Sunbeds as Vitamin D Sources

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ABSTRACT

The objectives of this work were: (1) To determine whether repeated exposures to small doses from a commercial sun bed (Wolff Solarium Super Plus 100 W) over 5 weeks gave less vitamin D than repeated exposures to twice as large, but still nonerythemogenic, doses. (2) To investigate whether the contribution to the vitamin D status from such sessions of exposures was dependent on the baseline status before the start of the sessions. (3) To determine the decay rate of the induced increment of vitamin D. The sun bed sessions raised the 25-hydroxyvitamin D levels from typical winter values to typical summer values. The mean value after exposure being 80 nM (± 14) and the increase being 15 nM on average. Persons with the lowest initial levels got the largest increase. The level in this group was back to the pre-exposure level after 2–4 weeks. To maintain a summer level through the winter, when no vitamin D is produced by the sun in northern countries, one should consider increasing the recommended intake of vitamin D intake significantly, or encouraging the population to get moderate, nonerythemal sun bed exposures.

INTRODUCTION

The health effects of vitamin D have been focused on for several years (1,2). A number of reports indicate that with a good vitamin D status prognosis is improved, adverse symptoms are alleviated and incidence rates are reduced for several forms of internal cancers (colon, prostate, lung, breast, lymphomas, *etc.*) (3,4), for multiple sclerosis (5), diabetes Type 1 and 2 (6,7), rheumatoid arthritis and several other autoimmune diseases (8), for influenza (9) and for cardiovascular diseases (10). Furthermore, rickets and osteomalacia, diseases related to a poor vitamin D status, are reappearing in certain population groups, notably immigrants with dark skin (11,12). Recently, a large IARC report (13) concluded that there was only limited evidence for any correlation between vitamin D levels and cancer risk or mortality. However, the report was criticized by a number of vitamin D experts for omissions, errors and lack of updating, and thus not describing the present state of knowledge correctly (14,15). Thus, the matter is not yet settled, and further investigations are certainly warranted.

In the United States and in a number of European countries a low vitamin D status has been reported for teenagers, the elderly and even for apparently healthy adolescents (16–19). The vitamin D level is usually estimated by measuring the serum concentration of 25-hydroxyvitamin D (25(OH)D). Optimal levels are being discussed, and are certainly different for avoidance of different diseases (20–22). Levels below 50 nM are likely to be inadequate, and much higher levels are probably needed for optimal health.

Sun exposure in the summer months is regarded as a main human source of vitamin D. Consumption of fat fish (herring, mackerel, salmon), cod liver oil and supplements are also good sources (23). At latitudes above 40° solar radiation contains too little UVB (280–320 nm) during the winter months (October to March) to produce significant amounts of vitamin D (24). Thus, higher serum levels of 25(OH)D are found in the summer than in the winter in practically all published investigations (25). Our review of published data indicates that summer values are about 70–80 nM, while typical winter values are 40–50 nM in a number of countries (25). We have found that cancer prognosis is significantly better for summer diagnosis than for winter diagnosis, and, on the background of a number of experimental and epidemiological studies reported in the literature, we have suggested that our findings are likely to be related to 25(OH)D variations through the year (24,26–29). This indicates that significant health benefits might be obtained by raising the winter level of 25(OH)D in a population to a level similar to that in the summer. This could be achieved either by exposure to sun beds or by ingestion of sufficient amounts of food and supplements containing vitamin D. Before recommending general sun bed use, one has to evaluate the vitamin D yield and the accompanying skin cancer risk of such use more thoroughly than has yet been done.

The present work was carried out with the following aims: (1) To determine whether repeated sun bed exposures,

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accumulating to a total dose of 6.75 minimal erythema doses (MEDs), from a commercial sun bed (Wolff Solarium Super Plus 100 W, Basel, Switzerland) over five weeks gave a significantly smaller improvement of the vitamin D status than repeated exposures accumulating to a total dose of 13.5 MEDs. (2) To find out whether the sun bed-induced contribution to the vitamin D status was dependent on the baseline vitamin D status. (3) To estimate the decay rate of the increased serum 25(OH)D level in groups with different baseline levels.

MATERIALS AND METHODS

Volunteers. Twenty-three healthy volunteers were included in the study, seven men and 16 women aged between 21 and 65 years. The average age was 34 years. All were living in Oslo (59°N). Most of the participants were Caucasians and had Fitzpatrick skin Types II or III, except two men with skin Type V.

The dietary vitamin D intake was estimated by using a specially designed food frequency questionnaire that was offered to all the participants at the beginning of the study. Questions about weight and height for calculation of body mass index (BMI) were included. The individual vitamin D intakes were estimated on the basis of the questionnaire. All participants were asked to stick to their normal diet during the study, to avoid any changes in vitamin D intake that might be caused by increased awareness of the problem of vitamin D deficiency.

To avoid any contribution from solar radiation, the study was conducted during the winter months (November to March), a time of the year when no vitamin D is synthesized in skin by sun exposure at our latitudes (24). None of the participants had used sun beds for at least 1 month prior to the start of the study.

The Regional Ethical Committee approved the study, and each participant gave informed consent. All completed the entire study. A pilot study had indicated that reliable trends would be obtainable even with the present low number of participants.

