The Time Course of UVB and UVC Erythema

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The time course of ultraviolet erythema was measured using six different exposure doses of UVC and UVB radiation in each of eight adult subjects. The intensity of erythema was measured by reflectance spectrophotometry at 4, 8, 24, 36, and 48 h after irradiation. In five subjects there was no significant difference between the form of the UVB and UVC erythema time-course. In three subjects a significant difference was observed, but this was random rather than systematic between subjects. The results do not confirm the previously reported major differences in time course between the two qualities of radiation. *J Invest Dermatol 91:454–457, 1988*

The dermatologic literature contains numerous references to a difference in the time course of erythema induced by UVB and UVC radiation [1–11]: UVC erythema is said to appear, become maximal, and fade earlier than UVB erythema. These observations are based on limited experimental data in early reports [1,2,5], which are unclear as to whether UVB and UVC erythema of similar intensity were compared. This reported difference in time course has been taken as evidence of a different mechanism of erythema production at these two wavelengths [7–11], particularly with regard to the role of prostaglandins as inflammatory mediators [8–10].

We have now used a method of quantifying erythema to determine objectively whether a difference in time course exists between UVB and UVC erythema.

METHODS

Subjects Eight adult subjects (4 female, 4 male; sun-reactive skin type II or III) were studied. No subject was known to exhibit abnormal sensitivity to sunlight, or was taking any medication known to provoke such a reaction. Three of the volunteers had normal skin and five were being investigated or treated for localized skin disease. In all cases, skin of the midback was studied, and all measurements were made on skin of normal appearance. No topical treatment was applied to any part of the back before or during the study.

Photo-irradiation Apparatus and Radiation Dosimetry The following two optical radiation sources were used a) UVC: a germicidal lamp (Philips type TUV 15W) was used for irradiation principally at 254 nm. The lamp was mounted inside an opaque plastic housing with a cylindrical collimator (15 mm internal diameter) positioned orthogonally to the mid-point of the long axis of the lamp. b) UVB: a 500-W medium-pressure mercury arc lamp was used in conjunction with Schott WG305 (3 mm thick) and UG5 (1 mm thick) color glass filters. Radiation from the lamp was focussed

into a liquid-filled light guide (1 m in length) with an applicator attached to the distal end of the light guide to produce a uniform beam of radiation (10 mm diameter) on the skin surface.

Spectral irradiance from both lamps (Fig 1) was measured in the plane of the skin surface using a double holographic grating spectroradiometer (Optronic Laboratories Inc., model 742) with bandwidth set at 1.5 nm, calibrated by reference to a deuterium spectral irradiance standard (obtained from the National Physical Laboratory, U.K.). The integrated irradiance from 200–290 nm (UVC waveband) from the germicidal lamp was 30 W/m²; this is 96% of the UV output and is almost entirely due to the 254 nm characteristic line. The integrated irradiance from 290–320 nm (UVB waveband) from the optically filtered mercury arc lamp was 80 W/m². Approximately 97% of the erythemally effective power from this source lies within the spectral interval 290–320 nm.

Subject Irradiation Six closely apposed circular sites (20 mm diameter) were marked on either side of the midback of each subject. One group of sites, chosen at random, was irradiated consecutively with UVC and the other with UVB radiation. On either side of the back one site was not irradiated and served as a control area. A geometric series of increasing exposures was used, the dose increment factor being approximately 2 for UVC and 1.3 for UVB radiation. All subjects were exposed to five different doses from each lamp. The lowest dose used ranged from 0.08–0.25 kJ/m² and 0.6–1.2 kJ/m² for UVC and UVB radiation, respectively.

