Sun exposure and vitamin D sufficiency[1–4]

Barbara A Gilchrest

ABSTRACT

Ultraviolet radiation is a carcinogen that also compromises skin appearance and function. Because the ultraviolet action spectra for DNA damage, skin cancer, and vitamin D_3 photosynthesis are identical and vitamin D is readily available from oral supplements, why has sun protection become controversial? First, the media and, apparently, some researchers are hungry for a new message. Second, the controversy is fueled by a powerful special interest group: the tanning industry. This industry does not target the frail elderly or inner-city ethnic minorities, groups for whom evidence of vitamin D_3 insufficiency is strongest, but rather fair-skinned teenagers and young adults, who are at highest risk of ultraviolet photodamage. Third, evolution does not keep pace with civilization. When nature gave humans the appealing capacity for cutaneous vitamin D_3 photosynthesis, life expectancy was <40 y; long-term photodamage was not a concern; and vitamin D_3 deficiency, with its resulting skeletal abnormalities (rickets), was likely to be fatal in early life. In the 21st century, life expectancy approaches 80 y in developed countries, vitamin D_3 is available at the corner store, and the lifetime risk of skin cancer is 1 in 3 among white Americans. Medical and regulatory groups should avoid poorly reasoned, sensationalistic recommendations regarding unprotected ultraviolet exposure. Instead, they should rigorously explore possible cause-and-effect relations between vitamin D_3 status and specific diseases while advocating the safest possible means of ensuring vitamin D_3 sufficiency. *Am J Clin Nutr* 2008;88(suppl):570S–7S.

INTRODUCTION

The media and certain elements within the biomedical research community have created a controversy regarding the allegedly conflicting goals of sun protection and skin cancer prevention on the one hand and achieving optimal vitamin D homeostasis on the other hand. I will attempt to distinguish this pseudo-controversy from the true controversy surrounding the rather poorly documented health benefits of very high vitamin D concentrations, however achieved.

The curious and somewhat elusive basis of the pseudo-controversy lies in the often unstated assumption that vitamin D concentrations, specifically those of the inactive pre-hormone 25-hydroxyvitamin D [25(OH)D] that is measured in serum, are best achieved from increased sun exposure, which enhances the cutaneous photosynthesis of vitamin D within the irradiated epidermis. This assumption has framed discussions in the popular press and on the Internet, even though virtually all intervention studies suggesting a benefit for increasing the conventional "normal" or "sufficient" 25(OH)D concentration in specific population groups have examined the effect of oral vitamin D supplements, not increased exposure to sun or other ultraviolet (UV) sources (1), and have shown that vitamin D obtained from diet or supplements can fully substitute for vitamin D synthesized in the skin. This formulation of the debate also fails to acknowledge that the major motivation for sun exposure in the population at large is tanning, not improved general health. Thus, reports continue on the "debate" between professional groups with primary interests in skin health versus endocrinologic health, often where no such debate exists, creating confusion among the general public regarding recommended health behaviors. I briefly review these complex areas, but principally seek to explain the controversy that continues to dominate media coverage and, more recently, health policy deliberations.

ULTRAVIOLET RADIATION CAUSES MELANOMA AND NONMELANOMA SKIN CANCER

UV radiation is a proven carcinogen (2) that is responsible for most of the estimated 1.3 million skin cancer cases in the United States each year (3), which account for more than one-half of all human malignancies. Experienced clinicians and epidemiologists have long suspected that UV irradiation has a causal role in both nonmelanoma skin cancer and melanoma. Studies of hairless mice and other animal models have demonstrated this relation repeatedly since the 1920s (4, 5). Particularly for squamous cell carcinomas, the relation is direct, with more UV irradiation resulting in earlier onset and higher prevalence of cancers in both mice and humans (4, 6). A direct cause-and-effect relation for UV irradiation and basal cell carcinomas has also been documented in a mouse model (7). Although the dose-response relation between UV irradiation and melanoma is less obvious than for nonmelanoma skin cancer, at least in humans, studies have documented a cause-effect relation in multiple animal models (8, 9). In addition, patients with the rare disorder xeroderma pigmentosum, caused by a mutation in 1 of 8 DNA repair enzymes

[1] From the Department of Dermatology, Boston University School of Medicine, Boston, MA.

[2] Presented at the National Institutes of Health conference "Vitamin D and Health in the 21st Century: an Update," held in Bethesda, MD, September 5-6, 2007.

[3] Supported by discretionary departmental resources.

[4] Address reprint requests to BA Gilchrest, Department of Dermatology, Boston University School of Medicine, Boston, MA 02118. E-mail: bgilchre@bu.edu.

Am J Clin Nutr 2008;88(suppl):570S–7S. Printed in USA. © 2008 American Society for Nutrition

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

required to correct UV-induced DNA damage, develop nonmelanoma skin cancers and melanomas at least 1000 times as frequently as the general population beginning early in life, even when they attempt to avoid all sun exposure (10).

PUBLIC ATTITUDES TOWARD SUN EXPOSURE

In 1903, Niels Ryberg Finsen received the Nobel Prize for observing that sun exposure was therapeutic for cutaneous tuberculosis (11), and the idea that UV radiation exposure was healthful rapidly took hold among the public (12). In the 1920s, Coco Chanel championed the idea that sun tanning was glamorous (13). Like many of her pronouncements, the concept of a tan's attractiveness became embedded in the public psyche and remains there to this day, nearly a century later, despite the revised medical and scientific perception of a tan as a DNA damage response (14) and widespread appreciation that UV radiation often leads to skin cancer (15).

The public perception that sunbathing is pleasant and that a suntan is attractive continues to motivate many people, especially teenagers and young adults, to attempt to tan their skin (16). These young people have a well-documented inability to imagine themselves being affected by photoaging and skin cancer when they become middle-aged or elderly.

