Abstract and Introduction

Abstract

Exposure to ultraviolet B radiation in sunlight provides the mechanism for more than 90% of the vitamin D production in most individuals. Concern has been expressed in recent years that the widespread use of sunscreens, particularly those with high sun protection factors, may lead to a significant decrease in solar-induced previtamin D₃ in the skin, resulting in a vitamin D level which is considered insufficient for protection against a wide range of diseases. In this article the published evidence to support and to question this view is presented. It is concluded that, although sunscreens can significantly reduce the production of vitamin D under very strictly controlled conditions, their normal usage does not generally result in vitamin D insufficiency.

Introduction

As solar ultraviolet (UV) irradiation provides the means for more than 90% of the vitamin D production in most individuals, it is crucial to have sufficient sun exposure to ensure optimal levels of this vitamin. The first step in the production of the biologically active form of vitamin D [1,25-dihydroxyvitamin D₃, 1,25(OH)D] is the conversion of 7-dehydrocholesterol (also known as provitamin D) in the skin to previtamin D₃ following solar UV radiation (UVR).[1] The action spectrum for this reaction indicates that it occurs in the UVB waveband (290–315 nm) with maximum efficiency at approximately 300 nm.[2,3] Vitamin D₃ is then formed from previtamin D₃ via a gradual thermal isomerization. Vitamin D₃ leaches into the blood and is hydroxylated to 25-hydroxyvitamin D₃ [25(OH)D, calcidiol] in the liver. The final step is the synthesis of 1,25(OH)D (calcitriol) in the kidney and other organs. Calcidiol [25(OH)D] circulates in the blood and is the most accurate measure of a person's vitamin D status.

Until recently a 'normal' or sufficient level of 25(OH)D was considered to be 50–250 nmol L⁻¹ (20–100 ng mL⁻¹), insufficient 25–50 nmol L⁻¹, deficient < 25 nmol L⁻¹, excess > 250 nmol L⁻¹ and intoxication > 325 nmol L⁻¹.[1] Information has now become available to indicate that a level of at least 80 nmol L⁻¹ (30 ng mL⁻¹) might be necessary to provide the optimal and full range of the health benefits of vitamin D.[1] It has been estimated in numerous surveys that a considerable proportion of people within a community may be vitamin D deficient or insufficient, including not only the elderly but also children and young adults. Many variables are of importance in determining the extent of previtamin D₃ production in the skin as a result of sunlight exposure such as age, skin colour, clothing habits, area of skin exposed and latitude of residence in addition to the season of the year, weather and time of the day.

Protection from the sun has been advised for more than 40 years as solar UVR causes sunburn and is a recognized carcinogen. It is the major risk factor for the nonmelanoma skin cancers (NMSCs) and is implicated in the induction of malignant melanoma. Although NMSC is rarely fatal, melanoma can be and, for example, accounts currently for about 2000 deaths per year in the U.K. The incidence of each of the skin cancers is increasing year by year in populations with fair skin.[4–7] Treatment of skin cancer imposes a huge burden on national health services, estimated at greater than $800 million per year in the U.S.A., and it can be disfiguring for the patient. In addition to tumorigenesis, chronic cumulative solar UVR causes photoageing. There are also immunosuppressive effects, leading to the possibility of a lowered ability to combat microbial infections.

Changes in society in the second half of the 20th century include the fashion for white-skinned individuals to be tanned, to wear minimal clothing as soon as the sun shines and to enjoy holidays in sunny locations, frequently in another country closer to the equator. Health campaigns in several countries have sought to increase public awareness regarding the inherent dangers of sunbathing and, as part of this advice, have recommended that
Sunscreens should be used.\textsuperscript{[8–11]} These were designed to protect against sunburn rather than against skin cancer, photoageing or photoimmunosuppression but it is likely that some degree of protection against all these effects will occur. Sunscreens are either inorganic, reflecting or scattering UVR, such as zinc oxide and titanium dioxide, or organic, absorbing UVR, such as cinnamates and salicylates.\textsuperscript{[12]} They give different levels of protection against sunburn, ranging from sun protection factors (SPFs) of 6 to > 50. One worry that has been expressed about their widespread and increasing use is that they could prevent or significantly lower the solar UVB-induced production of previtamin D\textsubscript{3} in the skin and hence lead to a vitamin D-insufficient or deficient state with reduced protection against a range of diseases. Published evidence to support this view and to question it is presented below.

