Some Light on the Photobiology of Vitamin D

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In this issue, Bogh et al. report a study that begins to address the important public health question of skin surface area and UVB exposure dose, related to erythema, necessary to achieve a given level of vitamin D status. They demonstrate the importance of baseline vitamin D status in conducting such studies. A smaller substudy suggests that skin pigment is not a barrier to vitamin D photosynthesis.


Introduction

The benefits of vitamin D and how best to obtain and maintain optimal levels are highly controversial topics that have enormous potential implications for human health. Nature has provided humans with two sources of vitamin D: solar UVB radiation and diet. However, most foods provide very little vitamin D, especially in typical Western diets. The exception is oily fish. Manmade interventions include food fortification in some countries, supplementation, and the use of tanning devices with UVB. Any discussion on vitamin D status should be based on vitamin D status performed in the same laboratories to minimize experimental variation.

The significance of this study

The study by Bogh et al. (2010, this issue) is a welcome and timely addition to our knowledge in the photobiology field. The baseline data show that 85% of 182 people screened for the study were either vitamin D (25(OH)D) insufficient (67% < 50 nmol l\(^{-1}\)) or deficient (18% < 25 nmol l\(^{-1}\)) in Denmark at 56°N during the winter. The limitation of these definitions of vitamin D status is discussed in this issue's Editorial, by Reddy and Gilchrest (2010). The backs and chests of volunteers with skin types I–VI were exposed to three standard erythema doses (SEDs) of UVB for 4 days over 1 week. The UVB source used was very rich in the spectral region that converts 7-dehydrocholesterol to pre–vitamin D in the skin. The sites exposed represent

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- 25% body surface area as estimated by the approach of Augustsson et al. (1992).

It should be stressed that an SED is independent of personal UVR sensitivity and is a measure of erythemal efficacy that is independent of source spectrum. A dose of 3 SEDs is equivalent to about 1 minimal erythema dose (MED) in skin types I/II and would be suberythemogenic (approximately 0.5 MED) in skin types III/IV (Harrison and Young, 2002). The authors show that baseline 25(OH)D is the determinant of the response to UVB exposure. The lower the baseline level, the greater the response, which supports homeostatic control. The regression line in Figure 3 in the article by Bogh indicates that individuals in the insufficient/deficient baseline range had an increase of 20–30 nmol l−1 25(OH)D, whereas those who were insufficient into sufficiency and those who were deficient into insufficient. However, it must be stressed that a relatively large surface area was exposed, and, at least in skin types I/II, the exposure doses would have been approximately erythemogenic.

The UVR doses used in the study by Bogh and co-workers should be placed into context. The same authors have performed several studies in which UVR exposure was measured over extended periods in different populations in spring/summer in Denmark (56°N) using time-stamped personal electronic dosimeters. In people working indoors without engaging in sun-seeking behavior, the median daily dose was 0.3 SED (range: 0–3.9) on working days and 0.6 SED (range: 0.1–3.5 SED) on their days off (Thieden et al., 2004). The measurements were taken on subjects’ wrists, and it is estimated that the dose to the face is twofold greater. Thus, the doses used in Bogh and colleagues’ study were 5–10 times higher than median wrist exposures at the same latitude. Not surprisingly, higher daily exposures have been measured in Queensland, Australia, with, for example, home workers in Brisbane (27.4°S) having weekday shoulder exposure medians of 2.0–8.0 SEDs, depending on the time of year. Outdoor workers at the same latitude showed values of 3.0–10.0 SEDs (Parisi et al., 2000). It has been estimated that the average American is exposed to about 250 SEDs per working year, mostly in the spring and summer (Godar et al., 2001). This can be increased by 78 SEDs (i.e., about 30%) with a 3-week vacation (i.e., by 3.7 SEDs per day). It is perhaps surprising that even studies in sunny climates have demonstrated suboptimal vitamin D status. This conundrum remains to be investigated and explained.

It is often said that short solar exposures to the face and the back of the hands are adequate to maintain optimal vitamin D status, but this does not seem to have been experimentally verified. Using the technique of Augustsson et al. (1992), this would be equivalent to ~10% of the body surface and would increase to ~20% if the lower arms are included, which is still less than the ~25% surface area in Bogh and colleagues’ study. Whether this is sufficient with lower UVR doses, which are more typical of daily exposure at given latitudes, over a longer period of time, remains to be tested under laboratory and/or field conditions. In this context it should also be noted that an SED of solar UVR will be less effective at vitamin D synthesis than an SED from the very UVB-rich source used in this study. This is because UVA in sunlight makes a much greater contribution to erythema than with the source used by Bogh et al.

