

Research and Professional Briefs

Adolescent Girls in Maine Are at Risk for Vitamin D Insufficiency

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ABSTRACT

The objective was to determine the seasonal fluctuations in serum 25-hydroxyvitamin D (25-OHD) in a group of healthy adolescents living in a northern climate. Twenty-three 9- to 11-year-old girls participated in the study from September 2000 to March 2003. Serum 25-OHD and parathyroid hormone levels were measured each September and March. Dietary intake of vitamin D was assessed each summer and winter. Summer-sun exposure was evaluated using reports of time spent outdoors. The mean decrease in serum 25-OHD from September to March was 28%. Vitamin D insufficiency (at least one serum 25-OHD level <50 nmol/L) was observed in 11 of 23 (48%) subjects. Four of 23 subjects (17%) exhibited vitamin D insufficiency in both September and March. Mean parathyroid hormone levels increased 4 pg/mL (15%) from September to March. Vitamin D intakes need to be increased in winter at northern latitudes.

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An adequate supply of vitamin D is important to maximize gains in bone mineral during puberty. Puberty is a time of rapid bone growth and mineralization, with up to 50% of total adult bone mass being accrued (1). Vitamin D plays an integral role in bone mineralization by promoting calcium absorption in the small intestine and stimulating osteoblastic activity to maintain serum calcium and phosphorus levels in the normal range (2). In adults, bone mineral density is pos-

itively associated with serum 25-hydroxyvitamin D (25-OHD) levels (3). Vitamin D insufficiency during puberty can negatively impact calcium balance and availability for mineralization of bone.

People living at northern latitudes are at increased risk of vitamin D insufficiency during winter. An individual's serum 25-OHD level, the standard indicator of vitamin D status, is determined by both dietary intake of vitamin D-2 and D-3 and cutaneous synthesis of vitamin D-3 after exposure to solar ultraviolet B (UV-B) radiation (2). Due to the increased zenith angle of the sun, most solar UV-B photons are absorbed by the earth's ozone layer 4 to 5 months per year in winter at northern latitudes, and the skin makes little or no vitamin D-3 (4). Serum 25-OHD levels fluctuate as the skin source is added and removed, with peak 25-OHD levels occurring in late summer and the lowest levels occurring in late winter at northern latitudes (5).

Significant rates of vitamin D insufficiency in winter have been documented in studies of adults and children in the United States and other countries (5-15). Tangpricha and colleagues (7) in Boston (latitude 42°N) found that 42% of adults not taking multivitamin supplements had serum 25-OHD levels below 50 nmol/L, the lower limit of normal, in March. At a lower latitude in winter (median latitude=32°N), data from the Third National Health and Nutrition Examination Survey showed that 29% of girls (ages 12-19) exhibited serum 25-OHD levels <50 nmol/L (15). In Canada (43°N), Vieth and colleagues (11) found mean serum 25-OHD levels in winter (November-May) of 58±24 nmol/L in women ages 18 to 35 years.

Adolescent girls living at northern latitudes may be at particular risk for the deleterious effects of vitamin D insufficiency because of rapid bone mineralization rates during puberty, lack of vitamin D synthesis during winter, and the decrease in milk consumption that often occurs during adolescence (16). Because milk has been the major food source fortified with vitamin D, adequate consumption of milk is necessary to meet the Adequate Intake (AI) of 5 µg vitamin D per day for adolescents (17). The purpose of this study was to document the extent of seasonal fluctuations in serum 25-OHD levels in healthy adolescent girls living at a northern latitude.

METHODS

During the summer of 2000, girls aged 9 to 11 years who lived in the area of Bangor, ME (latitude 44°N) were recruited for an observational study of bone mineralization through advertisements in newspapers and fliers posted in the community. Institutional Review Boards at

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Table. Mean serum and dietary intake data for adolescent girls over 3 years

	September 2000 (n=22 ^a)	March 2001 (n=22 ^a)	September 2001 (n=22 ^a)	March 2002 (n=22 ^a)	September 2002 (n=20 ^b)	March 2003 (n=20 ^b)
	← mean (standard deviation) →					
Age (y)	10.7 (0.8)	11.2 (0.8)	11.7 (0.8)	12.2 (0.8)	12.7 (0.8)	13.2 (0.8)
Body mass index	20.5 (3.8)	20.4 (4.1)	21.1 (4.3)	21.3 (4.2)	21.8 (4.6)	22.2 (4.6)
Serum 25-OHD (nmol/L) ^c	74.4 (22.2)	55.9 (16.5)	70.8 (20.6)	53.9 (15.2)	72.3 (19.8)	50.0 (14.4)
Serum PTH (pg/mL) ^d	25.1 (10.0)	28.9 (10.3)	28.7 (9.8)	32.3 (11.2)	26.1 (8.9)	29.4 (12.7)
Dietary vitamin D (μg/d)	—	5.4 (1.4)	4.4 (2.1)	5.7 (2.5)	5.3 (2.7)	4.8 (2.1)
Dietary calcium (mg/d)	—	1,028 (221)	989 (372)	1,070 (328)	1,038 (381)	916 (316)
Adjusted ^e time outdoors (min)	—	—	84 (39)	—	79 (49)	—