Protocol. The participants were split in two groups, similarly composed with regard to distribution of age, gender, BMI and vitamin D intake. The study extended over 12 weeks, including two phases: 1: intervention and observation and 2: only observation. For both groups a Norwegian summer was simulated by moderate exposures to a commercial sun bed two times per week. Individual MEDs were determined before starting the exposures (see below), to avoid any sun burns. Group A started with an exposure of 0.5 MED, and then the exposures were escalated by approximately 0.1 MED per session to reach 1 MED. Group B started with an exposure of 0.25 MED, escalating by 0.05 MED per exposure to reach 0.5 MED. In both groups the maximum exposure per session was reached at the fifth session. Exposures at this level continued up to 15 sessions, totally. After this part of the study (intervention), serum samples were collected for a 5 week observation period to determine the decay rate of serum 25(OH)D.

Ultraviolet exposure. The source of UV radiation was a commercially available and approved sun bed, equipped with Solarium Super Plus 100 W tubes (Wolff System). The spectrum given by the producer is shown in Fig. 1. The fluence rates were measured using a UV-meter (Solar Light Company Inc.) and the International Commission on Illumination (CIE) adjusted exposures were 16.4 mW cm^{-2} in UVA and 0.2 mW cm^{-2} in UVB. Figure 1 shows the spectral characteristics of the sun bed radiation compared with midsummer sun at noon in Oslo and at the Equator.

Individual MEDs were measured before the start of the study by exposing three skin areas on the anterior forearm to different doses of UV (14–19–25 min) from the sun bed. Erythema was clinically evaluated 24 h after the end of the test exposure. UV from the sun bed was administered to the whole body in incremental doses according to the group schedule described above.

Blood sampling and methods of analyses. Blood was sampled before the start of the exposure sessions and then every second week. The samples were collected in tubes, cells were removed by centrifugation and the serum was frozen to −20°C. At the end of the experiment the samples were shipped on dry ice in one batch to the Haukeland
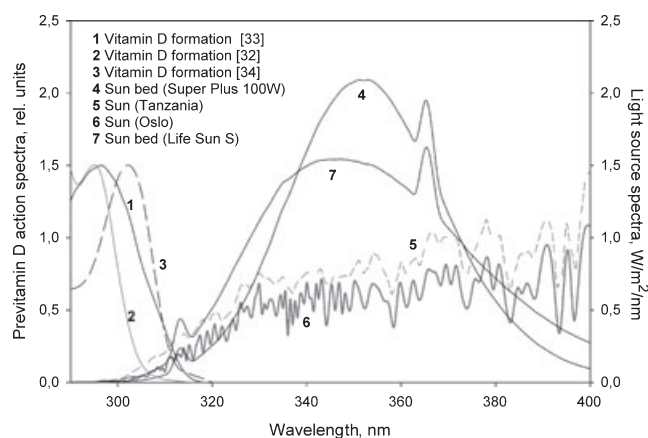
Figure 1. Spectral characteristics of the sun beds used by us and of the sun at noon midsummer in Oslo and at the Equator. Spectra relevant for vitamin D photosynthesis are also shown: That for 7-DHC absorption in an organic solution (32), that for vitamin D formation in human skin (33) and that for the yield of vitamin D and 1,25(OH)$_2$ vitamin D (they are similar) in human skin (34). To be comparable with the exposure set-up in a sun bed, the solar fluence rates are given for a plane surface perpendicular to the direction from the sun.

University Hospital, Bergen, for analysis. The 25(OH)D assay was performed according to the following method: Briefly, 100 µL serum samples were spiked with 26,27-dexadeuterium-25-hydroxy vitamin D$_3$ (Synthetica AS, Oslo, Norway) as internal standard and extracted with methanol and *n*-hexane. The *n*-hexane phase was collected, evaporated to dryness and ejected into a reverse-phase high-performance liquid chromatography system. Elution of 25(OH)D was performed with methanol/water (88:12, vol/vol, with 0.1% formic acid) and the eluate was monitored by a LC/MS-detector (LC/MSD SL; Agilent Technology, CA) equipped with a multimode ion-source. 25(OH) vitamin D$_2$, 25(OH) vitamin D$_3$ and internal standard were monitored at 395.0, 401.3 and 407.3 *m/z*, respectively, in the atmospheric pressure chemical ionization (APCI)-positive mode. The mean recovery of 25(OH) vitamin D was 77.2% (SD 3.9%) and the interassay variation was 4.9%, with a detection limit < 4 nM. Nodetectable levels of 25(OH) vitamin D$_2$ were found in the samples.

RESULTS

The spectrum of two sun beds, the one used in the present work and that used in our earlier work (30), compared with the solar spectrum at noon, midsummer in Oslo and under the Equator, are shown in Fig. 1. General characteristics of the study population are given in Table 1.

Moderate, nonerythemogenic exposures to the sun bed twice a week up to a total of 15 exposures were surprisingly efficient in increasing the serum 25(OH)D level (Fig. 2). The increase was almost the same for the two exposure patterns. The average MED was about 23 min (SD ± 3 min). The total exposure was 13.5 MEDs (5.4 h [SD ± 0.5 h]), with 1 MED in each of the last nine exposures for group A and 6.75 MEDs (2.5 h [SD ± 0.5 h]), with 0.5 MED in each of the last nine exposures for group B. Both exposure patterns gave a 25–30% increase in the 25(OH)D levels.

