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Ultraviolet Radiation and Human Health

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Ultraviolet Climatology

The sun is responsible for the development and continued existence of life on Earth. We are warmed by the sun's infrared rays, and we can see with eyes that respond to the visible part of the sun's spectrum. More importantly, visible light is essential for photosynthesis, the process whereby plants, necessary for our nutrition, derive their energy. Besides serving as the ultimate source of food and energy for humans, sunlight also acts on them to alter their chemical composition, control the rate of their maturation, and drive their biological rhythms; however the ultraviolet component, which comprises approximately 5% of terrestrial solar ultraviolet (UV) radiation, is largely responsible for the deleterious effects associated with sun exposure. Prior to the beginning of this century, the sun was our only source of exposure to UV radiation; but with the advent of artificial sources, the opportunity for additional exposure has increased. Exposure may be elective (eg sunbathing, cosmetic tanning with sunbeds, or medical therapy), or adventitious, often as a consequence of occupation (eg electric arc welders).

Both the quality (spectrum) and quantity (intensity) of terrestrial ultraviolet radiation varies with the elevation of the sun above the horizon, or solar altitude. The solar altitude depends on the time of day, day of year, and geographical location. On a summer's day, UVB (290–320 nm) comprises approximately 5% of terrestrial ultraviolet, and UVA (320–400 nm) the remaining 95%. But since UVB is much more effective than UVA at causing biological damage, solar UVB contributes about 80% towards the harmful effects we associate with sun exposure, with solar UVA contributing the remaining 20%.

The quality and quantity of solar UV are modified on its passage through the atmosphere. The principal interactions in the stratosphere (~10 to 50 km above sea level) are absorption by ozone and scattering by molecules such as nitrogen (N_2) and oxygen (O_2). In the troposphere (0 to ~10 km above sea level), absorption by pollutants such as ozone, nitrogen dioxide (NO_2) and sulfur dioxide (SO_2), and scattering by particulates (eg soot) and clouds are the main attenuating processes. Clouds reduce UV intensity, although not to the same extent as infrared (heat) intensity. This is because water in clouds attenuates solar infrared much more than ultraviolet; and so the risk of overexposure is increased, because the warning sensation of heat is diminished. Roughly speaking, the ambient annual UV radiation is about two thirds that estimated for clear skies in temperate latitudes, rising to about 75% for the tropics.[1] Light clouds scattered over a blue sky make little difference to UV intensity unless directly covering the sun, while complete light cloud cover reduces terrestrial UV to about one half of that from a clear sky. Even with heavy cloud cover, the scattered ultraviolet component of sunlight (often called skylight) is seldom less than 10% of that under clear sky;[2] however, very heavy storm clouds can virtually eliminate terrestrial UV, even in summertime. Reflection of solar UV radiation from most ground surfaces is normally less than 10%.[3] The main exceptions are gypsum sand, which reflects about 15–30%, and snow, which can reflect up to 90%. Contrary to popular belief, calm water reflects only about 5% of incident UV radiation, although up to 20% is reflected from choppy water. Since UV rays pass easily through water, swimming in either the sea or open-air pools offers little protection against sunburn.

Human Exposure to Natural UVR

The solar ultraviolet radiation to which an individual is exposed depends upon:

- Ambient solar ultraviolet radiation.
- The fraction of ambient exposure received on different anatomical sites.
- Behavior and time spent outdoors.

The UV dose absorbed by the skin is further modified by the use of photoprotective agents such as hats, clothing, and sunscreens.

Estimates of personal exposure can be obtained in two ways: (1) by direct measurement using UV-sensitive film badges; (2) or by independent determination of these three variables, either by measurement, modelling, or a combination of both.[4] The results obtained from a number of studies in northern Europe indicate that indoor workers in northern Europe receive an annual exposure of around

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0738-081X/98/$19.00
PII S0738-081X(97)00172-7

200 standard erythema doses (SED),* mainly from weekend and vacational exposure, and principally to the hands, forearms, and face. This value is approximately 5% of the total ambient available.

