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Ultraviolet radiation

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CONTENTS

INTRODUCTION

Of the various types of nonionizing radiation, ultraviolet (UV) is of special interest because of its relatively high photon energy as compared to the other

types included in this group. This could lead to greater variation in biological response. On the other hand, the low penetration will restrict most of the direct biological responses to the superficial tissues.

Although UV radiation can arise from a large number of man-made sources, the sun is the main source and both the general public and people working out of doors will be exposed to it. This natural background radiation and the variations in its magnitude must be taken into account when exposure limits are discussed.

It is well known that UV can initiate photochemical reactions and that some of these take place in the skin. The best known is the production of vitamin D_3, which is necessary for the prevention of rickets in man. The full extent to which UV affects human wellbeing is difficult to quantify. Artificially produced UV has, however, been used in mines and cellars and in far northern latitudes as a supplement to combat functional impairment among people *(1,2)*. Many of the observed effects, such as a decrease in the incidence of infectious diseases and in absenteeism, may be due to the bactericidal nature of the radiation *(3)*. On the other hand, large doses of UV have an acute destructive effect on the skin and eye. Doses so low that they give rise only to normally acceptable or even desirable acute effects can, if repeated, induce changes resulting in late effects such as elastosis of the skin, keratosis and skin cancers. These effects will be of greater significance in people with lightly pigmented skin.

Our goal in protecting the population against the harmful effects of UV is to establish the most appropriate exposure limits based on a biological risk–benefit analysis of all these factors in as quantitative a fashion as possible *(4)*.

PHYSICAL DESCRIPTION

Ultraviolet radiation is that part of the electromagnetic spectrum lying between the softest ionizing radiation on the one side and visible radiation on the other. For biological purposes, it is convenient to regard the range of wavelengths from 100 to 380–400 nm as constituting UV. The lower limit of 100 nm is equivalent to photon energies of 12.4 eV, which corresponds approximately to the limit for the production of ionization in biologically important materials. At the other end, the limit is the shortest visible wavelength; this varies slightly from individual to individual, and in adults lies between 380 and 400 nm.

Because of differences in physical properties and in biological effects, the UV region has been subdivided. Wavelengths shorter than approximately 180 nm are absorbed by air to such an extent that no biological effects would be expected, unless very powerful sources are used. The remainder can then be divided into the far-UV region between 180 and 300 nm and the near-UV region between 300 and 400 nm.

A somewhat different way of dividing the UV region takes some of the biological effects into account. In this arrangement the range 400–315 nm, the so-called "black light" region, is called UV-A. In this wavelength region,

fluorescence can be induced in many substances. UV-B covers the range 315–280 nm (the skin erythemal region). Most of the biologically active and potentially harmful UV from the sun reaching the surface of the earth falls within this spectral region. UV-C includes the radiation of wavelengths less than 280 nm (the germicidal region); it occurs in the radiation emitted by germicidal lamps and welding arcs, but not in sunlight reaching the earth's surface. These divisions are, however, arbitrary and usage varies from one worker to another.

PRODUCTION

Matter at a temperature of 2500 K or higher may emit a significant number of photons with energies inside the UV range. Such incandescent sources emit a smooth spectrum, a continuum, possibly with superimposed lines.

Most man-made sources of UV radiation can be grouped together in the categories shown below.

Incandescent sources
- tungsten halogen lamps

Gas discharges
- mercury lamps (low-, medium- and high-pressure)
- mercury lamps with metal halides
- xenon lamps
- hydrogen and deuterium lamps
- flash tubes

Electric discharges
- welding arcs
- carbon arcs

Fluorescent lamps
- fluorescent lighting tubes
- fluorescent sunlamps (UV-B emitters)
- fluorescent UV-A tubes

Lasers
- excimer lasers (several wavelengths)
- nitrogen lasers (337 nm)
- tunable UV lasers
- helium–cadmium lasers (325 nm)

The spectrum of the UV radiation emitted varies from one source to another. In the case of low-pressure mercury lamps, a line spectrum will be emitted. These lines are broadened into bands in high-pressure lamps (often called medium-pressure lamps by photobiologists) and there may also be emission of a continuum over a wide range of wavelengths. This continuum

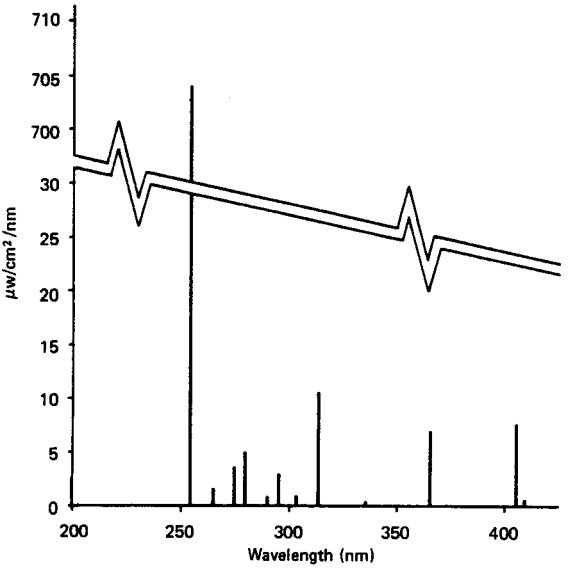
is most strongly marked in the highest pressure lamps. Addition of metal halides will increase both the continuum and the number of superimposed lines in the spectrum (Fig. 1 and 2). In high-pressure xenon lamps there is also a combination of distinct bands with a continuum (Fig. 3) *(5)*.

The emission spectrum of the arc produced during welding will depend not so much on the atmosphere in which the welding takes place but rather on the composition of the electrodes. An example of an emission spectrum produced by a welding process is shown in Fig. 4.

The spectrum of fluorescent lamps depends mainly on the properties of the fluorescent phosphors employed in the envelope. The amount of UV depends also on the absorption properties of the envelope glass used in the fluorescent tube (Fig. 5 and 6).

To permit the transmission of UV when the discharge does not take place in free air, gas discharge arcs and other UV sources must be contained within an envelope of quartz or UV-transmitting glass. On the other hand, sources that are designed primarily to emit visible radiation but which also produce significant but unwanted amounts of UV should be provided with an external filter that absorbs UV-B and UV-C radiation.

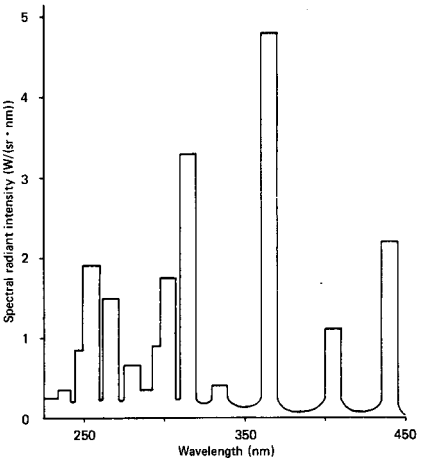
Fig. 1. Emission spectrum of a typical low-pressure mercury vapour lamp



Note. 55% of output is at the 253.7-nm resonance line of mercury.

Source: Courtesy F. Urbach.

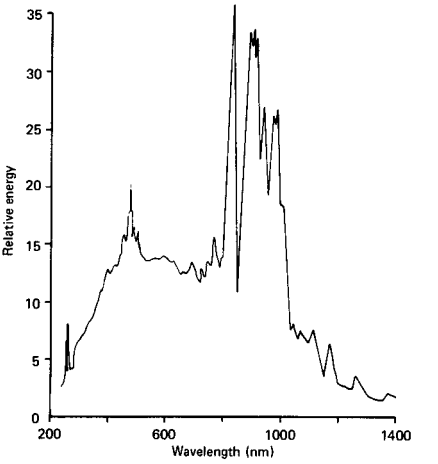
Fig 2. Emission spectrum of a typical mercury arc lamp operating at medium pressure



Note. The spectral lines of mercury are superimposed on a low continuum.

Source: Courtesy F. Urbach.

