommendations for vitamin D, published in 1997 by the Institute of Medicine (IOM), are 200 IU/day for children, adolescents, and adults up to 50 years of age, 400 IU/day for adults 51 through 70 years, and 600 IU/day for adults over 70 years. Calcidiol, the major circulating form of vitamin D, is used to assess vitamin D status. Accumulating scientific evidence suggests that higher levels of serum calcidiol (i.e., ~ 80 nmol/L) than previously indicated are associated with multiple health benefits. Recognizing the need for high-risk groups (e.g., the elderly, those with dark skin) to consume higher amounts of vitamin D than recommended by the IOM, the 2005 Dietary Guidelines for Americans recommends a vitamin D intake of 1000 IU/day for these groups.

Vitamin D deficiency is described as an unrecognized epidemic affecting all age groups, and especially African Americans and persons who cover most of their bodies with clothing for religious or cultural reasons. Poor vitamin D status is attributed to factors interfering with the cutaneous production of vitamin D (e.g., deep skin pigmentation, clothing, sunscreen use, aging, winter season, northern latitudes, etc.) and low dietary intake of vitamin D.

Vitamin D deficiency can cause rickets in infants and young children, poor bone health with the inability to attain genetically determined peak bone mass in children and adolescents, and osteomalacia and osteoporosis in adults. Emerging scientific evidence also indicates that poor vitamin D status may increase the risk of non-skeletal chronic diseases such as certain cancers, hypertension, metabolic syndrome, and autoimmune disorders. Moreover, vitamin D intakes in excess of current dietary recommendations are associated with reduced risk of these diseases. Based on recent findings, momentum is growing for increasing dietary recommendations for vitamin D to support overall health. D

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INTRODUCTION

A new appreciation for vitamin D, known as the "sunshine vitamin," is emerging (1). In the early 1920s, vitamin D deficiency was identified as the cause of rickets, a disease characterized by softening of bones and skeletal deformities (e.g., bowed legs) in growing infants and young children (1,2). In the 1930s, implementation of the public health measure to fortify milk with vitamin D made rickets a rare disease in the U.S. (2). In fact, until the last decade, it was assumed that vitamin D deficiency had been eliminated as a public health concern (1,2).

Recent increased interest in vitamin D is attributed to several developments. These include a re-appearance of vitamin D deficiency rickets in U.S. infants and young children, especially among African Americans; new findings of an epidemic of poor vitamin D status in both children and adults; research demonstrating that vitamin D deficiency not only adversely affects the skeleton, but also may be associated with increased risk of several chronic non-skeletal diseases (e.g., some cancers, autoimmune disorders, hypertension, metabolic syndrome); and observations indicating that, for optimal health, dietary recommendations for vitamin D need to be increased (1,2).

This *Digest* reviews the basic metabolism of vitamin D; sources of this fat-soluble vitamin; dietary recommendations for vitamin D; and vitamin D deficiency, its causes, and consequences (skeletal and non-skeletal). Heightened awareness of vitamin D deficiency across the life cycle and its consequences, along with considerations related to improving vitamin D status, are the subject of numerous recent symposia and scientific reviews (1,3-13).

A new appreciation for meeting vitamin D needs is emerging as a result of recent findings of a high prevalence of poor vitamin D status in many population groups and an expanded role for vitamin D in health.

VITAMIN D METABOLISM: AN OVERVIEW

The term vitamin D refers to vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol) (1,9,11-15). The former is derived from ultraviolet (UV) B irradiation of ergosterol, a yeast and plant sterol. Vitamin D_3 is produced in the skin upon exposure to UVB irradiation which catalyzes the conversion of 7-dehydrocholesterol (provitamin D_3) to vitamin D_3. Vitamin D_3 also occurs naturally in some animal products (e.g., oily marine fish). Because of its greater biological efficiency, vitamin D_3 is the preferred and most common form of vitamin D used in food fortification and over-the-counter dietary supplements (16).

