

# Physiological Variation in the Erythema Response to Ultraviolet Radiation and Photoadaptation

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**We have studied the cutaneous response to ultraviolet radiation, measured objectively as erythema in a sample of 12 body sites on 15 Northern European subjects with multiple doses of ultraviolet B (UVB). Skin pigmentation and the development of photoadaptation in response to five repeated doses of irradiation at three body sites was also measured. We report striking differences of up to 5-fold at different body sites to the same challenge dose ( $p < 0.001$ ) and demonstrate that for this population, site variation is just as important as between-person variation. Skin color at each body site is a strong predictor of response ( $p < 0.001$ ) and that this cannot be attributed to vascular differences, but instead we believe it reflects site-specific variations in melanin pigmentation. We also observed similar but smaller within-person effects for responses to another inflammatory agent, dithranol ( $p < 0.01$ ). Despite this, we did not find evidence for differences in the development of photoadaptation by body site. These results have clear clinical implications for the practice of phototesting prior to commencing phototherapy, for therapeutic failure in sites such as the legs in patients with psoriasis, and perhaps for melanoma body-site distribution.**

Key words: erythema/melanin/melanoma/minimal erythema dose/photoadaptation/ultraviolet radiation  
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Two methods are widely used to summarize and rank different persons' response to ultraviolet radiation (UVR). The minimal erythema dose (MED), and the Fitzpatrick phototype (Rees, 2002). The former is based on an assessment of a binary outcome, namely whether a particular degree of erythema occurs after exposure to a graded series of doses of UVR (Farr and Diffey, 1984; Farr and Diffey, 1986). The particular degree of erythema chosen as the endpoint varies among researchers. Reading of the MED is confounded by differences in pigmentation (i.e., the difficulty of recognizing erythema in the presence of different amounts of pigment) (Diffey and Robson, 1992), and because it is a threshold measure, the exact value of the MED depends on the dose increment chosen for the graded series of irradiation (Farr *et al*, 1989; Lock-Andersen and Wulf, 1996). It is usually performed at one body site only.

The second method, the Fitzpatrick phototype, is based on subjects' recall of their response to natural sunlight in terms of whether, and to what degree, they tan and develop erythema (Fitzpatrick, 1988). The response is summarized on an ordinal scale. The Fitzpatrick classification has found wide use in clinical practice, for instance, prior to phototherapy and in epidemiological examination of the risk between sunshine and skin cancer. Studies of reliability or

validity are few, but suggest that the classification has a low reproducibility (Rampen *et al*, 1988; Lock-Andersen and Wulf, 1996; Gordon *et al*, 1998). Unlike the MED, the measure is explicitly based on two qualities, erythema and pigmentation, and implicitly (if not explicitly) refers to more than one body site.

These two methods attempt to measure different aspects of the skin's response to UVR (Rees, 2002). The MED is a single snapshot of the erythema response to a single dose of UVR. By contrast, the Fitzpatrick scale attempts to summarize a dynamic response and involves pigmentation as well as erythema. It is worth outlining the rationale for the use of either measure prior to starting phototherapy. Worldwide, people vary by at least one to two orders of magnitude in their sensitivity to UVR measured as erythema following a single exposure. Even within Northern European populations, a 4–5-fold variation occurs (Farr and Diffey, 1984; Ha *et al*, 2003). The differences following repeated exposures have been poorly studied, but it seems reasonable to assume that they are also large as it is widely accepted that people tan to different degrees and at different rates. Since excessive doses of UVR may induce burning, the goal in determining the starting dose for phototherapy is to choose a dose of UVR that is not large enough to cause burning—but is as large as it is possible otherwise—and to increase the dose incrementally within the same constraints. It is also widely assumed that the degree of dose escalation can be greater in those who tan well, as tanning is protective against the development of erythema. The relation between acute erythema response and the propensity to tan—whatever the strength of this relation—determines

Abbreviations: MED, minimal erythema dose; MI, melanin index; SED, standard erythema dose; UVB, ultraviolet B; UVR, ultraviolet radiation

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the degree of covariance between the two measures (Rees, 2002).

In this paper, we examine experimentally how robust these clinical beliefs are by asking three related questions. First, how does variation in erythral response to UVR between people compare with variation in response within a person at different body sites? Some work has been carried out previously on such variation on one or two body sites, but no systematic attempt made to relate variation at a range of anatomical sites, to the variation seen between persons (Rhodes and Friedmann, 1992; Gordon *et al*, 1998). Second, irrespective of the absolute degree of erythema induced in response to a single dose of UVR at different body sites, do different body sites photoadapt to the same degree in response to repeated irradiation? Third, given site variation in response to single doses of UVR, can such differences be explained by site variation in pigmentation or other characteristics such as site variation in vascular responsiveness?

