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The Acute Effects of Long-wave Ultraviolet Radiation on Human Skin

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The erythematogenic and melanogenic properties of polychromatic long-wave ultraviolet light (UV-A) has been re-examined. Redness appeared immediately after exposure and persisted for 24 hr with doses of about 50 Joules/cm^2. With threshold erythemal doses, about 13 J/cm^2, the redness faded after a few minutes. The response was not biphasic. Pigmentation also appeared immediately after exposure and faded rapidly with threshold doses of 4 J/cm^2. With larger doses (18 J/cm^2) immediate pigmentation gave way without fading to delayed pigmentation (true melanogenesis).

Thus, the acute effects of UV-A, unlike other wavelengths within the UV-spectrum, are immediate and appear without latency. The responses are also most intense immediately after exposure.

Much has been learned about the erythemogenic, melanogenic and carcinogenic properties of sunburning radiation (UV-B, 290–320 nm). Long wave radiation (UV-A, 320–400 nm) to which we are regularly exposed, has been relatively neglected. For a long time, UV-A was thought to be more or less inert biologically. This view is no longer tenable. Prior exposure to UV-A enhances the sunburn reaction, a phenomenon termed photoaugmentation [1]. Conceivably, UV-A can potentiate other well known effects of UV-B such as aging changes and neoplasia. In experimental animals, long-term UV-A exposure has been reported to produce epidermal tumors [2,3] and cataracts [4]. It has long been appreciated that UV-A radiation can elicit both redness and pigmentation. However, there are conflicting reports concerning the onset and evolution of these reactions. Hausser, who in 1938 first described immediate pigment darkening (IPD), observed that tanning and erythema appeared immediately after exposure to UV-A wavelengths [5]. With large doses of 385 nm, the erythema persisted for over 12 hr and was followed by persistent pigmentation, that is, true melanogenesis. Henschke and Schulze later established that the action spectrum for IPD extended from 300 to 400 nm [6]. They too observed erythema which lasted for about 2 hr. In 1955, Bachem also found that both pigmentation and erythema from UV-A appeared without latency [7]. Moreover, the responses were intense from the very start. Interestingly, the erythema usually disappeared by 24 hr. Pigmentation, on the other hand either faded over 1 to 3 hr or persisted for over a year. Thus, the consensus among early workers was that UV-A provoked immediate rather than delayed erythema, and pigmentation was either transient (IPD) or persistent depending on the dose.

More recently, Pathak, Riley, and Fitzpatrick using a monochromator, re-investigated the cutaneous responses to UV-A [8]. They established that the action spectrum for IPD extended well into the visible range (600 nm). The immediate darkening faded within 1–3 hr and was followed in 48 to 72 hr by the reappearance of pigmentation. Delayed tanning reflected the formation of new melanin. They also noted that in fair-skinned persons, erythema appeared immediately, faded within 1–2 hr, and reappeared 10 to 18 hr later. Thus, their findings indicate that UV-A is capable of eliciting immediate as well as delayed erythema.

In view of recent interest in UV-A and its increasing use in photochemotherapy, we have re-investigated the erythemogenic and pigmentary effects of these wavelengths in humans.

MATERIALS AND METHODS

Subjects

These were healthy Caucasian college students between the ages of 19 and 24 yr. Since very fair-complexioned individuals who tan poorly (skin type 1) are inadequate for studying IPD and delayed melanogenesis, only Caucasian subjects who by history were capable of acquiring natural tans after repeated sun exposure were selected (skin types II and III). The untanned midback was the test site. Informed consent was obtained.

UV-sources

UV-A was secured from a 150-W xenon arc solar simulator [9]. To reduce infrared (IR) radiation, a UV-reflecting IR transmitting dichroic mirror is employed in the light path. The design and spectral distribution of this source have been published [9]. The radiation was filtered through a 2 mm Schott WG 345 filter to eliminate UV-B and through a 2 mm UG 5 colored filter to further attenuate heat and visible wavelengths. The proportion of UV-A in the filtered beam was calculated by using a 0.15 mm plastic "weatherable" Mylar film which has a sharp cut-off at 400 nm (50% transmission at 417 nm; 78% transmission >430 nm). Total flux at skin level ranged from 47.2 to 51.6 mW/cm^2; UV-A irradiance 27.0 to 32.0 mw/cm^2. Irradiance measurements were made by a Calibrated Eppley Thermopile (Eppley Laboratories). Intensity was measured and length of exposure determined prior to irradiation of each subject. UV-A effects were studied in 22 subjects (11 females).