Vitamin D_3 and vitamin D_2 are transported to the liver where they are hydroxylated to 25-hydroxyvitamin D [25(OH)D], also called calcidiol. This major circulating form of vitamin D is the indicator used to determine vitamin D status. A subsequent hydroxylation reaction occurs in the kidney and extra-renal sites to form 1,25-dihydroxyvitamin D [1,25(OH)2D], also called calcitriol. When formed by the kidney, calcitriol circulates in the blood as the metabolically active hormonal (endocrine) form of vitamin D, which enhances the efficiency of calcium and phosphorus absorption by active transport across the intestinal mucosa to maintain normal blood levels of these minerals.

Although the kidney is the main source of circulating calcitriol, most other tissues and cells in the body synthesize calcitriol for their own use and as such require an adequate amount of calcidiol as the substrate. The presence of the active metabolite calcitriol in extra-renal tissues is critical to the regulation of key autocrine functions, notably cellular proliferation, growth, and differentiation. The biological effects of calcitriol are mediated by the vitamin D receptor (VDR), which is present in most cells and tissues of the body (15). Since the 1980s, it has become increasingly apparent that calcitriol has a multitude of physiological functions beyond its beneficial role in calcium metabolism (15,17).

SOURCES OF VITAMIN D

Sources of vitamin D include exposure to sunlight and intake of foods (unfortified and fortified) and dietary supplements. Casual exposure to sunlight (i.e., 5 to 15 minutes of exposure of the arms and legs or the hands, arms, and face, two to three times a week) can provide 80 to 100% of the requirement for vitamin D (1,9,15,17). However, a

number of factors, by interfering with UVB exposure, reduce the cutaneous production of vitamin D_3 (9,18). These factors include increased melanin (skin pigment), sunscreen use, glass (windows), clothes, aging, winter season, northern latitudes, cloud cover, and smog (9,15,17). For example, in African Americans and other dark-skinned individuals with increased melanin pigmentation, the efficiency of cutaneous production of vitamin D_3 is reduced compared to that in Caucasians (18). Aging causes a decrease in the amount of 7-dehydrocholesterol (provitamin D_3) (9,15). Also, many people avoid exposure to sunlight due to concern that it will cause skin damage, including skin cancer and wrinkles (15). Some populations may be at risk of vitamin D deficiency because of the cultural or religious practice of covering most of their bodies with clothing (15).

In addition to sun exposure, foods are a source of vitamin D (1,9,11,12,19,20). However, only a few foods such as oily marine fish (e.g., mackerel, salmon, herring), cod liver oil, and sun-exposed mushrooms naturally contain vitamin D (1,9,11,19). In the U.S., milk and some other dairy foods (e.g., some yogurts, cheese), as well as some breakfast cereals, breads, and juices are fortified with vitamin D (20-22). While vitamin D fortification of milk is optional, nearly all milk sold in the U.S. is fortified with vitamin D_3 to obtain a standardized amount of 400 IU (10 µg) /quart. When a food is fortified with vitamin D, vitamin D must be listed on the nutrition label (21). An analysis of NHANES (National Health and Nutrition Examination Survey) 1999-2002 data found that fluid milk was the largest single food source of vitamin D (23). Data from national food intake surveys reveal that, across all age-gender groups, increased intake of vitamin D is synonymous with increased consumption of dairy products (23).

Supplements are another source of vitamin D (1). A variety of multivitamin supplements contain either 200 IU (5 µg) or 400 IU (10 µg) of vitamin D_2 or more commonly vitamin D_3. Also, vitamin D_2 and D_3 supplements are available in either 400 or 1000 IU capsules or tablets (1).

As a result of scientific advances in vitamin D nutrition, momentum is growing for considering an increase in dietary recommendations for this vitamin and providing new guidance to improve vitamin D status.

