

# An Optimal Method for Experimental Provocation of Polymorphic Light Eruption

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**Background:** There is controversy about the best method to induce polymorphic light eruption (PLE) experimentally.

**Objectives:** To review articles on PLE induction and design a UV radiation protocol that improves success rates with clinically relevant doses of environmentally relevant solar-simulated radiation (SSR).

**Design and Setting:** All articles on the experimental provocation of PLE published since 1980 were reviewed. Photoprovocation of lesions was studied in 25 PLE patients. The 24-hour minimal erythral dose (MED) of SSR was determined. Thereafter, six 4 × 4-cm adjacent sites on previously affected and previously unaffected skin were exposed to 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 MED of SSR for 3 to 4 consecutive days. The study period

was autumn to spring in London, England (51° north latitude).

**Main Outcome Measures:** Relationship between PLE induction and biological and physical exposure parameters.

**Conclusions:** The review shows that fractionated erythemally effective UV-A exposures were more successful than single-sunburning UV-B doses. Photoprovocation of PLE was successful in 68% of patients after 2 to 3 SSR exposures that were not necessarily erythral. There was no difference in success rate between previously affected and previously unaffected skin. Our data indicate that PLE is more likely to be induced when the natural causes of the disease are simulated.

*Arch Dermatol.* 2004;140:286-292

**P**OLYMORPHIC LIGHT ERUPTION (PLE) is the most common of the so-called idiopathic photodermatoses. In a recent population survey<sup>1</sup> in the United Kingdom, PLE was found to affect 15% of healthy people, with a female-male ratio of approximately 2:1. Genetic modeling using twin studies and families with PLE provides unequivocal evidence for a genetic basis for PLE and predicts that susceptibility to PLE is a polygenic trait with multiple susceptibility loci.<sup>2,3</sup> Polymorphic light eruption is characterized by a delayed abnormal reaction to the UV radiation (UVR) component of sunlight consisting of transient, nonscarring, pruritic papules and vesicles, typically developing hours or days after sun exposure and resolving over several days without sequelae. The pathogenesis of PLE is unclear, but histologic and immunologic studies suggest that the normal UVR-induced suppression of cell-mediated immunity is impaired and, as a result, these patients develop a T-cell mediated re-

sponse to a UVR-activated antigen (photoantigen).<sup>4,5</sup>

Investigations into the pathogenesis of PLE have been frustrated by the lack of reliable laboratory methods for the induction of clinical lesions. The results of such studies have varied considerably. The early PLE induction studies reported success rates from as low as 10% to 30%<sup>6-8</sup> to as high as 60% to 95%.<sup>9-11</sup> These studies were

*See also pages 295 and 351  
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based on one or more exposures of a single test site to between 1 and 10 times the minimal erythral dose (MED) of nominal UV-B radiation (ie, 290-320 nm), although these sources almost certainly contained other UVR wavelengths. Initially, induction was achieved with UV-B,<sup>6-13</sup> but several authors also succeeded in reproducing PLE lesions with UV-A irradiation (320-400 nm).<sup>12,14-21</sup>

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There are somewhat contradictory results about the wavelength dependence of PLE. In general, UV-A appears to be more effective than UV-B in eliciting lesions.<sup>14</sup> In a comprehensive study of 142 patients in which induction was attempted with increasing exposures of buttock skin to UV-A and/or UV-B daily for 4 to 8 days, the most effective waveband was UV-A (56%), followed by UV-A/UV-B combination (27%), then UV-B >(17%).<sup>12</sup> However, Miyamoto<sup>13</sup> has confirmed earlier reports<sup>22-24</sup> that UV-B can also be successful in a high proportion (57%) of selected patients. In a retrospective study of 30 patients by Mastalier et al,<sup>21</sup> the action spectrum fell within the UV-A range in 59% of patients, the UV-B range in 23%, and both ranges in 18%. The diversity in the wavelength-dependence studies remains unexplained. It would be puzzling if a single chromophore and a uniform mechanism could be activated by different parts of the UVR spectrum and result in such a morphologic diversity of lesions. This would indicate different pathogenic mechanisms or that there is a range of UVR-induced antigens.