Measurement of Erythema Erythema was measured using a reflectance instrument that compares the amount of red and green light reflected from the skin and thus obtains an "erythema index" related to the blood content of the dermis [12]. Before irradiation, three measurements of the erythema index were made at each of the sites with the subject lying prone on a couch. In all subjects, the erythema measurements were repeated at 4, 8, 12, 24, 36, and 48 h after irradiation. The increase in vasodilation due to the radiation is expressed as the difference (ΔE) between the mean post- and mean pre-irradiation erythema index at each site. This value has been shown to be a more reliable indicator of vasodilation than the post-irradiation erythema index alone [13]. A linear relationship between the measured increase in erythema index (ΔE) and logarithm of the exposure dose of radiation has been shown for wavelengths of radiation within the UVC, UVB, and UVA spectral intervals [14,15]. Values of ΔE around 0.05 correspond to the minimal erythema dose (defined as the least dose of radiation to result in uniform redness with sharp borders); values of ΔE around 0.3 correspond to "severe"
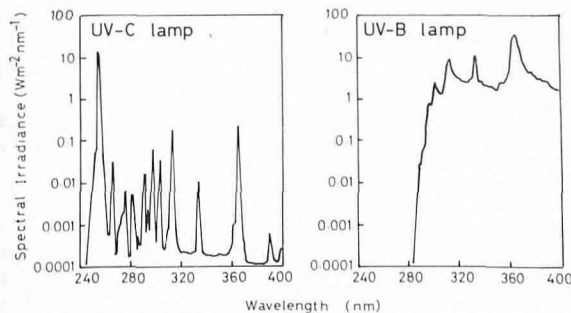
Figure 1. Spectral irradiance from the two lamps in the plane of the subjects' skin

erythema [14]. Erythema measurements made on each occasion were corrected by any change in basal erythema on the unirradiated control site.

In order to examine differences between the shape of the time course for UVB and UVC erythema, the erythema measurements at each exposure dose and for each subject were normalized to equal summed erythema indices over the 6 times of measurement. This procedure assumes that the shape of the time-course for a given subject and waveband is independent of dose.

Statistical Analysis A non-parametric statistical analysis was carried out for each subject in turn to test for systematic difference between the normalized time courses of UVB and UVC erythema. Details of the procedure are given in the appendix.
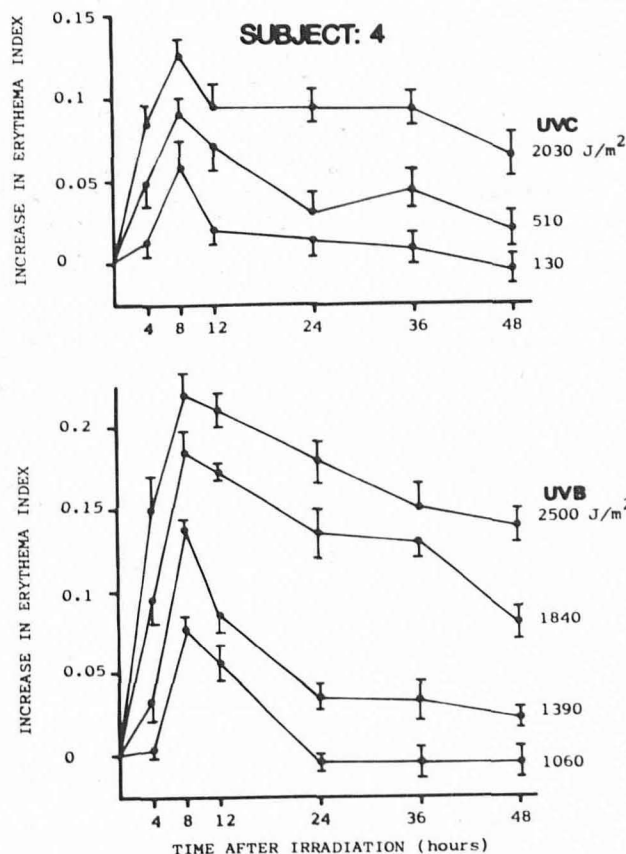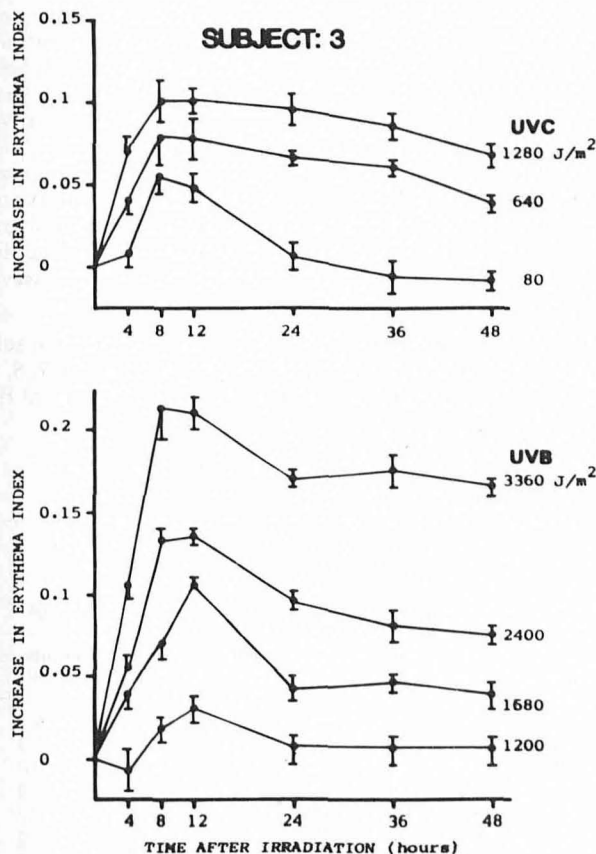
RESULTS

