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Abstract

Ultraviolet (UV) radiation has both beneficial and harmful effects on the human body. Its most important beneficial effect may be vitamin D production in the skin, also known as vitamin D photosynthesis. This is of particular interest for the elderly who often show vitamin D-deficiency. Intentional UV exposure has been recommended by different institutions in order to increase vitamin D levels. Nevertheless, UV radiation directly causes DNA damage and is verifiably responsible for carcinogenesis, potentially resulting in lethal skin cancers. Unfortunately, skin cancer incidence is rising worldwide, and there is still a lack of appropriate treatment for metastasized types. The only proven and avoidable risk factor is UV radiation. It has been shown that the earlier UV protection is started, the greater the benefit in terms of skin cancer prevention. Nevertheless, even if UV protection is started at older ages, individuals will benefit measurably. Because UV radiation is neither a reliable nor a safe method of achieving healthy vitamin D levels, intentional UV radiation is not recommended to increase vitamin D levels. In order to prevent skin cancer, UV protection is to be conducted as commonly recommended, by minimizing sun exposure, and especially sunburn, with appropriate sun protective behaviors, e.g. usage of sunscreen and clothing (hat, sunglasses, long sleeves, and pants). Infants must be protected with extra care. Tanning beds must be avoided.
Vitamin D, Ultraviolet Exposure, and Skin Cancer in the Elderly

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Key Words
Ultraviolet radiation · Sun exposure · Vitamin D · Photosynthesis · Skin cancer · Carcinogenesis · Cutaneous carcinoma

Abstract
Ultraviolet (UV) radiation has both beneficial and harmful effects on the human body. Its most important beneficial effect may be vitamin D production in the skin, also known as vitamin D photosynthesis. This is of particular interest for the elderly who often show vitamin D-deficiency. Intentional UV exposure has been recommended by different institutions in order to increase vitamin D levels. Nevertheless, UV radiation directly causes DNA damage and is verifiably responsible for carcinogenesis, potentially resulting in lethal skin cancers. Unfortunately, skin cancer incidence is rising worldwide, and there is still a lack of appropriate treatment for metastasized types. The only proven and avoidable risk factor is UV radiation. It has been shown that the earlier UV protection is started, the greater the benefit in terms of skin cancer prevention. Nevertheless, even if UV protection is started at older ages, individuals will benefit measurably. Because UV radiation is neither a reliable nor a safe method of achieving healthy vitamin D levels, intentional UV radiation is not recommended to increase vitamin D levels. In order to prevent skin cancer, UV protection is to be conducted as commonly recommended, by minimizing sun exposure, and especially sunburn, with appropriate sun protective behaviors, e.g. usage of sunscreen and clothing (hat, sunglasses, long sleeves, and pants). Infants must be protected with extra care. Tanning beds must be avoided.

Background

Ultraviolet Radiation and Skin Cancer
Skin cancer incidence is greatly increasing worldwide. The highest rates of non-melanoma skin cancer are registered in Australia, Ireland, and Switzerland. Together, basal cell carcinoma and squamous cell carcinoma account for one third of all cancers worldwide. Their incidence rates rise exponentially with age, as squamous cell carcinoma and basal cell carcinoma are present mainly in the elderly population. Due to the population pyramid, rapid increases of basal cell carcinoma and especially squamous cell carcinoma rates may be assumed for the future [1].

Epidemiological studies clearly indicate ultraviolet (UV) exposure as the major cause of skin cancer [2, 3]. In more than 95% of skin cancer cases in countries with high UV radiation burden, and in about 65% of cases worldwide, UV radiation is held at least partly responsible for the pathogenesis [4, 5].

Evidence for mutagenesis by UV radiation is further provided at the cellular level, where UV A radiation leads to oxidative damage of guanine bases on the DNA, and
UV B radiation induces characteristic cyclobutane pyrimidine dimers [6, 7]. Furthermore, skin cancer frequently reveals UV signatures seen as mutations in the tumor suppressor gene p53 [8, 9]. The UV-induced V600E mutation in the BRAF gene is detected in more than 60% of melanoma specimens, indicating UV radiation as a major cause of its pathogenesis [10].

