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Review

Who, what, where and when—influences on cutaneous vitamin D synthesis

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Abstract

The synthesis of vitamin D in skin is a two-stage process that begins with the production of previtamin D after irradiation of 7-dehydrocholesterol by ultraviolet (UV) radiation. A number of personal and environmental factors control the probability of a suitable UV photon reaching a molecule of 7-dehydrocholesterol in the skin. These are astronomical factors that govern the solar zenith angle (SZA), and the local state of the atmosphere, determining the available solar UV radiation; skin pigmentation and age, determining competing absorbers of UV radiation and available 7-dehydrocholesterol; individual behaviour in the local surroundings, determining exposure of unprotected skin to available UV radiation. The only one of these influences that can be determined unequivocally for any situation is the SZA. The other influences must be considered either as individual case studies, or be represented by "typical" and "idealised" situations for the weather, skin and behaviour. At large SZAs there is insufficient solar UV radiation to initiate significant vitamin D synthesis. At smaller SZAs assessment of solar exposure necessary for vitamin D synthesis can only be indicative and application of any such assessment necessarily requires awareness of both self- and the local environment.

Keywords: Vitamin D; Ultraviolet radiation; Solar zenith angle; Skin type; Age; Environment; Sunscreen

Contents

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1. Introduction

Vitamin D_3 is synthesised in human skin that is exposed to ultraviolet (UV) radiation, specifically to radiation of wavelengths shorter than about 315 nm. For solar radiation, the natural source of UV, we are thus discussing UVB (280–315 nm) radiation since shorter wavelengths are prevented from reaching the Earth's surface by stratospheric ozone.

UVB radiation incident on the cells of the skin photoisomerises 7-dehydrocholesterol (7DHC) to previtamin D_3. After this initial photoisomerisation the previtamin D_3 undergoes a heat isomerisation in the skin to vitamin D_3, a process that takes several hours. Alternatively, the previtamin D_3 can be photoisomerised further, into one of two inert isomers (lumisterol and tachysterol) or back to 7DHC. Each reaction has a different action spectrum, but all are in the UV range of wavelengths (MacLaughlin et al.,1982). With prolonged irradiation a quasi-equilibrium mixture of isomers will result. The relative amounts of each isomer depend on the irradiating spectrum and length of irradiation. In sunlight there is a limit to the amount of previtamin D_3 that forms within the mixture, this being less than 12–15% (Holick et al., 1981; Webb et al., 1988).

Vitamin D enters the circulation attached to a D-binding protein. If still present in the skin when further UV irradiation takes place the vitamin D_3 can be broken down by UV radiation and is no longer useful (Webb et al., 1989). The vitamin D_3 is first hydroxylated in the liver to 25-hydroxyvitamin D_3 (25(OH)D_3) and then again in the kidney to its active form, 1,25-dihydroxyvitamin D_3 (1,25$(OH)_2D_3$). The usual measure of vitamin D status is the circulating level of 25(OH)D, without distinguishing between vitamin D_2 from the diet and vitamin D_3 from solar exposure. Leaving aside the issue of dietary supplementation, most modern diets are low in vitamin D_3 and the majority of vitamin D is gained from exposure to sunlight (Holick, 2004a). The level of circulating 25(OH)D is observed to change (increase) with exposure to UVB. This is not the case for 1,25$(OH)_2$D which is tightly controlled by the endocrine system.

2. Factors influencing vitamin D_3 synthesis

For vitamin D_3 synthesis to begin a UVB photon must hit a molecule of 7DHC. Anything that helps or hinders the probability of this occurring is influencing vitamin D_3 synthesis. The major factors can be split into two categories: environmental or external, and personal or intrinsic to the individual.

The external factors control how much solar UV radiation is available and can be summarised by "where and when". They include latitude, season, time of day, ozone amount, cloud amount, aerosol and albedo (reflectivity of the surface). The personal factors (who and what) include skin type, age, clothing, use of sunscreen, and sometimes a choice of external factors, e.g. when to expose unprotected skin.

2.1. Where and when

Factors controlling ambient UV can be divided into the cyclical and very predictable, and the unpredictable, statistical expectation. The predictable factor is the solar zenith angle (SZA), the angle between the local vertical and the position of the sun in the sky (Fig. 1).

