

# Tanning is associated with optimal vitamin D status (serum 25-hydroxyvitamin D concentration) and higher bone mineral density<sup>1-3</sup>

Vin Tangpricha, Adrian Turner, Catherine Spina, Sheila Decastro, Tai C Chen, and Michael F Holick

## ABSTRACT

**Background:** Vitamin D is made in the skin on exposure to solar radiation, and it is necessary to optimal skeletal health. Subjects who use a tanning bed that emits ultraviolet B radiation (290–315 nm) are likely to have higher 25-hydroxyvitamin D [25(OH)D] concentrations than do subjects who do not regularly use a tanning bed.

**Objective:** The first objective of this study was to ascertain whether subjects who regularly use a tanning bed have higher 25(OH)D concentrations than do subjects who do not use a tanning bed. The second objective was to ascertain whether higher 25(OH)D concentrations correlated positively with bone mineral density.

**Design:** This cross-sectional analysis examined 50 subjects who used a tanning bed at least once a week and 106 control subjects. Each subject gave a blood specimen for measurement of serum 25(OH)D and parathyroid hormone concentrations. Each subject underwent bone mineral density testing of the hip and spine.

**Results:** Subjects who used a tanning bed had serum 25(OH)D concentrations 90% higher than those of control subjects ( $115.5 \pm 8.0$  and  $60.3 \pm 3.0$  nmol/L, respectively;  $P < 0.001$ ). Subjects who used a tanning bed had parathyroid hormone concentrations 18% lower than those of control subjects ( $21.4 \pm 1.0$  and  $25.3 \pm 0.8$  pg/mL, respectively;  $P = 0.01$ ). Tanners had significantly higher BMD and z scores at the total hip than did nontanners.

**Conclusion:** The regular use of a tanning bed that emits vitamin D–producing ultraviolet radiation is associated with higher 25(OH)D concentrations and thus may have a benefit for the skeleton. *Am J Clin Nutr* 2004;80:1645–9.

**KEY WORDS** Vitamin D deficiency, secondary hyperparathyroidism, vitamin D, bone mineral density, bone mineral content, tanning

## INTRODUCTION

Vitamin D is a secosteroid hormone that is made naturally in the skin. The precursor to vitamin D exists in the skin as 7-dehydrocholesterol, which is converted to previtamin D<sub>3</sub> when exposed to solar ultraviolet B (UVB) radiation of 290–315-nm wavelength (1, 2). Previtamin D<sub>3</sub> undergoes thermal isomerization to form vitamin D<sub>3</sub>. Once formed, vitamin D<sub>3</sub> enters the circulation and is bound to the vitamin D–binding protein. Vitamin D can also be obtained from the diet via consumption of vitamin D–fortified foods such as milk and cereals and foods that naturally contain vitamin D, including fatty fish such as salmon

and mackerel (3). Adequate vitamin D status is important for optimal bone health (4), and chronic vitamin D deficiency leads to osteomalacia and osteoporosis in adults (3–6). Clinical studies have shown a positive effect on bone mineral density (BMD) after supplementation with vitamin D (5, 6). Higher blood concentrations of 25-hydroxyvitamin D [25(OH)D] during childhood correlate positively with greater adult BMD (7). Furthermore, serum 25(OH)D was positively correlated with BMD in both men and women of all races (8).

There is increased concern about skin cancer, which has created a fear of causative sunlight exposure (9–12). Melanoma is the most serious form of skin cancer. It should be recognized that most melanomas occur in areas that are not exposed to the sun (13) and that it is the number of lifetime sunburn experiences, the number of moles, and red hair that increase the risk of this deadly disease (12). The use of sunscreen with a sun-protective factor (SPF) of  $\geq 8$  reduces the amount of vitamin D<sub>3</sub> produced in the skin by  $>95\%$  (14). A lack or scarcity of sunlight exposure leads to vitamin D deficiency (15–20). Adults who use tanning beds that emit vitamin D<sub>3</sub>–producing UVB radiation (17, 19, 21) should be able to make vitamin D<sub>3</sub> in their skin and increase the circulating 25(OH)D concentrations. We evaluated the possibility that higher serum 25(OH)D concentrations could correlate with higher BMD in subjects who were exposed to UVB radiation (ie, used a tanning bed) at least once a week.