ULTRAVIOLET ACTION SPECTRA AND BIOLOGICAL RESPONSES

In the 1980s, studies of healthy human volunteers and multiple narrow-band UV light sources determined the relative efficacy of different wavelengths of light in producing sunburn and suntan (17) as well as epidermal DNA damage (18). The action spectra for all these responses are strikingly similar, with peak efficacy in the UVB portion of the spectrum (≈290–300 nm) and efficacy reduced by approximately an order of magnitude at 313 nm (still in the UVB range) and by 4–5 orders of magnitude by 400 nm, the beginning of the visible spectrum (17, 18). An overlapping group of researchers determined the action spectrum for vitamin D photosynthesis in skin in the same manner and found it to be extremely similar, also peaking at ≈300 nm and falling off exponentially with longer wavelengths of light (19; **Figure 1**). The virtual identity of these multiple action spectra implies that DNA damage is responsible for tanning [experiments have confirmed this relation (14)] and that vitamin D photosynthesis cannot occur in the absence of DNA damage, even though vitamin D production is a consequence of UV effects on cell membranes rather than on DNA itself (20).

Formation of DNA photoproducts is linear with UVB dose over a very wide range (18). In contrast, pre-vitamin D conversion to the inactive photoproducts lumisterol and tachysterol balances vitamin D photosynthesis (conversion of 7-dehydrocholesterol to pre-vitamin D) (20). Hence, the concentration of pre-vitamin D reaches a maximum value after a relatively short UV exposure, less than one minimal erythema dose, and further UV exposure results only in more extensive conversion of the pre-vitamin to inactive metabolites (20). Following the formation of pre-vitamin D in the skin, gradual thermal isomerization of this compound occurs, yielding vitamin D. This vitamin D gradually leaches into the circulation, and the liver and kidney sequentially hydroxylate the vitamin into the active hormone 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] (20). The different UV dose-response relations for these biological endpoints are shown in **Figure 2**, which is derived from a literature review and not actual data.

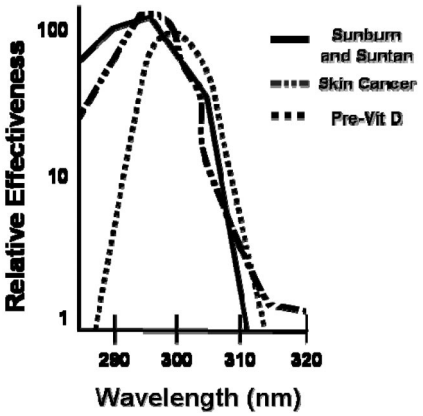

FIGURE 1. Ultraviolet (UV) action spectra for major biological responses, as determined in human volunteers by use of monochromatic light sources. Research has shown that sunburn, peaking 12–24 h after UV exposure, and suntan, peaking after 3–5 d, have virtually identical action spectra (17). UV-induced DNA photoproducts, determined identically but immediately after exposure, also display the same wavelength dependency (18), and investigators have extrapolated these data to define the action spectrum for nonmelanoma skin cancer in humans by de Gruijl (20). Pre-vitamin D (Pre-Vit D) synthesis deduced from increases in serum 25-hydroxyvitamin D concentrations over several days after UV exposure is very similar (1, 21). Modified from Wolpowitz & Gilchrest (1), as originally adapted from Matsuoka et al (22), de Gruijl (20), and Parrish et al (17).

SKIN PHOTOTYPE INFLUENCES ACUTE AND CHRONIC ULTRAVIOLET RADIATION RESPONSES

The content of epidermal melanin, a large polymer that efficiently absorbs photons across the entire UV and visible light range, and a related but less well understood set of determinants (termed *phototype*) substantially determine the effects of UV radiation on human skin (23). An individual's phototype reflects the extent of sunburning versus subsequent tanning after an initial moderate sun exposure after a long period of little or no exposure (27; **Table 1**). Phototypes strongly affect the acute and chronic risks of UV exposure and the rate of vitamin D photosynthesis (**Figure 3**).

Phototype I or II skin burns readily with a first moderate UV exposure and then tans minimally, if at all (23, 27). Persons with this type of skin achieve maximal vitamin D photosynthesis rapidly after, for example, ≈2–8 min of midday spring or summer sun exposure in New York or Boston and only slightly longer in Alaska or Scandinavia (28). With longer and repeated sun exposures, such persons suffer very substantial DNA damage that is eventually manifested as photoaging and skin cancer. Persons with phototype III skin, who commonly have a reasonably light baseline complexion, experience DNA damage and produce vitamin D at similar rates to persons with phototype I or II skin after a first UV exposure, but burn less and tan more readily (23, 27). With multiple exposures, the tanning response dominates, reducing the rate of vitamin D photosynthesis. After comparable UV exposure, persons with phototype III skin have considerably less cumulative DNA damage and hence less severe photoaging and less skin cancer risk than do those with phototype I or II skin (23). Constitutively high epidermal melanin content protects persons with phototype VI skin, who often have African

