The evolution of current medical and popular attitudes toward ultraviolet light exposure: Part 3

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In the 1930s, attitudes toward ultraviolet (UV) light exposure began to change significantly within the medical profession. UV radiation had been promoted as healthful since the century's start, and particularly after the discovery of its role in vitamin-D metabolism. Increasingly, however, attention would focus on the risks of UV light exposure from sunlamps and sunbathing. During this time, the American Medical Association established guidelines for the approval of UV lamps and the appropriate therapeutic uses of phototherapy. The landmark experiments of Findlay and other researchers, in which malignant skin tumors were induced in rodents after exposure to UV lamps or sunlight, would lead to widespread recognition of the carcinogenicity of UV radiation. The role of sunlight in the etiology of skin cancer was increasingly mentioned in articles in popular magazines in the 1940s and 1950s. There was rapid growth of the sunscreen industry as well, although product efficacy remained highly variable. In the 1950s, interest developed in the use of 8-methoxypsoralen ("the suntan pill") and dihyroxyacetone ("suntan in a bottle"). In spite of the known risks of UV exposure and attempts by physicians and other health professionals to educate the public and modify behavior, suntanning has remained tenaciously popular. Today, excessive UV light exposure is recognized as the major cause of the approximately 1.3 million cases of skin cancer in the United States each year. (J Am Acad Dermatol 2003;49:1096-106.)

UV LAMPS

Sunlamps and sunbathing became extremely popular in the latter 1920s, partly as a result of medical opinions regarding ultraviolet (UV) light exposure as beneficial to health and a form of preventive medicine.[1,2] As the decade came to a close, however, members of the medical profession began to respond with criticism to the extravagant claims being made for phototherapy and the aggressive marketing of UV lamps to the public. An editorial in the *Journal of the American Medical Association* (*JAMA*) stated that " . . . these machines are being sold to bath institutes, swimming pools, massage parlors, beauty parlors, clubs, barber shops and innumerable other businesses in which medical supervision is certainly not probable, indeed, hardly possible . . . Moreover, the rays are being advised as useful in a vast number of conditions for which the scientific evidence is extremely slim."[3] A physician and phototherapist wrote: "The use of actinotherapy by the public is and should be on the increase, since it is an additional method of preventive medicine and as such ranks with certain other ill understood yet definite adjuncts to modern medicine. We should through the medium of [The American Physical Therapy Association], acquaint both the medical and the lay public with the fact that, while this form of therapy is advantageous to the production and maintenance of good health, yet it is not without certain dangers, which can be understood only by properly educated and trained medical men."[4] Occasional articles in popular magazines warned of the possibility of severe burns and ocular complications from home sunlamps emitting short wavelength UV radiation (including wavelengths less than 280 nm).[5] One author noted: "It is exceedingly dangerous even to look at the source of light in these machines, unless the eyes are fully protected by suitable glasses."[6] By 1930, the US Public Health Service cau-

Abbreviations used:

AAD:	American Academy of Dermatology
AMA:	American Medical Association
DHA:	dihydroxyacetone
FDA:	Food and Drug Administration
JAMA:	Journal of the American Medical Association
MOP:	methoxypsoralen

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tioned that home UV lamps should be used only under medical supervision.[7]

The American Medical Association (AMA) sought to establish guidelines for UV lamps; these were outlined in a series of reports by the AMA's Council on Physical Therapy, beginning in 1932.[8-12] Specifications for the council's approval of sunlamps were indicated, and commercial sunlamps (like many other health-related products) could subsequently be rated to be either acceptable or unacceptable by the AMA. One requirement for acceptance of sunlamps advertised and sold to the public was that "the spectral range of wavelengths from sunlamps shall be limited largely from 2900 to and including 3132 angstroms and shall not include an appreciable amount of ultraviolet of wavelengths shorter than 2800 angstroms."[11] In addition, the total intensity of UV radiation was to be approximately the same as "clearest weather, midday, midsummer, midlatitude, sea-level, natural sunlight. . .."[10] Such stipulations were aimed not only at UV lamps considered to result in excessive exposure, but also at those believed by the council to provide too little UV radiation. Recommendations were also made regarding advertising to the public.[12-14] The council, recognizing that the medical profession's advocacy of UV light exposure was being exploited for commercial gain, explicitly qualified its recommendations for the use of UV lamps: "In general, the Council believes that more conservative claims for the necessity of strong sunlight should be made by the manufacturers of lamps for home use, such statements being restricted to those which can be justified by conclusive scientific evidence."[12] Therapeutic claims singled out as objectionable included statements "that exposure to UV rays increases or improves the tone of the tissues or of the body as a whole, stimulates metabolism, acts as a tonic, increases mental activity, maintains health or tends to prevent colds. . .."[10]