^aOne subject with a missing serum sample was excluded.
^bThree subjects with missing serum samples were excluded.
^c25-OHD=25 hydroxyvitamin D. Significant difference between each September value and the subsequent March value ($P<.001$).
^dPTH=parathyroid hormone. Significant difference between each September value and the subsequent March value ($P<.05$).
^eAdjusted to a standard of peak hour ultraviolet-B radiation.

St Joseph Hospital and the University of Maine approved the protocol. Informed consent was obtained from a parent. Exclusion criteria were medical problems influencing vitamin D metabolism; medication use, including vitamin, mineral, or herbal supplements; eating disorders; and plans for winter travel to warm climates for more than 1 week.

Subjects were seen for blood drawing and measurement of height and weight each September and March from September 2000 to March 2003. Serum 25-OHD levels measured in September and March reflect dietary vitamin D intake and sun exposure in summer and winter, respectively. The serum was frozen at -70°C until April 2003, and then analyzed for 25-OHD using a competitive protein-binding assay (18), and intact parathyroid hormone (PTH) using the Nichols Advantage System chemiluminescence assay (Nichols Institute Diagnostics, San Juan Capistrano, CA) at the Vitamin D, Skin, and Bone Laboratory, Boston University School of Medicine, Boston, MA. The intra- and interassay coefficients of variation for the 25-OHD assay were 3% to 4.5% and 6.4% to 14.5%, respectively, and for the intact PTH assay were 2.2% to 3.6% and 5.6% to 8.3%, respectively.

A registered dietitian trained the subjects in keeping food records, estimating portion sizes, and reading nutrient content labels. Four single-day (3 weekdays and 1 weekend day) food records were collected from the subjects each winter (January and February) and summer (July and August). Food records were analyzed using Nutritionist Pro software (First Data Bank, San Bruno, CA).

On the same 4 days the subjects kept food records, they also kept 24-hour records of their physical activity. During the summer only, subjects were questioned about whether the activity took place inside or outdoors, clothing worn, and sunscreen use. Minutes of time spent outdoors were tallied for each hour and adjusted for strength of UV-B radiation relative to peak hour UV-B levels as described by Sullivan and colleagues (19). Total minutes spent outdoors (adjusted for relative strength of UV-B radiation) were averaged for the 4 days.

Pearson's product-moment correlation was used to examine the relationship between 25-OHD levels in March and those of the previous September for each year using

Microsoft Excel software (Seattle, WA). Multivariate repeated measures analyses were done for dependent variables, serum 25-OHD, and PTH levels according to time (each 6 months between September 2000 and March 2003) using SYSTAT (SPSS Inc, Chicago, IL) for only those 19 subjects who had complete data for the 3 years. Level of significance was $P<.05$.

RESULTS AND DISCUSSION

Twenty-three white girls enrolled in the study in September 2000 and continued until March 2003. Complete dietary and serum data were available on 19 subjects for the 3 years. The other four subjects were missing one or two serum samples. The Table summarizes the data that were complete for each year of the study. Although 12 subjects reported some sunscreen use, all subjects reported times when they were outdoors and not wearing sunscreen. T-shirt and shorts was the usual dress, with about 50% of body surface area exposed.

Individual serum 25-OHD levels are shown in the Figure. Eleven of 23 subjects (48%) exhibited vitamin D insufficiency, defined as at least one serum 25-OHD level <50 nmol/L, at some point in the 3 years. Four of 23 subjects (17%) exhibited vitamin D insufficiency in both September and March. One 25-OHD value fell <17.5 nmol/L (the detection limit of the assay) and was reported as 17.5 nmol/L, which slightly elevated the mean for March 2003. A significant correlation between serum 25-OHD levels in March and those of the previous September was found each year ($r=0.83$ to 0.94 , $P<.001$). Repeated-measures analysis of variance (using the 19 subjects with complete data for the 3 years) showed no significant year-to-year difference in overall serum 25-OHD levels, but the difference between mean levels in September and March was significant ($P<.001$) and consistent across years with an average drop in serum 25-OHD of 20.1 nmol/L (28%). The change in serum PTH from September to March was also consistent across years ($P<.05$) in 19 subjects with an average increase of 4.0 pg/mL (15%).