We studied this further and divided the data into two (Fig. 3) and three (Fig. 4) groups, based on initial 25(OH)D level as given in the figure legends and in the discussion. BMI, within the range in the present population (19–29 kg m^{-2}), had a small influence on the initial level of 25(OH)D, but not on the increase (Fig. 5).
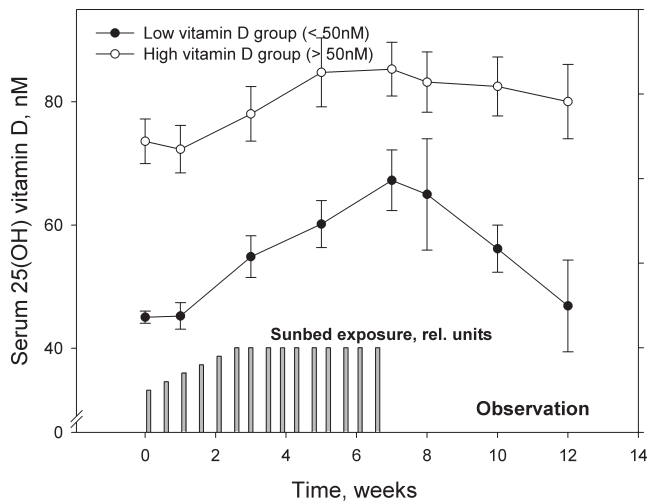
Table 1. General characteristics of the study population.

	40–50 nmol L^{-1}	50–75 nmol L^{-1}	75–100 nmol L^{-1}
Number of participants	9	8	6
Initial 25(OH)D levels, nmol L^{-1} (SD)	45.05 (±2.94)	63.9 (±6.09)	86.5 (±8.6)
25(OH)D after 15 exposures, nmol L^{-1} (SD)	67.3 (±14.7)	77.6 (±13.7)	95.6 (±14.2)
Absolute 25(OH)D increase, nmol L^{-1} (SD)	22 (±13)**	13.7 (±14)*	9 (±13.3)
Relative increase, %	49	22	11
BMI, kg m^{-2} (SD)	23.8 (±3.5)	23.07 (±3.4)	22.02 (±2)
Vitamin D intake, μg day^{-1}	5.4	3.9	6.2
Gender, % female	66.6	75	83.3

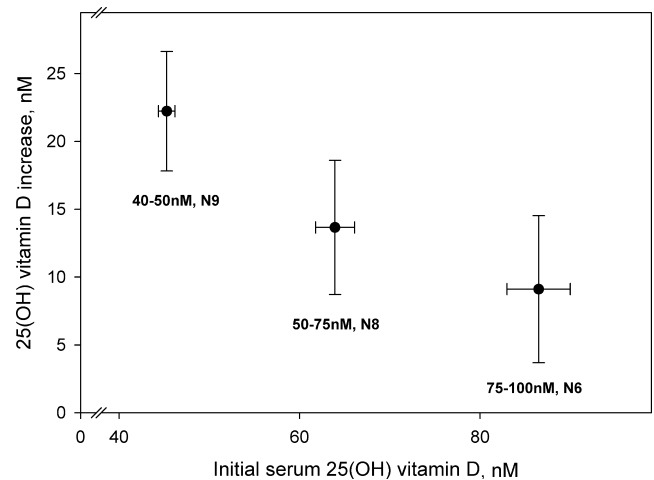25(OH)D = 25-hydroxyvitamin D; BMI = body mass index. *P = 0.022; **P = 0.0004.
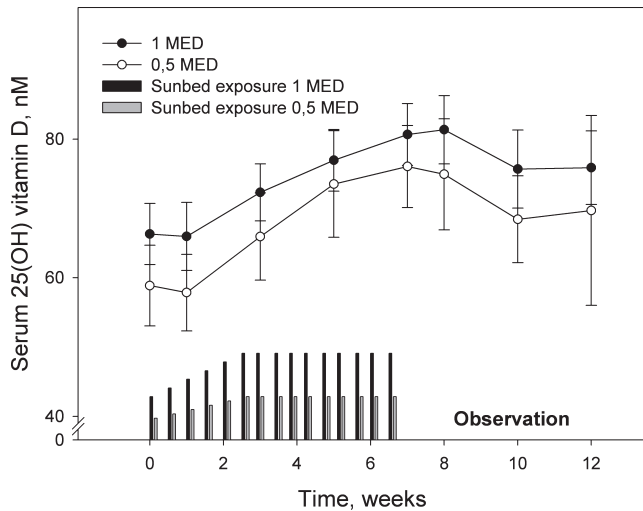
Figure 2. Level of 25(OH)D (nM) at baseline and as function of time in the intervention and observation phase for the two exposure patterns. The total exposure was 13.5 MEDs in group A and 6.75 MEDs in group B.