We conducted a study to ascertain the serum concentrations of 25(OH)D and BMD at the hip and spine in a group of adults who used tanning beds and in a control group of nontanners. We sought to ascertain whether there was a significant positive correlation between circulating serum 25(OH)D concentrations and BMD.

<sup>1</sup> From the Vitamin D, Skin and Bone Research Laboratory (AT, CS, SD, TCC, and MFH) and the Section of Endocrinology, Diabetes and Nutrition (AT, KS, SD, TCC, and MFH), Department of Medicine, Boston University School of Medicine, Boston, and the Section of Endocrinology, Metabolism and Lipids and the Department of Medicine, Emory University School of Medicine, Atlanta (VT).

<sup>2</sup> Supported by grant no. MO1RR00053 from the NIH and a grant from the UV Foundation.

<sup>3</sup> Address reprint requests and correspondence to MF Holick, Boston University School of Medicine, M-1013, 715 Albany Street, Boston, MA 02118. E-mail: mholick@bu.edu.

Received May 24, 2004.

Accepted for publication August 17, 2004.

## SUBJECTS AND METHODS

### Subjects

We recruited healthy adults between the ages of 18 and 70 y for participation in our study by placing advertisements in the local newspaper and on an online bulletin board. We classified as tanners those subjects who had regularly been using a tanning bed  $\geq 1$  time/wk for  $\geq 6$  mo. We classified as nontanners those subjects who did not use a tanning bed. Potential subjects were excluded if they had history of osteoporosis, took vitamin D supplements other than a regular multivitamin, took medications that interfered with vitamin D metabolism, were undergoing ultraviolet radiation as medical therapy, or were pregnant.

We obtained approval from the Institutional Review Board at Boston University School of Medicine to conduct the study and conducted the study in accordance with the Helsinki Declaration of 1975, as revised in 1983. All of the study subjects gave written informed consent for participation in the study.

### Protocol

Each subject came to the General Clinical Research Clinic at Boston University School of Medicine between 11 March and 17 June 2003. Each subject gave a blood sample for measurement of 25(OH)D and parathyroid hormone (PTH) concentrations. Women of childbearing age underwent a urine pregnancy test to exclude pregnant subjects. Each subject underwent a test of the BMD of the spine, hip, and total body with the use of a bone densitometer (QDR 4500W series; Hologic, Inc, Waltham, MA). We recorded the *z* score and BMD of the spine (L2-L4), total hip, and body.

Serum 25(OH)D was measured by using a method described by Chen et al (22). This assay has a limit of detection of 12.5 nmol/L. Values  $< 12.5$  nmol/L were assigned a value of 12.5 nmol/L. The assay has an intraassay CV of 8% and an interassay CV of 12%. Serum PTH was measured by using the Nichols Advantage system (Nichols, San Clemente, CA). To ascertain the prevalence of vitamin D deficiency, we considered any subject with a serum 25(OH)D concentration  $\leq 50$  nmol/L to be vitamin D deficient (23).

### Demographic information

A total of 166 subjects enrolled into the study. Three subjects were excluded from the study for the following reasons: they were aged  $> 70$  y with history of osteoporosis, unable to verify tanning status, and undergoing ultraviolet radiation therapy for psoriasis. Seven subjects did not complete the study protocol, either because they did not complete the BMD test or because their blood was not drawn for testing.

One hundred six subjects were classified as nontanners or control subjects, and 50 subjects were classified as tanners. Their background demographic data are shown in **Table 1**.

### Statistical analysis

The results are represented as means  $\pm$  SEM. The data were analyzed by using Microsoft Excel (Office 2000; Microsoft Corp, Redmond, WA) and ANALYSE IT (version 1.71; Analyse-it Software Ltd, Leeds, United Kingdom) software. Differences in concentrations of serum 25(OH)D and PTH and urine *N*-telopeptides of type I collagen were evaluated by using a two-tailed unpaired Student's *t* test. Differences in *z* score and

**TABLE 1**

Demographic information on tanner and nontanner (control) subjects

	Nontanners ( <i>n</i> = 106)	Tanners ( <i>n</i> = 50)
Age (y)	32.7 $\pm$ 0.9 <sup>1</sup>	34.2 $\pm$ 2.0
Sex, F/M ( <i>n</i> )	90/16	43/7
Percentage taking a daily multivitamin (%)	40	54
Milk intake (glasses/d)	1.0 $\pm$ 0.1	1.0 $\pm$ 0.1
Sunlight exposure (h/wk)	15.0 $\pm$ 2.0	24.3 $\pm$ 2.0 <sup>2</sup>
Ethnicity ( <i>n</i> )		
White	69	46
Asian	23	3
Black	4	—
Other	10	1
Duration of tanning bed use (y)	0	6.2 $\pm$ 0.7
Tanning (sessions/wk)	0	2.4 $\pm$ 0.2
(min/wk)	0	33.7 $\pm$ 5.0

<sup>1</sup>  $\bar{x} \pm$  SD (all such values).

