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The relationship of immediate pigment darkening to minimal erythema dose, skin type, and eye color*

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Immediate pigment darkening (IPD) was recorded in over 1,300 volunteers participating in routine sun protection factor (SPF) testing. Medical history obtained included skin type, hair color, eye color, sunburn sensitivity, tanning ability, and current medications. The presence of IPD and the energy needed to produce it were recorded immediately following exposure to a filtered 2500 W xenon arc solar simulator. Minimal erythema dose (MED) values were recorded 16-24 hours post-exposure.

The average MED was lowest for skin type I and highest for skin type IV. The IPD dose was also lowest for skin type I and highest for skin type IV. However, the average IPD dose was greater than the MED for skin type I and lower than the MED for skin type IV. For skin types II and III, the average IPD dose and MED were almost equivalent. For skin type I, 64% required equivalent or greater energy to produce IPD than their MED, and 30% showed no IPD at energy levels sufficient to produce erythema, whereas all skin type IV's had a measurable IPD response. For volunteers of skin type II and III showing no measurable IPD, the predominant eye color was blue or green (74%). Sunscreen usage altered the IPD response for all 4 skin types.

Key words: Immediate pigment darkening - minimal erythema dose - skin type - sunscreens.

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Sunlight exposure results in two distinct pigmentation processes, delayed tanning (DT) and immediate pigment darkening (IPD) (1, 2). IPD,

first described by Hausser in 1938 (3), has been said to result from stimulation of melanocytes by UVB, UVA, and visible wavelengths of light (2, 4). Oxidation of pre-existing melanin and/or redistribution of melanin granules within the melanocyte are two theories which have been sug-

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gested for the appearance of IPD (2). However, recent studies have suggested that IPD may be a passive photo-biochemical event, not an active movement of filaments and melanin granules as previously believed (5). Although the molecular mechanism for IPD has not been elucidated, IPD is considered to be of some value in photo-protection (6). It appears immediately after an exposure to a suitable light source, and fades within 1-4 h afterwards (7).

The classical skin typing system is based on an individual's ability to tan (DT) and to sunburn (8). It has also been used extensively to predict individual risk to skin cancer and melanoma (9, 10). The relationship between IPD and sunburn has been examined in several studies (11, 12). However, inconsistent results have been reported. Some authors have found no IPD response in skin types I and II (9), while others have reported IPD visible for all skin types (13). Some have found correlations between hair color and sunlight sensitivity to be striking for all skin types.

Our laboratory has an extensive data base of individual responses to ultraviolet light obtained in routine sun protection factor (SPF) testing. In previous studies, we have examined the relationship of skin type and MED to sunlight acclimatization for a large population (15). The present study correlates the sunburning sensitivity (MED) to the IPD response for the various skin types in a large population.

Material and methods

Solar simulator

The solar simulator used in this study has been previously described (16). Briefly, it is a 2500 W xenon arc filtered by a dichroic mirror to remove visible and infrared radiation, and by a secondary cut-off filter (1.0 mm WG320, Schott) to shape the short wavelength portion of the spectrum similar to that of natural sunlight. The solar simulator has a fluence of 21.8 mW/cm². The ultraviolet portion of the spectrum, shown in Fig. 1, has a fluence of 9.12 mW/cm². Less than 2.4 × 10⁻⁹ W/cm² is contributed by wavelengths shorter than 290 nm. The UVB, 290-320 nm, contributes a fluence of 2.4 mW/cm² which is

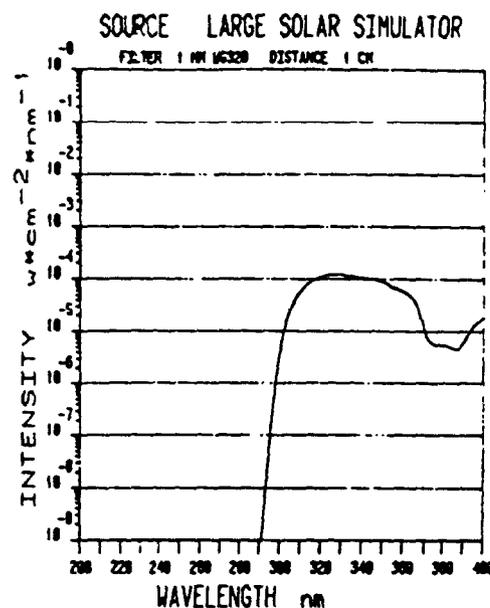


Fig. 1. Spectrum of the 2500 W xenon arc solar simulator filtered with a 1 mm WG-320 filter.