Figure 4. 25(OH)D increase in three groups: persons with initial levels in the regions 40–50 nM (nine persons), 50–75 nM (eight persons) and 75–100 nM (six persons).
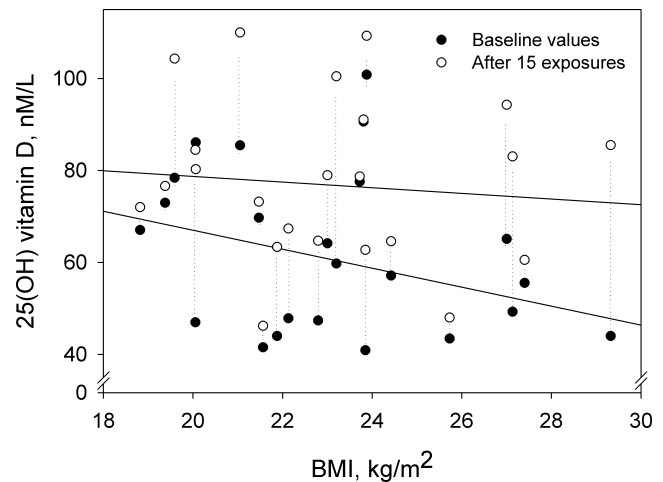

Figure 3. Level of 25(OH)D (nM) at baseline and as function of time in the intervention and observation phase for the groups with high (larger than 62 nM) and low (smaller than 62 nM) initial levels of 25(OH)D.

Figure 5. Initial and final 25(OH)D levels for persons of different body mass indexes (BMIs).

DISCUSSION

The sun bed UVB fluence rates were larger in our earlier study (30) than in the present one, but none of them are widely different from that in Equatorial sun. However, the UVA fluence rates are larger for the sun beds, notably for the one used in the present work. Several spectra relevant for photosynthesis of vitamin D are also shown in Fig. 1. The action spectra for generation of vitamin D *in vivo* are redshifted compared with the absorption spectrum of 7-dehydrocholesterol (7-DHC) in organic solutions (31). This is clearly shown

by the spectrum of Galkin and Terenetskaya (32) for solutions compared with action spectrum for human skin (33), and the spectra showing the yields of vitamin D and 1,25(OH)$_2$ vitamin D in skin (34). The latter spectra have peaks around 295–305 nm, a region where both the sun and the sun beds emit significant fluence rates. There are two reasons for the redshift. First, the penetration depth of UV radiation into human tissue decreases with decreasing wavelengths, due to absorption by chromophores like proteins, nucleic acids, urocanic acid and melanin, and to scattering, which is Rayleigh-dominated, as the majority of scattering elements are smaller than the wavelength. The cross section of pure Rayleigh scattering increases inversely with the fourth power of the wavelength, thus being 40% larger at 295 nm than at 320 nm. Secondly, the binding of 7-DHC in a lipid bilayer leads to a significant redshift (31). Without this redshift only small amounts of vitamin D would have been formed in skin by solar radiation, which contains very little radiation with wavelengths covering the 7-DHC spectrum in solution.

Our sun bed, being marketed as a ''UVA sun bed,'' gave significant contributions to the serum 25(OH)D level. It seems that even exposure pattern B (6.75 MEDs) gave saturation so that no more could be gained by increasing the total dose to 13.5 MEDs. However, as Fig. 2 shows, there is almost a linear increase up to the last exposure, so complete saturation probably did not occur. This is in contrast to our earlier work (30) which indicated that saturation might be approached as early as after 4 weeks. However, another type of sun bed—one emitting more UVB—was used in the first study, which included only 10 persons. Several investigations have indicated that larger exposures than those applied in the present work are needed before saturation occurs (35–39).

The reason for the similarity in increase for the two groups is probably that by chance the initial average level of 25(OH)D was lower in group B than in group A (Fig. 2). Thus, when all data were brought into one group and then divided in two similarly large groups on the basis of initial 25(OH)D level, one with initial levels below 62 nM (average 46 nM) and one with initial levels above 62 nM (average 72 nM), it is evident that those with low levels got more vitamin D from the exposures than those with high initial levels (Fig. 3). We studied this phenomenon in more detail and looked at the 25(OH)D increase in three groups: persons with initial levels in the regions 40–50 nM (nine persons), 50–75 nM (eight persons) and 75–100 nM (six persons) (Fig. 4). The increase in 25(OH)D was largest for the group with the lowest initial 25(OH)D level and decreased with increasing initial level. This cannot be explained by differences between the groups in BMI, in vitamin D intake or in gender composition (Table 1). Similar trends have been observed in other recent studies (40,41). In the study conducted by Carbone et al. a serial exposure to a broadband UV radiation source resulted in 170% increase in 25(OH)D levels in persons with initial 25(OH)D concentrations ≤75 nM and just 24% increase in the group with baseline levels > 75 nM (41). Other works (38,40) also showed that persons with serum 25(OH)D ≤ 30 nM respond earlier to seasonal changes in UV fluence rates. Moreover, the work by Steingrimsdottir et al. (42) showed that the amplitude of seasonal variation of 25(OH)D is highest for individuals not taking vitamin D supplements, and, therefore, having low circulating levels of 25(OH)D. Furthermore, Davie et al. (43)

found surprisingly large contributions to the vitamin D status by exposing only 600–900 cm^2 of skin to UV radiation at doses of only 3 min per day, three times per week. They even found that the 25(OH)D level reached steady state after 5–6 weeks.