When the SZA is small the sun is high in the sky, the solar radiation has a relatively short pathlength through the atmosphere (less chance of attenuation), and all the energy or photons in a beam fall on a small area. At large SZA the sun is low in the sky, radiation traverses a long path through the atmosphere (lots of attenuation), and at the surface the remaining energy is spread over a large area (inversely proportional to cosine (SZA)). The SZA is controlled by the motion of the Earth rotating around the Sun, and about its own axis, combined with position on the Earth's surface, i.e season, time of day and latitude. Small SZA are

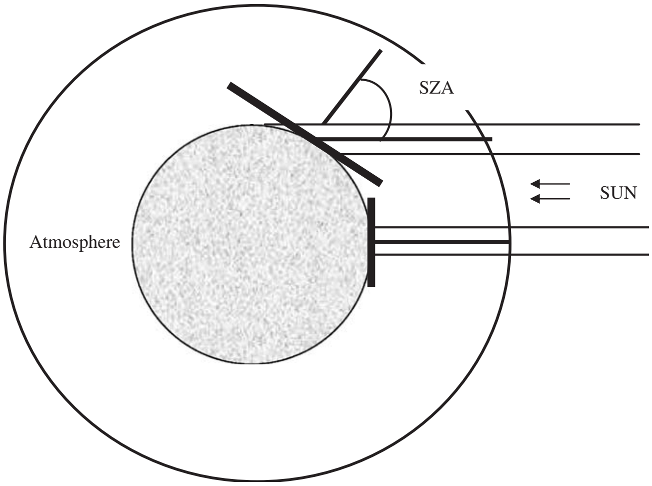

Fig. 1. Solar zenith angle is the angle between the local vertical and the direct solar beam. At a large SZA the radiation traverses a longer pathlength through the atmosphere, which can greatly attenuate shorter wavelengths, and the attenuated power is spread over a larger area of surface.

associated with summer, noon and low latitudes; large SZA are a feature of winter, early morning/late afternoon, and high latitudes.

Less certain than the turning of the Earth is the weather, or the state of the atmosphere, that encompasses several variables that control UV reaching the surface (Blumthaler and Webb, 2003). Ozone is a major absorber of UVB radiation. It is found predominantly in the stratosphere where there is a global pattern of distribution with a minimum in the source region of the Tropics and a maximum at high latitudes around the edge of the Polar regions. There is also a seasonal cycle, for example at mid-latitudes the ozone is a maximum in the spring and a minimum in autumn. Superimposed on this underlying climatology there can be great day to day and year-to-year variation in the stratospheric ozone. Atmospheric dynamics (e.g. the movement of high and low pressure systems that bring different weather patterns) can cause rapid changes in ozone that can easily be 10–20% in a day. Distinct from this is the long-term ozone change associated with ozone depletion and the Antarctic ozone hole. The extent of ozone depletion to date is latitude dependent, being insignificant in the Tropics and a maximum in the Antarctic springtime. In the 35–60° latitude bands the average depletion (1997–2001) from 1980 levels was 3% in the northern hemisphere and 6% in the southern hemisphere (WMO (World Meteorological Organization), 2003). Whether this trend will reverse remains to be seen.

The other major, and variable, atmospheric attenuator of radiation is cloud. The reduction in UVB by cloud depends on the height, thickness and spatial distribution of the cloud. Fair weather cumulus (“cottonwool”) clouds that do not cover the sun have little effect on UV reaching the surface, indeed they may enhance the UV for a brief period due to reflection from the cloud sides (Weihs et al., 2000). A thick layer of stratus cloud covering the whole sky (“heavy overcast”) will strongly reduce the radiation, including UV, at the surface, and all situations between these extremes can occur (Grant and Heisler, 2000; Josefsson and Landelius, 2000). Cloud is also very unpredictable, especially in the mid-high latitude regions characterised by the passage of low-pressure systems interspersed with regions of high pressure.

Aerosols (suspended particles) are another attenuator of radiation in the atmosphere, reducing the radiation at the surface by scattering and absorption. Polluted regions with high aerosol loads therefore have less UV than they would if the air were clean. Aerosols vary greatly both regionally and temporally and are often poorly characterised, yet their influence on UV radiation depends upon the make up of the aerosol (WMO, 2003).