In March, the rate of vitamin D insufficiency among these healthy adolescent girls living in Maine was high

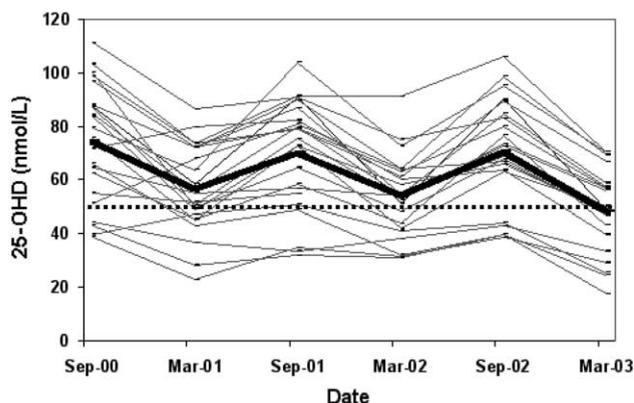


Figure. Individual serum 25-hydroxyvitamin D (25-OHD) levels over time. Dotted line (· · ·) indicates lower limit of normal (50 nmol/L). Bold line (—) indicates group mean.

and may compromise bone health. There is some evidence that low serum 25-OHD levels and increased PTH levels result in lower accumulation of bone mass. Outila and colleagues (6) observed that serum 25-OHD levels ≤ 40 nmol/L were associated with low forearm bone mineral density in 14- to 16-year-old females. Cheng and colleagues (20) found that 10- to 12-year-old girls with serum 25-OHD levels ≤ 25 nmol/L had secondary hyperparathyroidism and low cortical bone mineral density.

Oral vitamin D intake in winter was inadequate to maintain March serum 25-OHD levels in the normal range for many girls in this study. Reported intakes of vitamin D were at or near the current AI of $5 \mu\text{g}$ per day (17). Either the subjects' oral vitamin D intakes were overestimated, or the dietary intake goals should be higher than current recommendations. The latter is more likely, given that nutrient intakes are usually underestimated in food records (21). Researchers suggest that current dietary intake goals for vitamin D are markedly inadequate to sustain normal serum levels in the absence of sun exposure (2,11,22). Other studies documenting similarly high rates of vitamin D insufficiency support the conclusion that vitamin D insufficiency is prevalent at northern latitudes in winter and that increased vitamin D intakes are necessary (7,11,15).

Sources of vitamin D in summer in Maine were adequate for most girls to achieve serum 25-OHD levels > 50 nmol/L in September. Because higher 25-OHD levels in September were associated with higher levels the following March, increasing vitamin D intake over the summer can also help maintain adequate serum levels through the winter. Summer sun exposure is a potent source of vitamin D with one total body minimal erythemal dose (the amount of sun exposure that begins to redden the skin) supplying 250 to $625 \mu\text{g}$ of vitamin D-3 (2). Short exposures to midday sun (a few minutes) prior to applying sunscreen have been suggested as a source of vitamin D (2).

There was a subset of otherwise healthy girls (4 of 23) who exhibited vitamin D insufficiency in both September and March without a clear behavioral or dietary explanation. Whether this represents some disorder of vitamin D synthesis or metabolism is unclear. Individuals with

vitamin D insufficiency year-round can be identified by measuring serum 25-OHD levels at the end of summer (September).

The data analysis presented here uses 50 nmol/L as the conventional cutoff for adequate serum 25-OHD levels. Prominent researchers in the field suggest that the serum 25-OHD levels associated with optimal calcium absorption and normalization of PTH levels may be closer to 75 to 80 nmol/L (2,23). Viewing the above data in light of this proposed optimal serum level reveals a sizeable gap between current serum vitamin D status and desirable levels. Significantly higher intakes of vitamin D from food, sun, and/or supplements would be needed to shift the serum 25-OHD to 75 to 80 nmol/L year-round. Thus, dietetics professionals should anticipate future developments in the field of vitamin D, including changes in the Dietary Reference Intakes and in food fortification and supplementation practices, as research is ongoing.

CONCLUSIONS

- When stressing the importance of adequate calcium intake for bone building during adolescence, dietetics professionals should encourage adequate vitamin D intake for optimal calcium utilization.
- People of all ages living at northern latitudes should be encouraged to seek adequate sources of vitamin D, including milk and other emerging dietary sources, vitamin D supplements, and short periods of mid-day sun exposure between April and October.