Although such guidelines were binding only with respect to gaining the approval of the AMA, they did serve to promote reform. For example, in a 1947 review of 15 home sunlamps by the magazine, *Consumers' Research Bulletin*, certain products sold to the public were identified as either meeting or not meeting the AMA requirements. A Sun-Kraft quartz mercury sunlamp was specifically not recommended by the magazine because "radiations (according to the manufacturer) give peak intensity at 2537 angstrom units, which is outside the requirements of the American Medical Association Council on Physical Medicine."[15] The article also stated: "In spite of an early tendency to claim every good thing from [sunlamp] use, excellent publicity by the American Medical Association and some action by government control authorities has removed much of this from formal advertising."[15] By the 1940s, the Federal Trade Commission was initiating action against manufacturers of UV lamps that made misleading claims about their products.[16-19]

Home sunlamps enjoyed continued popularity after World War II.[15] A typical advertisement from 1948 proclaimed: "Give your children that glowing summer-tan look! G-E Sunlamp tans like the sun!"[20] Matthew Luckiesh, who had fanned public excitement about UV light as the director of General Electric's Lighting Research Laboratory in the 1930s,[2] was still promoting sunlamps to the public nearly three decades later in 1960.[21] However, by this time, Luckiesh had toned down his rhetoric considerably: "It would be difficult to prove the existence of any benefits for healthy or near-healthy persons beyond the cosmetic one of the pleasingly tanned skin."[21]

Today, sunlamps and tanning beds (now primarily emitting UVA [320-400 nm]) continue to be marketed to the public, although further regulations have been placed on these products as a protection to consumers. Federal guidelines in the United States now stipulate that the ratio of irradiance within the 200- to 260-nm wavelength range to the 260- to 320-nm wavelength range "may not exceed 0.003 at any distance and direction from the product or lamp."[22] Other federal requirements specify that sunlamps incorporate a timer system and be accompanied by protective eyewear. Labeling requirements stipulate the presence of a warning statement that informs users that repeated exposures may cause premature aging of the skin and skin cancer, and that failure to use protective eyewear may result in severe burns or long-term injury to the eyes.[22] Also, tanning devices may be marketed only for cosmetic use.[23] In spite of increased regulation, the consequences of the use and misuse of UV sunlamps and tanning beds, including their contribution to photoaging and skin cancer formation, remain an important concern.[23-25]

PHOTOTHERAPY

In addition to establishing guidelines for UV lamps, the AMA also attempted to rein in the medical use of phototherapy, which was being used by some advocates for a long list of medical conditions.[26] Initially, the AMA placed requirements on the therapeutic claims made by UV lamp manufacturers in their advertising and descriptive literature intended for members of the medical profession.[27,28] In 1942 and 1943, the AMA Council on Physical Therapy issued a report on the therapeutic value of UV radiation.[29-31] Noting that phototherapy was often "exploited beyond its limitations," the report served to

"set forth the views of the Council with respect to the conditions in which ultraviolet radiation therapy is of benefit."[29] Many purported medical benefits of phototherapy, such as increased resistance to upper respiratory infections, improved metabolism, and treatment of anemia, had not held up to scientific scrutiny, and the council's list was essentially limited to the treatment of rickets, numerous dermatologic conditions, and certain forms of tuberculosis. Potential harmful effects from UV radiation were also discussed, including mention of the risk of actinic keratoses and skin cancer.[31] Ocular risks were listed, including conjunctivitis, blepharitis, edema, corneal erosion, and functional disturbances such as color scotomas and constriction of the peripheral field.[31]