UV-B

Threshold doses for delayed erythema and pigmentation were determined with UV-B in 10 subjects (4 females). Radiation was obtained from a bank of 5 closely set fluorescent Westinghouse FS-20 Sunlamp tubes mounted in a reflector housing. The lamp-to-skin distance was 12 cm. UV-B irradiance, as measured by the Thermopile, was 0.61 mw/cm^2. This was calculated by using a 0.15 mm D plastic Mylar film with a sharp cut-off at about 315 nm.

Exposures and Grading

UV-A threshold doses for IPD, erythema and delayed tanning were determined by administering a series of increasing exposures (1 J/cm^2 increments), starting with 1.0 Joule/cm^2. For doses in excess of 10 J/cm^2, increments of 2.0 J/cm^2 were given, while for doses greater than 30 J/cm^2, 5.0 J/cm^2 increments were administered. The responses were graded immediately after irradiation, 4–6 hr later and at 1, 2, 3, 5, 7, and 14 days. In 12 of the subjects, the time-course of erythema was determined by visual evaluation immediately after exposure and at 6, 12, 18, 24 and 48 hr.

With UV-B, a series of 10-second increments, beginning with 30 seconds was given. Responses were graded 24 hr later and at 3, 5 and 7 days. The Minimal Tanning Dose (MTD) was the smallest dose required to produce minimally visible pigmentation at 7 days.

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Abbreviations:
IPD: immediate pigment darkening
IR: infrared
MED: minimal erythema dose
MTD: minimal tanning dose

UV-A Melanogenesis: Dose-Response

The influence of UV-A dose on delayed pigmentation was investigated in 10 subjects. Increasing doses were given to the midback; the intensity of the resultant pigmentation was recorded 14 days later, as follows: 0, no pigmentation; 1+, minimal visible pigmentation; 2+, moderate pigmentation; 3+, intense deep pigmentation; 4+, intense dark brown to black pigmentation.

RESULTS

UV-B Erythema and Pigmentation

The mean delayed erythema threshold dose was 26.8 ± 4.2 mJ/cm^2 (Table I). Erythema from one MED usually disappeared by 48 hr, but persisted for longer periods with doses of 2 MED's or larger. Delayed pigmentation usually appeared 3 to 4 days later. The MTD was 41.4 ± 9.0 mJ/cm^2.

UV-A

The threshold responses to UV-A were far more variable (Table II). Both pigmentation and erythema appeared maximally immediately after exposure. The mean threshold dose for the IPD was 4.0 ± 3.0 J/cm^2 (Table II). The 2 subjects with the highest values (12 and 14 J/cm^2) had the fairest complexion. With threshold doses, IPD usually faded within 5 to 10 min. Increasing exposures, however, produced progressively more intense IPD which required longer to disappear, fading over a period of 6 to 24 hr. After a certain threshold dose (MTD), IPD faded gradually but pigmentation never completely disappeared, persisting at the same intensity beyond 24 hr and lasting for the entire observation period (2 weeks). Thus, with doses equivalent to an MTD or larger, IPD blended into delayed melanogenesis. The mean MTD was 17.7 ± 8.0 J/cm^2 (Table II). In general, darker complexioned individuals had lower IPD and MTD threshold doses. At no time did delayed pigmentation develop without preceding intense IPD.