DIETARY RECOMMENDATIONS FOR VITAMIN D

Current dietary recommendations for vitamin D, published in 1997 by the Institute of Medicine (IOM), are 200 IU/day (5 µg/day) for children, adolescents, and adults up to 50 years of age, 400 IU/day (10 µg/day) for adults 51 through 70 years, and 600 IU/day (15 µg/day) for adults over 70 years (21). These recommendations assume that no vitamin D is available from sun-mediated cutaneous synthesis. The higher vitamin D recommendations for older adults reflect the decline in vitamin D metabolism with age.

Since 1997, accumulating scientific evidence suggests that a higher serum calcidiol level (i.e., ~ 80 nmol/L) than previously indicated is associated with multiple health benefits (e.g., optimal calcium absorption, improved bone density, decreased risk of falls, and reduced risk of chronic diseases such as osteoporosis, diabetes, and some cancers) and that a dietary intake of 1000 IU/day (25 µg/day) or more is needed to sustain healthy circulating levels of calcidiol at or above 80 nmol/L (1,7,9,13,14,24-28). Indeed, recognizing the need for high-risk groups (e.g., older adults, individuals with dark skin, those with insufficient exposure to sunlight) to consume higher amounts of vitamin D, the 2005 Dietary Guidelines for Americans recommends an intake of 1000 IU of vitamin D/day (25 µg/day) (29).

For some subgroups of the population, vitamin D recommendations may be higher than 1000 IU/day (13,27,28,30,31) and exceed the Tolerable Upper Intake Level (UL) of 2000 IU (50 µg) a day recommended in 1997 by the IOM (21). This current UL is criticized as being too low, thus curtailing clinical research of vitamin D nutrition, restricting the amount of vitamin D in foods and supplements, and limiting public health strategies to optimize vitamin D status (7,27). Based on a recent review of human clinical trials published since 1997, researchers suggest a UL of 10,000 I.U. (250 µg) of vitamin D_3 a day for healthy adults (32).

VITAMIN D DEFICIENCY

Prevalence and Causes. Vitamin D deficiency is described as an unrecognized epidemic affecting all age groups (1,3,6,9,14). The clinical indicator of vitamin D status is circulating calcidiol, which reflects the combined contribution of diet and cutaneous synthesis (1). A large body of data suggests that a circulating calcidiol level below ~ 80 nmol/L is indicative of suboptimal vitamin D status (1,13,18,24,26,30).

Numerous studies have identified poor vitamin D status in infants and their mothers, young children, teenagers, young and middle-age adults, and the elderly (1,9,33,34). Infants who are exclusively breast-fed, do not receive a vitamin D supplement, and are not exposed to sunlight are at risk of vitamin D deficiency because human milk contains little, if any, vitamin D (9,21). It is thought that vitamin D in breast milk depends on the mother's vitamin D status (35). Thus, African American infants are at risk of vitamin D deficiency because their mothers are often vitamin D deficient (35). Researchers suggest that increased vitamin D intake is needed to improve maternal and neonatal vitamin D nutriture, especially in African American mothers and in those living in northern climates (36).

Many young children and adolescents are at risk of vitamin D deficiency (9,15,37-39). A study of 307 multiethnic healthy adolescents in Boston found that vitamin D deficiency was highest in African American teens and that adolescents who chose soft drinks were at high risk of vitamin D deficiency, whereas consumption of milk or cold cereal was protective (37). A recent prospective study of prepubertal girls (49 white and 34 African American) in the southeastern U.S. found that more than 75% of the girls had blood calcidiol levels < 80 nmol/L and that white girls had higher calcidiol concentrations than the African American girls (39).

Older adults in particular are at high risk of vitamin D deficiency, especially those who are housebound, residents of nursing homes, or live in northern climates (1,9,12,27,40-42). In addition to lack of exposure to sunlight, many older adults consume low intakes of vitamin D (43). National survey data indicate that, even after considering vitamin D intake from dietary supplements, up to 90% of older adults still do not consume adequate amounts of vitamin D (43). Also, several age-related physiological changes in vitamin D potentially compromise vitamin D status and/or increase the requirement for this vitamin (27).