By the 1940s, dermatology was the one remaining field of medicine for which phototherapy was still commonly used in a variety of disorders. A 1948 review in *JAMA* on the use of "physical treatment" in dermatology, stated: "Ultraviolet radiations are not as extensively used in dermatology as in former years, but they are used more critically and in a more precise manner. The average dermatologist employs in his office or clinic an air-cooled and a water-cooled hot quartz mercury arc lamp and a 'cold quartz' type of lamp."[32] The indications for phototherapy were listed: "Ultraviolet rays have been found useful in a large number of diseases of the skin, the most important of which are acne vulgaris, dermatophytosis, neurodermatitis, eczema in infants, eczema seborheicum, furunculosis and folliculitis, pityriasis rosea, parapsoriasis, essential pruritus, psoriasis, tuberculodermas, including lupus vulgaris, scrofuloderma, erythema induratum and orificial tuberculosis, and some slowly healing ulcers and wounds."[32] The Goeckerman treatment (applying coal tar ointment before UV exposure) was recommended for recalcitrant psoriasis. Reflecting practices of the time, the author also listed skin diseases that were responsive to x-ray treatment or radium, including numerous benign conditions.[32]

SUNBATHING AND THE RECOGNITION OF UV LIGHT AS A CARCINOGEN

After the rapid growth in the popularity of recreational sunbathing that occurred in the late 1920s, apprehension was increasingly voiced by physicians concerning the dangers of excessive sun exposure. By 1932, the US Public Health Service was issuing warnings about the risks of sunbathing.[33] Specific recommendations included avoiding the summer sun between the hours of 10 AM and 3 PM, protecting the head from direct sunlight, and gradually increasing the time of sun exposure, starting with only 5 to 10 minutes and then extending the amount in increments of 5 to 10 minutes a day. The warning stated that "Blondes, especially those with red hair, fail to tan but always burn. Such persons must protect themselves from the sun's rays."[33] During the summer, dermatologists and public health workers also made recommendations for avoiding sunburn.[34,35] For example, Charles Pabst, a dermatologist at Greenpoint Hospital in Brooklyn, NY, issued an annual warning against overexposure to the summer sun[36] and emphasized that "heliophobes" (persons who do not tan) should be vigilant in their use of beach pajamas, wide-brimmed hats, and parasols.[35] The risks from sunbathing began to receive attention in popular magazines as well, which ran articles such as "Sunlight with Moderation,"[37] "Warnings for Sun-tan Worshipers,"[38] and "Are You a Heliophobe?"[39] A 1935 article entitled The Truth about Sunburn cautioned readers: "The spectacular results that have been attained in the treatment of some diseases have unfortunately led to a belief, now well-nigh universal, that ultraviolet rays are a kind of magic cure-all . . . it is not at all necessary to lie for hours in the midday sun to get the major benefits of solar irradiation. It is not only unnecessary; it is distinctly hazardous."[40]

It was in the 1930s that UV radiation became widely recognized as a carcinogen. Beginning with Paul Gerson Unna's report in 1894, numerous clinical observations had implicated chronic sun exposure in the etiology of skin cancer, although this work received little attention outside of the field of dermatology.[1] In the popular press, the association between UV light exposure and skin cancer was rarely mentioned before 1930, and it remained essentially unknown to the lay public. Further epidemiologic observations associating sunlight exposure and skin cancer appeared in the Australian medical literature in the late 1920s[41,42]; the high incidence of "squamous epithelioma" and "rodent tumor" in Australia was already a cause for serious concern. Edmund Molesworth, a dermatologist at the Royal Prince Alfred Hospital and the University of Sydney, Sydney, Australia, wrote in the *Medical Journal of Australia* in 1927: "One is frequently met with a surprised protest, on warning a patient with rodent ulcer to avoid unnecessary exposure, that he never dreamed that sunlight could harm anyone. But such is undoubtedly the case and sunbaking on the beaches has already begun to contribute its crop of rodent tumours. It may be that the installation of ultraviolet baths in private houses as recently described in the press, will also produce a quota [of skin cancers]. . .."[41]

In 1928, the British physician George Marshall Findlay[43] published the results of his classic study in

which malignant skin tumors were experimentally induced in albino mice by repeated exposure to UV light from a quartz mercury vapor lamp. Tumors developed whether the mice were exposed to UV light alone, or in combination with tar, although tar decreased the exposure time necessary to induce malignancy. Findlay concluded: "These experiments, therefore, are in favour of the hypothesis based on clinical evidence that in man exposure to ultra-violet light plays an important part in the aetiology of cancer of the skin of the face, neck and hands."[43]