**Sunscreens Prevent Production of Sufficient Vitamin D**

No randomized controlled trials or longitudinal studies have been reported showing that sunscreens significantly suppress cutaneous vitamin D synthesis, but three papers published about 20 years ago provide information that this might be the case. First, Matsuoka \textit{et al.},\textsuperscript{[13]} applied ethanol or ethanol containing 5\% \textit{para}-aminobenzoic acid (PABA) to pieces of human skin prior to exposure to 30 mJ cm\textsuperscript{-2} solar-simulated radiation. Without the sunscreen, 15\% of the 7-dehydrocholesterol in the basal layer of the epidermis, the site where most is located,\textsuperscript{[14]} was converted to previtamin D\textsubscript{3}, but this reaction was totally blocked by the sunscreen. Eight white-skinned subjects were then whole-body irradiated with one personal minimum erythemal dose (MED) from Philips TL-12 lamps (emission range 280–350 nm). One hour prior to the exposure, a PABA-based sunscreen, SPF 8, was applied to the total body surface of four of the volunteers. The method of application and the amount used were not stated. By day 1 postexposure the vitamin D\textsubscript{3} concentration in the serum rose from 1·5 to 25·6 ng mL\textsuperscript{-1} in the unprotected subjects but remained at the preirradiation level in the sunscreen-protected subjects. Thus the single application of the sunscreen had prevented the production of vitamin D\textsubscript{3} although, as each group contained only four individuals, the possibility of statistical uncertainty was high. Serum 25(OH)D levels were not measured.

Secondly, 20 white-skinned patients with a history of skin cancer who, in the previous 12 months had been applying PABA sunscreen (SPF not stated) on sun-exposed parts of the body before going outdoors were compared with 20 healthy controls (members of the same household or neighbours) of similar age who had similar sunlight exposure but did not use sunscreens.\textsuperscript{[15]} Blood samples were collected during the summer. It was found that the mean 25(OH)D level in the sunscreen user group was about half of that in the control group. However, no assays of 25(OH)D were performed before the sunscreen usage started, only a single blood sample from each individual was collected, the regular use of the sunscreen was determined retrospectively by history taking and, most importantly, no method was used to check whether the patients and controls had received similar sunlight exposure over the previous year. Indeed, as all the patients had a past history of skin cancer, it is possible that they would tend to avoid direct sunlight to a greater extent than the controls. In addition, more recent surveys have shown that sunscreen users in general expose themselves more frequently and for longer periods to sunlight than nonsunscreen users.\textsuperscript{[16,17]}

Thirdly, a sunscreen with SPF 15 was applied to different body areas of untanned white subjects (phototype III) 1 h prior to whole-body UVB irradiation (Philips TL-12 lamps) of just under one personal MED.\textsuperscript{[18]} Vitamin D\textsubscript{3} levels in the serum were measured before and 24 h after the irradiation, each group consisting of four or five individuals. Sunscreen coverage over the whole body completely blocked the UVB-induced synthesis of vitamin D\textsubscript{3}, and > 19\% of the body needed to be free of sunscreen for a significant rise in serum vitamin D\textsubscript{3} to occur. Serum 25(OH)D levels were not measured.

**Sunscreens Do Not Prevent Production of Sufficient Vitamin D**

Marks \textit{et al.},\textsuperscript{[19]} undertook the first longitudinal study relating to this topic by conducting a randomized double-blind controlled trial involving 113 subjects, aged 40 years and above, in Melbourne over the early spring to the early autumn. Half of the volunteers applied sunscreen, SPF 17, to the head, neck, forearms and dorsum of the hand at least once per day starting in the morning. Instructions were given regarding the correct application of
the cream. The other half of the volunteers applied placebo cream. Each individual, as wished, could wear hats and clothing, and avoid the sun around midday. Personal sun-badges, used in the final week of the study, demonstrated that the sunscreen and the control groups were exposed to similar doses of sunlight. Blood samples were collected at the beginning and end of the study and analysed for 25(OH)D and 1,25(OH)D. The concentration of 25(OH)D rose in both groups by a similar amount, and age, sex and skin phototype made no difference to the extent of the increase. Thus sunscreen usage could not be interpreted as a risk factor for vitamin D deficiency.\textsuperscript{[20]} The concentration of 1,25(OH)D increased in the control group only, a difference which could not be explained by Marks et al.\textsuperscript{[19]} although it was noted that the mean 1,25(OH)D levels remained in the upper half of the reference range during the entire period of the study in both groups and that no subject was outside the reference range at any time. Sunscreen use prevented the development of solar keratoses, the likely precursors of squamous cell carcinomas (SCCs). Marks et al.\textsuperscript{[19]} concluded that sufficient exposure to the sun is achieved during the Australian summer to allow adequate vitamin D production in subjects who regularly apply sunscreens.