## Results

**Different body sites show large differences in sensitivity to UVR** Ten areas, at 12 different body sites, on both left and right sides in 15 patients were irradiated giving a total of 3600 potential data points (1800 on each side). The correlations between the paired data points provide some information about reproducibility. Table I lists Spearman correlations ( $\rho$ ) between paired body sites, and shows that while correlations were as expected, high values for the inner forearm and outer forearm were the lowest. Although ten different doses of UVR were given at each paired body site for all individuals, given the known variability in response, many of these responses were zero as anticipated. Formal analyses were therefore carried out for the top dose (300 mJ per cm<sup>2</sup>), and are presented in most detail. We also examined the top 4 doses, incorporating dose as an explanatory factor and graphically present the results based on the MED.

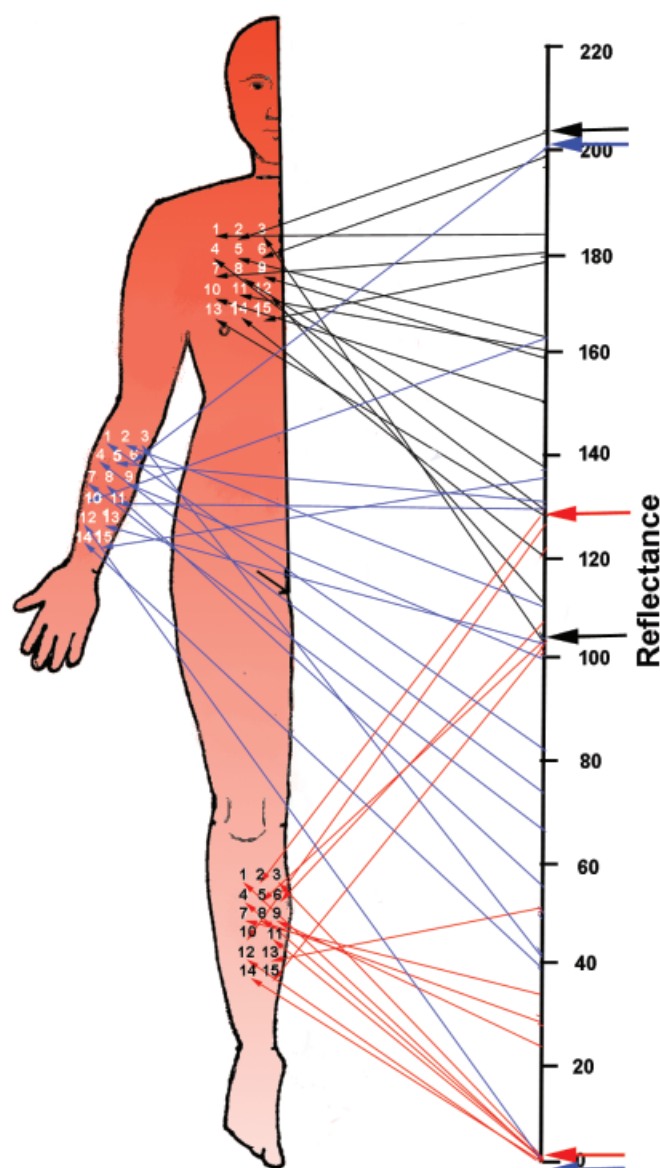
A mixed-effects model was fitted to the highest UVR dose data, with site and sex treated as fixed effects, and

person and side as random effects. Adding higher order functions did not appreciably alter results. It can be seen that there is a large site effect (Table II), and that there is also

**Table II. Summary of statistical model fitted for the degree of erythema induced by 300 mJ UVB**

	df	F-value	p-value
(Intercept)	1	131.3174	<0.0001
Site <sup>a</sup>	11	60.2171	<0.0001
Sex <sup>a</sup>	1	0.0342	0.8561
Site $\times$ sex <sup>a</sup>	11	1.3934	0.1743

<sup>a</sup>The symbol " $\times$ " refers to statistical interactions between (fixed) factors.



**Figure 1**  
**Examples of erythral response for three body sites for all persons.** Three representative body sites are shown, with the erythral response measured in reflectance units to a dose of 300 mJ per cm<sup>2</sup>. Numbers refer to each test subject. Note the spread of responses at each site (particularly the forearm), and the difference between sites (indicated by the arrows).