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

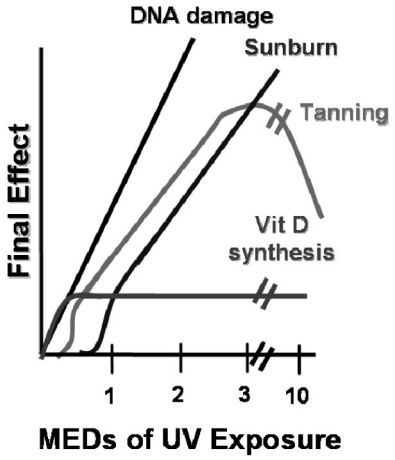

FIGURE 2. Ultraviolet (UV) radiation dose relations for sunburn, suntan, DNA photoproduct (thymine dimer) formation, and vitamin (Vit) D photosynthesis. Sunburn and suntan reactions become clinically apparent after a threshold or greater UV dose [in the case of sunburn, a minimal erythema dose (MED) by definition] after a considerable delay. The time to peak response is dose dependent, occurring at ≈12–24 h for sunburn and 2–5 d for suntan (23). Larger doses result in more intense peak reactions in a roughly linear fashion, with the slope of the lines largely genetically determined. At very high UV doses, blistering obscures sunburn and desquamation (peeling) obscures tanning. In contrast, DNA photoproduct formation is instantaneous and increases linearly across very small to very large UV exposures, with epidermal melanin content determining absolute amount. Few studies have investigated the rate of DNA photoproduct removal and the inversely related rate of mutation (24, 25) as a function of UV dose. The graph does not show these rates. The dose response for vitamin D synthesis increases linearly at small UV doses but differs strikingly from the other curves in that it reaches a plateau at doses well below the threshold dose for erythema (21). Pre-vitamin D forms rapidly, with excess compound converted to inactive metabolites. Remaining pre-vitamin D then thermally isomerizes over several hours to vitamin D, which enters the circulation gradually over several days and is hydroxylated in the liver to 25-hydroxyvitamin D, the conventionally measured but still inactive storage form of the vitamin (26). The plotted slopes for all curves are the author's arbitrary representations based on a review of multiple publications and not on actual measurements.

or aboriginal ancestry, from initial DNA damage. These persons do not sunburn after moderate UV exposure (23) but also photosynthesize relatively limited amounts of vitamin D because of UV absorption by melanin rather than other cellular targets (29). With repeat exposures, such persons tan darkly and have modest cumulative DNA damage and thus minimal photoaging and skin cancer risk, but also far less vitamin D synthesis per sun exposure than in persons with a lighter complexion (29).

TABLE 1
Skin phototypes

Phototype	Reaction to sun exposure[1]
I	Always burn, never tan
II	Burn slightly, then tan slightly
III	Rarely burn, tan moderately
IV	Never burn, tan darkly
V	Asian or Hispanic skin[2]
VI	Black skin[2]

[1] Reaction to 30 min of direct exposure after a long period of no sun exposure, eg, on the first warm day of spring.

[2] The original Fitzpatrick classification (27) defined these groups by racial heritage alone but not all individuals who identify themselves as members of these groups have more natural ultraviolet protection than do whites.

THE PSEUDO-CONTROVERSY

In recent years, numerous newspaper reporters, freelance journalists, and television news anchors have reported on the "medical controversy" that pits the unwanted effects of acute sunburn, photoaging, and skin cancer against both well-established and postulated benefits of vitamin D photosynthesis. These reports rarely note that sun exposure also produces tanning, at least in persons genetically capable of tanning, which is a cosmetic and lifestyle goal of many viewers or readers. Simplistically stated, the question posed by these articles and reports is: should the public maximize vitamin D levels through intentional UV exposure to reduce their risk of internal cancers, hypertension, diabetes, multiple sclerosis, and a litany of other disorders that some believe are due in part to "insufficient" vitamin D levels (28)? By framing the issue in this way, the media reports ignore the fact that people can obtain ample vitamin D from a combination of diet, supplements, and incidental protected sun exposure (30).

Reports often cite studies that measured low or low-normal concentrations of vitamin D in darkly pigmented individuals, such as inner-city minority groups, or among the frail elderly to justify promoting unprotected sun exposure. However, such coverage rarely notes that these at-risk groups have inefficient cutaneous vitamin D photosynthesis. In darkly pigmented people, melanin absorbs the UV photons that generate vitamin D (29), and in the elderly, their thinned epidermis may contain less 7-dehydrocholesterol, the cell membrane constituent that UVB converts to pre-vitamin D (30, 31). Such media coverage also fails to note that population groups most attracted to sunbathing—healthy, white teenagers and young adults, including many fair-skinned individuals who tan poorly (16)—are also at lowest risk of vitamin D insufficiency, yet at greatest risk of long-term photodamage.

A recent study (32) of a convenience sample of 93 healthy young adults recruited from the University of Hawaii and a Honolulu skateboard shop questioned the frequently suggested serum 25(OH)D sufficiency cutoff of 75 nmol/L. The investigators recruited these prototypic "surfer dudes" [mean age, 24 y; mean body mass index (in kg/m^2), 23.6] on the basis of a self-reported minimum outdoor sun exposure of 15 h (mean, 29 h) per week during the preceding 3 mo; 40% reported never using sunscreen, and the group overall reported an average of 22.4 h per week of unprotected sun exposure. All were clinically tanned. Nevertheless, the group's mean 25(OH)D concentration, measured by 2 standard techniques (HPLC and radioimmunoassay), was 79 nmol/L, and 51% had a level below the suggested 75-nmol/L cutoff for sufficiency (32). The study group was multi-racial, but even among the 37 white subjects, the mean value was only 92.8 nmol/L and the highest value was 155 nmol/L (32). These data suggest that a public health goal of >75 nmol/L, not to mention >150 nmol/L, for the entire population might be unachievable by sun exposure.