Examples of the time course of erythema induced by different doses of UVB and UVC radiation in two of the volunteers are shown in Fig 2. Erythema induced by both wavelengths was present by 4 h after irradiation. Although the time to maximum erythema varied from 8 to 24 h after irradiation between subjects, for any one subject it was similar for the two wavelengths. The duration of erythema was clearly related to the dose of radiation and, for both wavelengths erythema of minimal to mild intensity ($\Delta E < 0.1$) at 12 h had faded completely by 48 h (Fig 2). Because of this, in the analysis to normalize the data, only those exposures were included for analysis in which at least a mild erythema was present from 8 h onwards. The normalized time courses of UVB and UVC erythema for each subject are shown in Fig 3. The results of statistical analysis summarized in Table I show that there was no significant difference between the normalized time course of UVB and UVC erythema in five of the eight subjects. In the remaining three subjects (numbers 2, 6, and 7), the time courses were found to differ significantly (combined significance $< 5\%$).

DISCUSSION

For both wavelengths, the duration of erythema was clearly related to the exposure dose of radiation. As is widely known, low doses, which resulted in erythema of only minimal to mild intensity at 8 or 12 h, had faded completely by 48 h after irradiation. In order to make an objective comparison between the time courses of erythema of greater intensity induced by these two wavelengths some method of normalizing the data was required. We chose to normalize the data according to the total ΔE measured at each of the six times of observation. This procedure assumes that the shape of the time course for a given subject and waveband is independent of dose.
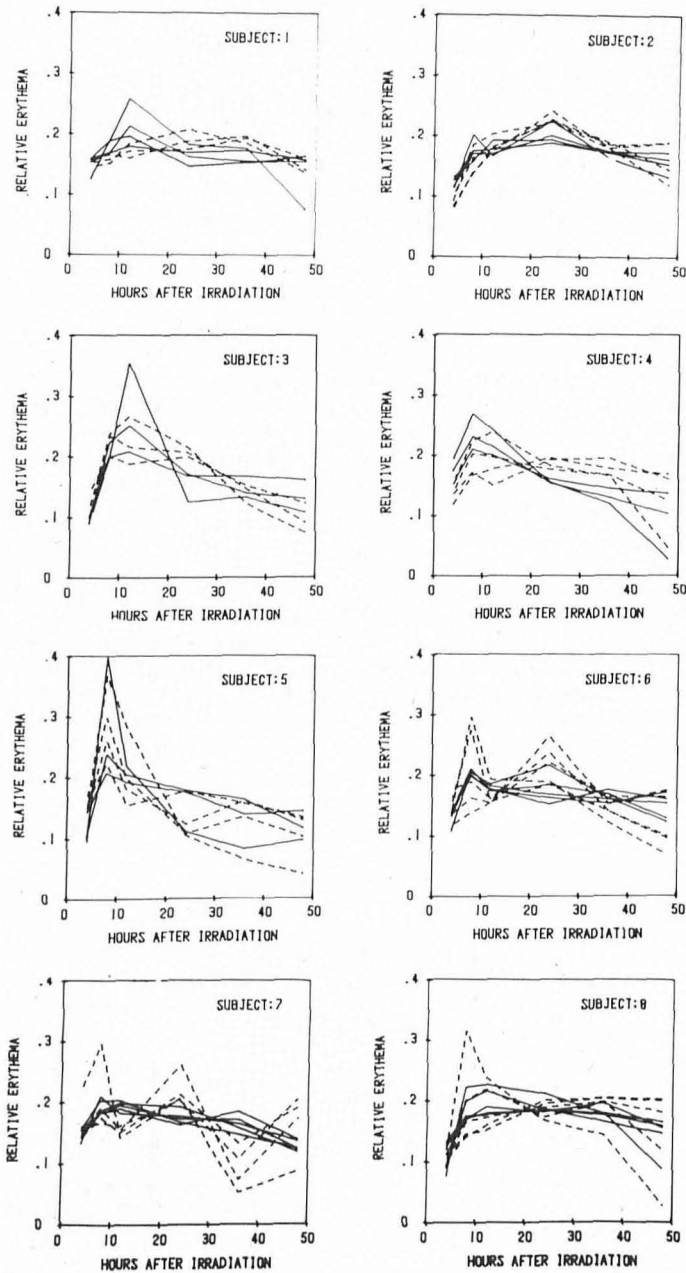

Figure 2. The time course of erythema in two subjects induced by different doses of UVB and UVC radiation. *Error bars* represent ± 1 standard deviation of the measured difference between the post- and pre-irradiation erythema indices