**Table I. Spearman's correlation coefficient ( $\rho$ ) for left side to right side comparisons by body site for whole dataset**

Body site	Correlation
Chest	0.96
Front upper arm	0.92
Inner forearm	0.60
Front thigh	0.92
Outer calf	0.71
Upper back	0.96
Lower back	0.95
Back of upper arm	0.92
Outer forearm	0.74
Back of thigh	0.95
Abdomen	0.98

considerable variation between persons, but with a minor degree of variation accounted for by side, (person (SD) = 33; side (SD) = 1.5; residual (SD) = 33, with an overall mean of 98). These results can be seen in context in Fig 1 in which the response in reflectance units for the highest dose of UVR is shown for three body sites, chosen to represent the range of sites examined. The numbers 1–15 refer to the 15 persons studied. It is clear that not only do responses for persons (for any site) differ, but that sites also differ, and that variation even within some sites is very large (e.g., forearm). By contrast, Fig 2 shows the ranking of response within each person by site, for all 15 persons. The clustering on the

**Table III. Summary of statistical model fitted for the degree of erythema induced by the upper four doses of UVB**

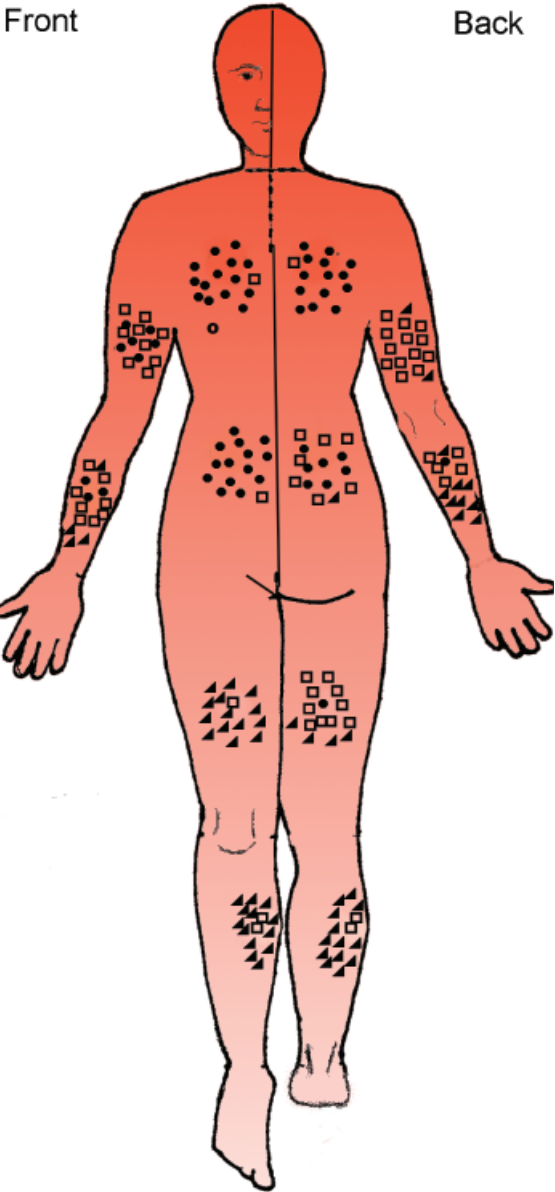
	df	F-value	p-value
(Intercept)	1	101.9203	<0.0001
Dose	3	305.7786	<0.0001
Site	11	233.8745	<0.0001
Sex	1	0.0358	0.8528
Dose × site <sup>a</sup>	33	2.4939	<0.0001
Dose × sex <sup>a</sup>	3	1.7035	0.1644
Site × sex <sup>a</sup>	11	4.6317	<0.0001
Dose × site × sex <sup>a</sup>	33	0.7870	0.8009

<sup>a</sup>The symbol “ × ” refers to statistical interactions between (fixed) factors.  
UVB, ultraviolet B.