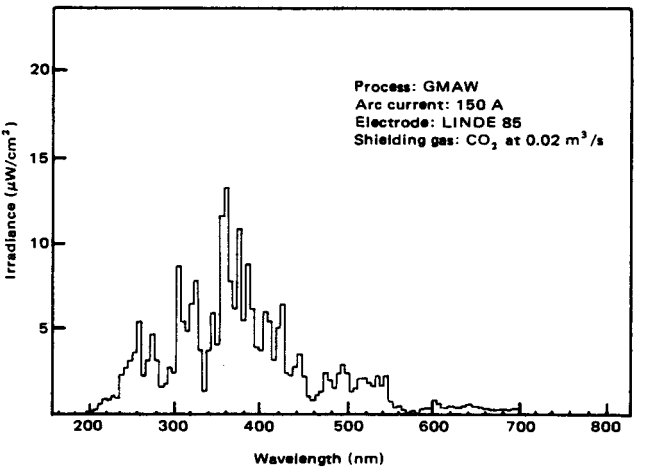
Fig 3. Emission spectrum of a compact xenon arc light source operating at high pressure



Note. Similarity to solar spectrum (above the atmosphere) and very high infrared output.

Source: Courtesy F. Urbach.

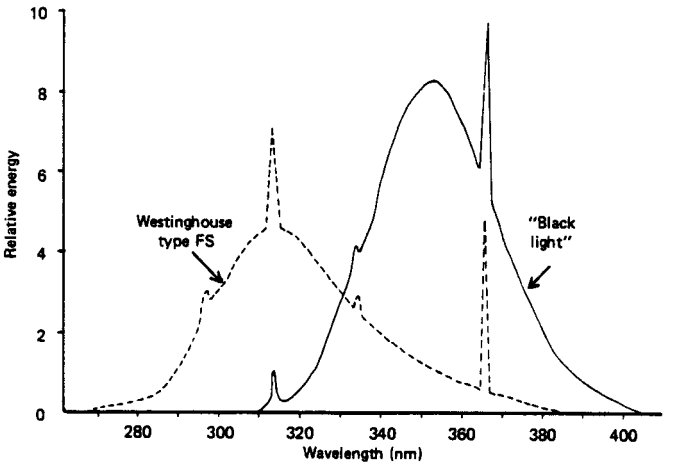
Fig. 4. Emission spectrum of gas tungsten arc welding



Note. The spectral emission from any kind of electric arc welding will depend on the composition of the electrodes, the plasma that is created and the shielding gas used.

Source: Adapted from Sliney & Wolbarsht *(6)*.

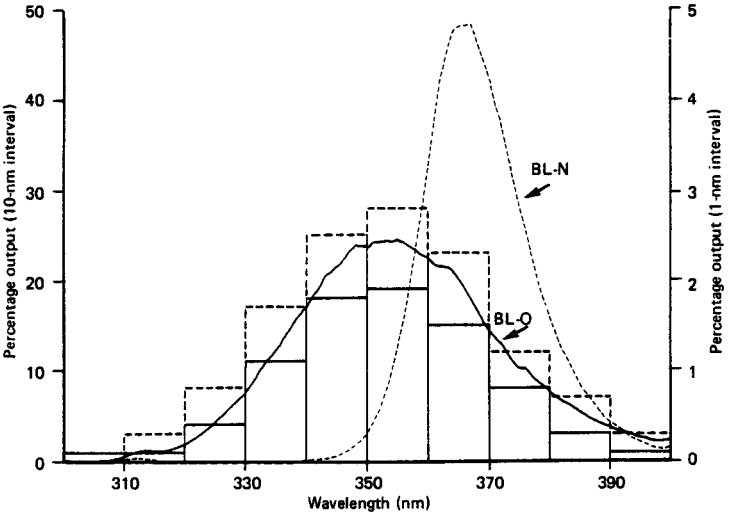
Fig. 5. Emission spectra of two medically used fluorescent lamps



Note. Type FS emits primarily in the UV-B, type "Black light" emits primarily in the UV-A.

Source: Courtesy F. Urbach.

Fig. 6. Emission spectra of two fluorescent lamps emitting primarily in the UV-A.



Note. Because of the use of two different phosphors, the spectral distribution between BL-O and BL-N differs markedly.

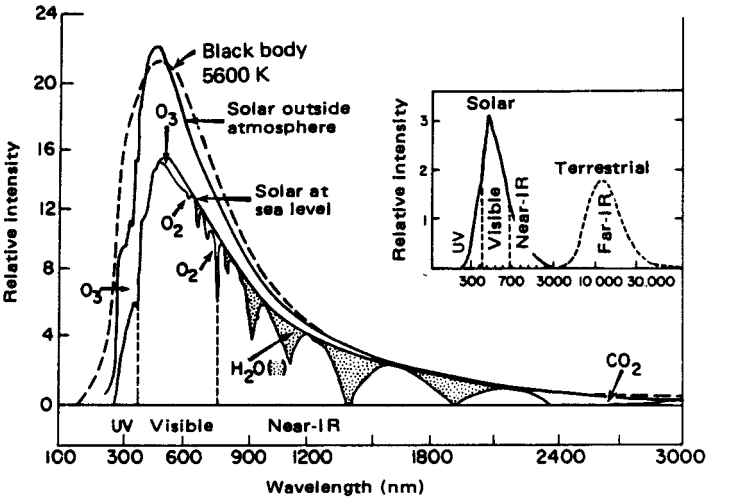
Source: Courtesy F. Urbach.

In the case of lasers, the emission lines will depend on the active medium and on the operating conditions.

SOLAR ULTRAVIOLET RADIATION

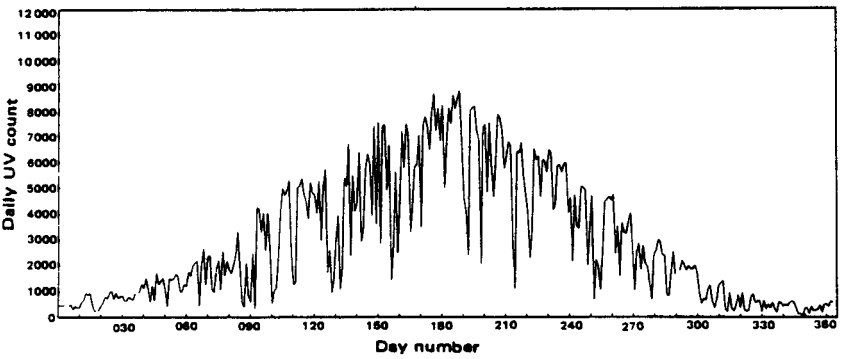
The sun is the main UV source. The broad spectrum and the intensity of the UV radiation from the sun are due to the high temperature at its surface and its size. The intensity is such that the UV radiation reaching the earth's atmosphere would probably be lethal to most living organisms on the surface. Fortunately, they are shielded by the atmosphere. The ozone layer in the upper atmosphere is particularly important in this connection. The spectrum, both before passage through the atmosphere and at sea level, is shown in Fig. 7. The path length traversed in the atmosphere by the UV radiation determines the irradiance at the surface of the earth; it is, therefore, affected by geographical latitude, altitude above sea level, and time of day and season. Scattering and absorption by dust, smoke and rain are also important. It should be noted that practically no UV radiation from the sun with wavelengths below 290 nm reaches the surface of the earth. The changes over the year in one location are shown in Fig. 8; it will be seen that large day-to-day changes occur.

Fig. 7. The sun's spectrum at the outer surface of the atmosphere and at sea level



Source: Giese *(7)*.

Fig. 8. Daily total erythemally effective UV count for 1974, Minneapolis, USA



Note. The measurements were performed with a Robertson-Berger meter, which weights the radiation spectrally according to a sensitivity curve, approximating the action spectrum for UV erythema in human skin.

Source: Scotto *(8)*.

When the yearly changes for discrete wavelengths (Fig. 9) are given as monthly averages, it can be seen that such changes are not the same for all wavelengths. A comparison between the curves obtained in open country and in an adjacent city (Sofia) show the effect of polluted air in reducing the UV in the city. Again, there is a difference between the wavelengths, the shortest showing the greatest reduction. Dependence on latitude is shown in Fig. 10.

If the ozone layer were to decrease in thickness, the absorption in the critical UV bands would decrease, and an increase in the biological effects of UV-B would be expected *(9)*.

Ozone is produced photochemically by UV from the sun at wavelengths largely below 242 nm. It is present in a concentration which is the outcome of a dynamic equilibrium between production and breakdown; there are daily, seasonal and geographical variations in this concentration. These variations add to the complexity of investigating long-term changes.