Figure 3. The normalized erythema time courses in each of the eight subjects (*solid line:* UVB; *broken line:* UVC)

We have shown previously [14] that the log (dose)-ΔE response curve for both UVB and UVC radiation is linear from 4 h to at least 48 h after irradiation. The assumption made concerning independence of dose and time course shape is therefore valid provided that measurements are confined to responses on the linear part of the dose-response curve. Because of this, only exposures that resulted in at least a mild erythema were included in the analysis. Other methods of normalizing the data, such as according to the area under the ΔE/time curve, or to the measured maximum increase in erythema, would be equally valid, but, in fact, do not affect the conclusions presented here. Between subjects, the overall form of the normalized time courses varied considerably, particularly with regard to time of maximum erythema and subsequent rate of fall of erythema. However, when compared within each subject (Fig 3) the responses were similar, suggesting a common mechanism of erythema production at the two wavelengths. In keeping with this, the within-subject statistical analysis described in the appendix showed no significant difference in time course of UVB and UVC in five of the subjects. In the remaining three patients the differences appeared to be random rather than systematic between subjects. For example, the considerable difference between UVC and UVB measurements seen in subjects 6 and 7 occurred at different times (8 and 24 h, subject 6; 24 and 36 h, subject 7) (Fig 3).

We were unable to make observations beyond 48 h after irradiation as the development of melanin pigmentation would invalidate the technique of erythema measurement [13]. Nevertheless, as there was no significant difference between the rate of fall of ΔE from 24 to 48 h for UVB and UVC erythema, it seems unlikely that a major difference in time course exists after 48 h.