It may seem that the decay of the levels of 25(OH)D after the sun bed sessions is fastest for the group with the lowest initial level (Fig. 3). This deserves further investigations, as it indicates that low 25(OH)D levels may be related to fast metabolism and degradation of vitamin D derivatives.

Body mass index seems to influence the initial level of 25(OH)D but not the increase (Fig. 5). The observation that the initial level decreases with increasing BMI is in agreement with other published investigations (44–47) and with a large yet unpublished study in our group. This can be explained by the fact that vitamin D and its precursors are lipophilic, and, therefore, partly stored in adipose tissue (47,48).

A main conclusion of our work is that small exposures to UV radiation, amounting to only 6.75 MEDs, from a commercial sun bed give large improvements of the vitamin D status. This finding is in agreement with our earlier investigation (30) as well as with the results of others (43,49,50), and may have significant health consequences. Regular use of sun beds with more than one exposure per week for 6 months or more resulted in 90% higher 25(OH)D serums values and in higher bone mineral densities (0.97 ± 0.03 vs 0.92 ± 0.01 g cm^{-2}) (39,50).

Sun beds are manufactured so as to follow the legislation in different countries. This means that the biologically weighted fluence rates have to be below a certain limit, often comparable with Mediterranean, midsummer and midday fluence rates (51). Furthermore, based on the belief that UVB is more carcinogenic than UVA (320–400 nm), according to the action spectrum of squamous cell carcinoma in mice (52), sun beds are made to emit orders of magnitude more UVA than UVB. A change in the legislation is the reason why we have used a different type of sun bed in the present than in the earlier work. Notably, the UVB/UVA ratio is lower in the present work than in earlier investigations (0.02 vs 0.039). However, even in the radiation of the present sun bed, the small UVB fraction is large enough to give summer levels of vitamin D.

As the action spectrum of vitamin D photosynthesis lies mainly in the UVB region (Fig. 1) and is similar to the DNA absorption spectrum (53), to the melanogenesis action spectrum and to the erythema action spectrum (54), or possibly slightly redshifted compared with these spectra (as argued for above), we can assume that whenever a sun bed can give erythema and DNA damage, it can also generate vitamin D. This would not be true for a sun bed emitting only UVA radiation, but even so-called ''UVA-sunbeds,'' such as our sun bed, emit small amounts of UVB.

The risk of cutaneous malignant melanoma (CMM) associated with sun bed use has been the topic of a number of investigations, as summarized in several reviews (55–58). Some investigations show a CMM-generating effect of sun bed use (59,60), while other investigations show no such effect, or even protective effects (61,62). It has been stated that the discrepancies may be related to methodological shortcomings (63,64), and that one has to wait for further results before firm conclusions can be drawn. A Norwegian investigation indicated that a relatively large melanoma risk might result from

sun bed use (60). However, it is possible that those who frequently use sun beds also expose themselves more than average to solar radiation in the summer. In construction of future sun beds and designing proper legislation, it should be kept in mind that UVA may be more CMM-generating than so far believed (65).

In view of the documented health effects of an adequate level of vitamin D, the vitamin D generating effect of sun beds should be weighted against the carcinogenic risk. We have earlier (24) estimated that the annual vitamin D-generating solar radiation dose would increase by 40–50% through a 10° southward migration, as from Tromsø to Oslo in Norway. Averaged over a year this would, under otherwise similar conditions, give a 10% improved vitamin D status. Such an increase might have a significant impact on death rates of internal cancers (4,66).

Raising winter levels of 25(OH)D up to summer levels (50 nM up to 80 nM in the Nordic countries [24]), would lead to a 22 nM higher average annual 25(OH)D level than the present one. This might be achieved by moderate sun bed exposures during the winter or by increasing the daily intake of vitamin D by 1500 IU (67), corresponding to 20 mL cod liver oil. According to the estimations of Giovannucci *et al.* (66) this would reduce the total number of cancer deaths by 29%, corresponding to a reduction in the annual number of cancer deaths in Norway by 3000 from the present level of 11 000. This is 10 times more than the number of melanoma deaths in Norway per year (about 250 at present) (68). However, before making any firm conclusion one should await more interventional investigations about the relationships between vitamin D levels and internal cancer.