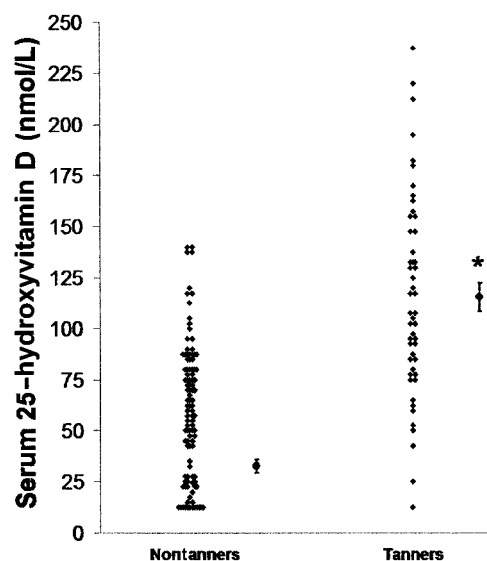
<sup>2</sup> Significantly different from nontanners, *P* = 0.003.

BMD were evaluated by using a two-tailed unpaired Student's *t* test. Differences in proportion were evaluated by using Fisher's exact test. The sample size was chosen to provide  $\geq 80\%$  power to detect a difference of 50% in 25(OH)D concentration and of  $\geq 4\%$  in BMD. A relation between serum 25(OH)D concentrations and BMD was evaluated by performing a Pearson correlation using the Analyze-It statistical software.

## RESULTS

### 25-Hydroxyvitamin D and parathyroid hormone

Tanners had higher mean 25(OH)D concentrations than did nontanners: 115.5  $\pm$  8.0 and 60.3  $\pm$  3.0 nmol/L, respectively (*P*  $< 0.001$ , *t* test; **Figure 1**). Tanners also had lower serum PTH



**FIGURE 1.** Mean ( $\pm$ SEM) serum 25-hydroxyvitamin D concentrations in tanners and nontanners. Single points for each category are means  $\pm$  SEMs. \*Significantly different from nontanners, *P*  $< 0.001$ .

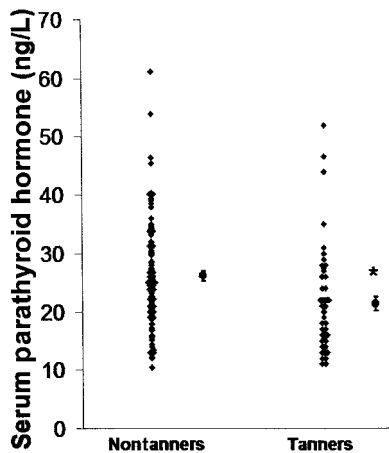


FIGURE 2. Mean ( $\pm$ SEM) serum parathyroid hormone concentrations in tanners and nontanners. Single points for each category are means  $\pm$  SEMs. \*Significantly different from nontanners,  $P = 0.01$ .

concentrations than did nontanners (control subjects):  $21.4 \pm 1.0$  and  $25.3 \pm 0.8$  ng/mL, respectively ( $P = 0.01$ ,  $t$  test; **Figure 2**). The prevalence of vitamin D deficiency among the nontanners was 41.5%, and that among the tanners was only 8% ( $P < 0.001$ , Fisher's exact test).

#### Bone mineral density

The tanners had significantly higher BMD and  $z$  scores at the total hip than did the nontanners (**Table 2**). No significant difference in BMD or  $z$  score at the spine (L2-L4) or total body was detected between the tanners and nontanners. No differences in bone mineral content were detected at either the hip or spine between tanners and nontanners (Table 2).

#### Correlation between 25-hydroxyvitamin D concentrations and bone mineral density

Because it was reported that higher 25(OH)D concentrations correlated with higher BMD (7), we wanted to see if this association existed in our subject population. We evaluated all subjects in the study to ascertain whether there was a relation between 25(OH)D concentrations and BMD. We calculated a Pearson's coefficient of correlation with 25(OH)D concentration as the independent factor and BMD as the dependent factor. We found that there was a positive but nonsignificant relation between 25(OH)D concentrations and BMD at both the hip ( $R^2 = 0.003$ ,  $P = 0.53$ ) and spine ( $R^2 = 0.004$ ,  $P = 0.42$ ).