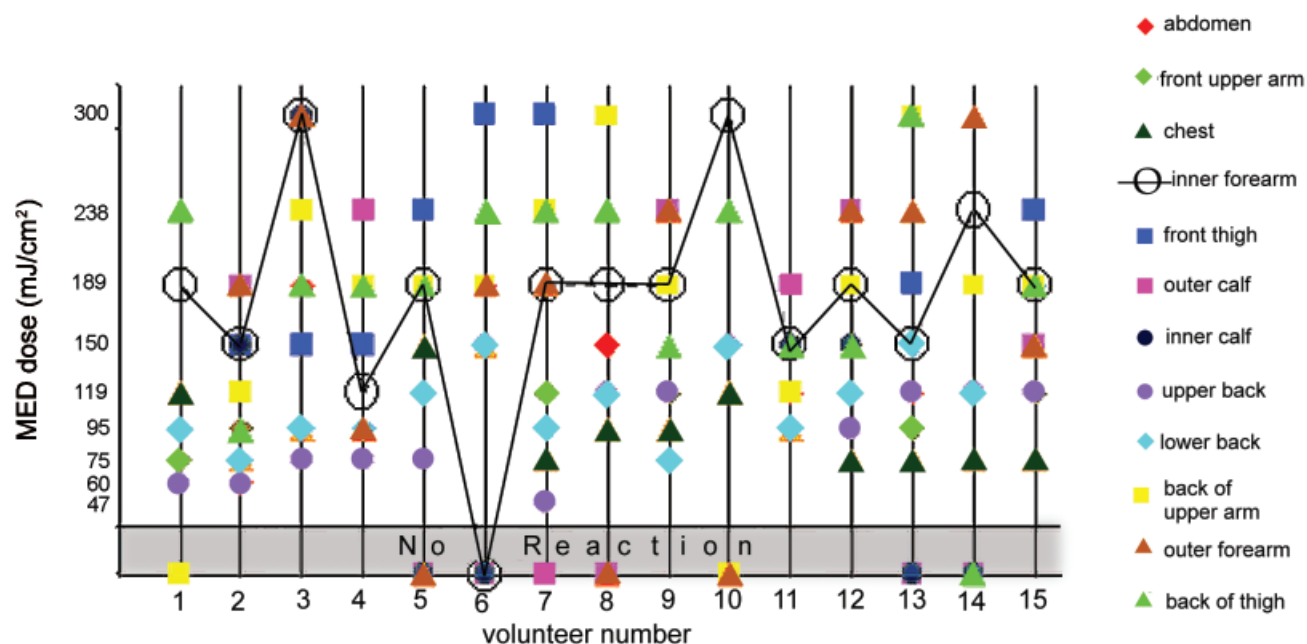
legs shows that for most persons, the leg is among the least sensitive sites. By contrast the chest and upper back are for most people among the most sensitive sites. Some sites such as the inner forearm are more variable, meaning that the ranking of sites by sensitivity within a person is not identical for all persons (probably mirroring the interactions with site seen in the formal analyses). Examination of a model incorporating the highest 4 doses, as expected, shows a large F value for dose and site but with a number of interactions between dose, site, and sex (Table III). We would caution against over-interpretation of this model because of poor fit to encompass many zeroes, but would also add that such interactions are plausible in the light of the MED data discussed below.

In order to relate these findings to clinical practice, Fig 3 shows the MED threshold measure for all body sites examined for all 15 persons. The y-axis is in (absolute) flux units, the vertical lines represent each of the 15 persons, and the different symbols refer to various body sites. The spread of points on each vertical line provides a measure of the spread of MED at each body site for each person, and the different ordering of the symbols between lines (i.e., between persons) reflects differences in the ranking of sites between persons. The checked line links the inner forearm, a site used in some units for phototesting, and shows the absolute range of doses required to elicit the MED (read off the y-axis) and the different position in the ranking of the various body sites in different persons. Figure 3 makes clear that the ranking of sites within persons shows some variation.

**Within-person pigmentary differences explain some site variation in UVR-induced erythema** Pigmentary differences between people are a major determinant of erythematous responses (Wagner *et al*, 2002; Ha *et al*, 2003). In order to examine whether pigmentary differences at different body sites explain some of the variation in UVR sensitivity at different body sites, we related erythema (reflectance) to melanin index (MI) at the various sites examined for the highest dose (300 mJ per cm<sup>2</sup>). The simple linear regression of erythema on MI was highly significant for each of the four individuals studied (all *p* < 0.001 with *R*<sup>2</sup> of 0.75–0.83). Use of the MI in such a way, however, assumes no systematic



**Figure 2**  
**Ranking of body site sensitivity to ultraviolet radiation for all subjects.** All 12 body sites are shown, with the left side representing the anterior body and the right side the posterior body. Within each site are a total of 15 symbols, one for each subject. The type of symbol shows how THAT person at THAT site ranks within ALL the subjects (•, upper third ranking; □, middle third; and ▲ for the lowest third). Note how sites like the upper back are the most sensitive and the lower leg the least sensitive for most persons, but sites like the forearm are more mixed.



**Figure 3**

**Minimal erythema dose (MED) readings for all subjects by body site.** Each of the body sites is represented by a different symbol and plotted along a vertical line for each subject (x-axis). The position of a symbol on the y-axis refers to the absolute erythema dose corresponding to the MED. Any site that failed to respond to any UVR dose is shown in the shaded gray area at the bottom of the figure. The symbol for the inner forearm (O) is joined by a dotted line for reference. Note the variation between body site MED, the differences between persons, and the different ordering of sites within different persons (e.g., the forearm shown by the checked line).