Findlay's results were independently reproduced in mice and rats, using either mercury arc radiation or natural sunlight.[44] The primary carcinogenic wavelengths in sunlight were determined to be from 290 to 320 nm.[44] Ironically, the sunlamp light bulb (S-1, General Electric) advertised to the public as "good for the whole family"[45] was the light source used to induce skin tumors in rats in a 1936 study.[44,46] The research of Findlay and others led to further concerns about the clinical consequences of sunbathing. In 1935, after the Argentinean researcher Angel Roffo[47] produced cutaneous tumors in rats by repeated exposure to sunlight for 7 to 10 months, he expressed the opinion that "sunlight baths have a cancerigenic action" in humans.[48] A 1935 review in *JAMA* on the etiology of cancer listed sunlight as a causative factor of skin cancer.[49] The author even made mention of a possible association between sun exposure and the development of malignant melanoma: "In certain cases of melanoma, sunlight has apparently been the chief irritant of a mole."[49] However, the author of a 1938 review on phototherapy argued that warnings to the public about the risk of skin cancer from sunbathing might be unnecessary: " . . . the physiologic response of the rat to ultraviolet radiation is greater than that of man and. . .the massive exposures necessary, even for the rat, to produce lesions, leave a wide margin of safety for man. In general, one might conclude that [animal experiments] indicate a possible but not a very probable danger for man. . .."[50] Such skepticism notwithstanding, the importance of sunlight exposure in the etiology of skin cancer was gaining acceptance in the medical profession.[51]

The study of the carcinogenic action of UV radiation (and chemical carcinogens) became an area of intensive experimental research. A leading investigator was Harold Blum[52-54] of the National Cancer Institute in Bethesda, Maryland. In 1941, Blum et al[52] reported the results of quantitative studies of UV light exposure in mice, demonstrating that relatively low intensity UV light was sufficient to induce skin tumors over time. This supported the concept that,

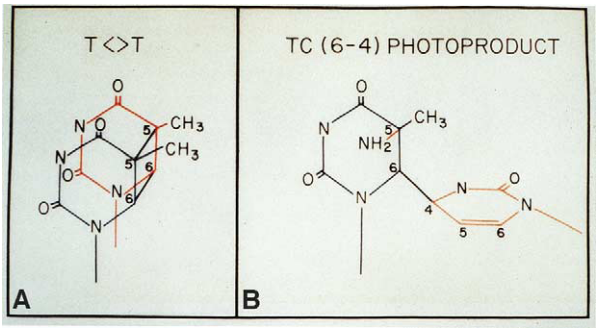

Fig 1. The two primary DNA lesions caused by UV light are (**A**) cyclobutane pyrimidine dimers between adjacent pyrimidine bases resulting from the formation of a cyclobutane ring structure involving carbons 5 and 6 and (**B**) 6-pyrimidine-4-pyrimidone photoproducts resulting from the formation of covalent bond between carbon 6 position of 5′pyrimidine and the carbon 4 position of an adjacent pyrimidine. A thymine dimer and thymine-cytosine photoproduct are shown respectively. (Courtesy of Dr Douglas E. Brash.)

in humans, "prolonged exposure to the relatively low intensities of sunlight may be effective [in producing skin tumors] if incident over sufficient time."[52] Blum published the textbook, *Carcinogenesis by Ultraviolet Light*,[54] in 1959, which discussed in detail the rapidly growing body of literature on the subject to which he contributed greatly.

Additional epidemiologic evidence was reported in the 1940s and 1950s implicating sunlight as a major cause of cutaneous malignancy in humans.[54-60] These studies reaffirmed earlier findings that skin cancer occurred more frequently on sun-exposed anatomic sites and was more common in individuals who were light-skinned, lived in southern latitudes, and were engaged in outdoor occupations. Importantly, reports from Australian investigators in the 1950s supported a role for UV radiation in the etiology of cutaneous melanoma.[61-63] With overwhelming clinical and experimental evidence identifying UV light as a carcinogen, the role of UV light exposure in photoaging and cutaneous malignancy formation was highlighted in a 1956 report by the AMA entitled "Ways and Means to Safe Sunbathing."[64] The report was intended to guide physicians in helping patients protect themselves from the harmful effects of UV light exposure.