The surface itself can also influence the incident radiation through its reflectivity (albedo). Some of the radiation reflected by the surface is back-scattered by the atmosphere above and returns again to the surface, enhancing the original incident radiation. This process becomes significant if surface albedo is high, e.g. if covered with fresh snow (albedo ~90%), and is further enhanced if there is a cloud layer to increase the radiation returned to the surface by reflection from the bottom of the cloud. With the exception of snow, most natural surfaces have a low albedo in the UV, of the order 5% for vegetation, 10% for soils and rocks, and up to 20% for dry sand, the same as some concretes and cement (Feister and Grewe, 1995; Webb et al., 2000). In addition, the altitude of the surface is important. The higher the altitude, the less atmosphere the radiation has to traverse and the more radiation will reach the surface (Blumthaler et al., 1994). As pollutants and aerosols tend to be concentrated in the lowest layers of the atmosphere, being at a significant altitude will also significantly reduce the effect of aerosols.

2.2. Spectrum and SZA

Given the great range of possibilities and transient nature of all the atmospheric and surface variables above, the following illustrations will take only SZA as the determinant of UV at the surface: the atmosphere and surface will be considered to be in a constant state. For calculations the conditions are: cloud free US standard atmosphere with specified ozone = 350DU, aerosol = rural type, albedo = zero (non-reflecting), altitude = zero (sea level). While these exact conditions would be found infrequently, they are reasonably representative of the conditions that might occur in many of the well-populated regions of the world. Any measurements shown are for the conditions at the time of measurement. Cloud and albedo effects are, to a first approximation, independent of wavelength in the UVB and would change the intensity but not the shape of any spectra illustrated. Ozone and altitude influence the shorter wavelengths more than the longer wavelengths and would change both the spectral shape and the intensity. There is also a wavelength dependence to aerosol attenuation that depends on the type of aerosol.

The SZA changes both the intensity and the spectrum of the incident radiation at the surface. When the pathlength is long the radiation is attenuated more than when the pathlength is short. A major attenuation process, even in a clean, clear atmosphere, is Rayleigh scattering by air molecules, a process that is inversely proportional to the fourth power of the wavelength, λ (i.e. scattering $\alpha\ \lambda^{-4}$). The short UVB wavelengths are therefore strongly scattered by this process. Ozone, the major absorber in the UVB, has a strong wavelength dependence in this spectral region that determines the steep shape and lowest wavelength limit of the solar spectrum. These two effects combined mean that the UVB wavelengths change more rapidly with SZA than the longer wavelengths in the solar spectrum, as illustrated in Fig. 2.

At any location the sun reaches its highest point in the sky at local solar noon. Note that due to political boundaries, time zones and artefacts such as summer time, solar noon may differ significantly from 12 o'clock local time.

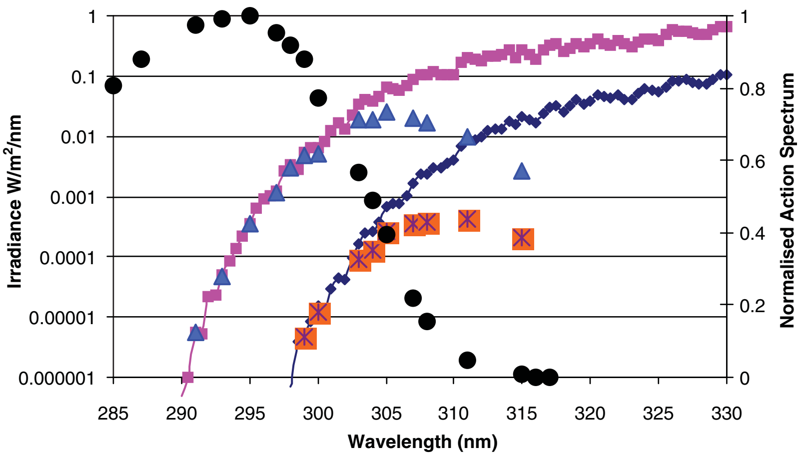

Fig. 2. The normalised vitamin D_3 action spectrum (Black dots, RH linear axis, from MacLaughlin et al., 1982) with solar spectra measured at solar zenith angles of 25° and 75° for cloud free sky (LH logarithmic axis). The blue triangles and red squares are the vitamin D_3 effective radiation for the two solar spectra, plotted on the logarithmic scale for visibility. Vitamin D_3 effective radiation is about 70 times more for the spectrum at SZA = 25° than at SZA = 75°.