According to Norris et al,<sup>25</sup> studies of laboratory-induced lesions have generally used UVR doses considerably in excess of the MED.<sup>26-28</sup> This makes histologic interpretation difficult because of coexistent sunburn, which results in mononuclear cell infiltration. Even recent studies have used high doses to provoke a PLE reaction (3.3 MED of UV-B<sup>19</sup>; 6 MED of UV-B<sup>20</sup>; and 2-4 MED of UV-B or UV-A<sup>29</sup>).

Different locations have been used to provoke PLE with varying degrees of success. Barnadas et al,<sup>18</sup> McFadden et al,<sup>30</sup> Mastalier et al,<sup>21</sup> and Norris et al<sup>31</sup> used previously affected skin with success rates of 30%, 100%, 57%, and 100% respectively. Boonstra et al<sup>29</sup> provoked PLE in previously affected skin to UV-B/UV-A combination exposure in 88% of men and 52% of women. Within this group, PLE was also induced by UV-B alone in 9% of the men and 24% of the women. Reactions to UV-A alone occurred in 3% of men and 24% of women and to visible light in 43% of men and 11% of women. Verheyen et al<sup>19</sup> and Lambert et al<sup>20</sup> used whole body and upper arm exposure and had UV-A success rates on previously affected sites of 100% and 87%, respectively, and 0% and 6.7% with UV-B. Holzle et al<sup>14</sup> tried to provoke PLE on previously exposed and previously unexposed skin. The success rates ranged from 0% to 90% on previously exposed skin, but it was 0% on previously unexposed skin.

A synopsis of findings from our literature review is provided in the **Table**. The aim of our investigation was to evaluate provocation test methods introduced since 1980 and to develop a reliable test using physiologically relevant doses of SSR to study the pathogenesis of PLE.

## METHODS

### VOLUNTEERS

Twenty-five patients diagnosed with PLE at the Photobiology Clinic of St John's Institute of Dermatology, London, England, were randomly recruited into the study (21 women, 4 men; age range, 18-55 years; mean age, 38 years; skin types I-V). Diagnosis was made on the basis of clinical history and

examination. All patients had PLE for at least 6 years, and the condition was defined as a fully resolving macular, papular, or papulovesicular photoeruption occurring 30 minutes to 48 hours after sun exposure and lasting for hours to at least a day.

Patients were screened by blood analysis to exclude those with porphyria and by estimation of antinuclear and extractable nuclear antigen autoantibodies to exclude those with lupus. Skin type was assessed by interview. Exclusion criteria for all volunteers included ingestion of any medication during or 2 weeks prior to the study (oral contraceptives excepted), phototherapy during or in the 6 months prior to the study, previous exposure of buttock skin to sunlamps or sunlight, and/or a recent sunburn. Pregnant or lactating women were also excluded. The local ethics committee approved the study, and each volunteer was fully informed of the procedures and gave written informed consent to participate.

### UVR SOURCE AND DOSIMETRY

Solar-simulated radiation (SSR) was generated by a 1-kW xenon arc solar simulator (Oriel, Stratford, Conn) fitted with a WG320/1-mm-thick glass filter, giving an even field of irradiance (approximately 290-400 nm) of about 15 mW/cm<sup>2</sup> on the skin surface at 11 cm from the source. Irradiance was routinely determined with a wideband thermopile radiometer (Medical Physics, Dryburn Hospital, Durham, England) calibrated against a DM150 double monochromator Bentham spectroradiometer (Bentham Instruments, Reading, England). See filter 2 of the first figure in Harrison and Young<sup>32</sup> for emission spectrum details. Eighty-eight percent of the erythemally effective energy of the source was in the UV-B range, and the remaining 12% was UV-A.

### INDUCTION OF LESIONS

In each patient, the just visibly perceptible 24-hour MED was determined on previously unexposed buttock skin using eight 25% dose increments. Photoprovocation was attempted on 2 body sites: (1) previously affected skin (either the arm or upper back) and (2) previously unaffected skin (buttock). Six adjacent sites (4 × 4 cm each), were exposed to 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 buttock MED in an attempt to induce PLE lesions. The exposures were repeated daily until a positive PLE response was obtained. If no lesions appeared after 3 or 4 days of exposure, the test was considered negative. (Twenty-three of 25 patients had a maximum of 3 exposures; only 2 of 25 patients had a maximum of 4 exposures.) Photoprovocation in 18 patients was performed from October 2001 to May 2002 and in a further 7 patients from November 2002 to March 2003.