Erythema appeared without latency and was most intense immediately after exposure, fading rapidly thereafter, but occasionally persisting for 5–6 hr following longer exposures. The threshold dose for immediate erythema was 13.2 ± 6.0 J/cm^2. With threshold doses, the immediate erythema was very evanescent; it usually disappeared within a few minutes and failed to reappear at later observation periods. Larger doses resulted in more intense immediate erythema which faded over progressively longer periods of time. Thus, on the average, about 30 J/cm^2 were required to produce erythema persisting for 4–6 hr (Table II). Again, once it disappeared, the erythema did not reappear at a later time. High doses (49.3 ± 17.6 J/cm^2) resulted in intense immediate erythema, often accompanied by a flare, which faded rapidly but remained visible 24 hr later. With still larger doses, erythema occasionally persisted beyond 48 hr, though it was far less intense. At no dosage level did we observe a biphasic erythemal response.

Dose-Response Studies

Although there was much individual variation, progressively larger doses of UV-A produced more intense delayed pigmentation (Figure).

TABLE I. *Threshold doses for UV-B*

Subject No.	Minimal erythema dose mJ/cm^2	Minimal tanning dose mJ/cm^2
1.	18.3	30.5
2.	30.5	61.0
3.	30.5	42.7
4.	24.4	36.6
5.	30.5	42.7
6.	24.4	36.6
7.	30.5	42.7
8.	24.4	42.7
9.	30.5	48.8
10.	24.4	30.5
Mean ± SD	26.8 ± 4.2	41.4 ± 9.0

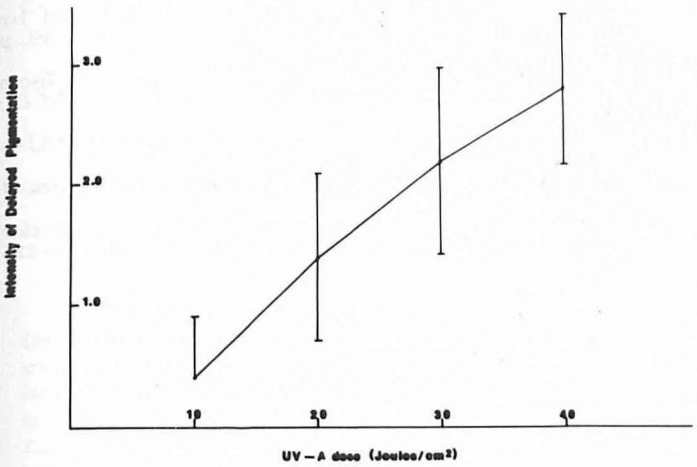
DISCUSSION

In the past, considerable disagreement arose over the shape of the erythema action spectrum curve simply because various investigators recorded their observations at different times and used different light sources [10,11]. It was later appreciated that these differences were at least partly due to the fact that UV-C

TABLE II. *Threshold doses (Joules/cm^2) for UV-A*

Subject No.	Tanning		Erythema		
	IPD	MTD[b]	Immediate	4–6 hr	24 hr
1.	5	12	14	14	40
2.	3	26	16	ND[c]	45
3.	5	8	24	30	70
4.	12	18	9	ND	35
5.	4	18	10	ND	45
6.	3	18	12	35	50
7.	2	10	18	ND	80
8.	2	10	10	ND	65
9.	4	10	12	16	25
10.	2	30	10	ND	40
11.	3	18	5	30	45
12.	4	12	7	18	30
13.	2	26	9	45	75
14.	4	30	20	60	80
15.	3	14	30	ND	60
16.	3	18	14	18	25
17.	2	12	6	ND	55
18.	2	16	12	ND	50
19.	2	14	14	ND	35
20.	14	16	8	16	30
21.	4	40	20	60	70
22.	5	14	12	20	35
Mean ± SD	4.0 ± 3.0	17.7 ± 8.0	13.2 ± 6.0	30.1 ± 16.7	49.3 ± 17.6

[a] IPD = Immediate Pigment Darkening.
[b] MTD = Minimal Tanning Dose.
[c] ND = Not determined.