26% of the UV fluence but only 11% of the total fluence. Because the UVB represents slightly more than 11% of the total fluence of the solar simulator flux, a small Robertson-Berger meter (Solar Light Co.) was chosen to monitor and control the exposure of the solar simulator. This meter has a response spectrum similar to the human erythemic response spectrum and has been used to measure sunburning radiation where the sunburning UV relative to the total fluence is small and potentially variable. Human MED responses in this study were obtained over an extended period of time; therefore, an exposure compensating system based on continuous UVB monitoring coupled to a microprocessor (SYVIM Mod 1, MOS 6502, programmed in its micro assembly language) was used. On each test site a simultaneous series of 5 graded exposures of 1 cm² each was administered based on a geometric progression of 1.25 n, with each exposure 25% greater than the previous one. Each exposure is integrated to be a predetermined total erythemic exposure, thereby compensating for erythemic fluence fluctuation. The total system is cal-

Table 1.
Our study population.

Skin type	I	II	III	IV	Total
# Total:	131	520	591	90	1,332
# No IPD:	28 (21%)	18 (4%)	5 (1%)	0	51 (4%)
# IPD = MED:	31 (24%)	221 (42%)	265 (44%)	26 (29%)	544 (41%)
# IPD < MED:	37 (28%)	154 (29%)	254 (42%)	56 (62%)	504 (38%)
# IPD > MED:	35 (27%)	123 (24%)	67 (11%)	8 (9%)	233 (17%)
Av. MED:	150±46 (1.33 J/cm ²)	221±75 (1.96 J/cm ²)	274±83 (2.43 J/cm ²)	336±116 (2.99 J/cm ²)	(RB Meter Counts) (Thermopile)
Av. IPD:	173±50 (1.53 J/cm ²)	212±66 (1.88 J/cm ²)	266±78 (2.35 J/cm ²)	273±93 (2.42 J/cm ²)	(RB Meter Counts) (Thermopile)
Hair color:					
Brown	92 (70%)	349 (67%)	401 (68%)	72 (80%)	914 (68%)
Blonde	15 (11%)	133 (26%)	160 (27%)	18 (20%)	326 (24%)
Red	16 (12%)	13 (2%)	21 (4%)	0	50 (4%)
Black	6 (5%)	8 (1%)	7 (1%)	0	21 (2%)
Gray	2 (2%)	17 (3%)	2 (0.3%)	0	21 (2%)
	<u>131</u>	<u>520</u>	<u>591</u>	<u>90</u>	<u>1,332</u>
Eye color:					
Blue	37 (35%)	199 (38%)	220 (35%)	5 (6%)	461 (35%)
Green	5 (5%)	71 (14%)	73 (12%)	39 (50%)	188 (14%)
Hazel	36 (34%)	165 (32%)	146 (23%)	3 (4%)	350 (26%)
Gray	0	2 (1%)	0	0	2 (0.1%)
Brown	29 (27%)	81 (15%)	190 (30%)	31 (40%)	331 (25%)
	<u>107</u>	<u>518</u>	<u>629</u>	<u>78</u>	<u>1,332</u>
All "Non-Brown"	78 (73%)	437 (84%)	439 (70%)	47 (60%)	1,001 (75%)

ibrated against a large Robertson-Berger meter (Solar Light Co.). Readings on each exposure are produced as RB meter counts and in seconds. Fluence was also measured with a thermopile and microvoltmeter; the average estimated total exposures are shown in Table 1.

Human testing

Human testing was performed according to proposed Food and Drug Administration guidelines for sunscreen testing (8). Informed consent was obtained. Two non-exposed test sites uniform in pigmentation and free of any observable defects were chosen on the lower back of each volunteer.

Immediate pigment darkening (IPD) was read immediately following the exposure for both control and product-treated sites. IPD was noted

when a definite blue-gray color was observed on the skin in any of the exposure squares. The minimal IPD dose was the lowest amount of irradiation needed for a visible response. The graduated series of exposures given on untreated, unprotected skin was also used to determine the subject's MED. An MED is defined as the lowest exposure which produces a minimally perceptible redness. These results were read 16–24 h post-exposure.