2.3. Direct and diffuse radiation

Radiation reaching the edges of the Earth's atmosphere arrives in a parallel beam direct from the sun. As the radiation passes through the atmosphere some of it is scattered out of the direct beam, by the Rayleigh scattering mentioned earlier, or by Mie scattering from larger particles. Some of the scattered radiation returns to space, but some of it goes on to reach the Earth's surface, arriving not in the direct beam but from any and all other directions. This diffuse or sky radiation is an important part of the total radiation that falls on a surface, especially in the UV. If the SZA is greater than about 30° then the diffuse fraction of the solar UV radiation will be more than 0.5, increasing as SZA increases. If the direct beam is blocked there is still a lot of radiation reaching the surface from the rest of the sky—a UV shadow is not as "dark" as a visible shadow. The fraction of the sky that can be viewed (i.e. is not occluded by buildings, mountains, trees, etc.) determines how much diffuse radiation you are exposed to. This is important when relating measured or calculated UV to human exposure. The ambient UV necessarily refers to the radiation falling on a standard surface, this being flat, horizontal and with an uninterrupted view of a flat horizon. The radiation falling on other surfaces, e.g. in the vertical differs from a horizontal surface and has a different diurnal pattern (Webb et al.,1999). It is a horizontal surface, and not the varied shape of the human body in a built environment, to which climatological data and weather forecasts refer. Thus the UV Index (UVI), a simple indicator of the erythemal UV for public forecasting (WHO (World Health Organisation), 2002), refers to the UV on a flat, horizontal surface.

Although the UVI is a scaled unit of erythemally effective UV radiation, with a different action spectrum to vitamin D synthesis, it is widely available in weather forecasts and can be used as a rough indicator of potential for vitamin D_3 synthesis: the higher the UVI, the more UV is available and the shorter the time required to produce a given amount of previtamin D_3 in the skin. What that time is will depend on skin type, and how close to a flat surface is the exposed skin, but it should be less than the time required for erythema in the same conditions.

2.4. Who and what

Location and season control the potential ambient UV while the weather determines what is actually available on a given day. Whether that UV is used for vitamin D synthesis, and sufficient for a healthy vitamin D status, depends on who you are and what you are doing.

2.4.1. Skin type

Skin type is genetically determined and affects the amount of previtamin D_3 that can be synthesised in the skin for a given dose of UVB radiation. It is closely related to the risk of suffering erythema (sunburn) and is associated with the amount of melanin pigment in the skin. Melanin absorbs UV radiation and in doing so prevents the UV photons from entering other skin cells and causing either damage (sunburn) or the conversion of 7DHC to previtamin D_3. It follows that the more melanin there is in the skin the lower the amount of previtamin D_3 synthesised for a given dose of UVB. The skin colour of indigenous races darkens as latitude decreases from poles to equator and the ambient UV increases. Fair-skinned, fair-haired races (skin types I/II) originated from high latitudes where pale skin maximises the use of any UV in weak sunlight for vitamin D_3 synthesis, and is at low risk of damage at these high latitudes. Dark-skinned races (skin types V/VI) originated where the sun is strong, damage must be prevented, and only a fraction of the available UVB need reach the 7DHC in cells for adequate vitamin D_3 synthesis. Migrant populations, or the descendants of migrant populations, who have moved significantly poleward or equatorward, have skin types that do not match the ambient UV environment. Fair-skinned people nearer the equator are at increased risk of erythema and skin cancer; dark-skinned people nearer the poles have a greater risk of sub-optimal vitamin D status than the indigenous people.

Although erythema and vitamin D synthesis are not exactly equivalent (the erythema action spectrum extends into the UVA (MacKinley and Diffey, 1987)), erythemally weighted irradiance values provide a good practical guide for estimating UV requirements for vitamin D synthesis. Every person has his or her own minimum erythema dose (MED), the amount of erythemally effective radiation that causes a just perceptible reddening of the skin. It has been shown (Lo et al., 1986) that people of different skin types synthesise equivalent amounts of vitamin D if they are each given the same UV dose in terms of their own MED. The absolute amounts of UV differ, but the biological effect, scaled by erythema, is the same. Note that adequate vitamin D synthesis occurs at sub-erythemal UV doses. In this case the MED is simply a tool for classifying skin types and UV requirements.