Volatile stable substances, released from the earth's surface as a result of human activities, can reach the ozone layer, and are decomposed there by photochemical reactions. Interest has concentrated on chlorofluorocarbons (CFCs), since photochemically produced chlorine can catalytically attack ozone and result in lower equilibrium concentrations *(10)*. Nitrogen oxides have also been investigated in this connection, as well as many other compounds and their interactions in the atmosphere *(11)*.

The computed long-term result, typically describing a development over several decades, depends strongly on the assumptions made for the future release of the various pollutants; projected changes of total ozone vary from an increase of 2–3% to a decrease of 10% or more. The latter possibility represents the case that the ozone chemistry would be dominated by chlorine; this is expected to occur only with a significant sustained growth in CFC emissions, of 3% or more per year. The production and release of CFCs have decreased since 1974, mainly as a result of restrictions on their use as propellants in spray cans. There is an increase, however, in their use for other purposes, such as refrigeration and foam blowing *(9)*.

The possibility of a decrease in ozone with a concomitant rise in UV-B has important biological implications. The consequences for human health are easiest to evaluate, owing to the availability of quantitative data. The predominant effect expected is an increase in the incidence of skin cancer. For every 1% reduction of the average thickness of the ozone layer, the incidence of basal-cell carcinoma would increase by about 3% and the incidence of squamous-cell carcinoma by about 5% *(12,13)*. It is uncertain whether there would be an influence on the incidence of malignant melanoma. UV-B radiation has been demonstrated to be harmful to several forms of plant and animal life; consequences for agriculture and fisheries are, therefore, likely. These are potentially at least as important as the direct effect on human health; because of lack of data it is as yet not possible to make quantitative predictions *(9)*.

Fig. 9. Monthly average UV intensity in Sofia, Bulgaria and in adjacent open country

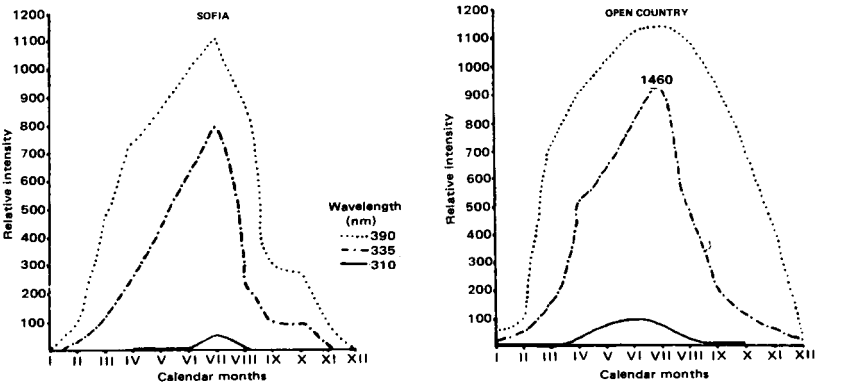
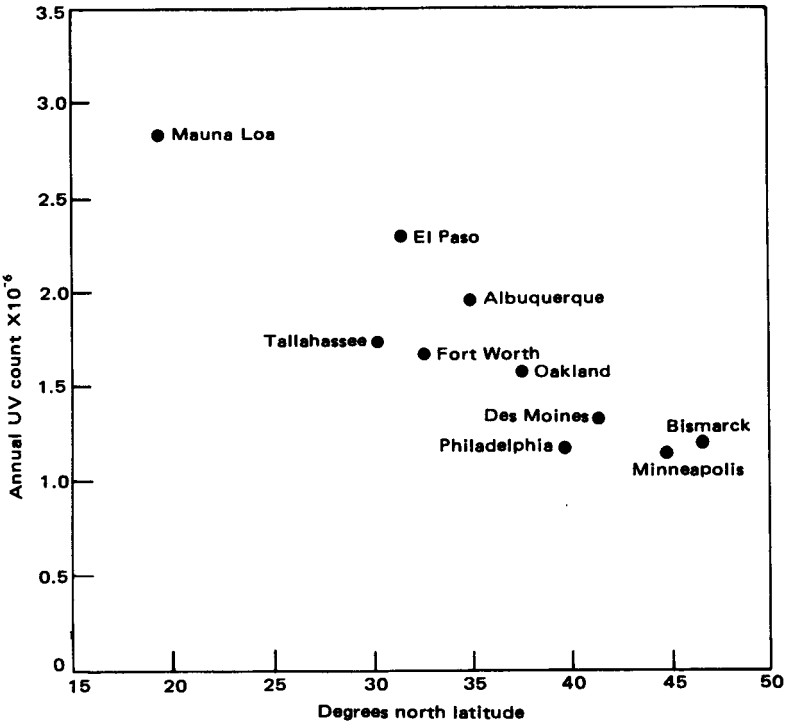


Fig. 10. Annual erythemal UV count by latitude



Source: Scotto *(8)*.

TRANSMISSION AND ABSORPTION IN BIOLOGICAL TISSUE

Most of the UV radiation incident on the skin is absorbed in the epidermis. Absorption is generally greater for the shorter wavelengths (Fig. 11).

The same is true for the eye. Most of the UV radiation is absorbed in the tear film, the cornea and the lens. The lens and the tissues in the anterior part of the eye may, however, be exposed to UV at wavelengths above 295 nm and the retina is exposed to a certain extent to UV-A. The penetration of different wavelengths into the eye is given in Table 1. Some doubt exists, however, as to the high transmission given for the vitreous humour at the longer wavelengths.

ABSORPTION AND PHOTOCHEMICAL PROCESSES

The primary process in a photochemical reaction is the absorption of radiant energy by a chromophore. In most molecules the ground or relaxed state consists of two paired electrons, the singlet state (S_0). On absorption of radiant energy one of the electrons can make a transition to an excited state (S_1), provided that the photon energy corresponds to an existing energy level in the absorbing molecule. From the excited state the molecule can release its energy by *(a)* transition of the excited electron to the ground state, giving off the energy as fluorescence, or *(b)* transition to the generally long-lived triplet excited state (T_1) and then discharging energy as phosphorescence. In addition, molecules in the S_1 or T_1 states can relax either by forming photoproducts or by transferring the energy to an acceptor molecule. Formation of photoproducts, as well as transfer of energy to an acceptor molecule, requires compatible energy levels for the donor molecule and the energy receptor.

In photosensitized reactions the photon energy is absorbed by a photosensitizer and then transferred directly or via an intermediate, such as oxygen, to the biochemical compound.

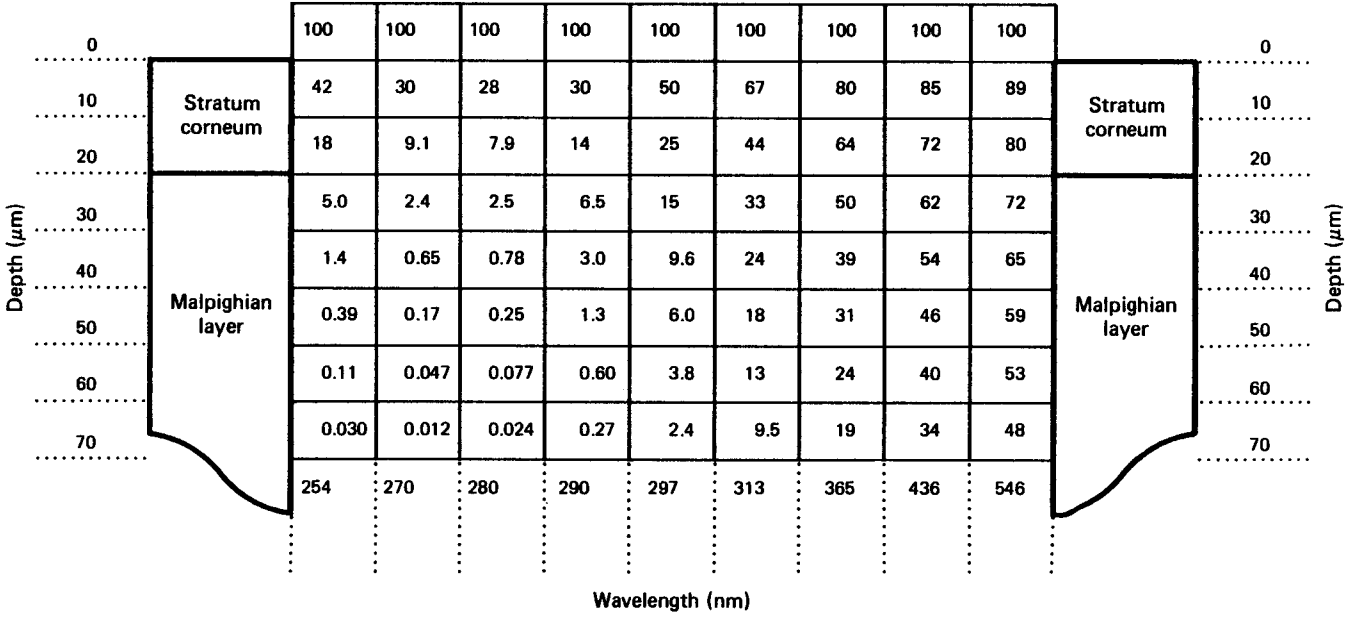
The photochemical process can be impeded by "quenchers". The quencher either brings the excited state molecule directly back to the ground state or neutralizes the reactive intermediates in the photosensitized reactions.