Health professionals need to be aware that vitamin D deficiency is an unrecognized epidemic with adverse health consequences for children and adults.

Contributing to African Americans' high prevalence of vitamin D deficiency (10,15,23,29,34,37,39,44,45) is their low intake of milk and other dairy products due in part to lactose intolerance (real and perceived) and reduced vitamin D production in their skin because of increased skin pigmentation (3,20,43,44). The National Medical Association, in a consensus report, recommends that African Americans consume 3 to 4 servings/day of low-fat milk, cheese, and/or yogurt, and offers strategies to help lactose intolerant individuals comfortably consume these foods (46).

Clearly, the cause of vitamin D deficiency is multifactorial and includes lack of or limited exposure to sunlight, an age-related decrease in cutaneous synthesis, obesity (i.e., decreased bioavailability of vitamin D from body fat stores), exclusive and prolonged breast-feeding, and low intake of vitamin D from foods (e.g., vitamin D-fortified milk) and supplements (1,3,9,10,12,14, 15,45). Nationally representative data from NHANES III indicate that few age, race, and gender groups meet current dietary intake recommendations for vitamin D established by the IOM (43).

Health Consequences. During the past decade, there has been an explosion of reports related to the health benefits (skeletal and non-skeletal) of vitamin D and to the consequences of inadequacy (1,3,6,9-15,17,21,31).

Vitamin D deficiency can cause rickets in infants and young children, poor bone health with the inability to attain genetically determined peak bone

mass in children and adolescents, and osteomalacia and osteoporosis in adults (5,9,47). Recognition of the recent resurgence of rickets, especially among African American infants and young children (2,48), led the American Academy of Pediatrics to issue guidelines for vitamin D intake to prevent rickets and vitamin D deficiency (49).

Vitamin D deficiency during pregnancy has been shown to adversely affect infants' body weight, growth, and bone mineral acquisition and may influence fetal "imprinting," which may affect neurodevelopment, immune function, regulation of cell growth, and risk of chronic diseases soon after birth as well as later in life (50-53). Based on a review of the evidence, researchers suggest that the current dietary recommendation of 200 IU of vitamin D/day for pregnancy and lactation is too low and that vitamin D intakes should be >1000 IU/day (35). In fact, a study suggests that a vitamin D intake of 4000 IU/day during lactation is necessary to prevent hypovitaminosis in both mothers and their nursing infants (54).

Considerable evidence indicates that vitamin D, especially in combination with calcium, protects the skeleton (12,21,47,55,56). A serum calcidiol level of at least 80 nmol/L is needed to achieve the maximal efficiency of vitamin D-induced intestinal calcium absorption (15,56,57). Adequate vitamin D status also reduces excessive bone remodeling, a risk factor for bone fragility (56). Studies in children and adolescents demonstrate that vitamin D deficiency limits accretion of bone mass and may have detrimental effects on the acquisition of maximal peak bone mass (58,59). Moreover, a vitamin D intake higher than the level currently recommended may be necessary to support bone health in adolescents, particularly those living in northern climates during winter (59).

Studies in older adults demonstrate that increased vitamin D intake enhances calcium absorption and reduces age-related bone loss or osteoporotic-related bone fractures (21,25,47,56). A meta-analysis of

Vitamin D status can be improved by moderate exposure to sunlight and increasing intake of vitamin D from foods naturally containing this vitamin (e.g., some oily fish), foods fortified with vitamin D (e.g., milk, some other dairy foods, some cereals), and, if indicated, supplements.

randomized controlled trials showed that 700 to 800 IU of vitamin D_3 per day reduced the risk of hip fractures by 26% and non-vertebral fractures by 23% in community dwelling and ambulatory institutionalized elderly (25). A vitamin D_3 supplement of 400 IU/day was insufficient to prevent fractures, supporting the need for an increase in dietary recommendations for older adults (25). The decline in fracture risk with vitamin D may be explained in part by the ability of vitamin D to improve balance (i.e., reduce risk of falls) and muscle strength (55,56,60-62). Poor vitamin D status in older adults has been shown to be a strong predictor of nursing home admissions (41).