Outdoor workers at the same latitudes receive about 2 to 3 times these exposure doses, while film badge studies on three groups of outdoor workers on the Sunshine Coast in Queensland (27°S) suggest that annual exposures would be considerably higher—certainly in excess of 1000 SED per year.[5]

Children have a greater opportunity for outdoor exposure and receive an annual dose in England of around 300 SED. For indoor workers the annual exposure associated with occupation (travelling to and from work, going outside at lunchtime) is about 40 SED, about 100 SED is contributed by weekend exposure, and the remaining 60 SED from vacational exposure. In the case of children, 'occupational' exposure (playtime and lunchtime exposure) may be about 60 SED, recreational about 180 SED (because children are at school for only about 190 days per year), and vacation with parents giving about 60 SED. It must be stressed, however, that there will be large variations in the annual exposure doses received by individuals within a given population group, depending upon propensity for outdoor activities.[6]

Effects of Solar UV Radiation on the Skin

The normal responses of skin to UV radiation can be classed under two headings: acute effects and chronic effects. An acute effect is one of rapid onset and generally of short duration, as opposed to a chronic effect, which is often of gradual onset and long duration.

Sunburn

Sunburn, or erythema, is an acute injury following excessive exposure to solar UV radiation. The redness of the skin that results is due to an increased blood content of the skin by dilatation of the superficial blood vessels in the dermis, mainly the subpapillary venules. Half an hour of midday summer sunshine in northern Europe on the unacclimatized skin of Caucasian subjects is normally sufficient to result in a subsequent mild reddening of the skin. Following this degree of exposure, erythema may not appear for about 4 hours, although measurements using an instrument more sensitive than the eye at detecting erythema showed that vasodilatation begins to occur much sooner.[7] The erythema reaches a maximum at about 8–12 hours after exposure, and it fades after a few days. Exposing the skin for increasing periods to strong summer sunshine progressively shortens the time before the appearance of erythema, lengthens its persistence, and increases its intensity. High doses may result in edema, pain, blistering, and, after a few days, peeling.

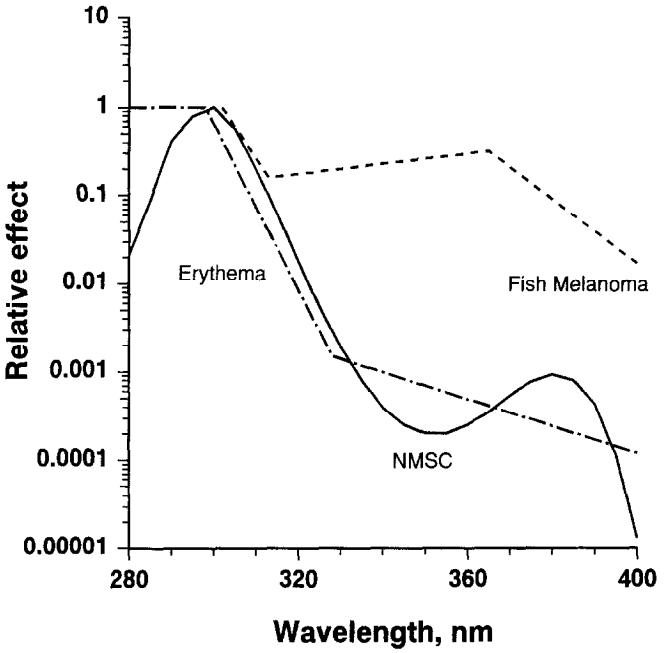

Figure 1. The action spectra for erythema in human skin,[9] nonmelanoma skin cancer in human skin (derived from data from hairless mice),[49] and melanoma in tropical fish.[51]

Action Spectrum for Ultraviolet Erythema

The ability of UV radiation to produce erythema in human skin is highly dependent upon the radiation wavelength, and it is expressed by the erythema action spectrum. Erythema action spectra have been the subject of experimental and theoretical interest for over 70 years. The International Commission on Illumination (CIE) first considered the adoption of a so-called standard erythemal curve in 1935.[8] More recently a new CIE reference action spectrum has been proposed that is represented by relatively simple functions over three clearly defined spectral regions (*Fig 1*).[9] Two experimental studies published since this action spectrum was introduced have shown that it is a valid predictor of the erythemal effectiveness of different wavelengths of ultraviolet radiation.[10,11]