That article also highlights a little-emphasized aspect of vitamin D insufficiency. Specifically, most persons with 25(OH)D concentrations <75 nmol/L have no detectable disease or health problems and probably never will. They appear perfectly healthy. Instead, the definition relies completely on statistical associations between a low vitamin D concentration and one or (sometimes) more diseases, a definition that is variably and imprecisely articulated in the literature (1), all of which affect only

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

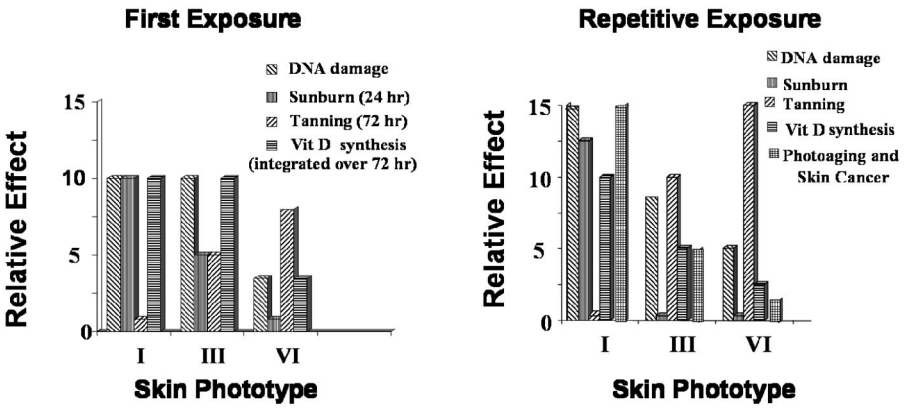

FIGURE 3. Effect of skin phototype on specific ultraviolet (UV) radiation responses. The graph shows relative consequences of first and multiple frequently spaced UV exposures on individuals of different complexion and genetic endowment by bar heights. These are the author's arbitrary representations based on a review of multiple publications and not on actual measurements.

a small minority of sufficient or insufficient groups. This suggests that the great majority of persons receive no detectable (at least no detected) benefit from a 25(OH)D concentration >75 nmol/L and, conversely, no harm from a lower level. Even more curious, in many instances, the statistical associations on which the insufficient status is based are not with measured 25(OH)D concentrations but instead with presumptive correlates such as insolation (amount and intensity of incident UV irradiation) in the general geographic region of residence. Latitude, altitude, season, cloud cover, smog, and other variables affect insolation, which is generally high near the equator and low near the poles; and lifestyle choices introduce enormous variation in sun exposure even among individuals in identical climates.

The safe sun position, as articulated by the American Academy of Dermatology (33) and other professional dermatologic organizations for many years, is based on the irrefutable facts that UV irradiation causes nonmelanoma skin cancer, melanoma, and photoaging; the only established health benefit of UV irradiation is vitamin D photosynthesis; and vitamin D can be obtained from the diet or from oral supplements. These organizations therefore recommend lifelong sun protection, especially for fair-skinned individuals at high risk of photodamage (1).

THE TRUE CONTROVERSY

The real controversy is whether increasing a person's conventionally normal serum 25(OH)D concentration has health benefits, as some epidemiologic studies have suggested but prospective randomized studies have not confirmed (1, 33). A thorough discussion of the quality and consistency of the epidemiologic and observational data, which some have interpreted to support a health benefit of serum 25(OH)D concentrations far above those associated with normal skeletal maintenance, is available elsewhere (1) and is beyond the scope of this discussion.

A recent example is illustrative. Several much-referenced reports link colorectal cancer incidence (26, 34, 35) to low vitamin D concentrations within the conventional normal range or a presumptive proxy, little sun exposure, which is usually based on residence in a poorly insolated area, as noted above. Although other epidemiologic or observational studies of similar size and design (grade B, level 2 or 3 in the hierarchy of evidence-based medicine; 36) found no statistical relation or even an inverse relation between sun exposure and colorectal cancer or closely related diseases (37–41), the popular media coverage of the topic has selectively and prominently cited the positive reports at the suggestion of interviewed "experts."

However, a prospective, randomized, placebo-controlled trial (grade A, level 1 for medical decision making; 36) of vitamin D supplementation (400 IU/d) for 7 y or longer involving >36 000 postmenopausal women found no relation between colorectal cancer risk (incidence or mortality; tumor grade, stage, or size) and supplement use, total vitamin D intake, or amount of sun exposure (crudely and indirectly calculated, as in the positive epidemiologic studies; 42). Although the investigators found an inverse correlation with baseline serum 25(OH)D concentrations, they found no indication that increasing initially low vitamin D concentrations by supplementation decreased cancer risk over the subsequent 7 y (42). An accompanying editorial (43) and the investigators themselves noted that 7 y of supplementation might be too short, the subjects might have received a dose of vitamin D that was too low, they might have had a lifestyle that was too healthy, or they might have been too young (62 y on average) to develop this cancer in large numbers. In brief, the authors concluded that no result is ever definitively negative. Nevertheless, it is most unlikely that even larger, longer-lasting randomized controlled trials than this multimillion dollar effort will ever be performed. Yet, <2 mo later, the media prominently covered a far less definitive multivariable model study inversely linking cancer, including colorectal cancer, risk statistically to 6 indirect historical measures of sun exposure and presumptively correlated vitamin D concentrations (44), with no reference to the gold-standard negative colorectal cancer study (42). Such selective reporting continues through the present.

IRRELEVANCE OF BOTH CONTROVERSIES TO SUN PROTECTION

A neglected but critical point is that the true, optimal level of 25(OH)D for musculoskeletal health, cancer prevention, or any of the other claimed benefits is irrelevant to the proven value of sun protection. Whatever this optimal level, ample vitamin D can be obtained from diet, supplements, and incidental sun exposure (45–48). Intentional unprotected sun exposure to increase vitamin D photosynthesis is not only unnecessary but also inefficient for populations at highest risk of vitamin D deficiency (29-31).

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

The groups most responsive to the media's unprotected sun exposure message are those at statistically lowest risk of vitamin D deficiency: healthy, fair-skinned adolescents and young adults. Indeed, surveys in the United States show that >70% of tanning bed users are white women aged 16–49 y (16), and 95% of all users exceed the exposure levels recommended by the US Food and Drug Administration (49) to maximize vitamin D photosynthesis. The demographics and exposure habits of the sunbathing public are similar to those of tanning bed users, although the average age is probably even younger and exposures even greater. The safe-sun message promulgated by dermatologists and the American Academy of Dermatology does not target dark-skinned persons, who already have excellent endogenous sun protection in the form of epidermal melanin. Moreover, the groups at demonstrated risk of vitamin D deficiency have not embraced the "UV advantage" message (28), perhaps because this message does not target them.