The most important biological UV radiation absorbers are proteins and nucleic acids. Examples of biologically active photosensitizers are methoxsalen and chlorpromazine. Important quenchers in biological tissue are vitamin E, carotenes and ascorbic acid.

The absorption spectrum describes the absorption of radiant energy as a function of wavelength. Nucleic acids have their main absorption peak close to 265 nm, due to the pyrimidine structure. The aromatic amino acids are the absorbing sites in protein, with tyrosine at 275 nm and tryptophan at 280 nm.

The action spectrum gives the relative response of a system to irradiation at different wavelengths, and ideally will correspond to the absorption spectrum. In biological systems, however, the action spectrum function is

Fig. 11. Penetration of UV and visible radiation into human epidermis for lightly pigmented Caucasian skin, at several wavelengths and to several depths



Note. The data apply to collimated, perpendicular irradiation and are expressed as a percentage of incident irradiance.

Source: Bruls et al. *(15)*.

Table 1. Percentage of energy incident on the corneal epithelium that impinges on the anterior surface of the various ocular media

Wavelength (nm)	Corneal stroma	Aqueous humour	Lens	Vitreous humour	Retina
230	3	—	—	—	—
235	11	—	—	—	—
240	19	—	—	—	—
245	26	—	—	—	—
250	26	—	—	—	—
260	26	—	—	—	—
265	27	—	—	—	—
270	29	—	—	—	—
275	31	—	—	—	—
280	33	—	—	—	—
285	42	—	—	—	—
290	52	2	0.4	—	—
295	63	9	3	—	—
300	70	27	14	—	—
305	75	50	37	—	—
310	78	64	51	—	—
320	81	78	74	0.3	0.3
330	84	80	77	0.5	0.5
350	87	86	83	2	2
360	89	88	85	4	4
370	90	90	87	12	11
380	93	91	88	28	26
390	94	93	91	49	45
400	95	94	93	69	64
450	—	96	96	84	81
500	—	96	96	87	84

Source: Modified from Kinsey *(14)*.

modulated by the shielding (i.e. thickness) of overlying tissue, energy transfer, and the action of sensitizers and quenchers.

A number of biologically important photochemical reactions have been shown to occur in biological tissue. DNA strand breaks and pyrimidine dimers are produced during exposure to UV radiation. Hydrates of cytosine and uracil may be produced, but have not been shown to produce biological effects after direct absorption of UV energy. Of greatest interest, at least in the UV-B region, is the photoproduction of covalent dimers of thymidine and other pyrimidines *(16)*. The biological effects of these lesions are reviewed by Smith *(17)*.

Defects in DNA are repaired in living cells principally by excision repair (dark repair), a process in which it has been possible to isolate at least five participating enzymes. These act by excision of thymidine dimers and dimers of other pyrimidines and reconstitution of the intact DNA strand. The primary biochemical mechanism has been studied both in bacteria and in mammalian and human cells and is now reasonably well understood *(18)*. Defects in the repair system are present in a number of rare diseases, of which xeroderma pigmentosum is the most important in relation to UV damage. Evidence has been presented to show that the genetic constitution, as measured by the ability of cells to repair UV lesions, may be important in relation to the development of UV-induced diseases *(19)*. When repair is in progress, it is easy to recognize in autoradiograms as unscheduled DNA synthesis after uptake of tritiated thymidine. The unscheduled synthesis disappears gradually during the 24 hours following the irradiation. The repair system is limited in its efficiency. In HeLa cells, the initial rate of repair increases linearly after doses of up to 30 J/m^2. At higher doses, no further increase in the rate of thymidine uptake is seen *(18)*. The incident dose needed for the induction of a given number of dimers is wavelength-dependent; at wavelengths of 254, 290 and 310 nm the doses are in the ratio 1 : 30 : 6000. At longer wavelengths, other types of DNA lesion become of increasing and ultimately of dominant importance *(20)*.

In addition, post-replication repair is active in mammalian cells and may be a more error-prone step. This repair system can also be deficient in xeroderma pigmentosum.

Photoreactivation is another independent repair system where exposure to longer wavelengths, whether UV or visible, can induce enzymatic repair. Enzymatic photoreactivation in human cells has been reported by several investigators *(21,22)*. Full agreement has, however, not yet been reached as to the significance of these results. It has been claimed that the enzyme is absent in xeroderma pigmentosum cells *(23)*.

Protein-DNA cross-links can also be repaired. The mechanism is not yet understood *(24)*.

Photochemical reactions induced by UV that have biological consequences are, however, not restricted to cellular constituents alone. Photo-oxidation of atmospheric constituents (smog formation) may, for example, indirectly influence human health.

PATHOLOGICAL EFFECTS IN MAN

For protection purposes these effects can be divided into two main groups, namely non-stochastic and stochastic *(25)*. The non-stochastic effects are related directly to the radiant exposure, while the stochastic effects take the form of an increase in the risk of contracting certain diseases, of which the late appearance of cancer is the most important.

Non-stochastic effects

In this group, the severity of the effects in the exposed individual varies with dose and there may be a threshold below which no effects occur *(25)*. These

effects may be either acute or late and can occur in any cell or tissue that can be reached by radiation or by photochemical by-products.

Because of its limited penetration, the primary effects of UV in man will essentially be restricted to the skin and eyes; only under special circumstances may such effects also extend to the oral cavity.

Skin

Four types of immediate change occur in the skin: *(a)* immediate pigment darkening; *(b)* the production of erythema (sunburn); *(c)* the production and upward migration of melanin granules (suntanning); and *(d)* changes in epidermal cell growth. The structure of the skin is shown in Fig. 12.