Following the determination of the MED, a sunscreen product was applied to the second test site at 2 µl/cm² and allowed to dry for 15 min. A second series of graded exposures was given, based on the predetermined MED and the expected SPF of the product. Products representing various SPF categories tested were divided into 2 groups. One group contained a UVB sunscreen

IV	Total
	1,332
	51 (4%)
(29%)	544 (41%)
(62%)	504 (38%)
(9%)	233 (17%)
±116 (RB Meter Counts) J/cm ² (Thermopile)	
±93 (RB Meter Counts) J/cm ² (Thermopile)	
(80%)	914 (68%)
(20%)	326 (24%)
	50 (4%)
	21 (2%)
	21 (2%)
	1,332
(6%)	461 (35%)
(30%)	188 (14%)
(4%)	350 (26%)
	2 (0.1%)
(40%)	331 (25%)
	1,332
(60%)	1,001 (75%)

ray color was observed on exposure squares. The minimum: lowest amount of irradiable response. The gradients given on untreated, unso used to determine the ED is defined as the lowest ces a minimally percept- sults were read 16-24 h

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alone (octyldimethyl PABA, homosalate, or ethylhexyl p-methoxycinnamate in various concentrations), the other group contained sunscreen formulas with both UVA and UVB absorbers, resulting in "broad spectrum" suncreening. The UVA sunscreens used were oxybenzone or titanium dioxide. IPD was again read immediately following exposure, and the MED was read 16-24 h later. The ratio of treated MED to untreated MED is the SPF.

Before initiating sunscreen testing, each volunteer was asked to supply a brief medical history. Skin type, eye color, hair color, sun sensitivity (ability to sunburn), tanning ability, current medications, and any notable dermatological conditions were recorded. Volunteers were disqualified if they were not currently in good health, were taking any known photosensitizing medications, or had had any forms of skin cancer or other serious skin conditions. In this study population, volunteers were chosen who normally needed sunscreen protection, i.e., who had sun-sensitive skin of types I, II, or III. The study volunteers, therefore, were not chosen "at random" from the general population, but were pre-screened for sun-sensitivity based on the SPF of the products to be tested. Male and female volunteers between ages 18-65 were tested.

Skin type was determined using the following criteria, as outlined by proposed FDA guidelines (8).

Skin type

- I Always burns easily; never tans
- II Burns easily; tans minimally
- III Burns moderately; tans gradually
- IV Burns minimally; always tans well

IPD, MED, and medical history were obtained on 1,332 volunteers for this study.

Results

The irradiation dose needed to produce a minimal sunburn (MED) and that needed to produce IPD for each skin type are shown in Table 1. The average MED increased from skin type I to skin type IV (i.e., it takes more radiant exposure to sunburn a skin type IV than a III, II, or I). IPD

also increases from skin type I to skin type IV. Comparing the MED and the IPD dose for each skin type, it can be seen that skin type I will generally require less irradiation to burn than to produce IPD, skin types II and III require about an equal dose to do both, and skin type IV individuals will produce pigment darkening at sub-MED dose levels. Fewer than 1% of all skin type IV's had "no IPD" or IPD > MED, whereas 48% of the skin type I's did. Of the skin type IV's, 63% had IPD < MED.

In our study, hair color did not appear to be related to IPD. Eye color, however, did seem to follow a pattern: 73% of the skin type I individuals who had no pigment darkening at irradiation levels sufficient to produce a sunburn had blue or green eyes. For skin type II's with no measurable IPD, 83% had blue or green eyes. 100% of the skin type III's with no measurable IPD had blue or green eyes. All skin type III and IV individuals with brown eyes had measurable pigment darkening. These results are shown in Tables 2 and 3.

The effect of using a broad spectrum sunscreen is shown in Table 4. Each skin type shows an increase in the number of individuals who had no pigment darkening while using a broad spectrum product. UVB (290-320 nm) sunscreens alone did not block the appearance of IPD. IPD can be inhibited using a broad spectrum sunscreen even for skin types III and IV, who tan easily and seldom burn.

Table 2. Relationship of IPD to MED by skin type.

	No IPD or IPD > MED:	IPD = MED:	IPD < MED:
I	48%	24%	28%
II	28%	44%	30%
III	12%	44%	42%
IV	1%	29%	63%

The greatest number of volunteers with no IPD measurable at exposures which produced a readable MED were skin type I (21%), 4% skin type II, and 0.8% skin type III.



Table 3.
No measurable IPD present: skin type and eye color.

	I	II	III	IV	Total
Eye color					
Blue/Green/Hazel:	16 (57%)	15 (83%)	5 (100%)	0	36 (71%)
Brown:	<u>12</u> (43%)	<u>3</u> (17%)	<u>0</u>	<u>0</u>	<u>15</u> (29%)
	28 (55%)	18 (35%)	5 (10%)	0	51 (100%)

More than half of those skin type I's with no measurable IPD had blue or green eyes (16/28). For skin type II, 15/18 with no IPD had blue or green eyes; skin type III 5/5. No skin types III or IV with brown eyes exhibited "no IPD".

Table 4.
Alteration of IPD following broad spectrum sunscreen.