### UVR-INDUCED ERYTHEMA

Using a reflectance meter (Diastron, Andover, England), we took 3 quantitative measurements of erythema 24 hours after the second SSR exposure and calculated the mean per site. For each site, the increase in erythema index was calculated by subtracting the mean background reading of adjacent nonirradiated skin.

### STATISTICAL METHODS

Microsoft (Redmond, Wash) Excel 2000 was used for statistical analysis. Linear regression was performed for increase in erythema index vs SSR dose (MED fraction) for each volunteer on previously exposed and previously unexposed test sites to generate erythema dose-response slopes (83% of the regressions had R<sup>2</sup> values ≥0.7), the slope being indicative of the overall erythema response. The distribution of the slopes was shown

# Provocation Tests Since 1980

Source	UV Source	Wavelengths	Exposures	Size Template	Location	Doses Given	Success Rate, %	Profile, No. of Patients	Skin Type
Tannenbaum et al <sup>26</sup>	Westinghouse FS-40 fluorescent sunlamp bulbs	UV-A + UV-B	Single/multiple	3 Separate 2 × 2-cm sites	Lower back	1 × 1 MED 1 × 5 MED 3 × 3 MED	0	10: 8 F, 2 M; age, 21-63 y	White
Jansen <sup>27</sup>	1. Medium-pressure mercury lamp	UV-A + UV-B + UVC	Single	Adhesive cover with 1-cm <sup>2</sup> rectangular holes	Upper back	1-12 MED	72 (for both 1. and 2.)	110: ? F, ? M; age 6-72 y	NS
	2. Xenon arc lamp	UV-A + UV-B + UVC	Single		Upper back	1-12 MED			
Holzle et al <sup>14</sup>	1. Monochromator	UV-A or UV-B or visible light	Single/multiple	2.7 cm in diameter	Prev aff and prev unaff	2-7.5 J/cm <sup>2</sup> UV-A, 1-8 MED UV-B, 2-5 J/cm <sup>2</sup> visible light	0	180: 163 F, 17 M; age 4-69 y	I, II, III
	2. Mercury lamp	UV-A	Single/multiple	4 cm in diameter	Prev aff and prev unaff	10-15 J/cm <sup>2</sup>	0		
	3. Cabin UV 1000	UV-B	Single/multiple	5 × 10 cm	Prev aff and prev unaff	2-5 MED	0		
	4. Philips TL12 lamp	UV-B	Single/multiple	5 × 10 cm	Prev aff and prev unaff	2-5 MED	0		
	5. Slide projector	Visible light	Single/multiple	5 × 5 cm	Prev aff and prev unaff	50 J/cm <sup>2</sup>	0		
	6. UVASUN 5000	UV-A	Single/multiple	At least 5 × 10 cm	Prev aff and prev unaff	20-100 J/cm <sup>2</sup>	90 in 43 patients		
Moncada et al <sup>28</sup>	A hot quartz high-pressure mercury lamp (Hanovia)	UV-A + UV-B + UV-C	Single	?	Back	20 MED	100	16: 13 F, 3 M; age, 7-60 y	NS
McFadden and Larsen <sup>15</sup>	UVASUN 2000	UV-A	Single	4 Test sites of 10 × 10 cm	Upper back	26, 52, 78, and 104 J/cm <sup>2</sup>	100	22: 13 F, 9 M	NS
Ortel et al <sup>12</sup>	1. Ultra-Vitalux (mercury high pressure)	UV-B	4-8	Two 4 × 4 cm	Prev aff	*	49 in total of which 56 in UV-A range, 17 in UV-B range, and 26 in both	142: 117 F, 25 M; age 5-82 y	NS
	2. Sellas (metal halogenide)	UV-A	4-8	Test areas	Prev aff	*			
	Both 1. and 2.	Both	4-8	Test areas	Prev aff	*			
Neumann et al <sup>16</sup>	2 UV-A devices	UV-A	Single/multiple	Whole body	Whole body	20-280 J/cm <sup>2</sup> in total meaning: Group 1: 2 × 70 J/cm <sup>2</sup> UV-A daily for up to 5 d	68	50: 41 F, 9 M; 25 in each group; age, 17-65 y; PLE >3 y	II, III
	1. SUPUVASUN 30000					Group 2: 20 J/cm <sup>2</sup> for up to 5 d	72		
Przybilla et al <sup>17</sup>	UVASUN 5000	UV-A	Multiple	Four 5 × 5 cm	Extensor site Upper arm	100 J/cm <sup>2</sup>	45 in at least 1 test site 26 in all sites	38	NS
Miyamoto <sup>13</sup>	Dermaray M-DMR-1	UV-B	Single/multiple	Two 2 × 2-cm areas	Lower abdomen	3 × 2 MED 1 × 3-5 MED	57	30: 27 F, 3 M; age, 9-66 y	Japanese
Norris et al <sup>25</sup>	Kratos 2500W xenon arc filtered	SSR	Single	Three 4 × 4-cm adjacent test sites	Prev aff	0.35-0.5-0.7 MED	79	14: 9 F, 5 M; age, 20-67 y; PLE, 1-43 y	II, III, IV
Barnadas et al <sup>18</sup>	Solar simulator (Solar Light) with filter	UV-A	Multiple	Circles 9-10 mm in diameter	Prev aff, but if tanned prev unaff	10-24 J/cm <sup>2</sup> daily for 2-4 d	30	29: ? F, ? M	NS
McFadden et al <sup>30</sup>	Kratos 2500W xenon arc filtered	SSR	Single	Three 4 × 4-cm adjacent test sites	Prev aff	0.7 MED	100	7: ? F, ? M; PLE, 1-43 y	NS
Verheyen et al <sup>19</sup>	PUVA cabin with Philips TL09	UV-A	Multiple	UV-A whole body	Whole body	15, 20, or 25 J/cm <sup>2</sup> UV-A for max 5 consecutive days	UV-A 100	26: 24 F, 2 M	White
	UV-B Philips TL12	UV-B	Multiple	UV-B 4 × 4 cm	Left upper arm	UV-B 3 × 3.3 MED	UV-B 0		