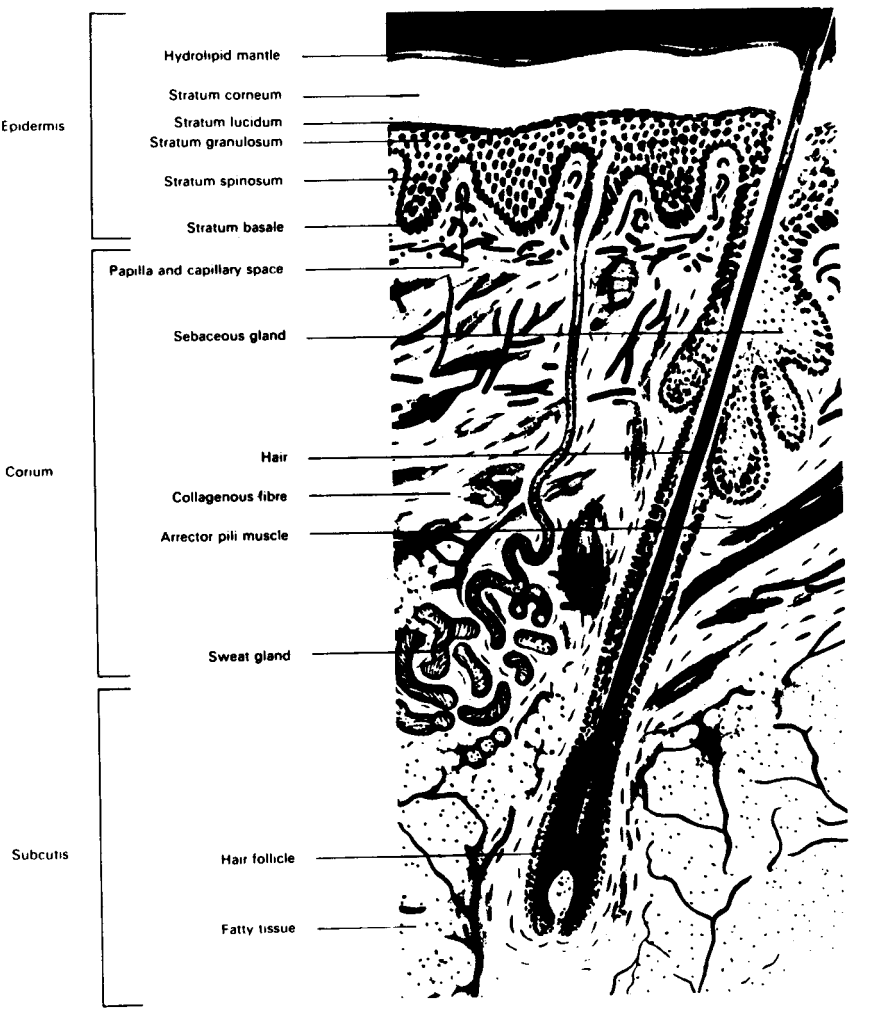
Immediate pigment darkening takes place during and immediately after irradiation. It is most strongly marked in pigmented skin. The action spectrum displays a maximum at 360 nm and extends to wavelengths above 400 nm. The phenomenon has long been ascribed to oxidation of existing premelanin *(27,28)*, but recent investigations do not confirm an increased amount of melanin pigment *(29)*.

The vascular reaction of the skin to UV known as erythema consists of vasodilation and an increased blood content; it may be accompanied by augmented blood flow and increased vascular permeability leading to cellular exudation, e.g. neutrophil leukocytes, and in severe cases by blistering. The erythema appears after a latent period of 1–8 hours, and lasts for one or more days. Higher doses of UV radiation lead to a shorter latent period and a longer duration of the erythema. The intensity of the erythema increases with increasing UV dose; the steepness of the increase in redness with increasing dose is different for the erythemas caused by the various wavelengths in the UV *(30,31)*. It appears likely that there are at least two different erythemal mechanisms, one based on direct action of the radiation on the superficial blood vessels, whose dilation causes the reddening of the skin, and one based on an indirect action, where the radiation acts on the epidermis and the vasodilation is effected by an active substance diffusing to the blood vessels in the dermis *(32)*. The involvement of prostaglandins has been suggested *(33)*.

The minimal dose that will provoke an erythema (the minimal erythema dose, MED) is the best defined threshold dose for acute effects following UV exposure in man. The MED depends on the properties of the individual's skin, probably mainly the transmission of UV radiation through the epidermal layers, which in turn is determined by the thickness of the epidermal layers and also by the pigmentation. Both factors are influenced by previous UV exposures. For the same reasons, the MED also depends on the skin region. In lightly pigmented Caucasian skin, not recently exposed, the MED on the trunk is on the average about 200 J/m^2 for wavelengths between 250 and 300 nm; it rises sharply between 300 and 330 nm and is of the order of $2 \times 10^5 J/m^2$ between 330 nm and 400 nm *(34,35)*.

The third reaction of the skin to UV exposure is an increase in pigmentation or "suntan", with an action spectrum close to that of erythema *(35)*. It is initiated by a spreading of existing pigment granules into neighbouring

Fig. 12. Cross-section of human skin



Source: Ciba-Geigy *(26)*.

cells throughout the exposed skin. Production of new pigment granules occurs later in the process.

UV radiation interferes with cell division in skin. Immediately after irradiation there is a cessation of cell division *(36,37)* for 24 hours or longer, depending on dose, followed by an increase in mitoses *(38)*. This increase reaches a maximum at 72 hours *(39)*. The increase in cell division after a

single dose of only short duration gives rise to hyperplasia of the epidermis with a maximum at 5–6 days *(40)*, often accompanied by a shedding of superfluous cellular material (peeling). After single very large doses, the outcome of UV irradiation in animals such as mice is ulceration and scar formation, but this occurs in man only if there is a secondary bacterial infection.

Sunburn cells constitute a special histological feature; these are cells characterized by dense nuclei lying in isolation within the middle layers of the epidermis *(39)*. These severely damaged cells may be dead and will be removed, but little direct information on them is available. The wavelengths between 260 and 290 nm appear to be of equal importance and photosensitizers, such as 8-methoxypsoralen, will increase the yield *(41)*.

In recent years there has been a great increase in the use of UV-A sources to produce rapid skin tanning. An imperfect knowledge of the effect of high-dose UV-A on the skin and eye has resulted in widespread concern as to whether cosmetic UV exposure is advisable. There is certainly a risk to the eyes if these are not adequately protected. As far as the skin is concerned there is an acute risk especially to photosensitive individuals, and a potential long-term risk for all, especially in the case of immoderate use. In many countries, regulations on UV exposure are in preparation or already in effect. Such regulations should be based on the best available knowledge of the biological effects; however, better knowledge, particularly on the biological effects of UV-A, is highly desirable *(42)*.

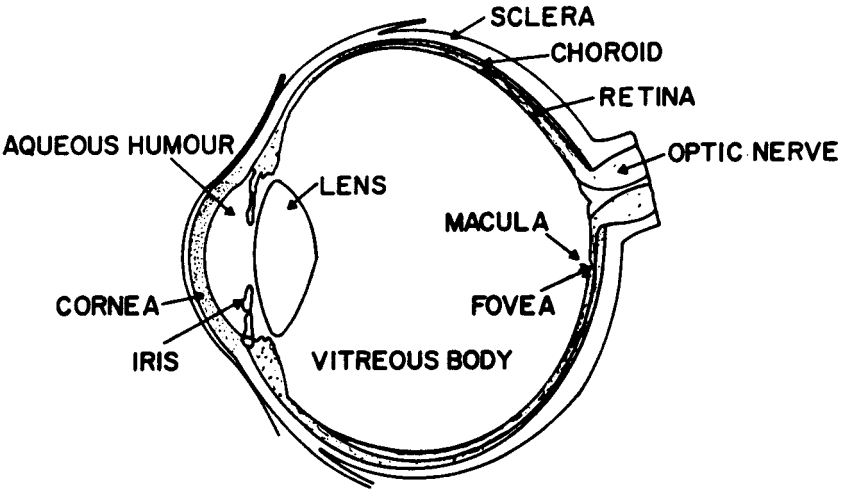
Mouth

As a consequence of dental practices, where plastic materials are hardened (or cured) by UV treatment, the mucous membrane of the mouth may be exposed to unwanted UV irradiation when defective apparatus is used *(43)*. Severe erythema of the skin around the mouth alone has been observed under such conditions. In recent years, the method has been largely replaced by visible light polymerization.

Eye

The structure of the eye is shown in Fig. 13. The main clinical effects of UV on the eye are photokeratitis and conjunctivitis, which appear 2–24 hours after irradiation. The symptoms are photophobia, foreign body sensation, and blepharospasm, which last from 1 to 5 days. In general, there is no residual lesion. Photokeratitis is caused preferentially by UV-C and UV-B but also by UV-A, though with less effectiveness. The peak sensitivity of the cornea is variously given as 270 nm *(44)* or 288 nm *(45)*. The effect is dose-related, which means that tissue damage depends on the total energy absorbed, not on the rate of absorption, at least if the exposure does not last for more than a few hours. Fairly accurate measurements have been made of the energy necessary for minimal photokeratitis. The threshold has a value of 50 J/m^2 at 270 nm, rising to 550 J/m^2 at 310 nm, followed by a steep increase to 22 500 J/m^2 at 315 nm *(46)*. Photoconjunctivitis has a similar action spectrum. Anterior uveitis was not found with exposure

Fig. 13. Cross-section of the human eye



at 315–325 nm until the dose received was about four times that required for a minimal effect. Studies on primate eyes tend to indicate a slightly lower threshold *(46)*.