Skin type	Volunteers with No IPD		
	UVA/UVB sunscreen	Study population	Increase
I	29	28	+ 1
II	39	18	+21
III	27	5	+22
IV	2	0	+ 2

Discussion

Interestingly, hair color did not seem to be related to the ability to produce IPD. Previous studies relating skin type to melanoma risk have found a high correlation between light hair color and skin cancer risk (11). These same studies found little relationship between light eye color and skin cancer risk. Another study found that skin type I individuals had a 4-fold increased risk of skin cancer when compared with skin type IV's, but that only a small increased risk could be linked to blue eyes (10). No significant risk was attached to hair color.

Other studies have described skin type I and II populations who lacked the IPD response (9, 12). We believe that there are definite sub-populations within skin type I – and perhaps also in skin types II and III who have no IPD response at dose levels sufficient to produce an MED. This is not to say that these individuals have no IPD

at all, but only that the irradiation needed to produce their IPD may be much greater than the dose needed to sunburn.

Wilson et al. (17) found that skin type I individuals had a lower MED and more prolonged erythema than did individuals of skin type IV. They were able to correlate prolonged erythema to fair complexion, sunburn sensitivity, and skin type. Tegner et al. (13) reported that the IPD reaction was most pronounced in individuals of skin type IV and weakest in those with skin type I. Unlike other studies, in our volunteer group of 4 skin types, all had representatives with IPD. We did not try to evoke IPD at greater exposure levels on those who did not exhibit IPD at MED energy levels, although this has been attempted by others (13).

Each skin type shows an increase in the number of individuals who had no pigment darkening while using broad spectrum sunscreen products. This would indicate that the IPD action spectrum is weighted towards the longer UVA and visible wavelengths than is the erythema action spectrum. Tests using a UVB sunscreen alone did not block the appearance of IPD. It is interesting to note that even for skin types III and IV who tan easily and seldom burn, IPD can still be inhibited using a broad spectrum sunscreen. Because the UVA sunscreen used in these tests was generally 2 or 3% oxybenzone – whose absorbance does not extend into the higher UVA wavelengths – we suggest that the lower UVA wavelengths (320–340 nm) contribute more to IPD.

It is interesting to note that 21% of our skin

type I population had "no IPD". Individuals who are at risk to acute skin damage may be related by their similar "no IPD" response, regardless of classical skin typing. Further, individuals subject to chronic sun damage may have in common the finding that their IPD dose is greater than their MED. The individual's IPD response, then, could be used as a refinement of the classical skin typing system. Since IPD and MED are easily measurable responses, recommendations on sun exposure and the need for sun protection could be based on the appearance of IPD, just as it has been for the classical skin types (8).

While many type I individuals may have similar energy requirements to produce an MED, this does not predict their ability to exhibit IPD. It has long been assumed that skin type I individuals, representing Caucasians at higher risk of developing skin cancer, were typically represented by the Celtic inheritance of red hair, blue eyes, and freckles and that all red-haired, freckled individuals were skin type I (7, 11, 14). In our study population, red-haired individuals were found in skin type classes I, II, and III, and did not automatically respond to sunlight in a similar manner. In fact, more red-haired individuals were found in skin type III than in skin type I. Comparison of the results of previous studies has demonstrated that skin type, MED, or phenotypic grouping has not been able to predict risk to melanoma or other skin cancers, except in the broadest sense (9-12). Our results indicate that the response of individuals classified within one skin type may differ widely to the same exposure. Indeed the differences in IPD responses represented in skin types I and II in other studies demonstrate that skin typing is not as straightforward as it would seem.

Immediate pigment darkening may provide some photoprotection to those individuals who can develop it, but it would be quite transient. The volunteers of skin type I who had no IPD visible at measurable MED levels are presumably also those who are at greatest risk to the development of skin cancer (9, 10). It is precisely these individuals who need to use high sun protection factor products. Correlation of diminished IPD in individuals with light eye color and skin type I or II is evident.

In summary, the average irradiation doses needed to produce minimal IPD for each of the 4 skin types examined are unique and increase from types I to IV, just as do the MED dose requirements. However, the IPD dose and MED values are only similar within skin types II and III. For skin type I, $IPD > MED$; for skin type IV, $IPD < MED$. Nevertheless, within skin types I, II, and III, there are individuals who exhibit no IPD at dose levels sufficient to produce minimal erythema. The lack of IPD response seems to correlate well with "non-brown" eye color, but is not related to light hair color. Our data suggest that the action spectra for IPD and for erythema diverge significantly at the longer UVA wavelengths; the peak of effectiveness for IPD would appear to be between 320-340 nm.

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IV	Total
0	36 (71%)
0	15 (29%)
0	51 (100%)

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