To correct for ethnic and sexual differences in BMD of the hip and spine, we calculated a Pearson's coefficient of correlation with 25(OH)D concentrations as the independent factor and  $z$  scores of the hip and spine as the dependent factors. We found that there was still a small positive relation between 25(OH)D concentrations and BMD. This relation was slightly stronger at both the hip ( $R^2 = 0.010$ ) and spine ( $R^2 = 0.012$ ) than was that between 25(OH)D and BMD, but, again, these relations were not significant.

#### DISCUSSION

Adults who used a tanning bed had 90% higher serum 25(OH)D and 18% lower PTH concentrations than did adults who did not use a tanning bed. The prevalence of vitamin D

TABLE 2

Bone mineral density (BMD) and bone mineral content (BMC) at the hip and spine in tanners and nontanners<sup>1</sup>

	Tanners	Nontanners
Total hip		
BMD (g/cm <sup>2</sup> )	$0.975 \pm 0.03$	$0.920 \pm 0.01^2$
BMC (g)	$33.2 \pm 1.0$	$31.1 \pm 0.8$
$z$ Score	$0.20 \pm 0.2$	$-0.18 \pm 0.01^2$
Spine (L2-L4)		
BMD (g/cm <sup>2</sup> )	$1.02 \pm 0.02$	$1.00 \pm 0.01$
BMC (g)	$61.5 \pm 0.8$	$62.1 \pm 1.0$
$z$ Score	$-0.036 \pm 0.20$	$-0.266 \pm 0.1$

<sup>1</sup> All values are  $\bar{x} \pm$  SEM.

<sup>2</sup> Significantly different from tanners,  $P = 0.04$ .

deficiency [25(OH)D  $\leq 50$  nmol/L] was significantly lower in the tanners (8%) than in the nontanners (41.5%) at the end of the winter. Tanners also had significantly higher BMD at the hip than did the nontanners, which confirms the findings of Bischoff et al (8). There was a small but nonsignificant positive relation between serum 25(OH)D concentrations and BMD at the hip and spine.

These findings have important clinical implications. The increased public awareness of the negative effect of sunlight in causing skin cancer has resulted in the fact that many adults and children always wear sun protection or completely avoid sunlight exposure. A lack of sunlight exposure can result in vitamin D deficiency. Humans produce most of the vitamin D found in the circulation in the skin through exposure to sunlight (2, 3), and adults who spend most of their time indoors are at risk of vitamin D deficiency (15–18, 20, 21, 23–26). Nursing home residents, medical inpatients, institutionalized persons, and blacks are at highest risk of vitamin D deficiency (18, 23–28). Subjects living in northern latitudes have low production of vitamin D in the skin because even the zenith of the angle of the sun's rays does not allow for cutaneous vitamin D<sub>3</sub> production (2, 3, 15, 17, 28). In addition, increased pigmentation (27–29) or the wearing of clothing that largely covers the body (30–32) impairs the production of vitamin D<sub>3</sub> in the skin. The regular use of sunscreens can also result in vitamin D deficiency (33): sunscreen with an SPF  $> 8$  can reduce the production of vitamin D in the skin by as much as 95% (2, 14).

Young adults are also at risk of vitamin D deficiency because of inadequate sunlight exposure that results from greater pursuit of indoor activities, greater use of sunscreen because of fear of skin cancer (34, 35), and less consumption of vitamin D–fortified milk (15, 36, 37) than were seen in previous generations. A recent survey of young adults living in Boston found that 36% of young adults were vitamin D deficient, even though many took a multivitamin and drank a glass of milk daily (15). African American adolescents and white preteen girls are also at risk for vitamin D deficiency (37, 38).

Vitamin D is important to bone mineralization because of its role in the maintenance of adequate serum calcium and phosphorus concentrations (2, 3). Vitamin D deficiency results in osteomalacia in adults and is a frequent source of occult muscle and bone pain (39–41). There is increasing evidence that vitamin D can protect against the development of many chronic diseases, including type 1 diabetes mellitus, hypertension, cardiovascular

disease, common cancers, multiple sclerosis, and rheumatoid arthritis (2, 3).