The interest among the media and public in the pseudo-controversy is nevertheless real and persistent. Why? The sun protection message is old, dating back at least 23 y (50), and its intended audience views it, like the "buckle up" seatbelt message, as wimpy. Real men and rebellious, fun-loving, and spontaneous adolescents do not wear sunscreen (or seatbelts). Moreover, many persons, especially teenagers, want to sunbathe not to decrease their risk of age-associated disease decades later but to acquire a "sexy" tan (15). In addition, relaxing in the sun and making one's own vitamin D have a back-to-nature holistic appeal for many persons. It is therefore not surprising that the print and electronic media continue to cover the pseudo-controversy; it sells. However, press releases crafted by representatives and employees of the indoor tanning industry have greatly facilitated the media's natural tendency to pursue a controversial story, especially if it is one their audience wishes to hear.

THE INDOOR TANNING INDUSTRY

In the United States alone, the indoor tanning business earns $5 billion per year (51, 52) and has >50 000 tanning facilities, 28 million customers annually (53), and >1 million visits per day (54). In some regions of the United States, more than half of all teenage girls have visited a tanning facility at least 3 times in the previous year (55).

Because professional groups such as the American Academy of Dermatology have requested stricter guidelines and better enforcement of existing regulations governing indoor tanning, over the past decade, at least 29 states have enacted legislation restricting access to tanning parlors for teenagers, and at least 3 additional states are considering similar legislation (R Bohannon, State Affairs Division, American Academy of Dermatology Association, personal communication, May 2006). The indoor tanning industry vigorously opposes such legislation through paid lobbyists and a well-orchestrated media campaign. The cornerstone of the industry's argument to curtail proposed restrictions on teenage use and general overuse is that more UV exposure is healthy, indoor tanning is safer than natural tanning, and UV radiation exposure reduces the risk of multiple diseases (56). The message that the tanning industry has shared with state legislatures and the media and that the UV Foundation's website publicizes is: "Vitamin D from UV exposure is free and easy to get—why pass up the simplest way to improve your odds of preventing cancer?" (57). Similar websites describe industry funding of research by the principal and perhaps only academically based proponent of UV exposure to increase vitamin D concentrations (58).

The indoor tanning industry's concern for the public's health would be more credible if its coverage of the issues were more balanced and a decade or so of extolling the virtues of UVA lamps (not the UVB lamps that it now touts as healthful) had not preceded the campaign (2, 59, 60). Before publication of the epidemiologic studies questioning the adequacy of conventional vitamin D recommendations, the industry argued strenuously that indoor tanning was superior to natural sun exposure precisely because people could tan with less UVB exposure (and, of course, less vitamin D photosynthesis; 61). Indeed, a review of the industry's public positions over the 30 y of its dramatic growth in annual revenues (12) reveals a series of opportunistic, contradictory positions. There can be no doubt that the business of the tanning industry is to sell tanning sessions, not to safeguard the public's health.

THE APPEAL OF NATURAL SOLUTIONS

Over millions of years, life has adapted beautifully to the earth's environment. Nature has devised elegant, efficient, and often surprising solutions to complex problems, and humans are rarely able to improve on them. Exceptions to this rule occur when the rate of change that civilization has imposed outpaces evolution by modifying the environment in ways that create previously nonexistent downsides for the natural solution. Vitamin D photosynthesis is a prime example.

Humans evolved as relatively hairless, darkly pigmented beings in a highly insolated tropical subsistence environment. Their abundant epidermal melanin absorbed most of the incident UV photons, allowing them to avoid painful sunburns while hunting and gathering food. However, sunlight's high UVB content permitted epidermal photochemistry, including conversion of membrane lipids to vitamin D, the biologically inactive precursor of the hormone $1,25(OH)_2D$ that requires hydroxylation steps in the liver and kidney before acquiring the ability to modulate genes in cells throughout the body (26). Metabolic spillover pathways that convert excess vitamin D to inactive metabolites in the skin during prolonged UV exposure prevented overproduction of the precursor molecule. The ability to photosynthesize vitamin D avoided the requirement for dietary vitamin D in this environment with its unpredictable and often inadequate food supply. Life expectancy was far <40 y (62) and therefore there was an enormous priority for health in the first decades, a time sufficient to permit reproduction. Very gradually, humans migrated away from the equator to far less insolated climates and skin color gradually lightened, giving rise, for example, to the fair-skinned, blue-eyed, blond populations of Scandinavia and northern Europe. Although quite speculative, one appealing explanation for the complexion change in humans who migrated north is that acute UV damage became less problematic and maintaining adequate vitamin D concentrations became a priority.

In recent centuries, humans have become far more mobile, migrating thousands of miles in weeks or, more recently, hours. During this period, many people moved to cities. As a result, large populations of dark-skinned individuals now live primarily indoors in poorly insolated climates, and many fair-skinned persons live in relatively well-insolated places, spending recreation and sometimes work time outdoors and intermittently traveling to highly insolated places for business or pleasure. Compounding

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

these trends, life expectancy has increased dramatically in recent centuries and now approaches or exceeds 80 y in much of the developed world (63). This has led to decades of progressive photoaging and an exponential increase in annual skin cancer incidence between the 4th and 8th decades that is due, at least in part, to age-associated decreases in DNA repair capacity (24, 25). In addition, childhood rickets has emerged among dark-skinned, inner-city ethnic minorities in the northern United States and Europe (64, 65), and fair-skinned whites now have a 1 in 3 lifetime skin cancer risk.