2.4.2. Age

As the body ages the amount of 7DHC in skin cells decreases, which in turn decreases the capacity to synthesise vitamin D (MacLaughlin and Holick, 1985). It is still possible for the elderly to acquire and maintain an adequate vitamin D status through casual, short exposures to sunlight (Webb et al., 1990) but recent work has indicated that the elderly may need more 25(OH)D than younger adults (Vieth et al.,2003) because of the changing relation between 25(OH)D, parathyroid hormone (PTH) and hyperparathyroidism with age. In addition to these physiological changes, behaviour often changes with age, affecting exposure to the available solar UV radiation.

2.5. Clothing and sunscreen

Vitamin D is synthesised in the skin, but measured as a product in the blood. While the volume of blood in a body varies with season the change is small, while the skin area that can be exposed to sunlight is highly variable. Any association between UV dose and vitamin D status must therefore be qualified by the amount of skin exposed. For example, using the rule of nines, exposing a (bald) head and neck to sunlight for 20 min would produce about the same vitamin D as exposing the full body for 2 min. It is thus more efficient (for vitamin D synthesis), and less risky (for sunburn), to expose a large amount of skin for a short period of time, particularly as previtamin D_3 plateaus with prolonged exposure. Whether this is practical or desirable depends on culture, religion, air temperature, age, fashion and other sensibilities.

Clothing is an obvious physical barrier between solar radiation and the skin. Sunscreen is also a barrier that has been specially designed to prevent UVB radiation (and more recently UVB and UVA radiation) from reaching the skin. It follows that wearing sunscreen prevents the cutaneous synthesis of vitamin D (Matsuoka et al., 1987). Proper application of an SPF 15 sunscreen will reduce vitamin D synthesis by 99.9%, SPF 8 by 97.5% (Holick, 2004a), although it is very rare that ‘‘proper application’’, as used in sunscreen testing, occurs in everyday sunscreen use (Thieden et al., 2005). Nonetheless, for efficient cutaneous vitamin D synthesis, unprotected skin should be exposed to solar radiation.

2.6. Behaviour patterns

Vitamin D_3 is synthesised in the skin and later appears as a circulating metabolite that is measured for vitamin D status. It is fat soluble and can be stored in fat cells for use when there are insufficient new supplies of the vitamin available. It is used constantly in the process of calcium metabolism and bone remodelling. Clearly there is no instant physiological response to sunlight exposure (or lack thereof). Instead, for latitudes with clear seasonal changes in availability of solar UV, there is a well-documented seasonal cycle in vitamin D status, with a maximum in late summer and a minimum in late winter when stores from the previous summer are depleted and there is not yet sufficient sunlight for new cutaneous synthesis. Providing summer status reaches a good level each year then long-term vitamin D insufficiency is avoided.

The best way to increase vitamin D status is by short, regular exposures of unprotected skin to sunlight. There is no benefit to prolonged exposure for several reasons. First, there is the limit to the amount of previtamin D_3 that will form in the skin. Once this limit is reached only the inert isomers increase (Webb et al.,1988). It takes several hours for the previtamin D_3 to be isomerised to vitamin D_3 and then enter the circulation, a process that does not require UV radiation. However, vitamin D_3 itself is photolabile and can be broken down by sunlight of both UVB and UVA wavelengths (Webb et al., 1989). Sunbathing while vitamin D_3 remains in the skin cells is therefore counter-productive. Thus a regular daily exposure is far more effective than a single long exposure once a week. Short regular exposures will also prevent sunburn and the associated discomfort and long-term risks associated with erythema. Once a short exposure has been achieved on unprotected skin, sunscreen or clothing can be used to protect the skin if there is further outdoor activity. It is never necessary to sunburn in the quest for vitamin D_3.

Activity and local environment also play a role in vitamin D_3 synthesis because they change the geometrical relation between the radiation and the skin surface. Lying on a beach with a flat horizon will incur a far greater UV dose than wandering the narrow streets of the town behind when the body is often in shadow and only a small part of the sky is visible (reducing diffuse radiation).

3. How much sunlight?

The preceding sections have shown that there is no one-size-fits-all answer to how much solar radiation is needed to achieve and maintain an adequate vitamin D status. In absolute and easily identifiable terms (e.g. minutes in the sun) it depends on where you are, the time of year and day, the weather, your age, skin type, clothing, activity and environment. Given the infinite possibilities of all these variables it is only possible to provide an idealised indication of what might be possible or necessary.