The problem of acute or lasting damage to deeper-lying ocular structures has become increasingly important with the availability of strong UV sources, including lasers. The effects will depend on the transmittance of UV through the ocular media, figures for which are given in Table 1, which shows that an effect on the lens is possible at wavelengths longer than 290 nm. The action spectrum for acute damage to the lens lies between 295 and 320 nm *(47)*. Animal experiments show that both a single, high radiant exposure and exposures of long duration but of low irradiance induce opacities in the lens. Some epidemiological studies on man suggest that sunlight, especially UV radiation, appears to be active in producing cataracts *(48,49)*. One particular type of cataract (nuclear cataract) may be due to photochemical processes in the lens involving tryptophan, resulting in the formation of a brown pigment (brunescent cataract). Discussions of the possible biochemical mechanism have been presented *(47,49)*. The most efficient wavelength for the production of transient lenticular opacities was 300 nm, but only when the exposure exceeded a threshold value of 1500 J/m^2 *(46)*. The damage became permanent at radiant exposure levels of approximately twice this figure. It has been suggested that a characteristic change in the conjunctiva, pterygium, is caused by exposure to UV radiation *(6)*.

Retinal damage by high-intensity UV-A has been demonstrated in experimental animals *(50–52)*. In the adult human eye such damage appears unlikely, due to the strong absorption of UV-A by the lens. Persons with the

crystalline lens removed (aphakics) are, however, more vulnerable *(6,53)*. The modern practice of implanting intraocular lenses in the eye of aphakic persons increases the risk of UV damage to the retina.

Chemical photosensitization

Photosensitization is both an area of great interest and one of importance in industrial hygiene. It manifests itself in a number of ways, involving somewhat different mechanisms.

The photodynamic effects of organic substances all appear to be based on the same principle and are associated with UV-A and extend into the visible region. The energy is first absorbed by the photosensitizer, a relatively low-molecular-weight substance present in the cells, e.g. a fluorescent dye (acridine orange, riboflavines). It can then be transferred to a target molecule, oxygen serving as an intermediate. The effect of this transfer is most serious when the target is DNA in the nucleus or in a virus, when chain breaks and cross-linking may result *(54)*.

Other substances, such as the naturally occurring psoralens, will be bound to DNA after irradiation and will react with thymine and cytosine. After irradiation with UV-A, they form covalent photo-adducts sometimes leading to inter-strand linking. This results in a high degree of DNA damage.

From a clinical point of view, photosensitivity is a general term describing the combined action of UV and a chemical substance; this can lead to either phototoxic or photo-allergic reactions. Phototoxicity is the common response in all those whose skin is irradiated with sufficient energy and at the appropriate wavelength in the presence of a phototoxic substance. Although the result may only be the common sunburn reaction, it will be more marked with the photosensitizer. Photo-allergy is less common and is thought to depend on an acquired altered reactivity due to an antigen–antibody or cell-mediated hypersensitivity to the photosensitizer. Clinically immediate urticarial or delayed papular or eczematous reactions may appear. Photo-allergy may result in an increased sensitivity to light even without the sensitizer. The incident exposure may be relatively small. The UV of wavelengths 300–320 nm present in white fluorescent lamps *(55)* may suffice. With respect to the eye, photosensitizers such as psoralens do enhance cataract formation and chlorpromazine may have an effect on the retina.

Immunological effects

A great number of experiments performed during the past decade have shown that UV-B irradiation alters responses of the immunological system *(56,57)*. UV-B depresses contact sensitivity reactions, reduces the number and functions of Langerhans' cells in the skin, and changes the distribution of subpopulations of circulating lymphocytes in mice and man. Repeated irradiation of mice with UV-B induces an immunological change that inhibits the animals' ability to reject transplanted tumours induced by UV-B radiation in syngeneic mice *(58)*. Such an effect of UV-B radiation also appears to decrease the animal's defence against primary tumours induced by UV-B radiation in its own skin *(59)*.

An action spectrum for UV-induced immune suppression was found to peak between 260 and 270 nm *(60)*. An entire field of new findings and insights is opening up. It is not yet clear what the implications will be for the ideas about benefit and risk of human exposures to UV radiation, and about protection against the risks.

Late effects

Late non-stochastic effects
These occur in the skin and in the eye.

Skin. After prolonged exposure to sunlight over a period of years, the dermis will begin to degenerate, with a decrease in elasticity due to degeneration of the collagen fibres combined with other histological changes *(61)*. The visible symptoms will be deep furrows in the skin giving an appearance of premature aging. No dose–effect relationship is known for this reaction in man.

The epidermis may also be involved, with the development of actinic keratosis. The importance of this lesion is difficult to evaluate, but the occurrence of an increased cellular proliferation rate *(62)* and a certain amount of cellular atypia *(63)* suggest that it may represent a precancerous stage in the development of squamous-cell carcinoma. Many of these carcinomas are surrounded by areas of actinic keratosis *(63)*. It has been suggested that actinic keratosis may be a universal disorder of epithelial growth *(64)*.

Eye. As mentioned earlier, some of the types of cataract seen in elderly people may be due to repeated exposure to UV radiation over many years. The quantitative dose–effect relationship is unknown.

Late stochastic effects
Late stochastic effects are those for which the probability of an effect occurring, rather than its severity, is a function of dose. A threshold cannot be expected in effects of this type *(25)*. The typical lesion following UV exposure is a malignant tumour. There is no reason to expect heritable damage since UV cannot reach the gonads but is absorbed in the overlying tissues.

Skin. Cancer of the skin is a well recognized effect of UV irradiation, both in experimental animals and in man.

Three types of cancer are concerned: basal-cell carcinoma, squamous-cell carcinoma and malignant melanoma. The evidence for the production of skin cancer by UV is good for squamous-cell carcinoma and reasonably good for basal-cell carcinoma *(65–68)*; it is still uncertain for malignant melanoma *(9)*. The evidence incriminating UV radiation comes basically in two steps. The first step is to establish the involvement of sunlight, from epidemiological or clinical observations. Such observations deal with influences of full-spectrum sunlight and therefore do not point to any particular

wavelength region within the solar spectrum. The wavelength range involved has to be found by a second step, usually experimental investigations on animals.

Clinical observation shows that squamous-cell and basal-cell carcinomas appear preferentially on the most sun-exposed skin sites of lightly pigmented individuals. Malignant melanomas do not show such a convincing preference, though the incidence of all three types of skin cancer is higher in geographical areas with more intense sunlight. An inverse relationship between incidence and geographical latitude has been found for melanomas in white people in the United States. Similar, even stronger, correlations have been found for squamous-cell and basal-cell carcinomas. These and many other epidemiological observations suggest a causative role for sunlight in human skin cancer, including malignant melanoma *(69–76)*.

Animal experiments indicating a specific wavelength region have been performed mainly on mice. Such experiments yield mainly squamous-cell carcinomas and fibrosarcomas; the results apply directly only to these types of skin cancer, and not to basal-cell carcinomas or melanomas. That the wavelengths causing tumours are mainly below 320 nm was first shown by Roffo *(77,78)* and by Funding et al. *(79)*. The peak in the action spectrum appears to be between 280 and 320 nm *(80)* and the shorter wavelengths from the sun, i.e. 295–320 nm, are thus active *(67)*. Several observations suggest that the action spectrum for UV carcinogenesis is similar to that for UV erythema. Experiments with lamps emitting only UV-A showed that this can also induce skin tumours in mice *(81,82)*. An occasional clinical incident has been reported suggesting the induction of basal-cell carcinoma in man by UV-B radiation *(83)*.

Data incriminating a particular wavelength range for the induction of malignant melanoma are not available. There are no reports on the induction of melanoma in experimental animals by UV radiation alone.

In general, irradiation is effective only when the dose is spread over an extended period *(62,84,85)*, and the carcinogenic effect will depend on the number of doses and the duration of the irradiation. A single exposure may induce tumours in mice or rats, but only with doses so high that acute tissue damage is caused *(86,87)*. With regular daily exposure to UV-B, the tumours usually appear on nearly normal-looking skin *(88)*. Induction of tumours is mainly related to the doses of UV radiation administered, but dose delivery also plays a role. In general, doses are more effective if administered over longer periods of time *(89)*. With the dose delivery standardized, the relationship between the doses administered regularly and the time at which the tumours appear may be established quite accurately, and described by mathematical equations *(90)*. The same type of equations may be used, with different parameters, to describe skin cancer data for more or less homogeneous human populations *(91)*. The human data show much more spread than data from animal experiments and allow, therefore, different mathematical descriptions *(13,92)*. A dose–effect relationship in practical terms for human populations states that the incidence of skin cancer is approximately proportional to the square of the UV doses regularly received *(85)*. Such a relationship suggests that, although no dose of UV radiation is

completely without risk, small doses have a minor effect; the important risk is caused by large doses received over long periods of time.