Factors Influencing the Development of Sunburn

Skin color is an important factor in determining the ease with which the skin will sunburn. Whereas fair-skinned people require only about 15–30 minutes of midday summer sunshine to induce an erythemal reaction; people with moderately pigmented skin may require 1–2 hours exposure; and those with darkly pigmented skin will not normally sunburn. Other phenotype characteristics that may influence the susceptibility to sunburn

* *SED is equivalent to an erythemal weighted exposure dose of 100 J/m^2; a minimal erythema on unexposed skin in subjects with skin types I to IV would be expected to require an exposure of between 1.5 to 6 SED.*

are hair color, eye color, and freckles.[12,13] Based on a personal history of response to 45–60 minutes of exposure to midday summer sun in early June, individuals can be grouped into one of six sun-reactive skin types.[14]

There are anatomical differences in erythemal sensitivity. The face, neck and trunk are two to four times more sensitive than the limbs.[15] These anatomical differences are compounded by the variations in solar exposure on different parts of the body. Vertical surfaces of an upright person receive about one third of the ambient UV radiation, whereas horizontal surfaces, such as the epaulette region of the shoulder, receive up to 75%. There is no difference in sunburn susceptibility between sexes. Although erythemal sensitivity may change with age, in that young children and elderly people are said to be more sensitive, quantitative studies of erythemal sensitivity in subjects of these age groups have not confirmed this.[16,17]

Heat, humidity, and wind have been shown to alter the erythemal sensitivity of mice exposed to artificial UVB radiation, but the significance of these atmospheric conditions upon the induction of sunburn in humans has not been clearly identified.

Epidermal Hyperplasia

Thickening (hyperplasia) of the epidermis is a significant component of a mild sunburn reaction. A single moderate exposure to UVB can result in up to a threefold thickening of the stratum corneum within one to three weeks, and multiple exposures every one to two days for up to seven weeks will thicken the stratum corneum by about three to fivefold.[18] Skin thickness returns to normal about one to two months after ceasing radiation.

Thickening of the skin, especially of the stratum corneum, after sun exposure can lead to a significant increase in protection against UV radiation by a factor of five or even higher. In Caucasians, skin thickening is probably more important than tanning in providing endogenous photoprotection, although in darkly pigmented races it is likely that skin pigmentation is the most important means of protection against solar UV radiation.

Tanning

A socially desirable consequence of exposure to unfiltered sunlight is the delayed pigmentation of the skin known as tanning, or melanin pigmentation. Melanin pigmentation of skin is of two types: (1) constitutive—the color of the skin seen in different races and determined by genetic factors only; and (2) facultative—the reversible increase in tanning in response to solar UV radiation (and other external stimuli).

Immediate Pigment Darkening

This is a transient darkening of exposed skin that can be induced by UVA and visible radiation.[19] In general, the greater the constitutive tan, the greater is the ability to exhibit immediate pigment darkening (IPD). Immediate tanning can become evident within 5–10 minutes of exposure to summer sun, and it normally fades within 1–2 hours. Electron microscopic studies suggest that melanin photochemistry is the predominant mechanism of IPD.[20,21] The function of IPD has not yet been demonstrated.

Delayed Tanning

The more familiar delayed tanning becomes noticeable about one to two days after sun exposure, gradually increases for several days, and it may persist for weeks or months. Following solar UV radiation exposure, there is an increase in the number of functioning melanocytes; and activity of the enzyme tyrosinase is enhanced.[22] This leads to the formation of new melanin and, hence, an increase in the number of melanin granules throughout the epidermis. Although a tanned skin does confer a degree of photoprotection, such protection seems to be no more than moderate, a factor of only two to three being achieved by a deep UVA-induced tan in the absence of skin thickening.[23] Melanin is not an effective sunscreen for Caucasian skin, and it has been suggested that, contrary to popular belief, melanin is not an evolutionary adaptation to protect humans from the damaging effects of sunlight.[24] Instead it is postulated that hominids developed melanin as a camouflage and as a device to keep their bodies warm in a forest environment.