These facts imply that fair-skinned persons benefit enormously from regular, lifelong safe sun practices. Moreover, while wearing sunscreen with a high sun protection factor (SPF) in season, such persons probably generate vitamin D maximally in exposed areas during incidental sun exposure (1). Although some have claimed that sunscreens block all UV and hence all vitamin D photosynthesis (22), this is not the case. By definition, sunscreens allow continuous transmission of a fraction of erythemogenically weighted incident UV photons equal to 1/SPF of the total (eg, 1/15th or 7% for an SPF 15 product). Moreover, studies have shown that sunscreen users customarily apply half or less of the FDA-stipulated amount of product required to generate the stated level of protection (2 mg/cm^2) and hence achieve far less protection (66). If persons require 2–8 min of unprotected summer sun exposure to optimize cutaneous vitamin D synthesis (28), they could accomplish this in ≈10–20 min of exposure after applying an SPF 15–30 sunscreen in the customary manner (66, 66). Most critically, regardless of one's complexion or extent of UV exposure, daily oral vitamin D supplementation can completely compensate for lack of cutaneous vitamin D photosynthesis (1).

AREAS OF UNCERTAINTY AND RESEARCH NEEDS

The longstanding pseudo-controversy has led many responsible professional groups to wonder whether to recommend a safe or prudent amount of unprotected sun exposure to the public concerned about skin and overall health or even cosmetic tanning. The risk-benefit ratio of sun exposure and probably of high 25(OH)D concentrations varies enormously within the population. Moderate or even generous sun exposure might have little effect on a darkly pigmented person's risk of subsequent photoaging and skin cancer while promoting higher 25(OH)D concentrations, but it could promote development of precancerous and even cancerous lesions in already photodamaged fair skin without increasing the already maximized vitamin D photosynthesis.

Solar UVB intensity varies enormously with latitude, altitude, time of day, and time of year, among many other variables (68). UVA radiation varies far less in intensity and is far more abundant in sunlight than UVB radiation (69), so unprotected late-summer-afternoon or midday-winter exposure might involve almost no UVB exposure (and hence no vitamin D synthesis) but might still contribute to photoaging and photocarcinogenesis. A rule of thumb might be that any sunburn dose is too much by a factor of ≥3, because maximal vitamin D synthesis is achieved after approximately one-third of a minimal erythema dose (21). Individuals who never sunburn or who live in climates that never allow then to sunburn are relatively safe from the damaging effects of unprotected sun exposure. Persons with complexions or living circumstances associated with the possibility of frequent sunburns probably have no safe minimum unprotected exposures, because these would be only a few minutes and would almost certainly be exceeded cumulatively on a daily basis during the course of routine activities.

All clinicians, investigators, and public health officials interested in vitamin D biology, photocarcinogenesis, or skin biology and pathophysiology can probably agree that more research in overlapping areas is desirable. Perhaps the most clinically important questions are: Does an inverse cause-effect relation exist between higher 25(OH)D concentrations and cancer incidence, hypertension, diabetes, multiple sclerosis, and other conditions for which research has noted inverse epidemiologic associations (1)? Does having a higher than conventionally recommended serum 25(OH)D concentration produce a health benefit, or even a future health benefit, in healthy children and adults? If such a benefit exists, what is the minimum duration required for maintaining high 25(OH)D concentrations (eg, throughout life or only for a period of months or years)? Implicit in these questions is the fact that one cannot deduce cause-and-effect relations from epidemiologic studies, which are inevitably confounded by indirect and group-averaged measures of key variables, socioeconomic factors, racial and genetic factors, and lifestyle associations.

In contrast with these understudied areas, randomized, prospective controlled trials among frail elderly groups strongly suggest that such individuals benefit from daily oral supplementation of ≥800 IU of vitamin D, which enhances muscle strength and decreases falls, reducing bone fracture risk (1). These data imply that the present recommended daily allowance (600 IU/d) for vitamin D in those ≥70 y old (69) is probably inadequate and that increasing vitamin D intake in frail older individuals, particularly those who are housebound or institutionalized, would probably confer a health benefit. Other research has shown that doubling or tripling the standard vitamin D supplement doses or fortifying more foods with vitamin D would be very safe (45, 70). Signs of vitamin D toxicity only appear after daily doses exceeding 10 000 IU (45), so the safety margin is broad.

One area does not require further research, at least to resolve the present controversy. Overwhelming data, briefly summarized above, establish UV radiation as a carcinogen responsible for >1 million skin cancers per year in the United States alone (3), as well as for photoaging (71), an essentially universal problem among whites in middle age and beyond. These data also show that lifelong safe sun practices minimize both risks. With continued goodwill and enhanced communication, one can hope that the "controversy" surrounding the "sunshine vitamin" will become a thing of the past.

The author had no conflicts of interest.

REFERENCES

1. Wolpowitz D, Gilchrest BA. The vitamin D questions: how much do you need and how should you get it? J Am Acad Dermatol 2006;54:301–17.
2. National Toxicology Program, Department of Health and Human Services. Report on carcinogens. 11th ed. Internet: http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s183uvrr.pdf (accessed 23 September 2005).
3. Jemal A, Tiwari RC, Murray T, et al. Cancer statistics, 2004. CA Cancer J Clin 2004;54:8–29.
4. Blum HF. Carcinogenesis by ultraviolet light. Princeton, NJ: Princeton University Press, 1959;
5. Findlay GM. Ultraviolet light and skin cancer. Lancet 1928;215:1070.
6. Vitasa BC, Taylor HR, Strickland PT, et al. Association of nonmelanoma skin cancer and actinic keratosis with cumulative solar ultraviolet exposure in Maryland watermen. Cancer 1990;65:2811–7.
7. Aszterbaum M, Epstein J, Oro A, et al. Ultraviolet and ionizing radiation