REFERENCES

1. Holick, M. F. (2006) High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin. Proc.* **81**, 353–373.
2. Zittermann, A. (2003) Vitamin D in preventive medicine: Are we ignoring the evidence? *Br. J. Nutr.* **89**, 552–572.
3. Holick, M. F. (2006) Vitamin D: Its role in cancer prevention and treatment. *Prog. Biophys. Mol. Biol.* **92**, 49–59.
4. Schwartz, G. G. and H. G. Skinner (2007) Vitamin D status and cancer: New insights. *Curr. Opin. Clin. Nutr. Metab. Care* **10**, 6–11.
5. Munger, K. L., L. I. Levin, B. W. Hollis, N. S. Howard and A. Ascherio (2006) Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. *JAMA* **296**, 2832–2838.
6. Littorin, B., P. Blom, A. Scholin, H. J. Arnqvist, G. Blohme, J. Bolinder, A. Ekbom-Schnell, J. W. Eriksson, S. Gudbjornsdottir, L. Nystrom, J. Ostman and G. Sundkvist (2006) Lower levels of plasma 25-hydroxyvitamin D among young adults at diagnosis of autoimmune type 1 diabetes compared with control subjects: Results from the nationwide Diabetes Incidence Study in Sweden (DISS). *Diabetologia* **49**, 2847–2852.
7. Pittas, A. G., J. Lau, F. B. Hu and B. Dawson-Hughes (2007) The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J. Clin. Endocrinol. Metab.* **92**, 2017–2029.
8. Adorini, L. and G. Penna (2008) Control of autoimmune diseases by the vitamin D endocrine system. *Nat. Clin. Pract. Rheumatol.* **4**, 404–412.
9. Cannell, J. J., R. Vieth, J. C. Umhau, M. F. Holick, W. B. Grant, S. Madronich, C. F. Garland and E. Giovannucci (2006) Epidemic influenza and vitamin D. *Epidemiol. Infect.* **134**, 1129–1140.
10. Wallis, D. E., S. Penckofer and G. W. Sizemore (2008) The "sunshine deficit" and cardiovascular disease. *Circulation* **118**, 1476–1485.
11. Beck-Nielsen, S. S., T. K. Jensen, J. Gram, K. Brixen and B. Brock-Jacobsen (2008) Nutritional rickets in Denmark: A retrospective review of children's medical records from 1985 to 2005. *Eur. J. Pediatr.* **168**, 941–949.
12. Holvik, K., H. E. Meyer, E. Haug and L. Brunvand (2005) Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway: The Oslo Immigrant Health Study. *Eur. J. Clin. Nutr.* **59**, 57–63.
13. International Agency for Research on Cancer (2008) Vitamin D and cancer. Lyon, France.
14. Holick, M. F. (2009) Shining light on the Vitamin D—Cancer Connection IARC Report. *Derm. Endocrinol.* **1**, 4–6.
15. Garland, C. F., W. B. Grant, B. J. Boucher, H. S. Cross, C. Garland, O. Gillie, E. D. Gorham, R. P. Heaney, M. F. Holick, B. Hollis, J. Moan, M. Peterlik, J. Reichrath and A. Zittermann (2009) Open letter to IARC Director Christopher P. Wild: Re IARC Working Group Report 5—Vitamin D and Cancer. *Derm. Endocrinol.* **1**, 119–120.
16. Andersen, R., C. Molgaard, L. T. Skovgaard, C. Brot, K. D. Cashman, E. Chabros, J. Charzewska, A. Flynn, J. Jakobsen, M. Karkkainen, M. Kiely, C. Lamberg-Allardt, O. Moreiras, A. M. Natri, M. O'Brien, M. Rogalska-Niedzwiedz and L. Ovesen (2005) Teenage girls and elderly women living in northern Europe have low winter vitamin D status. *Eur. J. Clin. Nutr.* **59**, 533–541.
17. Gordon, C. M., K. C. DePeter, H. A. Feldman, E. Grace and S. J. Emans (2004) Prevalence of vitamin D deficiency among healthy adolescents. *Arch. Pediatr. Adolesc. Med.* **158**, 531–537.
18. Holick, M. F. and T. C. Chen (2008) Vitamin D deficiency: A worldwide problem with health consequences. *Am. J. Clin. Nutr.* **87**, 1080S–1086S.
19. MacFarlane, G. D., J. L. Sackrison Jr, J. J. Body, D. L. Ersfeld, J. S. Fenske and A. B. Miller (2004) Hypovitaminosis D in a normal, apparently healthy urban European population. *J. Steroid Biochem. Mol. Biol.* **89–90**, 621–622.
20. Bischoff-Ferrari, H. A., E. Giovannucci, W. C. Willett, T. Dietrich and B. Dawson-Hughes (2006) Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am. J. Clin. Nutr.* **84**, 18–28.
21. Dawson-Hughes, B., R. P. Heaney, M. F. Holick, P. Lips, P. J. Meunier and R. Vieth (2005) Estimates of optimal vitamin D status. *Osteoporos. Int.* **16**, 713–716.
22. Heaney, R. P. (2008) Vitamin D in health and disease. *Clin. J. Am. Soc. Nephrol.* **3**, 1535–1541.
23. Lu, Z., T. C. Chen, A. Zhang, K. S. Persons, N. Kohn, R. Berkowitz, S. Martinello and M. F. Holick (2007) An evaluation of the vitamin D(3) content in fish: Is the vitamin D content adequate to satisfy the dietary requirement for vitamin D? *J. Steroid Biochem. Mol. Biol.* **103**, 642–644.
24. Moan, J., A. C. Porojnicu, T. E. Robsahm, A. Dahlback, A. Juzeniene, S. Tretli and W. Grant (2005) Solar radiation, vitamin D and survival rate of colon cancer in Norway. *J. Photochem. Photobiol. B, Biol.* **78**, 189–193.
25. Moan, J., Z. Lagunova and A. C. Porojnicu (2006) Vitamin D, photobiology and relevance for cancer. In *Proceedings of the Meeting "Sunlight, Vitamin D and Health"*, pp. 33–40. House of Commons, London.
26. Porojnicu, A. C., T. E. Robsahm, A. Hansen Ree and J. Moan (2005) Season of diagnosis is a prognostic factor in Hodgkin lymphoma. A possible role of sun-induced vitamin D. *Br. J. Cancer* **93**, 571–574.
27. Porojnicu, A. C., T. E. Robsahm, A. Dahlback, J. P. Berg, D. C. Christiani, O. S. Bruland and J. Moan (2007) Seasonal and geographical variations in lung cancer prognosis in Norway. Does vitamin D from the sun play a role? *Lung Cancer* **55**, 263–270.