Action Spectrum for Delayed Tanning

The doses of UV radiation at different wavelengths necessary to induce delayed tanning were determined by one group of investigators for subjects with sun-reactive skin types I and II (poor tanners) and by another group for subjects who tan well (skin types III and IV).[25,26] The action spectra obtained corresponded broadly with the erythema action spectrum. The threshold doses at all wavelengths for erythema and pigmentation were similar to those for poor tanners; whereas in those subjects who are genetically capable of tanning easily, the melanogenic doses in the UVA region were approximately one quarter of the doses required to produce a minimal erythema. That melanogenesis can be stimulated in individuals who tan well with suberythemal doses of solar UV radiation has been confirmed by field studies using unfiltered and optically filtered sunlight.[27]

Production of Vitamin D_3

The only thoroughly established beneficial effect of solar ultraviolet radiation on the skin is the synthesis of vitamin D_3. Solar radiation in the UVB waveband photochemically converts 7-dehydrocholesterol in the epidermis to previtamin D_3. This previtamin immediately isomerizes to vitamin D_3 in a reaction controlled by skin temperature, and it takes two to three days to reach completion. Previtamin D_3 is photolabile, and excessive exposure to sunlight causes its photolysis to biologically inert photoproducts, lumisterol and tachysterol. In fact, production of previtamin D_3 is limited to no more than 5–15% of the 7-dehydrocholesterol content in the skin, no matter how long a person is exposed to sunlight. Once vitamin D_3 is made in the skin, it enters the blood for transport to the liver to be metabolized to 25-hydroxyvitamin D.[28] If vitamin D_3 does not enter the circulation before sun exposure the following day, it can rapidly be degraded in the skin by sunlight to suprasterol 1, suprasterol, and 5,6 transvitamin D_3, products that are believed to be biologically inert.[29] Thus sunlight, through its photochemical activity, is able to regulate the production of both previtamin D_3 and vitamin D_3 in the skin.

Only short exposures to sunlight are required to synthesize vitamin D_3 in the skin; from spring until autumn 15 minutes exposure to the hands, arms and face between 9:00 AM and 4:00 PM is adequate to provide our vitamin D_3 requirement; however, in England it is likely that there is insufficient ambient UVB during the winter to synthesize vitamin D_3.[30] Furthermore, increased melanin pigmentation in the skin can limit the production of vitamin D_3, as can increasing age.[31,32] It is not surprising, therefore, that the seasonal variation of solar UVB, and hence plasma 25-hydroxyvitamin D_3 levels, has led to calcium imbalance in the elderly and nutritional osteomalacia in Asian immigrants to the UK.[33–34]

Photoaging

The clinical signs of a photoaged skin are dryness, deep wrinkles, accentuated skin furrows, sagging, loss of elasticity, mottled pigmentation and telangiectasia.[36] These characteristics reflect profound structural changes in the dermis.[37] It has been speculated that perhaps as much as 80% of solar UV induced photoaging occurs within the first 20 years of life, with the exception of those whose occupation or life style results in extensive exposure as adults.[36]

Action Spectrum for Photoaging

The relative importance of different wavelengths in aging human skin cannot be readily determined because of the long latent period and slow evolution of photoaging. Instead, extrapolation from experiments using hairless mice or the miniature pig is relied upon.[38–40] Because approximately one third of UVA radiation and less than 10% of UVB radiation incident on white skin penetrates to the dermis, it is not surprising that results from animal studies have shown that chronic UVB and UVA irradiation in hairless mouse skin both result in histological, physical, and visible changes characteristic of photoaging.[38,41] UVB radiation was only 20–50 times more efficient than UVA; this is in marked contrast to sunburn, suntan, and nonmelanoma skin cancer where UVB is about 1000 times more effective than UVA.

It should be remembered that solar radiation includes not only UV radiation but also visible and infrared radiation. Visible light is thought to be unimportant in photoaging,[37] but studies have confirmed that infrared radiation can certainly damage the dermal matrix.[37,42]

Skin Cancer

The three common forms of skin cancer, listed in order of seriousness are: basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma (MM). Around 90% of skin cancer cases are of the nonmelanoma variety (BCC and SCC) with BCCs being approximately four times as common as SCCs. Exposure to UV radiation is considered to be a major etiological factor for all three forms of cancer.[43] For basal cell carcinoma and malignant melanoma, neither the wavelengths involved nor the exposure pattern that results in risk have been established with certainty; whereas for squamous cell carcinoma, both UVB and UVA are implicated, and the major risk factors seem to be cumulative lifetime exposure to UV radiation and a poor tanning response.