These findings appear to be at variance with earlier reports which suggest an earlier onset and shorter duration for UVC than for UVB erythema [1–11]. Although reference is often made to a difference in time course, only Hausser and Vahle [1], Bachem [2], and Breit and Kligman [5] provide any data to support this notion. Few details are given by these workers, but it would appear that comparisons were made in terms of multiples of the MED (for example the time course of a 3 MED UVB erythema would be compared with a 3 MED UVC erythema). The significant difference in slope of the dose-response curve at these two wavelengths [14] means that, when compared in this fashion at doses greater than the MED, UVB erythema will always be of much greater intensity. Therefore, they will be seen to persist longer than UVC erythema. It is suggested that normalizing the time course curves allows a more valid comparison to be made. Our results do not confirm the previously reported major differences in time course and provide no evidence for a different mechanism of erythema production at the two wavelengths.

Details of Statistical Analysis Suppose that in a particular subject erythema was achieved at n irradiated sites (here n = 6, 7, 8, 9, or 10), of which b are chosen at random to receive UVB and the

Table I. Summary of Statistical Analysis

| Subject | Sex | Age | No. irradiated sites in which erythema was achieved | | | No. points in reference distribution | Rank of test statistic at time | | | | | | Combined | |
			UVB (b)	UVC (c)	Total (n)	(N)	4h (t_1)	8h (t_2)	12h (t_3)	24h (t_4)	36h (t_5)	48h (t_6)	Rank	Significance %
1	M	34	4	3	7	35	34	3	4	4	1	33	3	<9
2	F	38	4	4	8	35	1	8	15	2	1	28	1	<3
3	F	42	3	3	6	10	2	2	5	1	7	2	1	10
4	F	58	3	4	7	35	1	4	9	1	1	15	3	<9
5	F	22	3	4	7	35	1	33	35	10	33	23	13	37
6	M	21	5	5	10	126	46	99	10	6	6	31	2	<2
7	M	20	5	4	9	126	23	110	1	1	1	21	1	<1
8	M	68	5	5	10	126	93	118	77	73	57	118	115	91

remaining $c = n - b$ receive UVC (here b, c = 3, 4, or 5). Data are then collected on n time courses, of which b are labeled UVB and c are labeled UVC, at times t_i (i = 1, 2, . . . , 6). These measurements lead to a particular value of our chosen test statistic. However, according to the null hypothesis, the b time courses labeled UVB might, equally well, have been selected at random from the n observed time courses because UVB and UVC are indistinguishable. We can use this fact to generate a reference distribution for the test statistic, because there are N different labelings available (N = n!/b!c! half this number when b = c), of which we have observed one; and if the recorded value of our test statistic ranks kth most extreme among the N possible values, then the null hypothesis is just rejected at the k/N probability level (i.e. 100k/N% level). Note that when, as here, b and c are small, the realizable significance levels of the test are highly discrete, and, hence, the usual approximations based on the normal distribution can be severely awry.

The obvious statistic with which to test the null hypothesis at a particular time t_i is the absolute difference between the UVB and UVC group means at t_i. Thus, Table I shows the observed rank of this statistic among all possible values for each subject and each time point. For example, in the case of subject number 2 at time t_4 (24 h) the observed absolute difference between the UVB and UVC means ranked second among the 35 possible values and so the corresponding significance level is calculated as $100 \times 2/35 = 5.7\%$. Other significance levels can be calculated similarly: We have reported ranks in Table I to emphasize the discreteness of the tests. Thus, for subject 3, with b = c = 3, it is not possible to obtain a significance level less than 10% because the reference distribution contains only ten points.

The results in Table I for the individual t_i's suggest that there may be evidence to reject the null hypothesis for six of the subjects. A combined test over the t_i's for each subject is required. A common procedure for combining independent significance levels is to consider their geometric mean, or equivalently their product, and to apply an approximation to the null distribution of this statistic based on the chi-squared distribution. Here this procedure fails for two reasons: because the tests are dependent, and because of the discreteness of the significance test. We can, however, assess the geometric mean of the significance levels against the reference distribution for each subject, and this leads to the ranks and significance levels given in the final two columns of Table I. We now see clear evidence against the null hypothesis for three of the subjects.

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