28. Porojnicu, A. C., Z. Lagunova, T. E. Robsahm, J. P. Berg, A. Dahlback and J. Moan (2007) Changes in risk of death from breast cancer with season and latitude: Sun exposure and breast cancer survival in Norway. *Breast Cancer Res. Treat.* **102**, 323–328.

29. Robsahm, T. E., S. Tretli, A. Dahlback and J. Moan (2004) Vitamin D$_3$ from sunlight may improve the prognosis of breast-, colon- and prostate cancer (Norway). *Cancer Causes Control* **15**, 149–158.

30. Porojnicu, A. C., O. S. Bruland, L. Aksnes, W. B. Grant and J. Moan (2008) Sun beds and cod liver oil as vitamin D sources. *J. Photochem. Photobiol. B, Biol.* **29**, 125–131.

31. Moriarty, R. M., R. Schwartz, C. Lee and V. Curtis (2008) Formation of vitamin D$_3$ in synthetic lipid multibilayers. A model for epidermal photosynthesis. *J. Am. Chem. Soc.* **102**, 4257–4259.

32. Galkin, O. N. and I. P. Terenetskaya (1999) "Vitamin D" biodosimeter: Basic characteristics and potential applications. *J. Photochem. Photobiol. B, Biol.* **53**, 12–19.

33. MacLaughlin, J. A., R. R. Anderson and M. F. Holick (1982) Spectral character of sunlight modulates photosynthesis of previtamin D$_3$ and its photoisomers in human skin. *Science* **216**, 1001–1003.

34. Lehmann, B., P. Knuschke and M. Meurer (2000) A novel pathway for hormonally active calcitriol. *Horm. Res.* **54**, 312–315.

35. Chel, V. G., M. E. Ooms, C. Popp-Snijders, S. Pavel, A. A. Schothorst, C. C. Meulemans and P. Lips (1998) Ultraviolet irradiation corrects vitamin D deficiency and suppresses secondary hyperparathyroidism in the elderly. *J Bone Miner. Res.* **13**, 1238–1242.

36. Gronowitz, E., O. Larko, M. Gilljam, A. Hollsing, A. Lindblad, D. Mellstrom and B. Strandvik (2005) Ultraviolet B radiation improves serum levels of vitamin D in patients with cystic fibrosis. *Acta Paediatr.* **94**, 547–552.

37. Reid, I. R., D. J. Gallagher and J. Bosworth (1986) Prophylaxis against vitamin D deficiency in the elderly by regular sunlight exposure. *Age Ageing* **15**, 35–40.

38. Snell, A. P., W. J. MacLennan and J. C. Hamilton (1978) Ultraviolet irradiation and 25-hydroxy-vitamin D levels in sick old people. *Age Ageing* **7**, 225–228.

39. Thieden, E., H. L. Jorgensen, N. R. Jorgensen, P. A. Philipsen and H. C. Wulf (2008) Sunbed radiation provokes cutaneous vitamin D synthesis in humans—A randomized controlled trial. *Photochem. Photobiol.* **84**, 1487–1492.

40. Edvardsen, K., M. Brustad, O. Engelsen and L. Aksnes (2007) The solar UV radiation level needed for cutaneous production of vitamin D$_3$ in the face. A study conducted among subjects living at a high latitude (68 degrees N). *Photochem. Photobiol. Sci.* **6**, 57–62.

41. Carbone, L. D., E. W. Rosenberg, E. A. Tolley, M. F. Holick, T. A. Hughes, M. A. Watsky, K. D. Barrow, T. C. Chen, N. K. Wilkin, S. K. Bhattacharya, J. C. Dowdy, R. M. Sayre and K. T. Weber (2008) 25-Hydroxyvitamin D, cholesterol, and ultraviolet irradiation. *Metabolism* **57**, 741–748.

42. Steingrimsdottir, L., O. Gunnarsson, O. S. Indridason, L. Franzson and G. Sigurdsson (2005) Relationship between serum parathyroid hormone levels, vitamin D sufficiency, and calcium intake. *JAMA* **294**, 2336–2341.

43. Davie, M. W., D. E. Lawson, C. Emberson, J. L. Barnes, G. E. Roberts and N. D. Barnes (1982) Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anticonvulsant-treated subjects. *Clin. Sci. (Lond).* **63**, 461–472.

44. Bischof, M. G., G. Heinze and H. Vierhapper (2006) Vitamin D status and its relation to age and body mass index. *Horm. Res.* **66**, 211–215.

45. Carlin, A. M., D. S. Rao, A. M. Meslemani, J. A. Genaw, N. J. Parikh, S. Levy, A. Bhan and G. B. Talpos (2006) Prevalence of vitamin D depletion among morbidly obese patients seeking gastric bypass surgery. *Surg. Obes. Relat Dis.* **2**, 98–103.

46. Reinehr, T., G. de Sousa, U. Alexy, M. Kersting and W. Andler (2007) Vitamin D status and parathyroid hormone in obese children before and after weight loss. *Eur. J Endocrinol.* **157**, 225–232.