There are many factors complicating the straightforward relationship between UV radiation and skin cancer in man. Latitude correlations are significant only in reasonably homogeneous populations. In populations mixed with regard to pigmentation, the picture may be entirely different. Darkly pigmented skin is much less susceptible than white skin to UV carcinogenesis. The carcinogenic action of UV radiation also depends on dietary influences *(93–95)* and on skin temperature *(96,97)*. Diseases such as certain types of inherited albinism and xeroderma pigmentosum *(98)* lead to an increase in the incidence of skin tumours, the latter probably as a result of defects in DNA repair mechanisms *(99)*. Incomplete or erroneous repair of DNA damage appears to be important in the development of skin tumours *(100)*. Certain medical therapies also result in an increase in malignant skin tumours, such as immunosuppressants *(2)* and dermatological photochemotherapy with 8-methoxypsoralen and UV-A *(101)*.

Eye. So far no direct evidence has been presented that tumours in the anterior chamber of the eye, and especially melanomas at this site, can be produced by UV irradiation. It should be noted that melanoma of the eye is commonest in blue-eyed individuals, and that melanoma of the iris occurred only in blue eyes in a series of ocular melanomas *(102)*. Tumours of the cornea, both fibrosarcomas and haemangioendotheliomas, have been induced in experimental animals *(103)* and tumours, including melanomas, are known to occur in domestic animals and in man in tropical regions *(104)*.

HAZARDS DUE TO OVEREXPOSURE

The risk of damage following either acute or chronic exposure to UV is encountered in a number of situations.

Solar UV is the most important source of such exposures. All those who work out of doors are potentially at risk from overexposure, the consequences of which may be both acute and long-term effects. The fashion of exposing a large part of the body to sunlight has during recent years increased the exposure of the skin, resulting in quite high UV doses. This is true not only for outdoor work but is now also normal during leisure periods, as exemplified by the holiday exodus of a large part of the population of the northern European countries to the Mediterranean coast.

UV-emitting arcs are an integral part of the working conditions at a number of workplaces. In welding, such arcs constitute a serious risk. Not only UV, but also visible and infrared radiation as line spectra with a continuous component are emitted during welding. The shape of such spectra will be different for the different welding procedures *(105)*.

The use of UV in some graphic reproduction techniques also represents an exposure risk for the workers concerned.

UV, and especially UV-C, is used for the sterilization of food and air, and pathological effects due to accidental exposures, often as small doses but of long duration, may result.

A number of sources available to the general population are known to emit UV, either as a normal part of the emission or after accidental breakdown. The normal white-light fluorescent tubes usually emit small amounts of UV. This may be enough to induce a phototoxic reaction if a photosensitizer is present. Under certain conditions the UV output of lighting tubes is by itself large enough to contribute appreciably to a worker's annual UV dose *(106)*. In addition, UV sources have for many years been available for home use, partly for the semi-cosmetic purpose of tanning. This may result in overexposure if the instructions on the equipment are not followed. The spectrum of fluorescent sunlamps is not always restricted to the solar spectrum; it differs greatly from that of solar radiation in the UV-B range, and UV-C components may be present.

The use of black-light lamps to control the effectiveness of tooth brushing will, in general, not constitute a hazard as the sources used are weak and the exposure short. The same is true where fluorescent black-light tubes are used, for instance for crack detection, chromatography, philately, mineral identification or document inspection.

Accidental short-term exposure with resultant symptoms has, however, occurred after breakage of the protective shield around high-pressure mercury lamps used for lighting *(107)*.

Medical irradiation in the form of phototherapy is at present expanding. In the blue light phototherapy of infants with neonatal jaundice (hyperbilirubinaemia), incorrectly selected fluorescent tubes have given rise to erythema. The use of certain photodynamic dyes and light for the treatment of herpes, or of psoralens and UV-A for other skin diseases such as psoriasis (PUVA), will expose the patient to risk. Up to now the action spectrum that has been studied the most extensively is that for ultraviolet erythema *(108)*. The action spectrum of the effect on psoriasis appears to be similar *(109)* and the same applies to the carcinogenic action spectrum *(110)*. If adequate safety precautions are not taken, the treatment personnel may also be at risk.

Excimer lasers may pose new problems, as these produce high-intensity radiation of wavelengths as short as 193 nm, which have not been available to any great extent from conventional sources. At present little is known about the biological effects of these short wavelengths. UV lasers are considered in detail in Chapter 2.

DOSIMETRY

From the point of view of establishing standards, it is desirable not only to be able to make measurements of emitted radiation but also to be able to record the doses received by the persons to be protected. It must, however, be appreciated that the dose absorbed by the sensitive cells may be difficult to estimate. Most of the equipment available for dose measurements in relation to protection is cumbersome and delicate and not too well adapted

for field use. In general, a phototube (photomultiplier) or photodiode detector is used. When it is necessary to determine the spectral distribution the different wavelengths can be separated, e.g. by a diffraction grating monochromator or by filters, and the transmitting optics must be made of quartz to allow all the UV to pass. The quality of broad-band measurements can be good, but considerable errors may be introduced when a full spectral description is required. One such error is the lack of precision in narrow wavelength bands when filters are used.

Instruments have been constructed that weight the radiation according to a sensitivity curve representative for certain biological effects, such as the action spectrum for UV erythema or a more generalized ultraviolet hazard curve *(8,111)*.

Personal dosemeters integrate the effective dose received by people over time, for instance during their work. The device consists, for instance, of a piece of polysulfone film in a badge carried by the person. The method is still under development, but has already produced several useful results *(111–115)*.

SAFETY STANDARDS

Any safety standards developed must take into consideration not only the harmful effects of UV radiation but also the need for a certain minimal irradiation, so as to ensure that sufficient vitamin D_3 is produced; this is of greatest importance during infancy and childhood. Vitamin D is supplied in two ways: through diet and by production in the skin. Yet deficiencies do occur, especially among children and elderly people. In children this leads to rickets and in the elderly to osteomalacia.

The synthesis of vitamin D_3 in the skin, its regulation and metabolism have been studied extensively in recent years *(116)*. A photoregulation process ensures that there is no danger of overproduction leading to vitamin D intoxication. The action spectrum for the production of vitamin D_3 shows some similarity to that for UV erythema *(117)*. It is therefore possible to estimate the UV doses needed for a sufficient production of vitamin D_3 in terms of erythemally effective radiation. From recent measurements *(118,119)* it may be calculated that for production in the skin of the daily vitamin D requirement of 400 IU, a UV dose on the head, neck and hands of about 60 MED per year is necessary.

Another reason that the skin needs at least some UV radiation, especially in long winters, is that it helps the skin to maintain some of its tolerance to UV. Many people have difficulty in adapting when UV irradiance increases again in the spring. This leads to many patients developing photodermatoses in areas with long winters. This difficulty may be prevented by maintaining some tolerance in winter *(120)*; doses required are of the same order of magnitude as those required for the production of vitamin D_3.

On the other hand, too much UV is not beneficial either. Up to now the standard established by the American Conference of Governmental Industrial Hygienists (ACGIH), which specifies a threshold limit value, has been

used in preparing guidelines for other countries *(121)*. This is based on the action spectrum for photokeratitis and erythema in normal white-skinned individuals. This means that acute effects have alone been taken into consideration. For the UV-B region and at lower wavelengths, it states that the radiant exposure in an 8-hour period must not exceed the value given in Table 2. For the wavelength range 320–400 nm, the total irradiance on the unprotected skin or eye must not exceed 10 W/m^2 for periods exceeding 10^3 seconds (about 17 minutes). For radiant exposures of shorter durations, it should not exceed 10 kJ/m^2.

A procedure has been suggested for characterizing the relative levels of UV from illumination sources and derived guideline numbers given for the maximum illumination level of the source that will not exceed the ACGIH standards *(122)*.