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

enhance the growth of BCCs and trichoblastomas in patched heterozygous knockout mice. Nat Med 1999;5:1285–91.
8. Kannan K, Sharpless NE, Xu J, O'Hagan RC, Bosenberg M, Chin L. Components of the Rb pathway are critical targets of UV mutagenesis in a murine melanoma model. Proc Natl Acad Sci U S A 2003;100:1221–5.
9. Yamazaki F, Okamoto H, Matsumura Y, Tanaka K, Kunisada T, Horio T. Development of a new mouse model (xeroderma pigmentosum a-deficient, stem cell factor-transgenic) of ultraviolet B-induced melanoma. J Invest Dermatol 2005;125:521–5.
10. Kraemer KH, Lee MM, Andrews AD, Lambert WC. The role of sunlight and DNA repair in melanoma and nonmelanoma skin cancer. The xeroderma pigmentosum paradigm. Arch Dermatol 1994;130:1018–21.
11. Geise AC. Is sunlight good for you? In: Living with our sun's ultraviolet rays. New York, NY: Plenum Press, 1976;35.
12. Albert MR, Ostheimer KG. The evolution of current medical and popular attitudes toward ultraviolet light exposure: part 3. J Am Acad Dermatol 2003;49:1096–106.
13. Gilchrest B. Anti-sunshine vitamin A. Nat Med 1999;5:376–7.
14. Gilchrest BA, Eller MS. The tale of the telomere: implications for prevention and treatment of skin cancers. J Investig Dermatol Symp Proc 2005;10:124–30.
15. Geller AC, Brooks DR, Colditz GA, Koh HK, Frazier AL. Sun protection practices among offspring of women with personal or family history of skin cancer. Pediatrics 2006;117:688–94.
16. Swerdlow AJ, Weinstock MA. Do tanning lamps cause melanoma? An epidemiologic assessment. J Am Acad Dermatol 1998;38:89–98.
17. Parrish JA, Jaenicke KF, Anderson RR. Erythema and melanogenesis action spectra of normal human skin. Photochem Photobiol 1982;36:187–91.
18. Freeman SE, Hacham H, Gange RW, Maytum DJ, Sutherland JC, Sutherland BM. Wavelength dependence of pyrimidine dimer formation in DNA of human skin irradiated in situ with ultraviolet light. Proc Natl Acad Sci U S A 1989;86:5605–9.
19. Adams JS, Clemens TL, Parrish JA, Holick MF. Vitamin-D synthesis and metabolism after ultraviolet irradiation of normal and vitamin-D-deficient subjects. N Engl J Med 1982;306:722–5.
20. de Gruijl FR. Skin cancer and solar UV radiation. Eur J Cancer 1999;35:2003–9.
21. Holick MF, MacLaughlin JA, Clark MB, et al. Photosynthesis of previtamin D3 in human skin and the physiologic consequences. Science 1980;210:203–5.
22. Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. J Clin Endocrinol Metab 1987;64:1165–8.
23. Walker SL, Hawk JLM, Young AR. Acute and chronic effects of ultraviolet radiation on the skin. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, eds. Fitzpatrick's dermatology in general medicine. 6th ed. New York, NY: McGraw-Hill, 2003;1275-82.:
24. Bohr VA, Anson RM. DNA damage, mutation and fine structure DNA repair in aging. Mutat Res 1995;338:25–34.
25. Moriwaki S, Ray S, Tarone RE, Kraemer KH, Grossman L. The effect of donor age on the processing of UV-damaged DNA by cultured human cells: reduced DNA repair capacity and increased DNA mutability. Mutat Res 1996;364:117–23.
26. Holick MF. Vitamin D: photobiology, metabolism, mechanism of action, and clinical applications. In: Favus M, ed. Primer on the metabolic bone diseases and disorders of mineral metabolism. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999;92–8.
27. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988;124:869–71.
28. Holick MF, Jenkins M. The UV advantage. ibooks, Incorporated, 2004.
29. Clemens TL, Adams JS, Henderson SL, Holick MF. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. Lancet 1982;1:74–6.
30. Bell NH. Vitamin D metabolism, aging, and bone loss. J Clin Endocrinol Metab 1995;80:1051.
31. Need AG, Morris HA, Horowitz M, Nordin C. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. Am J Clin Nutr 1993;58:882–5.
32. Binkley N, Novotny R, Krueger D, et al. Low vitamin D status despite abundant sun exposure. J Clin Endocrinol Metab 2007;92:2130–5.
33. Robinson JK, Amonette R, Wyatt SW, Bewerse BA, Bergfeld WF, Farris PK. Executive summary of the national "Sun Safety: Protecting Our Future" conference: American Academy of Dermatology and Centers for Disease Control and Prevention. New York, May 1 and 2, 1997; J Am Acad Dermatol 1998;38:774–80.
34. Garland CF, Garland FC, Gorham ED. Can colon cancer incidence and death rates be reduced with calcium and vitamin D? Am J Clin Nutr 1991;54(suppl):193S–201S.
35. Garland CF, Garland FC, Gorham ED. Calcium and vitamin D. Their potential roles in colon and breast cancer prevention. Ann N Y Acad Sci 1999;889:107–19.
36. Bigby M, Szklo M. Evidence-based dermatology. In: Corona R, Wolff K, Goldsmith LA, et al, eds. Fitzpatrick's dermatology in general medicine. 7th ed. New York, NY: McGraw-Hill, 2007:8–18.
37. Grau MV, Baron JA, Sandler RS, et al. Vitamin D, calcium supplementation, and colorectal adenomas: results of a randomized trial. J Natl Cancer Inst 2003;95:1765–71.
38. Tuohimaa P, Tenkanen L, Ahonen M, et al. Both high and low levels of blood vitamin D are associated with a higher prostate cancer risk: a longitudinal, nested case-control study in the Nordic countries. Int J Cancer 2004;108:104–8.
39. Gross MD. Vitamin D and calcium in the prevention of prostate and colon cancer: new approaches for the identification of needs. J Nutr 2005;135:326–31.
40. Hartman TJ, Albert PS, Snyder K, et al. The association of calcium and vitamin D with risk of colorectal adenomas. J Nutr 2005;135:252–9.
41. Majewski S, Skopinska M, Marczak M, Szmurlo A, Bollag W, Jablonska S. Vitamin D3 is a potent inhibitor of tumor cell-induced angiogenesis. J Investig Dermatol Symp Proc 1996;1:97–101.
42. Wactawski-Wende J, Kotchen JM, Anderson GL, et al. Calcium plus vitamin D supplementation and the risk of colorectal cancer. N Engl J Med 2006;354:684–96.
43. Forman MR, Levin B. Calcium plus vitamin D3 supplementation and colorectal cancer in women. N Engl J Med 2006;354:752–4.
44. Giovannucci E, Liu Y, Rimm EB, et al. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst 2006;98:451–9.
45. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. Am J Clin Nutr 1999;69:842–56.
46. Boucher BJ. Sunlight "D"ilemma. Lancet 2001;357:961.
47. Calvo MS, Whiting SJ, Barton CN. Vitamin D intake: a global perspective of current status. J Nutr 2005;135:310–6.
48. Utiger RD. The need for more vitamin D. N Engl J Med 1998;338:828–9.
49. Hornung RL, Magee KH, Lee WJ, Hansen LA, Hsieh YC. Tanning facility use: are we exceeding Food and Drug Administration limits? J Am Acad Dermatol 2003;49:655–61.
50. Robinson JK, Rigel DS, Amonette RA. Trends in sun exposure knowledge, attitudes, and behaviors: 1986 to 1996. J Am Acad Dermatol 1997;37:179–86.
51. Dellavalle RP, Parker ER, Cersonsky N, et al. Youth access laws: in the dark at the tanning parlor? Arch Dermatol 2003;139:443–8.
52. Demierre MF. Time for the national legislation of indoor tanning to protect minors. Arch Dermatol 2003;139:520–4.
53. Kwon HT, Mayer JA, Walker KK, Yu H, Lewis EC, Belch GE. Promotion of frequent tanning sessions by indoor tanning facilities: two studies. J Am Acad Dermatol 2002;46:700–5.
54. Whitmore SE, Morison WL, Potten CS, Chadwick C. Tanning salon exposure and molecular alterations. J Am Acad Dermatol 2001;44:775–80.
55. Oliphant JA, Forster JL, McBride CM. The use of commercial tanning facilities by suburban Minnesota adolescents. Am J Public Health 1994;84:476–8.
56. ITA responds to flawed study on links between indoor tanning, skin cancer. The National Tanning Training Institute. Internet: http://www.tanningtraining.com/hotnews/61h181519848010.html (accessed October 25, 2007).
57. UV foundation applauds vitamin D research results. Your Alzheimers Resource. Internet: http://www.alzheimersupport.com/library/showarticle.cfm/ID/2279/T/Alzheimers/searchtext (accessed October 24, 2007).
58. What we know about the positive effects of UV light. Total Tan. Internet: http://totaltancorp.com/article_tanning_8.html (accessed October 24, 2007, and January 31, 2008).
59. Westerdahl J, Ingvar C, Masback A, Jonsson N, Olsson H. Risk of