Emerging evidence, mainly from epidemiological studies, suggests that optimal vitamin D status may reduce the risk of various non-skeletal disorders (1,6,9,15,17,28). For example, vitamin D may have a role in the prevention and treatment of certain cancers (e.g., colon, breast, prostate, pancreatic) (63-66), hypertension and heart disease (1,67,68), metabolic syndrome (69), type 1 diabetes mellitus (70), autoimmune disorders such as multiple sclerosis (71) and rheumatoid arthritis (72), and periodontal disease (73).

Although further research is needed to determine optimal vitamin D intake and status for several health outcomes, there is growing support for an increase in the currently recommended intake of vitamin D (10,13,14,17,18,24,26-29,35,56,63).

CONCLUSION

Because of the recent identification of widespread poor vitamin D status and numerous potential health benefits associated with optimal vitamin D status, assessment of vitamin D status as part of annual physical examinations is encouraged (1,9,15,17,71). Approaches to meet vitamin D requirements are sensible sun exposure (i.e., usually 5 to 15 minutes of exposure to the arms and legs or the hands, arms, and face, two to three times a week) and dietary vitamin D intake (1,15). In the absence of sun exposure, vitamin D status can be improved by

consuming at least 1000 IU (25 µg) of vitamin D a day from foods naturally containing or fortified with vitamin D and, when indicated, vitamin D supplementation. Because of problems with adherence related to taking supplements and because supplements often contain a limited number of nutrients, vitamin D-fortified foods are the preferred option (56). Consuming three servings/day of vitamin D-fortified milk, some cheeses and/or yogurt provides vitamin D as well as many other nutrients such as calcium, potassium, phosphorus, protein, vitamins A and B_{12}, riboflavin, and niacin, which contribute to overall health and reduced risk of chronic diseases (74). D

REFERENCES

1. Holick, M.F. J. Nutr. *135(11s)*: 2739s, 2005.
2. Weisberg, P., K.S. Scanlon, R. Li, et al. Am. J. Clin. Nutr. *80*: 1697s, 2004.
3. Raiten, D.J., and M.F. Picciano. Am. J. Clin. Nutr. *80*: 1673s, 2004.
4. Vitamin D Workshop Advisory Committee. J. Steroid Biochem. Mol. Biol. *97*: 1, 2005.
5. Holick, M.F. J. Nutr. *135*: 2726s, 2005.
6. Calvo, M.S., and S.J. Whiting. J. Nutr. *135*: 301, 2005.
7. Whiting, S.J., and M.S. Calvo. J. Nutr. *136*: 1114, 2006.
8. The American Society for Bone and Mineral Research. *Contemporary Diagnosis and Treatment of Vitamin D-related Disorders.* Arlington, VA: December 4-5, 2006.
9. Holick, M.F. In: *Nutrition and Bone Health.* M.F. Holick and B. Dawson-Hughes (Eds). Totowa, N.J.: Humana Press, 2004, p. 403.
10. Holick, M.F. Mayo Clin. Proc. *81*: 353, 2006.
11. Norman, A.W., and H.H. Henry. In: *Present Knowledge in Nutrition*. 9th Ed. Volume 1. B.A. Bowman and R.M. Russell (Eds). Washington, D.C.: International Life Sciences Institute, 2006.
12. Johnson, M.A., and M.G. Kimlin. Nutr. Rev. *64*: 410, 2006.
13. Heaney, R.P. J. Steroid Biochem. Mol. Biol. *97*: 13, 2005.
14. Whiting, S.J., and M.S. Calvo. J. Steroid Biochem. Mol. Biol. *97*: 7, 2005.
15. Holick, M.F. Am. J. Clin. Nutr. *80*: 1678s, 2004.
16. Houghton, L.A., and R. Vieth. Am. J. Clin. Nutr. *84*: 694, 2006.
17. Holick, M.F. Am. J. Clin. Nutr. *79*: 362, 2004.
18. Dawson-Hughes, B. Am. J. Clin. Nutr. *80*: 1763s, 2004.
19. U.S. Department of Agriculture, Agricultural Research Service. *USDA National Nutrient Database for Standard Reference, Release 19.* Nutrient Data Laboratory, 2006. www.ars.usda.gov/nutrientdata
20. Calvo, M.S., S.J. Whiting, and C.N. Barton. Am. J. Clin. Nutr. *80*: 1710s, 2004.
21. Institute of Medicine, National Academy of Sciences. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Washington, D.C.: National Academy Press, 1997.