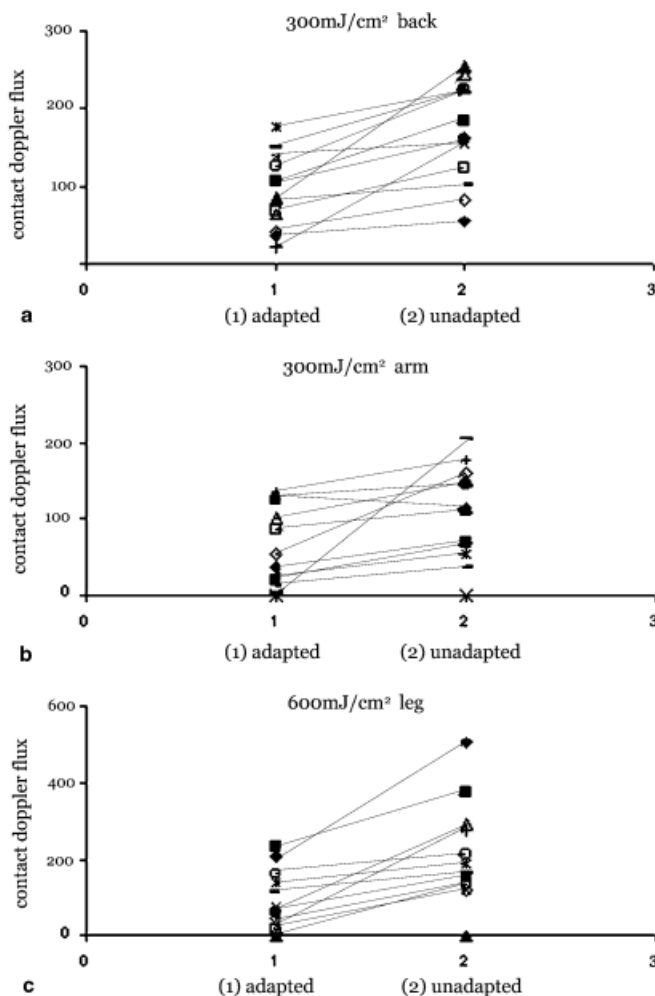
differences in blood flow that would confound the reflectance measure of pigment. In order to exclude this possibility, laser Doppler basal readings at a number of sites in nine individuals were taken. We found no relation between basal blood flow and MI nor between peak blood flow following UVR and basal blood flow (data not shown). We took these experiments to exclude the possibility that the relation between melanin pigment and erythema at different body sites was confounded by differences in basal blood flow.

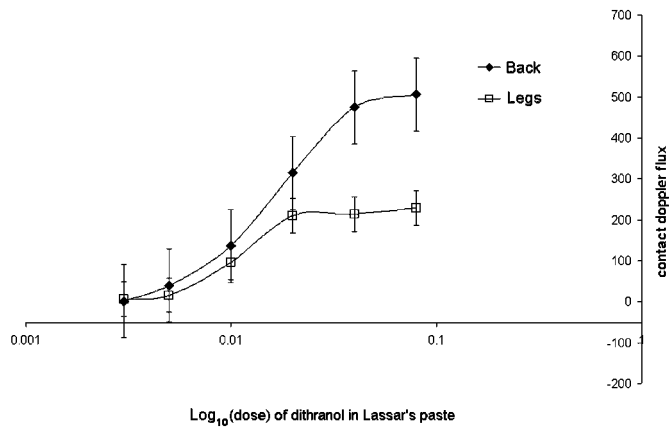
**Experiment 2: photoadaptation** Photoadaptation was operationally defined as the difference in flux response to a unit dose of UVR between an area of skin that has been previously treated with UVR (on five occasions over 5 d—see Materials and Methods) and a paired skin site that had not been irradiated before.

In order to ensure that there was no residual change in blood flow, due to the previous irradiations on the photoadapted site, baseline flux readings were taken. No differences were evident (data not shown). Examples of the results are shown in Fig 4. For most challenged doses, photoadapted sites showed a 2–3-fold reduction in mean erythema, and examples for the highest doses are shown (Fig 4, all  $p < 0.01$  paired  $t$ -tests). We were unable to detect any obvious differences between sites in the degree of photoadaptation nor any obvious relation between the

**Figure 4**

**Response to ultraviolet radiation measured as Doppler flux following photoadaptation.** Flux responses following challenge at three paired body sites are shown (a, back; b, arms; c, legs). Each subject is shown by a different symbol and lines link photoadapted with non-photoadapted paired body sites (all pairwise comparisons  $p < 0.001$ , paired  $t$  tests). Note that the dose used on the leg was larger than on the other sites (600 mJ per  $\text{cm}^2$  vs 300 mJ per  $\text{cm}^2$ ).