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010

cutaneous malignant melanoma in relation to use of sunbeds: further evidence for UV-A carcinogenicity. Br J Cancer 2000;82:1593–9.
60. Spencer JM, Amonette RA. Indoor tanning: risks, benefits, and future trends. J Am Acad Dermatol 1995;33:288–98.
61. Levine JA, Sorace M, Spencer J, Siegel DM. The indoor UV tanning industry: a review of skin cancer risk, health benefit claims, and regulation. J Am Acad Dermatol 2005;53:1038–44.
62. Oeppen J, Vaupel JW. Demography. Broken limits to life expectancy. Science 2002;296:1029–31.
63. Hoyert DL, Heron MP, Murphy SL, Kung HC. Deaths: final data for 2003. Natl Vital Stat Rep 2006;54:1–120.
64. Welch TR, Bergstrom WH, Tsang RC. Vitamin D-deficient rickets: the reemergence of a once-conquered disease. J Pediatr 2000;137:143–5.
65. Kreiter SR, Schwartz RP, Kirkman HN Jr, Charlton PA, Calikoglu AS, Davenport ML. Nutritional rickets in African American breast-fed infants. J Pediatr 2000;137:153–7.
66. Bech-Thomsen N, Wulf HC. Sunbathers' application of sunscreen is probably inadequate to obtain the sun protection factor assigned to the preparation. Photodermatol Photoimmunol Photomed 1992;9:242–4.
67. Pinnell SR. Cutaneous photodamage, oxidative stress, and topical antioxidant protection. J Am Acad Dermatol 2003;48:1–19; quiz 20-2.
68. Diffey BL. Human exposure to ultraviolet radiation. In: Hawk JLM, ed. Photodermatology. London, United Kingdom: Arnold Publishers, 1999: 5–24.
69. 1997 RDA Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes of calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, DC: National Academy Press, 1997.
70. Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. J Nutr 2005;135:317–22.
71. Yaar M, Gilchrest BA. Aging of skin. In: Corona R, Wolff K, Goldsmith LA, et al, eds. Fitzpatrick's dermatology in general medicine. 7th ed. New York, NY: McGraw-Hill, 2007:963–74.

The American Journal of Clinical Nutrition

Downloaded from www.ajcn.org by on March 25, 2010