22. Food and Drug Administration, U.S. Department of Health and Human Services. Fed. Regist. *70 (No. 220)*: 69435s, 2005 (Nov. 16).
23. Keast, D.R., S.L. Hoerr, V.L. Fulgoni, et al. FASEB J. *V19(4)*: A59 (abst. # 62.5), 2005.
24. Dawson-Hughes, B., R.P. Heaney, M.F. Holick, et al. Osteoporos. Int. *16*: 713, 2005.
25. Bischoff-Ferrari, H.A., W.C. Willett, J.B. Wong, et al. JAMA *293*: 2257, 2005.
26. Hollis, B.W. J Nutr. *135*: 317, 2005.
27. Heaney, R.P. J. Nutr. *136*: 1123, 2006.
28. Bischoff-Ferrari, H.A., E. Giovannucci, W.C. Willett, et al. Am. J. Clin. Nutr. *84*: 18, 2006.
29. U.S. Department of Health and Human Services, U.S. Department of Agriculture. *Dietary Guidelines for Americans 2005.* 6th ed. Washington, D.C.: U.S. Government Printing Office, 2005. www.healthierus.gov/dietaryguidelines.
30. Weaver, C.M., and J.C. Fleet. Am. J. Clin. Nutr. *80*: 1735s, 2004.
31. Heaney, R.P. Am. J. Clin. Nutr. *78*: 912, 2003.
32. Hathcock, J.N., A. Shao, R. Vieth, et al. Am. J. Clin. Nutr. *85*: 6, 2007.
33. Calvo, M.S., and S.J. Whiting. Nutr. Rev. *61*: 107, 2003.
34. Hanley, D., and K.S. Davison. J. Nutr. *135*: 332, 2005.
35. Hollis, B.W., and C.L. Wagner. Am. J. Clin. Nutr. *79*: 717, 2004.
36. Bodnar, L.M., H.N. Simhan, R.W. Powers, et al. J. Nutr. *137*: 447, 2007.
37. Gordon, C.M., K.C. DePeter, H.A. Feldman, et al. Arch. Pediatr. Adolesc. Med. *158*: 531, 2004.
38. Sullivan, S.S., C.J. Rosen, W.A. Halteman, et al. J. Am. Diet. Assoc. *105*: 971, 2005.
39. Willis, C.M., E.M. Laing, D.B. Hall, et al. Am. J. Clin. Nutr. 85: *124*, 2007.
40. Dawson-Hughes, B., S.S. Harris, and G.E. Dallal. Am. J. Clin. Nutr. *65*: 67, 1997.
41. Visser, M., D.J.H. Deeg, M.T.E. Puts, et al. Am. J. Clin. Nutr. *84*: 616, 2006.
42. Lappe, J.M., M. Davies, D. Travers-Gustafson, et al. J. Am. Coll. Nutr. *25*: 395, 2006.
43. Moore, C.E., M.M. Murphy, and M.F. Horbick. J. Nutr. *135*: 2478, 2005.
44. Harris, S.S. J. Nutr. *136*: 1126, 2006.
45. Calvo, M.S., and S.J. Whiting. J. Nutr. *136*: 1135, 2006.
46. Wooten, W.J., and W. Price. J. Natl. Med. Assoc. *96*: 1s, 2004.
47. U.S. Department of Health and Human Services. *Bone Health and Osteoporosis. A Report of the Surgeon General.* Rockville, MD.: U.S. Department of Health and Human Services, Office of the Surgeon General, 2004. www.surgeongeneral.gov/library.