The values given in Table 2 apply directly only to sources emitting essentially monochromatic UV. The maximal permissible exposure for a broad-band source can be calculated by summing the relative contributions from all its spectral components, each contribution being weighted by means of the relative spectral effectiveness, as given in Table 2. In addition, the guidelines should not be used for determining exposure limits for photosensitive individuals.

Table 2. Threshold limit values (TLV) and relative spectral effectiveness by wavelength for any 8-hour period of exposure

Wavelength, λ (nm)	TLV (J/m^2)	Relative spectral effectiveness, S_λ
200	1 000	0.03
210	400	0.075
220	250	0.12
230	160	0.19
240	100	0.30
250	70	0.43
254	60	0.50
260	46	0.65
270	30	1.00
280	34	0.88
290	47	0.64
300	100	0.30
305	500	0.06
310	2 000	0.015
315	10 000	0.003

The guidelines discussed so far do not take into account the long-term risk of skin cancer. As the action spectrum for UV carcinogenesis appears to be similar to that for UV erythema, the cancer risk may also be discussed in terms of erythemally effective doses. Thus the Health Council of the Netherlands *(123)* has tried to define "acceptable levels" for long-term unintended exposures to UV radiation. The reasoning was based on the clinical observation that skin cancer in the Netherlands occurs mainly in outdoor workers even though there are many more indoor workers. The difference in the UV doses received apparently brings the outdoor workers into the risk zone. The difference in erythemally effective UV doses received by outdoor workers and indoor workers was estimated with the help of data collected with Robertson–Berger meters *(8)* and personal dosimeters *(111)*. The acceptable level for long-term occupational exposures from man-made sources was defined as a small fraction of this difference. This led to an acceptable level corresponding to an average daily exposure of 3–9 minutes of full local summer sunlight.

This is a rather strict limit, but those given in Table 2 for short-term exposure are equally strict. Where these limits are observed there appears to be little need for additional limits for long-term exposure *(124)*.

PROTECTION

Solar ultraviolet radiation

The weak penetration of UV makes a simple form of protection possible, since it is excluded by most types of clothing. This, of course, may not provide protection for the face and hands during work out of doors. Furthermore, it should be remembered that not all clothing will adequately exclude UV. Relatively open-weave clothing or that made of UV-transparent material may result in sunburn being caused by sunlight penetrating the clothing. It is also the experience of dermatologists that synthetic material used for dresses and shirts permits sufficient UV to pass for a skin reaction to occur when phototoxic substances are being tested *(125)*. Apart from clothing, protection may also be afforded by the application of sun-blocking or sun-screening substances that act by absorbing or scattering the radiation. Of the former, *p*-aminobenzoic acid or some of its esters have proved to be the most successful. They can easily be applied as a lotion, a cream or preferably in an alcoholic solution *(97)*. The results are a decrease in UV-B-induced erythema and a slower rate of suntanning.

It has been suggested that β-carotene could act as a systemic protector *(126)*. Since even its possible effectiveness in erythropoietic protoporphyria, a photosensitive disease, has been questioned, the evidence in support of the general usefulness of this treatment is not very strong. The recent observation that the related retinoic acid decreases the dose necessary for the successful PUVA treatment of psoriasis *(127)* is interesting, in view of the inhibiting effect of this substance on skin tumour production *(128,129)*. Since animal experiments suggest that all transretinoic acids may increase cell growth *(128)*, some caution is necessary.

Industrial sources

Protection against UV in the working environment should preferably consist of containment of the radiation by appropriate design of the source or of the apparatus in which it is placed.

As mentioned previously, a large number of sources can be shielded by the use of an appropriate covering, which may be a filter that selects only those wavelengths corresponding to the purpose for which the lamp is to be used. In the case of high-intensity lamps containing UV sources, attempts are being made to introduce safety devices that will interrupt the emission if the covering glass is broken.

When containment is not possible and the irradiance is high, appropriate eye protection is mandatory together with protection of the skin. This may consist of appropriate clothing or the application of effective sunscreens. Standards for eye protection exist in most countries. Welding is an example of a type of work where sufficient protection can be obtained by suitably designed and fitted welding masks or hoods. When welding is started, however, the shield may have to be removed and this can give rise to photolesions of the eye.

It is fortunate that a certain degree of control of the hazard can be achieved by the welder himself, as the eye will reject filters of insufficient absorbing capacity in the visible light at wavelengths close to UV-A *(130)*. It is not sufficient to protect the welder himself; the surrounding area must also be monitored and screened so as to ensure that nobody is accidentally exposed. This requires fixed shielding between and around welders; such shielding work must be treated with non-reflecting paint in order to protect the neck of the welder from exposure by reflection.

CONCLUSIONS AND RECOMMENDATIONS[a]

Conclusions

All people are exposed to UV radiation from sunlight, and the risk to health varies with geographical, genetic and other factors. Similar risks are involved in the increasing exposure of people to UV radiation from artificial sources, such as those used for suntanning, in phototherapy and in industrial processes. The biological effects of a single exposure differ significantly from the effects of repeated and cumulative exposures. Both types of risk increase markedly with excessive exposure.

For UV radiation exposures the spectral composition of the source and action spectrum weighted irradiance (W/m^2) and radiant exposure (J/m^2) are the important parameters that determine the biological effect.

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[a] These conclusions and recommendations are those pertaining to ultraviolet radiation made by the WHO Working Group on Health Implications of the Increased Use of NIR Technologies and Devices, Ann Arbor, USA, October 1985.

The essential measurements and determination of the hazard should include:

— careful estimation of the output spectrum of the source in narrow intervals (1–5 nm bands);

— knowledge of the action spectrum for the effect of concern;

— the irradiance in the individual wavelength bands;

— the exposure duration;

— the distribution of the radiation impinging over the exposed area;

— the characteristics of the reflecting surfaces;

— the frequency of the repetition of the exposure; and

— the effective irradiance (dose rate) in repeated exposures.

The interaction between biological tissues and UV radiation depends on:

— the spectral distribution of the source;

— the radiant exposure (dose) weighted against the action spectrum; and

— the number of exposures.

The interaction of UV radiation and biological tissues is mainly photochemical. However, there are some UV sources that emit sufficient energy to produce thermal effects in tissues.

Because of the relatively superficial absorption, the major biological effects are on the skin and the eye. Through its optical properties, the eye has an increased vulnerability to injury to UV radiation.

The major health hazards to the skin are both acute and chronic. Acute hazards are sunburn and photosensitized reactions, the chronic hazards accelerated aging and photocarcinogenesis. The major health hazards to the eye are photokeratitis, corneal burns, ocular inflammation, photochemical cataract, and photochemical injury to the retina.

Recommendations

Control measures should include education and training of all personnel working with UV sources. Engineering controls such as proper layout of working areas, enclosures, and ventilation of instruments should be selected as appropriate. Personal protection may consist of special eyewear, and appropriate clothing or protective sunscreens applied to the skin. Warning signs and other administrative controls may supplement these measures.

Various national and international bodies have dealt with the problem of maximum permissible exposures of the eye and skin. Despite the lack of data in some areas, there is a fair degree of consensus on the exposure limits, such as those recommended by the IRPA and ACGIH, and those in preparation by the IEC and CIE.

It is also recommended that additional specific studies be performed on the health effects of UV radiation. Epidemiological studies are recommended in the following areas:

— malignant melanoma in skin in relation to sunlight;

— cataract formation as produced by solar radiation, if possible separately for UV-A and UV-B radiation;

— risks to aphakic people and those with intraocular lens implants for retinal changes, mainly from UV-A and short wavelengths in the visible part of the spectrum;

— pterygium formation as the result of exposure to UV-A and UV-B radiation; and

— malignant melanoma in the uvea.

Experimental studies are recommended in the following areas:

— the action spectrum for photocarcinogenesis;

— the action spectrum for cataract formation, macular changes in aphakic animals, and pterygium formation;

— the chronic effects of UV-A radiation on human skin; and

— the effect of chronic exposures to UV-A and UV-B radiation on the lens, the retina and the uvea, as well as the cornea and conjunctiva.

There are widespread public misconceptions as to the benefits and risks to health of exposure to UV radiation. Information programmes are necessary to educate people about risks from excessive exposure.

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