Further research provided insights into the molecular mechanisms by which UV light induces the formation of skin cancer. In the 1960s, the two major DNA lesions caused by UV light were described: the formation of cyclobutane pyrimidine dimers and 6-pyrimidine-4-pyrimidone photoproducts (Fig 1).[65-69] These photoproducts may result in characteristic "C to T" or "CC to TT DNA" mutations. Another

significant advance occurred in 1968, when Cleaver[70] demonstrated defective DNA repair in UV light-exposed fibroblasts from patients with xeroderma pigmentosum. His findings suggested the importance of such repair mechanisms to preserving the normal health of human skin. The study of diseases with cellular hypersensitivity to UV radiation, such as xeroderma pigmentosum, proved to be a useful tool for better understanding the carcinogenic action of UV light.[71,72]

Recent investigations have focused on the presence of UV-induced mutations in specific regulatory genes in malignant skin tumors. The tumor suppressor gene, p53, frequently shows characteristic UV-type mutations in DNA obtained form squamous cell carcinomas, basal cell carcinomas, and actinic keratoses.[73-75] Mutations in p53 may also be present in clones of keratinocytes in normal appearing, sun-exposed skin.[75,76] Another gene of interest is PTCH, the human homologue of the *Drosophila*-patched gene, which encodes a protein inhibiting an intracellular signaling pathway. The PTCH gene is defective in patients with nevoid basal cell carcinoma syndrome,[77,78] and somatic mutations (predominantly UV-type) were found in the DNA of approximately one third of sporadic basal cell carcinomas tested in one study.[79] Currently, many other genes that may play a role in the multistep process of carcinogenesis in the skin and other organs are being studied.[80]

Additional factors that are thought to be related to the carcinogenicity of UV light are also under investigation, including cytokine activation and immune suppression; eicosanoid and proteinase production; and the generation of reactive oxygen species.[75,81]

INCREASED PUBLIC AWARENESS OF THE CARCINOGENICITY OF UV LIGHT

Increased recognition of the deleterious effects of UV light, and particularly its carcinogenicity, would have a major impact on public health recommendations. In 1936, *JAMA* editors, in a reversal of previous editorial positions, wrote: "As far as is known, man actually requires only a relatively small amount of sunshine for the maintenance of normal health, and the greatest danger perhaps at the present time lies in too much exposure to sunlight rather than too little."[82] The dermatologist Paul Bechet, addressing the Section on Dermatology and Syphilology at the AMA meeting in 1933, emphasized the need for greater education of the public regarding the risks of sunbathing: "The fact that excessive exposure to actinic rays, either natural or mechanical, is an important etiologic factor in certain diseases of the skin is supported by the evidence submitted. While all dermatologists know this, they have not emphasized it sufficiently, with the result that there exists complete ignorance among laymen as to the ill effects of prolonged actinic exposure."[83]

The message that excessive UV light exposure was associated with skin cancer development would start to be directed to the public in the 1930s. Warnings by physicians began to appear sporadically in newspaper articles and letters to the editor.[84-87] Popular magazines occasionally cited concerns in articles about sunbathing. A 1935 article in the *American Mercury* described the findings of "sailor's skin" noting that "It is actually found among farmers, golfers, and inveterate sunbathers rather more often than among sailors."[40] An article about sunbathing in *Woman's Home Companion* in 1937 stated: "Dermatologists are frankly concerned about the possible after-effects of all this ill-regulated sun exposure. They point out that not only is excessive sun very drying and aging to the skin but that it may bring on serious skin conditions later in life."[88] In addition, in 1941 a writer for *Life* warned that "Extensive sunning also produces scaly, wrinkled skin and a predisposition to skin cancer."[89] That same year, the *Ladies' Home Journal* published an article entitled "Sunlight Cancer," which described a sunbather in whom a changing dark brown mole developed: "This is a dangerous malignant cancer, long quiescent, but probably incited to growth by the unusual exposure to sunlight."[90]

Publicity about the carcinogenicity of UV light gradually increased in the 1940s. A 1948 article in the *Saturday Evening Post* cited medical authorities who stated that "There is probably no fact regarding the cause of cancer better established beyond question than that habitual actinic exposure. . .causes [skin] cancer in certain types of skins. The chief conditions are maturity, fair skin and habitual exposure. . .."[91] Still, the same article noted: "Some doubts come from doctors who say that the causal connection between steady sun exposure and skin cancer is not well enough established to suit them."[91] A review of sunscreens in *Consumers' Research Bulletin* in 1949 warned:

> The present vogue of excessive sunbathing is not so healthy a practice as its devotees are wont to think. For some years, [*Consumers' Research Bulletin*] has warned that too much ultraviolet from the sun may be a predisposing cause of cancer. It is now coming to be well known that both skin and lip cancer are more prevalent among fishermen, farmers, and Navy personnel than in other occupations. Even popular magazines and newspapers are beginning to discuss the dangers of too much sunshine. Women are discovering too, from sad experience, that acquiring a heavy