47. Wortsman, J., L. Y. Matsuoka, T. C. Chen, Z. Lu and M. F. Holick (2000) Decreased bioavailability of vitamin D in obesity. *Am. J. Clin. Nutr.* **72**, 690–693.

48. Rosenstreich, S. J., C. Rich and W. Volwiler (1971) Deposition in and release of vitamin D$_3$ from body fat: Evidence for a storage site in the rat. *J. Clin. Invest.* **50**, 679–687.

49. Koutkia, P., Z. Lu, T. C. Chen and M. F. Holick (2001) Treatment of vitamin D deficiency due to Crohn's disease with tanning bed ultraviolet B radiation. *Gastroenterology* **121**, 1485–1488.

50. Tangpricha, V., A. Turner, C. Spina, S. Decastro, T. C. Chen and M. F. Holick (2004) Tanning is associated with optimal vitamin D status (serum 25-hydroxyvitamin D concentration) and higher bone mineral density. *Am. J. Clin. Nutr.* **80**, 1645–1649.

51. European Commission (2007) Safety of Tanning Devices for Cosmetic Purposes. Commission opinion of 27 October 2004. Available at: http://ec.europa.eu/enterprise/electr_equipment/lv/opinions.htm.

52. de Gruijl, F. R., H. J. Sterenborg, P. D. Forbes, R. E. Davies, C. Cole, G. Kelfkens, H. van Weelden, H. Slaper and J. C. van der Leun (1993) Wavelength dependence of skin cancer induction by ultraviolet irradiation of albino hairless mice. *Cancer Res.* **53**, 53–60.

53. Setlow, R. B., E. Grist, K. Thompson and A. D. Woodhead (1993) Wavelengths effective in induction of malignant melanoma. *Proc. Natl Acad. Sci. USA* **90**, 6666–6670.

54. Parrish, J. A., K. F. Jaenicke and R. R. Anderson (1982) Erythema and melanogenesis action spectra of normal human skin. *Photochem. Photobiol.* **36**, 187–191.

55. Autier, P. (2004) Perspectives in melanoma prevention: The case of sunbeds. *Eur. J. Cancer* **40**, 2367–2376.

56. Bataille, V., M. Boniol, E. De Vries, G. Severi, Y. Brandberg, P. Sasieni, J. Cuzick, A. Eggermont, U. Ringborg, A. R. Grivegnee, J. W. Coebergh, M. C. Chignol, J. F. Dore and P. Autier (2005) A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe. *Eur. J. Cancer* **41**, 2141–2149.

57. Gallagher, R. P., J. J. Spinelli and T. K. Lee (2005) Tanning beds, sunlamps, and risk of cutaneous malignant melanoma. *Cancer Epidemiol. Biomarkers Prev.* **14**, 562–566.

58. International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light, skin cancer (2007) The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. *Int. J. Cancer* **120**, 1116–1122.

59. Fears, T. R., C. C. Bird, D. Guerry, R. W. Sagebiel, M. H. Gail, D. E. Elder, A. Halpern, E. A. Holly, P. Hartge and M. A. Tucker (2002) Average midrange ultraviolet radiation flux and time outdoors predict melanoma risk. *Cancer Res.* **62**, 3992–3996.

60. Veierod, M. B., E. Weiderpass, M. Thorn, J. Hansson, E. Lund, B. Armstrong and H. O. Adami (2003) A prospective study of pigmentation, sun exposure, and risk of cutaneous malignant melanoma in women. *J. Natl Cancer Inst.* **95**, 1530–1538.

61. Bataille, V., A. Winnett, P. Sasieni, J. A. Newton Bishop and J. Cuzick (2004) Exposure to the sun and sunbeds and the risk of cutaneous melanoma in the UK: A case–control study. *Eur. J. Cancer* **40**, 429–435.

62. van der Rhee, H. J., E. De Vries and J. W. Coebergh (2006) Does sunlight prevent cancer? A systematic review. *Eur. J. Cancer* **42**, 2222–2232.

63. Autier, P. (2004) Issues about solaria. In *Prevention of Skin Cancer* (Edited by D. J. Hill, J. M. Elwood and D. R. English), pp. 157–176. Kluwer Academic Publishers, Dordrecht.

64. Gallagher, R. P., J. M. Elwood and G. B. Hill (1986) Risk factors for cutaneous malignant melanoma: The Western Canada Melanoma Study. *Recent Results Cancer Res.* 102: **38-55**, 38–55.

65. Moan, J., A. Dahlback and R. B. Setlow (1999) Epidemiological support for an hypothesis for melanoma induction indicating a role for UVA radiation. *Photochem. Photobiol.* **70**, 243–247.

66. Giovannucci, E., Y. Liu, E. B. Rimm, B. W. Hollis, C. S. Fuchs, M. J. Stampfer and W. C. Willett (2006) Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. *J. Natl Cancer Inst.* **98**, 451–459.

67. Heaney, R. P., K. M. Davies, T. C. Chen, M. F. Holick and M. J. Barger-Lux (2003) Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am. J. Clin. Nutr.* **77**, 204–210.

68. Cancer Registry in Norway (2004) *Cancer in Norway 2001*, pp. 36–37. Cancer Registry in Norway, Oslo.