(continued)

## Provocation Tests Since 1980 (cont)

Source	UV Source	Wavelengths	Exposures	Size Template	Location	Doses Given	Success Rate, %	Profile, No. of Patients	Skin Type
Lambert et al <sup>20</sup>	PUVA cabin with Philips TL09	UV-A	Single/multiple	UV-A whole body	Whole body	15, 20, or 25 J/cm <sup>2</sup> UV-A for max 5 consecutive days	UV-A 87	45: 40 F, 5 M; mean age, 35 y	I, II, III
	UV-B Philips TL12	UV-B	Single/multiple	UV-B 4 × 4 cm	Upper arm	UV-B 3 × 3.3 MED	UV-B 6.7		
Mastalier et al <sup>21</sup>	1. Sellas Sunlight 2001	UV-A	3-5	2 symmetrical 6 × 6-cm sites	Upper chest	0.7 MED first dose, then daily increase of 0.2 MED	57 OK (17/30) in total of which 59 in UV-A range (10), 23 in UV-B range (4), and 18 in both ranges (3)	30	I, II, III, IV
	2. Sellas 1200 UV-B source	UV-B	3-5	2 symmetrical 6 × 6-cm sites	Upper chest				
	3. Waldmann (8001, 7001K, or 4001)	UV-A + UV-B	3-5	2 symmetrical 6 × 6-cm sites	Upper chest				
Norris et al <sup>31</sup>	Kratos 2500W xenon arc filtered	SSR	Single	?	Prev aff	0.7 MED	100	5: 3 F, 2 M; age, 35-49 y	NS
Boonstra et al <sup>29</sup>	1. CHM45-20, filtered (ORC, Japan)	UV-A	Multiple	Small area = up to 2 cm in diameter	Small area on back	3-4 MED small area for max 6 d	1. or 2.: UV-A alone 3 M, 24 F	93: 59 F, 34 M; mean PLE, 9.2 y	NS
	2. Mutzhas UVASUN 3000S	UV-A	Multiple	Large area = 5 × 10 cm	Large area on arm	2 MED large area for max 6 d			
	3. Kromayer lamp	UV-B	Multiple	Small area = up to 2 cm in diameter	Small area on back	3-4 MED small area for max 6 d	3. or 4.: UV-B alone 9 M, 24 F		
	4. Philips TL20W/12 sunlamps	UV-B	Multiple	Large area = 5 × 10 cm	Large area on arm	2 MED large area for max 6 d	1. or 2. and 3. or 4.: UV-A + UV-B 88 M, 52 F		
	5. CHM45-20, filtered (ORC, Japan)	Visible light	Multiple	Small area = up to 2 cm in diameter	Small area on back	3-4 MED small area for max 6 d	5. or 6.: visible light 43 M, 11 F		
	6. CHM45-20, filtered (ORC, Japan)	Visible light	Multiple	Large area = 5 × 10 cm	Large area on arm	2 MED large area for max 6 d			