**Figure 5**  
**Dithranol dose-response curves for two body sites.** Response to various challenge doses measured in flux units for back (◆) and legs (□). Error bars refer to standard error of the mean. Pairwise comparisons are  $p < 0.01$  for the three highest doses.

individual's skin type and response, but would suggest larger studies will be required to explore such effects in detail.

**Experiment 3: dithranol** Because we found large differences between body sites in the erythral response to UVR, we wish to examine whether this was a generalized phenomenon or something specific to UVR. Figure 5 shows the dose responses measured as increase in blood flux, for different doses of dithranol on the lower legs and back. It is immediately apparent that there are differences with, like UVR, the legs being less sensitive. The back produced consistently higher Doppler flux readings than the legs at all doses in all volunteers, with a 2-fold difference at the highest three doses ( $p < 0.0001$ , paired  $t$ -tests; Fig 5).

## Conclusions

Using an experimental approach with attention to exposure dosimetry and objective reading of response, we have shown systematic differences between body sites in the response to UVR. We have also confirmed the well-known differences in response between persons (Wagner *et al*, 2002; Ha *et al*, 2003). Within the group of Northern Europeans we studied, there was approximately a 4-fold difference between persons and a 5-fold difference within persons at different body sites. Obviously, if a group with a broader genetic ancestry (with respect to skin color) had been selected, the range between persons would have been larger. We will discuss these results under two headings: mechanistic causes of variation to UVR, and implications for clinical practice and future work.

The major determinant of response to UVR between different people is skin color (Wagner *et al*, 2002; Ha *et al*, 2003), itself a proxy for the photoprotective effects of melanin (Rees, 2003). It is therefore not surprising that we have also shown that even within a person, site variation in skin color accounts for some of the variation in the vascular response to UVR. We believe that this reflects site variation in melanin, and that we have excluded confounding due to

differences in basal flux; but our results with dithranol, although not as striking as those seen with UVR, and the study not as detailed, suggest that other factors need to be considered. Dithranol sensitivity was least on the legs, like UVR sensitivity, and although the pharmacology of dithranol inflammation is distinct (Lawrence and Shuster, 1985a, b), our results suggest that some common mechanism needs to be identified to explain these results. We are aware of some work incriminating skin color (or skin type) in the dithranol response but we feel more work is required (Kingston and Marks, 1983; Maurice and Greaves, 1983) (LN, KW, JLR, unpublished).

Although there were large differences in response to UVR by body site, photoadaptation did not obviously differ at the various sites examined. This surprised us and we would suggest that whatever the initial UVR sensitivity, repeated irradiation causes photoadaptation to track along the "same line" at different body sites. Again, future studies need to explore this further, particularly the fact that the degree of basal pigmentation is different at the various sites.

**Clinical relevance and future work** We believe our results have major implications for the way the clinical usefulness of phototesting is viewed prior to phototherapy. Indeed, given the site variation within a person, it might be tempting to imagine that our results suggest that it is unlikely to be helpful. How do we reconcile our data with the widespread use of phototesting? In practice, phototesting is carried out on some of the most sensitive body sites (such as the back), and usually a lower dose (say 50%–70%) of the MED is then used as a guide to therapy. This ensures that the patient does not usually burn (on one of the most sensitive sites). Many, if not most, other body sites are of course less sensitive and will—in erythral standards—receive a far lower biological dose (perhaps as low as 10%). Furthermore, it is likely that since our data suggest some differences in body site ranking with respect to sensitivity between persons, the degree to which this occurs will differ between persons. Our data demonstrate that discussing dosing of phototherapy with respect to some threshold measure such as the MED at a particular body site has little meaning when applied to the whole patient. A dose that is erythral in one region is not in another, and the difference may be 5-fold or more. We would note in passing that the familiar clinical observation that psoriasis on the lower legs responds less well to phototherapy may be related to the low sensitivity of the legs to UVR.