**Vitamin D Production**

The most striking UV radiation-induced benefit is the cutaneous photosynthesis of vitamin D. Cutaneous membrane lipids, 7-dehydrocholesterol (provitamin D), absorb UV B radiation between wavelengths of 280 and 315 nm and are thereby converted into previtamin D3 (precholecalciferol). Previtamin D3 isomerizes into vitamin D3 (cholecalciferol). By binding to vitamin D-binding protein, vitamin D3 is transported to the liver. Here, it is hydroxylated by the cytochrome P450 27A1 into the stored form of vitamin D3, calcidiol [25(OH)D3, 25-hydroxyvitamin D]. For activation, further hydroxylation into calcitriol [1,25(OH)2D3] by the cytochrome P450 27B1 is required. Generally, this step takes place in the kidneys, but other tissues, such as the skin, are also able to perform this hydroxylation. By binding to nuclear vitamin D receptors in various tissues, calcitriol leads to the transcription of specific genes which are responsible for cell cycle control, antiproliferation and apoptosis. Vitamin D production depends on several factors. In the elderly, vitamin D production capacity is lowered due to atrophy of the skin with a lower amount of membrane lipids. Vitamin D receptor polymorphisms and hormone status as well as various further factors influence possible effects of vitamin D [11, 12].

**Effects of Vitamin D**

Vitamin D is essential for enteral and renal calcium and phosphate uptake as well as their integration into bones [13]. Vitamin D, at adequate levels, allows for adequate calcium absorption in the kidneys and prevents induction of secondary hyperparathyroidism [11]. Furthermore, it influences the muscular system. One further advantage of vitamin D, particularly in the elderly population, is the prevention of falls and fractures [14–16].

Several studies associated low vitamin D levels (less than 75 nmol/l) with increased risk for numerous diseases (e.g. cardiovascular diseases [17, 18], colorectal carcinoma [44], autoimmune diseases such as diabetes mellitus type I [19], and others [20]). However, direct implication of vitamin D and increased risk of various diseases are difficult to grasp. A healthy lifestyle in terms of adequate body mass index, nutrition, and physical activity may directly affect disease risk, and, besides, increase vitamin D levels as well [21]. However, other large randomized trials could not prove any benefit from vitamin D supplementation on cancer risk [22].

**The Vitamin D Controversy**

Unfortunately, vitamin D deficiency is a problem worldwide, specifically in older, dark-skinned, and overweight populations [23]. Exposure to UV radiation was considered an easy and cost-effective means of increasing vitamin D levels: intentional UV radiation is frequently promoted by various authors despite the fact that UV-induced vitamin D production is especially poor in the populations suffering most from vitamin deficiency: the elderly and populations with dark skin complexions. Several authors even promote the use of UV B lamps or tanning beds in order to increase vitamin D production [24, 25]. Besides the fact that tanning beds do not increase vitamin D levels, as they emit UV A, not UV B radiation [26], and tanning lowers the skin’s capacity for vitamin D production due to absorption of UV by melanin, the hazardous consequences of UV radiation, particularly carcinogenesis, are ignored in these recommendations [27]. Besides, maximal vitamin D production is achieved already with very low UV doses. Nevertheless, concurrent with the start of UV exposure, DNA damage and thus carcinogenesis take place [28].

Furthermore, after production of a specific amount of vitamin D, further UV exposure leads to photolysis of precholecalciferol into tachysterol and suprasterol. Additionally, cholecalciferol is photolyzed into the degradation products suprasterol I, II and transvitamin D3 [11]. Remarkably, cholecalciferol absorbs UV B as well as UV A radiation and becomes more fragile with further radiation [12]. Because repeatedly sun-exposed skin tans, vitamin D production diminishes, due to the increased UV absorption in the skin.

Research shows that accidental UV exposure, even if sunscreen is applied, is sufficient for maximal photosynthesis and cannot be increased by additional sun exposure [29]. Seasonal variability of vitamin D levels is common for sunscreen users as well as for individuals who do not use sunscreen [30].