The use of tanning beds has been promoted to the public for the cosmetic purpose of tanning, but this study shows that a moderate use of tanning beds may also provide some medical benefit. Higher concentrations of 25(OH)D throughout the year may have a significant effect in enhancing intestinal calcium absorption and improving bone health (7, 8, 42). Blood concentrations of 25(OH)D in tanners are > 75 nmol/L, which is considered to be necessary for maximum intestinal calcium transport (23, 42). This may explain why higher serum 25(OH)D concentrations are associated with higher bone density. There is mounting evidence that a healthy concentration of 25(OH)D (ie, >75 nmol/L) may reduce the risk of colon, breast, and prostate cancers, hypertension, and autoimmune diseases (2, 3, 39–42).

In conclusion, the regular use of a tanning bed results in higher 25(OH)D concentrations and prevents increased seasonal prevalence of vitamin D deficiency during the winter. The subjects who had used tanning beds for a mean of  $\geq 5$  y had higher BMD at the hip than did the nontanners (control subjects). Larger studies should be conducted to investigate the potential positive effect of chronic use of tanning beds on vitamin D status and bone health.



VT participated in the design of the study, the recruitment of subjects, the review of the original data and their compilation, and the preparation of the manuscript. AT participated in the analysis of the bone density measurements. CS and SD participated in the recruitment of subjects. TCC participated in the biochemical measurements of 25(OH)D and PTH concentrations. MFH participated in the design of the study, the recruitment of subjects, the review of the original data and their compilation, and the preparation of the manuscript.

VT, AT, CS, SD, and TC declare no conflict of interest in the regards to this manuscript. MH serves as a consultant to the UV Foundation.