Abbreviations: aff, affected area; F, female; M, male; max, maximum; MED, minimal erythema dose; min, minimum; NS, not stated; PLE, polymorphic light eruption; prev, previously; PUVA, psoralen-UV-A phototherapy; SSR, solar-simulated radiation; unaff, unaffected area.

\*All sites started with 0 to 8 MED and increased by 1.4 times per exposure if no effect.

to be normal (Kolmogorov-Smirnov test), and so unpaired *t* tests were used to compare the slopes between patients who showed a PLE response and those who did not on both treatment sites. Significance was assumed at *P* < .05.

## RESULTS

### CLINICAL PRESENTATION

The morphologic features of PLE lesions induced by photoprovocation were consistent with the response reported by each patient after previous sun exposure. Thus, with SSR we were able to produce lesions comparable to those seen in the genuine disease. The PLE lesions developed 1 to 24 hours after the last irradiation and consisted of macular, small papular (**Figure 1A**), or papulovesicular (**Figure 1B**) lesions scattered over the irradiated site. The papular or papulovesicular lesions were sometimes sparsely scattered over the irradiated area, although almost confluent lesions developed as well.

In all patients, the recurrence of the rash was associated with pruritus. Shortly thereafter, patchy or confluent erythema developed in which the characteristic skin lesions emerged. Lesions persisted for at least 12 hours and up to 2 weeks after the last exposure. **Figure 1A** shows

a papular reactions of increasing severity after 3 consecutive exposures to 0.75, 1.0, 1.25, and 1.5 MED. **Figure 1B** shows a papulovesicular PLE reaction after 3 consecutive exposures on 1.25 and 1.5 MED sites. Experimentally induced skin lesions usually resolved over the next 1 to 3 days, but it generally took 1 to 3 weeks before they completely disappeared.

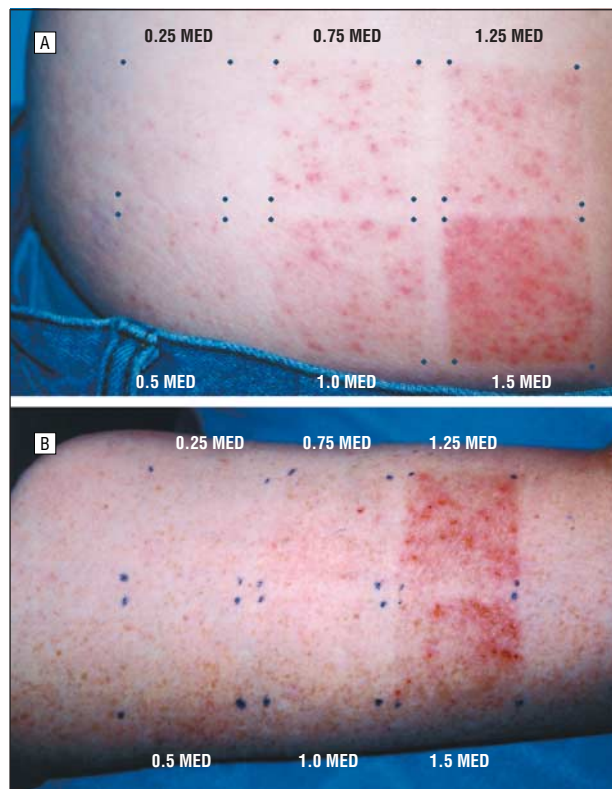
### ERYTHEMA

Erythema was shown to be SSR dose dependent, and the slopes were significantly steeper on the buttock site than on the previously exposed site (**Figure 2**). There was no difference in the erythema response on either test site between patients in whom PLE was successfully induced and those in whom it was not (**Figure 2**).