> coat of tan, year in and year out, robs the skin of its natural oils and leaves the tissues dry, roughened, coarsened, and a fertile field, as it were, for lines and wrinkles.[92]

By the 1950s, it was fairly common for popular articles relating to suntanning and sunburn to mention the risks of photoaging and skin cancer from excessive sunlight exposure.[93-97] This message eventually made it to television when the skin cancer authorities Harold Blum, Rudolph Baer, and J. B. Howell appeared in a panel discussion on the AMA-associated television series, *Ask Your Doctor*.[98]

SUNSCREENS AND SUNTAN STIMULANTS

Physical sunblocks had been used since the century's start, but it was not until the explosion in the popularity of recreational sunbathing that there was intensive interest in the development of products that might enhance suntan or prevent sunburn. The first commercial chemical sunscreen, containing benzyl salicylate and benzyl cinnimate, was introduced in the United States in 1928.[99] In his 1936 textbook, *Cosmetic Dermatology*,[100] Herman Goodman listed the compounding for numerous preparations that were sunburn deterrents or suntan stimulants. The "physical parasols," contained zinc oxide or titanium dioxide, whereas the primary agents in "chemical parasols" were benzyl salicylate and phenyl salicylate. Goodman considered the fluorescing chemical parasols, quinine and esculin, to be unreliable sunburn preventives.

All of the suntan stimulants listed included oil of bergamot, later recognized to contain 5-methoxypsoralen (MOP). Oil of bergamot was known to promote hyperpigmentation in combination with sunlight; in 1916, Freund first described 4 patients with the condition that was later named "berloque dermatitis."[101] The sale of suntan activators containing 5-MOP would continue, even to recent times in certain countries. However, 5-MOP has now been identified as a potent mutagen in the presence of UVA and has been reported to be photocarcinogenic in animals and humans.[102-105] In 1995, the European Commission banned suntan lotions containing more than 1 part per million of psoralen.[106]

A final category listed by Goodman[100] was sun simulants. These preparations included brown pigment, which dyed the skin, giving the appearance of a suntan. Coloring agents such as cudbear and henna were used. Although not mentioned by Goodman, tannic acid was also used as a skin dye and sun protectant.[107]

In 1942, Rothman and Rubin of the University of Chicago, demonstrated that 10% to 15% *para*-aminobenzoic acid (PABA) ointment was an effective sunburn protectant.[108] In addition, PABA was chemically stable, colorless, odorless, and did not stain clothing. Its potential to act as a contact sensitizer was also soon reported.[109] During World War II, dark red veterinary petrolatum was found to be an effective physical sunscreen agent by the US military, becoming standard equipment on life rafts and in vehicles in tropical areas.[110] The answer to a *JAMA* query to the editor in 1950 stated that preparations designed to prevent sunburn usually contained 10% phenyl salicylate, 15% quinine, 2% tannic acid, or 15% PABA.[111] Benzophenone compounds, which provide partial UVA coverage, were introduced in the late 1950s.[112]

Despite the proliferation of commercial sunscreen preparations, it was difficult for the public to be certain of the efficacy of a given product. Unlike today, labeling was of little help to consumers. In 1940, a federal policy was established whereby products referring to sunburn protection were regulated as drugs whereas those claiming to promote tan were considered cosmetics. To circumvent regulation, therefore, manufacturers commonly promoted sunscreens as a means of acquiring a tan.[113] A survey by the AMA in the 1950s found that 30 of 56 commercial sunscreens did not list the active ingredient.[64] In 1950, *Consumer Reports* tested 46 sunscreens, concluding that 14 brands provided reliable protection, 17 provided intermediate protection, and 15 offered little or no protection.[114] A report by the AMA Committee on Cosmetics stated in 1956: "The selection of one brand of suntan preparation over another is virtually a hit-and-miss procedure. When the screening ingredient is listed on the label, it furnishes some point of reference from which to operate; but this is not sufficient for reliable evaluation."[64] Motivated individuals could have pharmacists compound sunscreen formulas provided by the US Public Health Service.[115] Better labeling of sunscreens, and emphasis on sun protection instead of tanning, resulted from the establishment of the Over-The-Counter Drug Review by the Food and Drug Administration (FDA) in 1972.[113] This led to recommendations such as considering the efficacy of certain sunscreen agents to be generally recognized as established, and requiring the listing of a sun protection factor on a sunscreen product's label. Federal guidelines for sunscreens have recently been revised by the FDA.[116]