An often cited study concluded that a sun protection factor 8 suppresses vitamin D when irradiated with minimal erythema dose [31]. However, the study only found this effect within the first 2 days. Afterwards, the vitamin D level diminished, and after 8 days, there was no significant difference between the group that used sunscreen and the group that did not use sunscreen. Conse-
quent, the correct conclusion would be that the population should be sunburned every 2nd or 3rd day in order to keep an increased vitamin D level—which is not realistic due to the well-known risks of UV radiation.

Furthermore, the amount of vitamin D photosynthesized from UV radiation varies according to season and latitude and, therefore, cannot be guaranteed to be delivered in a reliable manner. Elderly people have a fourfold lower capacity for vitamin D production when compared to younger people, due to atrophy of the skin and a lower amount of cutaneous membrane lipids [28]. The repeatedly recommended daily UV exposure of one quarter of the body surface, with one third to one quarter of the minimal erythema dose, is based on an in vitro study [32] and cannot be applied to in vivo physiology by implication. Furthermore, UV doses far below the minimal erythema dose cause DNA damage and should be avoided. Carcinogenesis cannot be risked in order to gain the potential benefits of UV radiation, which can be achieved in relatively riskless ways with little effort.

**Vitamin D Supplementation**

There is much debate over the amount of calciferol required [33, 34]. Leading groups of clinicians investigating the role of vitamin D in several diseases recommend a daily intake of 800 IU vitamin D for adults. Vitamin D from nutrition cannot reach this level [35], even when the diet consists of products containing high levels of vitamin D (e.g., fatty fish) [13]. Fortified food, which is common in the US, particularly dairy products and orange juice, indeed increases vitamin D levels by approximately 200 IU; nevertheless, the intake of 800 IU vitamin D daily is still not achieved. Therefore, the vitamin D deficient population would have to be supplemented with vitamin D drops or tablets, or in the case of malabsorption, intramuscular injections [36]. However, the overall benefit of vitamin D needs to be proven in well-designed prospective placebo-controlled randomized trials.

**Conclusion**

Vitamin D is a complex molecule with various, not yet fully understood effects on the human body. Most studies reporting the benefits of vitamin D were not adjusted to lifestyle, e.g., activities and nutrition. Therefore, a causative risk reduction for the development of several diseases with normal serum vitamin D levels is not proven yet. On the other hand, one may presume a healthy lifestyle to improve vitamin D serum levels.

Studies with vitamin D supplementation reported increased risks of prostate and esophageal cancer [37, 38]. Furthermore, supplementation of vitamin D in childhood has been associated with increased risk for atopy [39, 40].

Considering these facts, vitamin D supplementation should be used very carefully in order to minimize unpredictable and unforeseeable hazards until large controlled trials have excluded hazardous effects.

The vitamin E experience is a good example to remember. In a clinical trial, patients were supplemented with alpha-tocopherol and beta-carotene in the hope of preventing carcinogenesis. However, supplemented patients showed a higher incidence of lung cancer [41].

The World Health Organization assumes that the health threats caused by UV exposure outweigh the health risks induced by UV underexposure and vitamin D deficiency [21, 42].

In conclusion, adequate levels of vitamin D are essential, particularly for the elderly. In the light of (a) the fluctuation of UV radiation due to time of day and season, (b) a decrease in the capacity for vitamin D, particularly for the elderly, and above all (c) the proven carcinogenetic and other harmful characteristics of UV radiation, there is no such thing as so-called ‘safe sun exposure’, and sun exposure should not be prolonged in order to increase vitamin D levels. Rather, vitamin D should be carefully supplemented orally or, in case of malabsorption, parenterally. At-risk populations, e.g., the elderly, should especially be targeted. Serum vitamin D levels should be carefully controlled, and oversupplementation should be avoided until randomized studies clearly indicate ideal vitamin D serum levels.

Generally recommended sun protection measures in order to decrease the risk for skin cancer should be continued [43]: (a) minimizing sun exposure (particularly between 11 a.m. and 3 p.m.), sunburn, and tanning beds; (b) wearing hats, sun glasses and appropriate clothes; (c) usage of sunscreen (waterproof, SPF at least 20, including UV A protection, multiple applications during the day, 15–30 min prior to sun exposure); (d) protecting infants from direct sun exposure, and (e) periodic self-examination of the skin.

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