The simplest statement becomes that of where it is not possible to make any appreciable vitamin D_3 in the skin from solar exposure, because there is too little UVB radiation in the solar spectrum. Webb et al. (1988) exposed solutions of 7DHC to solar radiation for up to 3 h throughout the year at a range of latitudes and showed that no previtamin D_3 (and hence no vitamin D_3) was synthesised during the winter months in Boston, and for a longer period in Edmonton, while year round synthesis took place in Los Angeles and Puerto Rico. Engelsen et al. (2005) used a radiative transfer model to calculate that poleward of 51° latitude no vitamin D synthesis could occur for at least some period of the year, but no limit was put on exposure times.

When vitamin D_3 synthesis is possible we have to consider how much vitamin D is required before calculating how long it will take to synthesise it. That question is under debate and is not a subject for this paper. For illustrative purposes only, let us assume that the vitamin D requirement is 1000 i.u. per day and that this can be achieved by exposing 0.25 skin surface area to 0.25 of the personal MED (Holick, 2004b). The atmosphere is assumed to be in a single state, as described in Section 2.2 and calculations have been made with the FastRT simulation tool (Engelsen and Kylling, 2005) for radiation on a flat horizontal surface. Fig. 3 then shows the time to synthesise the required vitamin D for skin type I as a function of latitude and season. Given the assumptions made in the calculations, most practical situations will require longer times (due to more pigmented skin, cloud, imperfect horizon, skin not horizontal).

An alternative, practical approach is to use the available information in the form of the UVI, and knowledge of self, to estimate solar exposure. Using the same criteria as above, if you know that for UVI of 7

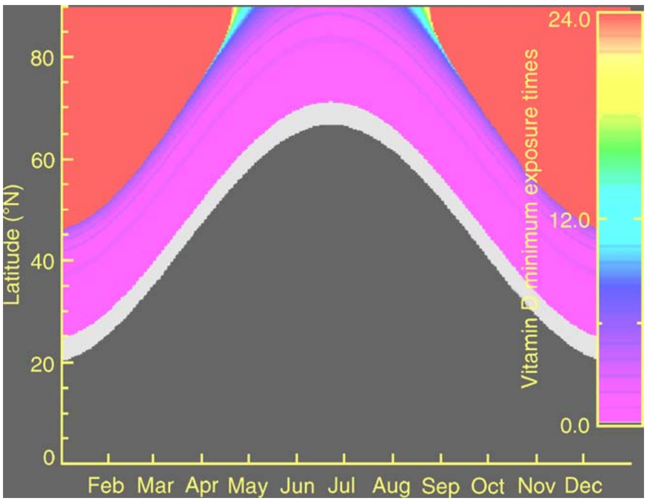

Fig. 3. Exposure times (in hours) required to synthesise the equivalent of 1000 i.u. vitamin D. Assumptions include irradiance on a horizontal surface and fixed atmospheric conditions. The red area indicates where no vitamin D synthesis is possible, the black area shows where synthesis occurs in minutes rather than hours.

you will get an MED in 40 min, then only expose unprotected skin for 10 min in those conditions. A quarter of skin surface area equates to full arms and head, or lower arms and lower legs, protecting the face. This method accounts for personal skin type, and to a certain extent for activity and local environment.

4. Conclusion

The capacity to synthesise vitamin D in the skin depends on a large number of factors. The basic determinants are solar zenith angle, controlling the potential available UVB (latitude, season and time of day), and skin pigmentation and age. Further confounding factors are atmospheric variables (weather), unprotected skin area exposed, local surroundings (fraction of potential ambient UVB available) and activity (skin orientation).

There are regions of the world where it is not possible to synthesise significant amounts of vitamin D_3 in realistic exposure times for several months of the year. Where vitamin D_3 synthesis is hypothetically possible in short exposure times the efficiency of the process depends upon personal characteristics and behaviour.

Due to the two stage process of synthesising vitamin D_3 in the skin, and the photo-instability of the intermediate product, previtamin D_3, short, regular exposures to sunlight are more beneficial than infrequent, extended exposures. The benefits of vitamin D exposure are acquired well before there is a danger of erythema.

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