48. Holick, M.F. J. Clin. Invest. *116*: 2062, 2006.
49. Gartner, L.M., and F.R. Greer. Pediatrics *111*: 908, 2003.
50. Mannion, C.A., K. Gray-Donald, and K.G. Koski. Can. Med. Assoc. J. *174*: 1273, 2006.
51. Hollis, B.W., and C.L. Wagner. Can. Med. Assoc. J. *174*: 1287, 2006.
52. Copper, C., K. Javaid, S. Westlake, et al. J. Nutr. *135*: 2728s, 2005.
53. Javaid, M.K., S.R. Crozier, N.C. Harvey, et al. Lancet *367*: 36, 2006.
54. Hollis, B.W., and C.L. Wagner. Am. J. Clin. Nutr. *80*: 1752s, 2004.
55. Vieth, R. Ann. Med. *37*: 278, 2005.
56. Heaney, R.P. Am. J. Clin. Nutr. *85*: 300s, 2007.
57. Heaney, R.P., K.M. Davies, T.C. Chen, et al. Am. J. Clin. Nutr. *77*: 204, 2003.
58. Valimaki, V.V., H. Alfthan, E. Lehmuskallio, et al. J. Clin. Endocrinol. Metab. *89*: 76, 2004.
59. Viljakainen, H.T., A.-M. Natri, M. Karkkainen, et al. J. Bone Miner. Res. *21*: 836, 2006.
60. Bischoff-Ferrari, H.A., B. Dawson-Hughes, W.C. Willett, et al. JAMA *291*: 1999, 2004.
61. Bischoff-Ferrari, H.A., T. Dietrich, E.J. Orav, et al. Am. J. Clin. Nutr. *80*: 752, 2004.
62. Snijder, M.B., N.M. van Schoor, S.M. Pluijm, et al. J. Clin. Endocrinol. Metab. *91*: 2980, 2006.
63. Kushi, L.H., T. Byers, C. Doyle, et al. CA Cancer J. Clin. *56*: 254, 2006.
64. Garland, C.F., F.C. Garland, E.D. Gorham, et al. Am. J. Public Health *96*: 252, 2006.
65. Holick, M.F. Prog. Biophys. Mol. Biol. *92*: 49, 2006.
66. Skinner, H.G., D.S. Michaud, E. Giovannucci, et al. Cancer Epidemiol. Biomarkers & Prev. *15*: 1688, 2006.
67. Li, Y.C., J. Kong, M. Wei, et al. J. Clin. Invest. *110*: 229, 2002.
68. Zittermann, A., S.S. Schleithoff, and R. Koerfer. Heart Fail. Rev. *11*: 25, 2006.
69. Martini, L.A., and R.J. Wood. Nutr. Rev. *64*: 479, 2006.
70. Harris, S.S. J. Nutr. *135*: 323, 2005.
71. Mark, B.L., and J.A.S. Carson. J. Am. Diet. Assoc. *106*: 418, 2006.
72. Merlino, L., J. Curtis, T. Mikuls, et al. Arthritis Rheum. *50*: 72, 2004.
73. Dietrich, T., M. Nunn, B. Dawson-Hughes, et al. Am. J. Clin. Nutr. *82*: 575, 2005.
74. Miller, G.D., J.K. Jarvis, and L.D. McBean. *Handbook of Dairy Foods and Nutrition.* 3rd ed. Boca Raton, FL: CRC Press, 2007. D

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