Finally, although we have used erythema as an endpoint, a series of questions must now be asked about other biological endpoints. Erythema, or blood flux, has the great virtue that is easy to measure and non-invasive, allowing multiple and complex designs. It also has a lot of biological coherence to it: the action spectrum for erythema and DNA damage are similar; patients with DNA repair defects, such as xeroderma pigmentosa, show abnormal erythema responses; and the erythral action spectrum is a good predictor of non-melanoma skin cancer rates in animals (Young, 1997; Young *et al*, 1998; Urbach, 1999; de Gruijl, 2000). Nonetheless, our data need to be followed up using other markers of UVR damage, for example, apoptosis and UVR effects on the cutaneous immune function. Our data



may also be relevant to attempts to interpret the relation between UVR and the different body site distributions of melanoma and non-melanoma skin cancers (Green *et al*, 1993).

## Materials and Methods

All studies had appropriate ethics committee approval and were made in the light of the declaration of Helsinki (<http://www.wma.net/e/policy/b3.htm>) and subsequent amendments on the World Medical Association web site (<http://www.wma.net/e/>). All volunteers gave informed, signed consent for the study in which they participated. None of the volunteers received fees for taking part in any experiment.

**Experiment I: variation in erythral response at different body sites** Fifteen healthy individuals resident in Edinburgh, Scotland, were recruited during October and November. None of the participants had been exposed to vocational UVR (or sun beds) for at least 3 mo prior to taking part. The age range was 23–48 y (median, 36 y), and there were eight males and seven females.

**Phototesting protocol** The irradiation source was a 12.5 cm broadband UVB lamp (Philips PLS 9 W per 12) housed in a fully enclosed luminaire designed and built under the supervision of Professor Brian Diffey, Regional Medical Physics, Newcastle, UK. Ten closely spaced apertures, each 8 mm × 12 mm, were milled into the lamp diffuser to enable ten different doses to be delivered simultaneously. The apertures were arranged in a horseshoe design of five doses to a side, with the lowest dose roughly parallel to the highest dose, so that all doses were within an area 7 cm × 3 cm. One aperture was open; the rest were backed with metal foil filters, each perforated with a grid of holes of differing sizes (the highest dose administered with an open aperture). The filters were designed to increase the UVB incrementally with doses of 38, 47, 60, 75, 95, 119, 150, 189, 238, and 300 mJ per cm<sup>2</sup> ( $\sqrt[3]{2}$  increments). The lamp casing is of UV opaque transparent plastic, thus avoiding the need for additional lamp shielding. The unit also contained a digital photodiode that switched off the lamp automatically when the correct dose at the open aperture was delivered. All doses used are traceable to national standards.

All participants were phototested at the following 24 body sites: right and left pectoral area, right and left anterior abdominal wall, right and left bicep area, right and left tricep area, right and left flexural forearm, right and left extensor forearm, right and left upper back, right and left lower back, right and left anterior thigh, right and left posterior thigh, right and left lateral calf, and right and left medial calf.

The UVR lamp was handheld against the body and the UVB delivered with the open aperture to the upper right region of each site. The top and bottom of the phototesting unit was "land-marked" with ink at each site to ensure symmetry of application between left and right sides of the body.

**Erythema measurements** Twenty-four hour post-irradiation of each body site was assessed visually for erythema, and any visible erythema plus one lower dose site (to catch non-visible erythema) was objectively measured in triplicate using a reflectance instrument (Dia-Stron, Andover, Hampshire, UK). UVR-induced erythema was expressed as the erythema index derived from reflectance spectroscopy ( $\log 10[632 \text{ nm per } 546 \text{ nm}] \times 1000$ ) (Diffey *et al*, 1984).

A baseline recording was also taken in triplicate from non-irradiated skin laterally adjacent to the lowest delivered dose at each body site. A mean value was calculated from the three measurements, along with the mean of the baseline recordings. The erythema response was described as the change in erythema index (baseline values subtracted). The MED, defined as the dose of UVR required to produce a barely perceptible erythema, was also recorded (Lock-Andersen and Wulf, 1996).

In four of the volunteers, the MI was measured in triplicate at each site in the same location as the baseline erythema recordings made using the Dia-stron machine. The MI measurement is a function of remittance at 632 nm (for melanin absorption) and 905 nm (the reference signal) (Flanagan *et al*, 2001; Ha *et al*, 2003). On this scale, increase in pigmentation leads to a higher MI, and there is a strong inverse relation between MI and erythema in response to a defined dose of UVR between individuals (i.e., the MI is a useful predictor of an individual's sensitivity defined as erythema to UVR) (Ha *et al*, 2003).

**Experiment II: photoadaptation** Fourteen healthy volunteers, seven male and seven female, resident in Edinburgh, Scotland, age range 22–49 y (median, 35 y), were recruited into the study. Seven persons also took part in experiment I, and the history of their vocational UVR exposure was as for experiment I. Participants were skin typed according to the Fitzpatrick scale. Two persons were type I, eight type II, one type III, two type IV, and one type VI phototype. The individual with type VI skin failed to respond to any UVR and was excluded from any subsequent analysis.