USE OF 8-MOP: "SUNTAN PILL" AND POTENT PHOTOCARCINOGEN

In the 1950s, there developed interest in the use of 8-MOP as a tanning aid, on the basis of its action of enhancing pigmentation secondary to sunlight

exposure. The drug, which had recently become available as a treatment for vitiligo, was touted as the "suntan pill" in the popular press. A front-page article in the *Wall Street Journal* in 1956 declared: " '8-MOP' Drug May Speed Mellow Tans, Prevent Painful Burns."[117] *Life* ran a feature article 1 month later entitled "A Suntan in a Capsule."[118] Other popular magazines ran titles such as "The New Sun Tan Pill,"[119] and "Take a Powder: Get a Suntan."[120] These articles fanned public excitement by citing possibilities, such as one stated in the *Life* article, that "within two or three years a pill a day will banish painful sunburns from the beaches."[118]

Many physicians were troubled by the prospect of the use of 8-MOP for suntanning. This was reflected in a report to the AMA in 1958 by dermatologists Marion Sulzberger and Aaron Lerner.[121] The authors expressed concern about potential adverse effects from the use of 8-MOP by suntanners, who formed "a large and not easily controllable segment of the population."[121] Such misgivings proved justified; Samuel Becker, a dermatologist at the University of Illinois, would write in a separate report to the AMA in 1960: "Early publicity labeling the psoralens 'suntan pills' led many physicians and patients to regard these compounds as an equivalent to proprietary suntan lotions. . .. Casual prescribing, inadequate instructions to patients, passing around the medication, and experimentation by patients have all led to instances of severe, blistering dermatitis."[22]

The gravest issue raised in the report by Sulzberger and Lerner was 8-MOP's potential carcinogenicity. It was difficult to predict on purely theoretic grounds the effect that psoralens such as 8-MOP had on the formation of skin cancers. The authors articulated the uncertainties: "Will the incidence of basal-cell or squamous-cell carcinomas be changed, either decreased or increased? Will other senile skin changes be delayed or accelerated? Will there be any effect on the formation of melanomas?"[121]

Concern about the potential carcinogenicity of psoralens was warranted. In 1956, it was reported that 8-MOP combined with a nonmutagenic dose of UV light caused mutations in *Drosophila*.[123] Initial animal studies in which 8-MOP was administered in combination with primarily short- and middle-wavelength UV light yielded conflicting results as to whether the drug increased, decreased, or had no effect on skin tumor formation.[124,125] However, in 1958, a landmark study by Griffin et al[126] was published that first reported the surprising finding that 8-MOP combined with long wavelength UV light (UVA) produced malignant tumors in the skin and cataracts in the eyes of exposed mice. These authors demonstrated that mice treated with 8-MOP, administered either by an oral or intraperitoneal route, developed skin carcinomas when exposed to UVA, whereas control mice exposed to UVA alone did not develop tumors.[126,127] Commenting on the clinical implications of the findings, one of the authors, John Knox, a dermatologic researcher at Baylor University College of Medicine, stated: "In consideration of possible [sun] protection from psoralens, our studies to date in animals indicate that for light-skinned individuals the psoralens are possibly carcinogenic and we do not advocate them except where definitely indicated in selected cases of vitiligo."[128] The eminent dermatologist and skin biologist Stephen Rothman remarked: "If this [365 nm] wavelength, by virtue of the photosensitizing effect of psoralens, acquires the potency of producing cancers and cataracts, I just wonder whether all the dermatologists should not take a very strong stand against use and propagation of this material."[129] However, the applicability of the results of these animal studies to human patients remained a point of contention.[130,131] Specifically, it was argued that the intensity and duration of UVA that had been used could not be obtained from sunlight exposure, and that a much larger dose of 8-MOP was given than what was used clinically.[130] Thus, 8-MOP continued to be used by some clinicians to theoretically induce "sun tolerance" in patients who were light-sensitive.[132] In vitro studies in the late 1960s and early 1970s provided greater insight into the mechanism of mutagenicity and carcinogenicity of psoralens; the UVA wavelengths were found to produce a photoreaction in which the psoralen molecules formed photochemical adducts with pyrimidine bases and interstrand cross-links in DNA.[133,134]