Influence of UV-A dose on the degree of true melanogenesis. *Bars* indicate standard deviation.

and UV-B erythema evolved differently, the former peaking in 8 hr and the latter in 24 hr. We encountered a similar problem while attempting to determine the energy requirements for threshold UV-A responses. Initially, we sought to determine the delayed MED by recording observations at 24 hr. It quickly became clear that delayed erythema was not elicitable with doses that provoked immediate reactions. In several recent communications, the "MED" with UV-A in humans was reported to be about 20 J/cm^2 [12,13]. Parrish et al, used these values to argue that the delayed erythemogenic effects of UV-A and UV-B were in fact additive, an explanation they preferred to photoaugmentation [13]. This implied that both wavebands produced delayed erythema, although the time-course of the UV-A reaction was not described. Our present findings clearly show that UV-A responses appear without a latency period, in contrast to UV-C and UV-B. These effects are not likely to be due to heat or nonspecific energy absorption since the irradiances used were less than half the reported immediate heat erythema thresholds [9,14]. Nonetheless, we cannot rule out some contribution by heat. Since delayed erythema implies that redness appears after a latency period, it is inaccurate to use this term for describing UV-A erythema. The 24-hr erythema would be more appropriate. Large doses of UV-A were needed in the majority of subjects to produce erythema persisting for 24 hr or longer. This suggests that "delayed" UV-A erythema is not a type of response which occurs under usual conditions of exposure, at least in individuals who are capable of acquiring natural tans.

The reported threshold dose for 24-hr UV-A erythema has differed considerably. Parris et al [13] and Tannenbaum et al [15] obtained values of 20–30 J/cm^2, using a 150-w xenon source and high pressure mercury lamps. With a 1600-w xenon source, we have previously reported a value of about 90 J/cm [16]. In the present study, the dose was 50 J/cm^2. There are several reasons for these discrepancies. Measurements of radiation intensity are greatly influenced by the type and nature of detector used [17]. Another factor is the variability of erythema which is often difficult to reproduce, even in the same individual (unpublished observations). Skin type and complexion are also important factors; the subjects in this study were capable of tanning. Lastly, although it is convenient to lump all wavelengths between 320–400 nm together as "UV-A," it should be remembered that erythemal efficiency is wavelength dependent. The erythema action spectrum in the UV-A region has not been adequately determined. Maximal efficiency is said to occur at about 385 nm [18]. Threshold doses for polychromatic radiation will be influenced by the spectral distribution of the source.

With monochromatic UV-A, both Pathak et al [8] and Parrish et al [19] reported biphasic erythema after threshold exposures. The average threshold dose for 24-hr erythema was 21.6 J/cm^2 with 337.1 nm radiation emitted from a pulsed nitrogen gas laser [19]. Larger doses, however, resulted in more intense immediate erythema which persisted over 24 hr. The tanning response was also biphasic, consisting of IPD followed in 3–5 days by true or delayed melanogenesis. This is in contrast to our observation with polychromatic UV-A, where both erythema and pigmentation could not be clearly separated into 2 distinct phases. These differences may be due to selection of subjects. Reactions in very fair skinned Caucasians who tan poorly (skin type 1) may evolve differently than in normally complexioned individuals. This is an interesting possibility that needs further study. However, we think it is more likely that the effects of monochromatic and polychromatic radiation are dissimilar. There is evidence to suggest that this may be the case. The law of reciprocity, for example, which applies over a wide range of intensities for monochromatic UV-B [20] and UV-A [19] does not apply to polychromatic UV [21].

Clearly, melanogenic efficiency is also wavelength dependent. UV-B is far more efficient in stimulating delayed melanogenesis. Since the MTD for UV-B was larger than the MED, single exposures to UV-B will not induce tanning without prior erythema. Our findings compare well with those of Langen who also found that the threshold tanning dose was about 50% larger than the threshold erythema dose [22]. UV-A on the other hand was far less efficient. The MTD was about 400 times that of UV-B.

In this study, we have employed the term MTD in a manner analogous to the more familiar MED. We believe that MTD determinations will be important for future quantitative investigations of UV-melanogenesis. The latter, unlike erythema, has not been adequately studied. Our present findings, though clearly preliminary, do show that delayed UV-A melanogenesis is dose dependent.

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Announcement
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