**Photoadaptation protocol** Each subject was irradiated at three body sites (chosen to be representative of the range of responses seen in experiment I), upper left back (anterior scapular region, 5 cm from spine); inner left forearm (midway from wrist to elbow), and outer left calf (midway from ankle to knee). The UVR source was a Waldmann 801 BL (Herbert Waldmann GmbH & Co., KG, Villingen-Schwenningen, Germany) bank of ten Philips TL 20 W/01 55 cm each fitted into a multi-directional hood. Volunteers were positioned so that the area to be irradiated was parallel to and of equal distance from the tubes. The area irradiated measured 11.5 cm × 5 cm and the surrounding skin was protected with UVR opaque fabric. Each area was marked with ink at the edges to ensure same site re-application.

Irradiation was performed daily for 5 d (Monday–Friday) with the dose increments being based on the work of Diffey, and are those used routinely for phototherapy of psoriasis in our unit. The doses used were as follows: 0.3, 0.33, 0.36, 0.39, and 0.43 J per m<sup>2</sup>, corresponding to standard erythema doses (SED's) of 1.5, 1.67, 1.83, 2.05, and 2.23. (The SED (Diffey *et al*, 1997), is an international standard measure of UVR weighted by the erythema action spectrum). The starting dose would be expected to produce erythema below detection with the human eye (but measurable instrumentally) for an individual with skin types I or II. The UVB was delivered to the upper back with the subject prone, to the outer calf with subject lying on alternate sides, and to the outer forearm with the subject sitting upright. Ninety-six hours after the last irradiation, the three areas of skin plus adjacent (matching) areas (right upper back, inner forearm, and outer calf) were "challenged" with five incremental doses of TL12 UVB using the device described above in experiment I only with the lower five doses blocked off with UVR opaque card (as they would not be expected to induce erythema based on the finding of experiment I).

Twenty-four hours after challenge, measurements of blood flow were taken with a contact laser Doppler flowmeter instrument (moorLAB satellite, Moor Instruments Ltd., Axminster, UK). This method, rather than a reflectance device, was used because of the spectra for melanin and hemoglobin overlap, and therefore use of color as a proxy for blood flow is invalid if, as in this case, basal pigment may have changed. Doppler flux is expressed as an arbitrary number in "flux units" (Farr and Diffey, 1986).

Because experiment I and other pilot data show that the lower legs are less sensitive to UVR than most other body sites, the legs were challenged with increased doses of UVB so that measurable erythema was obtained. Because there was overlap in the dosing regimes, comparisons can also be made with the other body sites examined.

**Experimental III: site variation in sensitivity to dithranol** Nine volunteers took part in experiment III. There were eight females and

one male, one of whom took part in experiment I (median age, 44 y, range, 16–54 y). Doubling doses of dithranol (0.005%, 0.01%, 0.02%, 0.04%, and 0.08%, and final volume of 0.15 mL) in Lassar's paste (zinc oxide, 24%; salicylic acid, 2%; starch, 24% in white soft paraffin, 50%) were applied to left and right mid-back and left and right outer calves. A control of Lassar's paste only was used at each site, and all applications were occluded under 8 mm Finn chambers (Epitest Ltd, Hyryla, Finland) and secured *in situ* for 24 h with Mepore tape (Tendra, Mölnlycke Health Care AB (Publ), Göteborg, Sweden ([www.tendra.com](http://www.tendra.com))).

The resulting erythema at each dose site (including control) was measured at 48 h with contact laser Doppler flowmetry along with baseline flux measurements taken from a site closely adjacent to the control dose. Laser Doppler flowmetry was used because of the potential for confounding by pigmentation. Erythema was defined as the increase in flux units after baseline measurements were subtracted from the flux at test sites.

**Experiment IV: baseline blood flux at different body sites** To further determine whether variation in dermal microvasculature and basal pigmentation at different body sites varied to a degree which might partly explain any variation in the erythema response to UVR-induced erythema, nine volunteers had basal blood flow measurements at nine body sites (right and left pectoral area, abdomen, biceps, flexural forearms, anterior thighs, upper back, extensor forearms, posterior thighs, and lateral calves) using the contact laser Doppler, and the MI was measured.

**Data handling and statistical analyses** Data were tabulated in Microsoft Excel (Microsoft, Seattle, USA) and imported into S-Plus 6 Version 2 (Insightful Inc, Seattle, USA [www.insightful.com](http://www.insightful.com)). Details of the statistical models used are described in the Results section.

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