Farrerons et al.\textsuperscript{[21]} followed 24 elderly sunscreen users (mean age 71 years) and 19 controls on five occasions throughout a period of 24 months. Serum 25(OH)D and 1,25(OH)D levels were measured together with several bone markers and parathyroid hormone. All subjects were vitamin D sufficient at the start. The individuals in the sunscreen group were instructed to apply the cream (SPF 15) each morning to sun-exposed parts of the body in the spring and summer months, to avoid sun exposure around noon and to wear adequate clothing. The 1,25(OH)D levels did not change significantly in either the sunscreen or the control groups with the season of the year. The values of 25(OH)D decreased in the winter by 31–35% in the controls and by 17–40% in the sunscreen users. In the summer the serum 25(OH)D levels increased a little more (by 55% and 24% in the 2 years) in the controls than in the sunscreen users (by 35% and 33% in the 2 years). Most importantly, no secondary hyperparathyroidism developed in the winter months and no increase in the bone markers was detected in either group. In a follow-up report\textsuperscript{[22]} the bone mass of a subset from each group was evaluated over the 24-month period. No seasonal change in bone mass was observed and no significant difference in this parameter between the sunscreen and control groups occurred throughout the 24 months. It was concluded that sunscreen protection did not increase the risk of osteoporosis in elderly women. These studies were carried out in Barcelona (41°N) where solar UVR is high and the authors speculate that the sunscreen may not have been applied adequately or not to all the sun-exposed body areas.

In an examination of 381 volunteers aged 65 years and above, resident in Boston, Massachusetts, to determine why greater adiposity is associated with lower blood levels of vitamin D\textsubscript{3} and 25(OH)D, sunscreen usage was included in a questionnaire exploring sun exposure habits over a 3-month period.\textsuperscript{[23]} The percentage of body fat did not differ with sunscreen use. While hours spent outside and percentage of skin exposed were significantly and positively associated with serum 25(OH)D levels, this was not found for sunscreen use. Another study measured the impact of various lifestyle factors including sun exposure, sunscreen use, dietary and supplemental vitamin D intake and medical history, on 25(OH)D status in older adults (60–91 years).\textsuperscript{[24]} Sunscreen use was shown to be positively correlated with serum 25(OH)D levels. One explanation for this relationship is provided by Thieden et al.\textsuperscript{[17]} who demonstrated that sunscreens are used particularly as a means of avoiding sunburn on days of sunbathing with the intention to tan.

Kimlin et al.\textsuperscript{[25]} assessed serum 25(OH)D status in 124 healthy adults, aged 18–87 years, living in Queensland at the end of the winter months to find out whether some phenotypic characteristics and sun behaviour patterns were important determinants. The participants completed a questionnaire covering the previous month which included the use of sunscreens, their SPF and the body site of application. Although the association between sunscreen use and 25(OH)D levels was not statistically significant, the mean 25(OH)D level increased with increasing frequency of sunscreen use, and the participants who regularly used sunscreens not only had sufficient 25(OH)D levels but also some of the highest concentrations. These findings contrasted with other sun-protective measures, such as wearing long-sleeved shirts or long trousers, where lower 25(OH)D levels tended to be seen. Similar results were revealed in a study of photoprotective behaviour in Irish patients with cutaneous lupus erythematosus.\textsuperscript{[26]} Decreased 25(OH)D levels were only very weakly correlated with sunscreen usage but strongly correlated with sun avoidance by wearing protective clothing and limiting outdoor exposure.
In summary, the evidence described above demonstrates that, in real-life situations, the regular use of sunscreens is unlikely to affect vitamin D status adversely and, indeed, may even enhance it.