Skin color and vitamin D synthesis

Of particular interest is the substudy on the effect of pigmentation (see Table 2 in the article by Bogh et al.) on vitamin D synthesis; people with darker skin tend to have suboptimal vitamin D status. Although the sample size is small (n = 9 pairs matched with similar baseline 25(OH)D), the data indicate that skin type and measured pigmentation have no effect on the synthesis of vitamin D after exposure to the same fixed doses of UVB; this means that from an erythemal (MED) point of view the darker skin types, which included V and VI, had lower doses. This study should be confirmed with a larger sample size, and broadened in its remit, but it calls into question much of the dogma about the relationship between pigmentation and vitamin D status, and perhaps even the hypothesis that vitamin D was a major factor in the evolution of skin color (Yuen and Jablonski, 2009). However, the data of Bogh et al. are in contrast with those recently published by Armas et al. (2007) in a larger study. Armas et al. exposed 90% of the body surface area three times per week for 4 weeks. The doses given to skin types I/II would be expected to be in the MED range, and doses up to fourfold greater were given to individuals with darker skin types. The estimated increase of 25(OH)D in skin types I/II for a dose of 30 mJ/cm² over 4 weeks was comparable to that obtained in 1 week in Bogh and colleagues’ study. Higher doses were required for darker skin types. Thus, overall, the outcomes of the two studies, with very different designs, are contradictory. However, it should be noted that the study population of Armas et al. (2007) indicated a relationship between skin color and baseline 25(OH)D, with higher values for fairer skin types. The current study shows that this difference in baseline 24(OH)D levels could have influenced the outcome.

Clinical Implications

• Baseline 25(OH)D is a determinant of UVB-induced vitamin D synthesis.
• Vitamin D photosynthesis is independent of skin pigmentation for a fixed UVB dose and similar baseline 25(OH)D level.
• Is adventitious solar exposure of face and hands sufficient to maintain vitamin status?
were at the high end of suberythemal. This UVR protocol was equivalent to a vitamin D dose of 250 µg/day, which is 10,000 international units. A level of about ~100 nmol 1\(^{-1}\) was reached at 3 weeks, with about 70 nmol 1\(^{-1}\) reached in 2 weeks. This daily supplement dose is 10 times higher than that recommended by the US Department of Health and Human Services and the US Department of Agriculture (Johnson and Kimlin, 2006).

Much of the advice pertaining to “safe sun” is based on the prevention of erythema because it is a readily accessible clinical readout, and sunburn is a risk factor for malignant melanoma in susceptible skin types. It is possible to compare, in theory, the relative risks and benefits of solar exposure using action spectra (wavelength dependence) for erythema and the synthesis of pre–vitamin D (not 25(OH)D) as biological weighting functions with solar spectra with different UVB/UVA ratios. The amount of UVB increases with the height of the sun, which is dependent on latitude, season, and time of day. Such calculations indicate that the optimal benefit-to-risk ratio occurs when the sun is high in the sky (Sayre and Dowdy, 2007), which is when people are advised to avoid the sun (e.g., about noon). These calculations are based on action spectra, which are likely to have large margins of error, and it would be desirable to test these results under field or laboratory conditions using 25(OH)D as the readout.

Understanding the relationship among UVR spectrum, skin area and exposure dose, skin color, tanning, photoprotection, and vitamin D outcome. Some of these issues in the context of risk/benefit are currently being investigated in a multinational European Community–funded project, “ICEPURE: The Impact of Climatic and Environmental Factors on Personal Ultraviolet Radiation Exposure and Human Health” (see http://www.icepure.eu for details). Furthermore, we need a much better understanding of the relationship between the maintenance of vitamin D status by UVB versus diet/supplementation and their interactions.

CONFLICT OF INTEREST
The author states no conflict of interest.

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See related article on pg 563

Cutaneous T-Cell Lymphoma: Two Faces of the Same Coin
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Primary cutaneous anaplastic large-cell lymphoma (C-ALCL) and cutaneous peripheral T-cell lymphoma not otherwise specified (C-PTL-NOS) are cutaneous T-cell lymphomas with distinct clinical behaviors. Whereas C-ALCL has a favorable prognosis with frequent spontaneous disease regression, C-PTL-NOS runs a more aggressive course. The molecular pathogenesis of these cutaneous T-cell lymphoma types has not yet been studied in detail. In this issue, van Kester et al. report new imbalances that could contribute to our understanding of the differences between these two lymphoma types.


Cutaneous T-cell lymphomas (CTCLs) are non-Hodgkin’s lymphomas characterized by the clonal proliferation of skin-homing mature T lymphocytes. The

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