More recently, the photocarcinogenicity of 8-MOP in human beings has been well documented. In 1958, Becker[122,135] reported that psoralens combined with UV light were therapeutically effective for light-responsive dermatoses such as psoriasis and eczema. In 1967, Oddoze et al[136] reported the successful use of oral 8-MOP combined with UV light to treat recalcitrant cases of psoriasis. This treatment became popularized in the 1970s; at this time, Parrish et al[137] used high-intensity UVA-emitting light bulbs, and the term "PUVA" (psoralen-UVA) was coined. Patients who received PUVA have subsequently been found to have a high incidence of cutaneous malignancy.[138-141]

DIHYDROXYACETONE: "SUNTAN IN A BOTTLE"

Shortly after 8-MOP was popularized as the "suntan pill," public attention was focused on dihydroxyacetone (DHA), a topical suntan-simulating agent

that was coined "suntan in a bottle." In the fall of 1959, a 5% aqueous solution of DHA was marketed as an aftershave lotion called Man-Tan.[142] An enormous commercial success, sales of Man-Tan totaled $20 million in the first 6 months after its introduction.[143] Within 2 years, numerous competing DHA-containing products had been marketed such as Tan-O-Rama; Magic Tan; Tanfastic; Tansation; Quick Tan; Tan Tone; One, Turn Tan; Rapid Tan; and Tan Perfect.[143,144]

Critical evaluation of DHA soon appeared in the medical literature[145-148] and consumer magazines like *Consumer Reports*.[149,150] Caveats included the fact that DHA was inadequate as a sunscreen. In addition, poor cosmetic results were possible, such as a mottled or streaked appearance, or unnatural orange coloration of the skin. In spite of these drawbacks, the agent was considered innocuous and of modest cosmetic usefulness for certain patients with hypopigmentation or depigmentation.[148] The action of DHA was determined to be on the basis of its binding to keratin in the outer epidermal layers.[147,148]

CONCLUSION

Tracing the evolution of attitudes toward UV light exposure provides a historic framework for current issues related to skin cancer prevention. Popular opinions regarding UV light exposure as desirable and healthful solidified in the late 1920s, after the discovery of its role in vitamin-D synthesis. Members of the medical profession contributed to the formation of these attitudes with exaggerated claims about the medical benefits of UV radiation, ignorance of its deleterious effects, and the misuse of phototherapy. Public health advocacy of UV light exposure was also commercially exploited–most importantly by manufacturers of home UV lamps–further influencing popular opinion. By the 1930s, the medical profession began to correct its course by issuing warnings about sunbathing and establishing guidelines for sunlamps and phototherapy. Over subsequent decades, the message that sunlight plays a role in the cause of skin cancer increasingly reached the public. Once established, however, popular beliefs and practices related to sunbathing and suntanning proved difficult to modify. Even at present, favorable attitudes toward suntanning persist; a 1996 telephone survey of 1000 adults by the American Academy of Dermatology (AAD) showed that 56% of respondents believed that persons looked more healthy when they had a suntan, and 25% reported that they intentionally worked on a tan.[151] Tanning parlors are frequented by approximately 1 million US citizens each day, and the annual revenues for the indoor tanning industry in the United States were recently estimated to exceed $1 billion.[23]

Today, the high incidence of nonmelanoma and melanoma skin cancer has been termed an epidemic.[152,153] In 2000, there were an estimated 1.3 million skin cancers diagnosed in the United States, including 47,700 cases of malignant melanoma.[154] Approximately 7700 person died from melanoma in the United States in that year.[155] Such statistics underscore the importance of primary prevention of skin cancer, as well as skin cancer screening and early detection. In spite of the challenges inherent in attempting to change societal attitudes toward suntanning, there is evidence that such prevention efforts can be effective over time. Two decades of public health campaigns in Australia have led to a large shift in knowledge and beliefs about sunlight exposure, and behavior.[156-158] Moreover, the incidence of melanoma and basal cell carcinoma in younger Australian cohorts has been reported to be leveling off or decreasing.[156,158,159] However, these trends must be interpreted with caution because they may also be related to the changing racial composition of Australia.[160] In the United States, organizations including the AAD, the Skin Cancer Foundation, and the American Cancer Society sponsor primary prevention programs emphasizing sun protection.[161] Although recent assessments of sun protection behaviors in the United States highlight the need for additional education,[154,162] ongoing public health efforts should serve to influence popular attitudes and ultimately may have an impact on prevention practices and skin cancer incidence.

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