## REFERENCES

- Holick MF, MacLaughlin JA, Clark MB, et al. Photosynthesis of previtamin D<sub>3</sub> in human skin and the physiologic consequences. *Science* 1980;210(4466):203–5.
- Holick MF. Vitamin D. A millennium perspective. *J Cell Biochem* 2003;88(2):296–307.
- Matsuoka LY, Ide L, Wortsman J, Hanifan N, Holick MF. Chronic sunscreen use decreases circulating concentrations of 25-hydroxyvitamin D: a preliminary study. *Arch Dermatol* 1988;124:1802–4.
- Suda T, Ueno Y, Fujii K, Shinki T. Vitamin D and bone. *J Cell Biochem* 2003;88(2):259–66.
- Chapuy MC, Arlot M, Duboeuf F, et al. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992;327:1627–42.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age and older. *N Engl J Med* 1997;337:670–6.
- Jones G, Dwyer T. Bone mass in prepubertal children: gender differences and the role of physical activity and sunlight exposure. *J Clin Endocrinol Metab* 1998;83:4274–9.
- Bischoff HA, Dietrich T, Orav JE, Dawson-Hughes B. Positive association between 25-hydroxyvitamin D levels and bone mineral density: a population-based study of younger and older US adults. *Am J Med* 2004;116:634–9.
- Grodstein F, Speizer FE, Hunter DJ. A prospective study of incident squamous cell carcinoma of the skin in the Nurses' Health Study. *J Natl Cancer Inst* 1995;87:1061–6.
- Ziegler A, Jonason AS, Leffell DJ, et al. Sunburn and p53 in the onset of skin cancer. *Nature* 1994;372:773–6.
- Kennedy C, Bajdik CD, Willemze R, de Grujil FR, Bavinck JN. The influence of painful sunburns and lifetime of sun exposure on the risk of actinic keratoses, seborrheic warts, melanocytic nevi, atypical nevi and skin cancer. *J Invest Dermatol* 2003;120:1087–93.
- Veierod MB, Weiderpass E, Thorn M, et al. A prospective study of pigmentation, sun exposure, and risk of cutaneous malignant melanoma in women. *J Natl Cancer Inst* 2003;95:1530–8.
- Garland CF, Garland FC, Gorham ED. Rising trends in melanoma. An hypothesis concerning sunscreen effectiveness. *Ann Epidemiol* 1993;3:103–10.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 1987;64:1165–8.
- Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D insufficiency among free-living healthy young adults. *Am J Med* 2002;112(8):659–62.
- Looker AC, Gunter EW. Hypovitaminosis D in medical inpatients. *N Engl J Med* 1998;339(5):344–5 (letter).
- MacLaughlin JA, Anderson RR, Holick MF. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 1982;216(4549):1001–3.
- Chuck A, Todd J, Diffey B. Subliminal ultraviolet-B irradiation for the prevention of vitamin D deficiency in the elderly: a feasibility study. *Photochem Photobiophys* 2001;17(4):168–71.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. A one-year study to evaluate the roles of exposure to sunlight and diet on the circulating concentrations of 25-OH-D in an elderly population in Boston. *Am J Clin Nutr* 1990;51:1075–81.
- Chel VG, Ooms ME, Popp-Snijders C, et al. Ultraviolet irradiation corrects vitamin D deficiency and suppresses secondary hyperparathyroidism in the elderly. *J Bone Miner Res* 1998;13:1238–42.
- Chen TC, Lu Z, Perez A, Holick MF. Cutaneous synthesis of vitamin D<sub>3</sub> in response to sun-tanning bed radiation. In: Holick MF, Jung EG, eds. *Biologic effects of light*. Berlin: Walter De Gruyter & Company, 1994: 28–33.
- Chen TC, Turner AK, Holick MF. Methods for the determination of the circulating concentration of 25-hydroxyvitamin D. *J Nutr Biochem* 1990;1:315–9.
- Malabanan A, Veronikis IE, Holick MF. Redefining vitamin D insufficiency. *Lancet* 1998;351:805–6.
- Dawson-Hughes B, Harris SS, Dallal GE. Plasma calcidiol, season, and serum parathyroid hormone concentrations in healthy elderly men and women. *Am J Clin Nutr* 1997;65:67–71.
- Gloth FM, 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.
- Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *N Engl J Med* 1998;338(12):777–83.
- Harris SS, Soteriades E, Coolidge JA, Mudgal S, Dawson-Hughes B. Vitamin D insufficiency and hyperparathyroidism in a low income, multiracial, elderly population. *J Clin Endocrinol Metab* 2000;85(11):4125–30.
- Nesby-O'Dell S, Scanlon KS, Cogswell ME, et al. Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: third National Health and Nutrition Examination Survey, 1988–1994. *Am J Clin Nutr* 2002;76(1):187–92.
- Clemens TL, Adams JS, Henderson SL, Holick MF. Increased skin pigment reduces the capacity of skin to synthesize vitamin D<sub>3</sub>. *Lancet* 1982;1(8263):74–6.
- Mukamel MN, Weisman Y, Somech R, et al. Vitamin D deficiency and insufficiency in Orthodox and non-Orthodox Jewish mothers in Israel. *Isr Med Assoc J* 2001;3(6):419–21.
- Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. *Osteoporosis Int* 2001;12(11):931–5.
- Sedrani SH. Low 25-hydroxyvitamin D and normal serum calcium concentrations in Saudi Arabia: Riyadh region. *Ann Nutr Metab* 1984;28(3):181–5.
- Holick MF, Matsuoka LY, Wortsman J. Regular use of sunscreen on vitamin D levels. *Arch Dermatol* 1995;131(11):1337–9.
- Tripp MK, Herrmann NB, Parcel GS, Chamberlain RM, Gritz ER. Sun protection is fun! A skin cancer prevention program for preschools. *J School Health* 2000;70(10):395–401.

35. Robinson JK, Rigel DS, Amonette RA. Summertime sun protection used by adults for their children. *J Am Acad Dermatol* 2000;42:746–53.
36. Gordon CM, Nelson LM. Amenorrhea and bone health in adolescents and young women. *Curr Opin Obstet Gynecol* 2003;15(5):377–84.
37. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. *Arch Pediatr Adolesc Med* 2004;158(6):531–7.
38. Sullivan SS, Rosen CJ, Chen TC, Holick MF. Seasonal changes in serum 25(OH)D in adolescent girls in Maine. *J Bone Miner Res* 2003;28(suppl):S407 (abstr).
39. Gloth FM III, Lindsay JM, Zelesnick LB, Greenough WB III. Can vitamin D deficiency produce an unusual pain syndrome? *Arch Intern Med* 1991;151:1662–4.
40. Malabanan AO, Turner AK, Holick MF. Severe generalized bone pain and osteoporosis in a premenopausal black female: effect of vitamin D replacement. *J Clin Densitometr* 1998;1:201–4.
41. Holick MF. Vitamin D deficiency: what a pain it is. *Mayo Clin Proc* 2003;78(12):1457–9.
42. 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(2):142–6.