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References

1. Gordon CL, Halton JM, Atkinson SA, Webber CE. The contributions of growth and puberty to peak bone mass. *Growth Dev Aging*. 1991;55:257-262.
2. Holick MF. Vitamin D: The underappreciated D-lightful hormone that is important for skeletal and cellular health. *Curr Opin Endocrinol Diabetes*. 2002; 9:87-98.
3. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. Positive association between 25-hydroxy vitamin D levels and bone mineral density: A population-based study of younger and older adults. *Am J Med*. 2004;116:634-639.
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;67:373-378.

5. Rapuri PB, Kinyamu HK, Gallagher JC, Haynatzka V. Seasonal changes in calciotropic hormones, bone markers, and bone mineral density in elderly women. *J Clin Endocrinol Metab.* 2002;87:2024-2032.
6. Outila TA, Karkkainen MUM, Lamberg-Allardt CJE. Vitamin D status affects serum parathyroid hormone concentrations during winter in female adolescents: Associations with forearm bone mineral density. *Am J Clin Nutr.* 2001;74:206-210.
7. Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D insufficiency among free-living healthy young adults. *Am J Med.* 2002;112:659-662.
8. Rosen CJ, Morrison A, Zhou H, Storm D, Hunter SJ, Musgrave K, Chen T, Lui WW, Holick MF. Elderly women in northern New England exhibit seasonal changes in bone mineral density and calciotropic hormones. *Bone Miner.* 1994;25:83-92.
9. Lehtonen-Veromaa MKM, Mottonen TT, Nuotio IO, Irjala KMA, Leino AE, Viikari JSA. Vitamin D and attainment of peak bone mass among peripubertal Finnish girls: A 3-y prospective study. *Am J Clin Nutr.* 2002;76:1446-1453.
10. Woitge HW, Scheidt-Nave C, Kissling C, Leidig-Bruckner G, Meyer K, Grauer A, Scharla SH, Ziegler R, Seibel MJ. Seasonal variation of biochemical indexes of bone turnover: Results of a population-based study. *J Clin Endocrinol Metab.* 1998;83:68-75.
11. Vieth R, Cole DE, Hawker GA, Trang HM, Rubin LA. Wintertime vitamin D deficiency is common in young Canadian women, and their vitamin D intake does not prevent it. *Eur J Clin Nutr.* 2001;55:1091-1097.
12. Davies PSW, Bates CJ, Cole TJ, Prentice A, Clarke PC. Vitamin D: Seasonal and regional differences in preschool children in Great Britain. *Eur J Clin Nutr.* 1999;53:195-198.
13. Guillemant J, Cabrol S, Allemandou A, Peres G, Guillemant S. Vitamin D-dependent seasonal variation of PTH in growing male adolescents. *Bone.* 1995;17:513-516.
14. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *CMAJ.* 2002;166:1517-1524.
15. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal sub-populations from NHANES III. *Bone.* 2002;30:771-777.
16. Park YK, Meier ER, Bianchi P, Song WO. Trends in children's consumption of beverages: 1987-1998. *Fam Econ Nutr Rev.* 2002;14:69-79.
17. Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Washington, DC: National Academy Press; 1997:250-287.
18. Roth HJ, Zahn I, Alkier R, Schmidt H. Validation of the first automated chemiluminescence protein-binding assay for the detection of 25-hydroxycalciferol. *Clin Lab.* 2001;47:357-365.
19. Sullivan SS, Cobb JL, Rosen CJ, Holick MF, Chen TC, Kimlin MG, Parisi AV. Assessment of sun exposure in adolescent girls using activity diaries. *Nutr Res.* 2003;23:631-644.
20. Cheng S, Tylavsky F, Kroger H, Karkkainen M, Lyytikainen A, Koistinen A, Mahonen A, Alen M, Halleen J, Vaananen K, Lamberg-Allardt C. Association of low 25-hydroxyvitamin D concentrations with elevated parathyroid hormone concentrations and low cortical bone density in early pubertal and prepubertal Finnish girls. *Am J Clin Nutr.* 2003;78:485-492.
21. Hill RJ, Davies PSW. The validity of self-reported energy intake as determined using the doubly labeled water technique. *Br J Nutr.* 2001;85:415-430.
22. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr.* 2003;77:204-210.
23. Heaney RP, Dowell MS, Hale CA, Bendich A. Calcium absorption varies within the reference range for serum 25-hydroxyvitamin D. *J Am Coll Nutr.* 2003;22:142-146.