Squamous Cell Cancer

The evidence that exposure to sunlight is the predominant cause of squamous cell cancer in humans is very convincing. These cancers occur almost exclusively on sun-exposed skin such as the face, neck, and arms; and the incidence is clearly correlated with geographical latitude, being higher in the more sunny areas of the world.[44] Recent epidemiological studies suggest that sun exposure in the 10 years prior to diagnosis may be important in accounting for individual risk of SCC.[45]

Basal Cell Cancer

The relationship between basal cell carcinoma and sunlight is less compelling, but the evidence is sufficiently strong to consider it also to be a consequence of exposure to sunlight. While SCC is strongly related to cumulative lifetime exposure to sunlight, this relationship is not so convincing for BCC;[46,47] and it may be that sun

exposure in childhood and adolescence may be critical periods for establishing adult risk for BCC.[46]

Action Spectrum for Nonmelanoma Skin Cancer

Clearly an action spectrum for skin cancer can be obtained only from animal experiments. The most extensive investigations to date are those from groups at Utrecht and Philadelphia. These workers exposed a total of about 1100 white hairless mice to 14 different broad-band ultraviolet sources, and by a mathematical optimization process derived an action spectrum referred to as the Skin Cancer Utrecht-Philadelphia (SCUP) action spectrum.[48] The SCUP action spectrum is that for skin tumor induction in hairless mice, a species which has a thinner epidermis than humans. By taking into account differences in the optics of human epidermis and hairless albino mouse epidermis, the experimentally determined action spectrum for tumor induction in mouse skin can be modified to arrive at a postulated action spectrum for human skin cancer.[49] The resulting action spectrum resembles the action spectrum for erythema (*Fig 1*).

Malignant Melanoma

During the past 40 years or so there has been an increase in the incidence of malignant melanoma in white populations in several countries. There exists an inverse relationship between latitude and melanoma incidence, and this has been taken as evidence for a possible role of sunlight as a cause of malignant melanoma; however, this pattern is not always consistent. In Europe, for example, the incidence and the mortality rates in Scandinavia are considerably higher than those in Mediterranean countries. This inconsistency may reflect ethnic differences in constitutional factors and customs. Also, the unexpectedly low incidence in outdoor workers, the sex and age distribution, and the anatomical distribution have pointed to a more complex association.[50]

There is now growing evidence that intermittent sun exposure—mainly from recreational activities—rather than cumulative or chronic exposure associated with occupation is associated with increased risk of developing malignant melanoma. Several studies have established a history of sunburn as an important risk factor for melanoma development, although in these studies a potential for recall bias exists. Migration studies have led to the suggestion that sun exposure in childhood is a particularly critical period in terms of melanoma risk.

Action Spectrum for Melanoma

The only data that exist on an action spectrum for melanoma induction are those obtained from irradiating hybrids of a small tropical fish with different wavelengths of ultraviolet irradiation.[51] The action spectrum obtained in this study (Fig 1) shows that all wavelengths of UV radiation may be important in melanoma, unlike nonmelanoma skin cancer in which the causative wavelengths are largely within the UVB spectrum.

Other Cancers

There is some evidence that solar radiation may play a role in ocular melanoma and cancer of the lip; however both cancers are rare, and there is not the clear relationship with geographical latitude that is seen with skin cancers. Non-Hodgkin's lymphoma has increased in incidence in several countries over the past few decades, with geographical and temporal trends that are similar to those seen in nonmelanoma skin cancers, raising the possibility of a link with sun exposure.[52,53] Further support for this hypothesis comes from observations that both melanoma and nonmelanoma skin cancers occur appreciably more often than would be expected among patients who have previously been diagnosed as having non-Hodgkin's lymphoma.[54]

Eye Damage

Exposure to sunlight, particularly the UVB component, is believed to be associated with a variety of eye disorders, including damage to the cornea, lens, and retina.[55] Cataracts are the most frequent effect, while photokeratitis (snowblindness) and pterygium (a fleshy growth on the conjunctiva) also result from UVB exposures. Cataracts are a major cause of blindness in both developed and developing countries; however, the relative importance of different wavelengths in cataractogenesis, as well as dose relationships, are extremely uncertain.

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