Discussion

Sunscreens were designed primarily to prevent sunburn. In humans, they also reduce the severity of solar elastosis,[27] the development of solar keratoses,[28,29] new naevi,[30] SCCs[31,32] and cutaneous photodamage,[33] and the reactivation of herpes labialis.[34] By 1984 sunscreens generally had SPFs of 4–6 but this increased to SPF 15 in the 1990s and currently higher SPFs are often preferred in many northern European countries.[35] Indeed, a sunscreen of SPF 30 is recommended for use in some official health guidelines,[36] and advice from the World Health Organization and other health agencies stresses the need for re-application at regular intervals.[37]

By definition sunscreens do not block all UVR but allow the transmission of a fraction of incident UVB photons, equal to 1/SPF. For example, for a product of SPF 30, one-thirtieth or 3.3% of the erythemal UV radiation, the majority of which is UVB, is transmitted. What is probably more relevant is that sunscreens are rarely, if ever, applied at the concentration, 2 mg cm\(^{-2}\), that provided the tested level of protection. Most commonly individuals use only about 0.5 mg cm\(^{-2}\).[16,17,38,39] Recently Faurschou and Wulf[40] demonstrated that the relationship between the amount applied and the SPF was nonlinear. Thus a sunscreen with stated SPF 16 is reduced to SPF 2 when 0.5 mg cm\(^{-2}\) is used. Furthermore, the coverage is not even as sunscreens tend to accumulate in the furrows of the stratum corneum while leaving the ridges relatively unprotected.[41] The frequency of re-application may also be inadequate,[42] especially if the individual is sweating, coming into contact with sand, swimming or engaged in vigorous activity.[43] Finally, it is unrealistic to imagine that absolutely all exposed parts of the body will be protected by the sunscreen. For example, Diffey[42] reported that fewer than half the subjects questioned about their sunscreen habits applied the cream to all uncovered body sites. Similarly, Robinson et al.[44] found that adults using sunscreen on their children in the summer months frequently missed the ears, neck, feet and legs.

Attempts have been made to estimate personal exposure to sunlight, such as by using UV-sensitive film badges or electronic dosimeters. One series of studies in Denmark, based on such an approach, found that the yearly UV dose was highly variable between individuals and correlated with days of sunbathing/exposing the upper body and with participation in outdoors sports and gardening.[45,46] In the six winter months, 10.5% of the annual ambient UV dose was received by indoor workers but this was increased markedly by sunshine holidays outside Denmark.[47] It was concluded that no photoprotection is required during the winter months in Denmark or during winter holidays above 45°N, but sun protection measures are required all year round at lower latitudes, particularly on days when risk behaviour occurs.

Most recently Diffey[48] has provided a behavioural model based on parameters that affect personal erythemal behaviour. He noted particularly the increasing trend for northern Europeans to choose holiday destinations in areas of low latitude, a societal change that will significantly increase the overall annual UV dose received. This period of high UV exposure is likely to be of benefit in improving the vitamin D status of the individual in the short term, but could be the reason for the observed increase in skin cancer development. Therefore the use of protective measures, including sunscreens, is considered of particular benefit at such times.

Gilchrest[49] has demonstrated the relationships between UV dose and sunburn, suntan, DNA photoproducts and previtamin D\(_3\) in the skin. For sunburn and suntan, the response is dose dependent above a threshold until, at large doses, blistering and peeling occur. For the DNA photoproducts, the response increases linearly from very small to very large UV doses. For previtamin D\(_3\) formation, the amount increases linearly at small UV doses but plateaus at doses below 1 MED. This is because higher UV exposure results in the conversion of previtamin D\(_3\) to the inactive photoproducts, luminsterol and tachysterol.[1] Thus the efficiency of previtamin D\(_3\) production is higher than the generation of erythema so that exposure to suberythemal doses of solar UVR allows the synthesis of previtamin D\(_3\) in the skin without causing reddening.

Conclusions
Although sunscreens could almost entirely block the solar-induced production of cutaneous previtamin D$_3$ on theoretical grounds or if administered under strictly controlled conditions, in practice they have not been shown to do so, as summarized above. This is mainly due to inadequacies in their application to the skin and because people using sunscreens may also expose themselves to more sun than nonsunscreen users. However, as the advantageous properties of vitamin D for the prevention of an increasing list of diseases, including bone deformities, several autoimmune diseases and internal cancers and various viral infections, are becoming apparent, care should be taken not to limit sun exposure unduly in daily life. The adoption of what might be termed a sensible approach is advocated so that circulating 25(OH)D is maintained at what is considered a sufficient level. Diffey[50] and Thieden et al. [17] have shown that, for north European populations, much of the high dose-rate exposure which largely accounts for the harmful effects of solar UVR occurs during recreational activities, particularly during sunshine holidays. These represent the times when the use of sunscreen would be of most benefit rather than application daily all year round to all exposed skin.

References


Conflicts of interest

None declared.