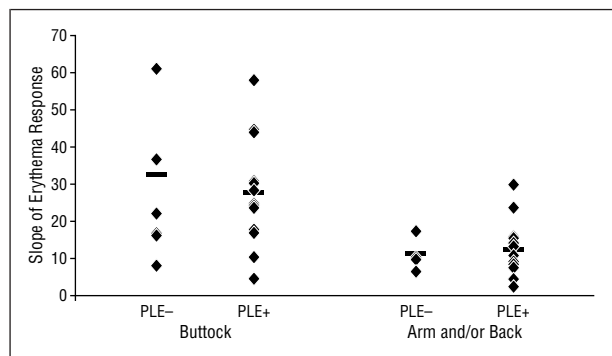
### LEVEL OF RESPONSE

Seventeen (68%) of 25 patients developed PLE on at least 1 test site. **Figure 3** shows the number of sites with a positive response at a given dose level, regardless of the number of exposures. Six patients developed PLE only on previously affected sites (upper back or arm); 4 patients developed PLE only on previously unaffected sites





**Figure 1.** Polymorphic light eruption (PLE) is provoked with solar-simulated radiation. A, Typical papular PLE lesions are seen on buttock skin after 3 exposures of 0.75, 1.0, 1.25, and 1.5 minimal erythemal doses (MEDs). As shown here, reactions were generally stronger with higher doses. B, Papulovesicular PLE lesions are visible on the arm after 3 exposures of 1.25 and 1.5 MED.

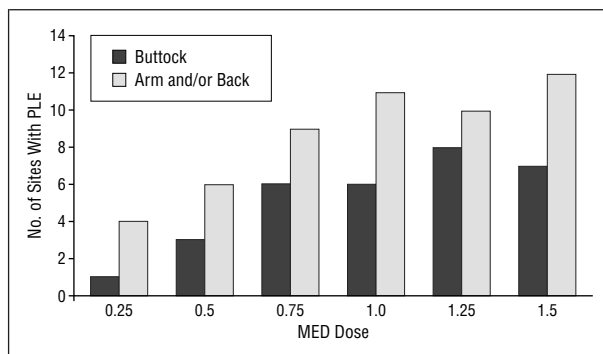


**Figure 2.** Erythematous polymorphic light eruption (PLE) responses are greater on previously unexposed sites. The slopes of erythema dose-response curves were significantly steeper on previously unexposed sites in all patients ( $P=.02$  in nonresponders [PLE-] and  $P=.002$  in responders [PLE+]). There was no difference in the erythema responses, on either site, between patients who responded and those who did not.

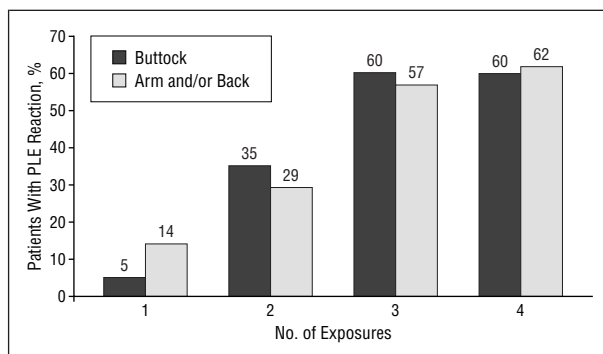
(buttock); and 7 patients showed responses on both sites. Polymorphic light eruption was readily provoked on both previously exposed and previously unexposed skin. Eleven (65%) of 17 patients responded on buttock skin and 13 (77%) of 17 responded on arm and/or back.

#### NUMBER OF EXPOSURES

Successful provocation of PLE was dependent on the number of exposures. In both skin sites, success increased with



**Figure 3.** Patients respond to a wide range of solar-simulated radiation (SSR) doses. Seventeen (68%) of 25 patients showed a polymorphic light eruption (PLE) reaction on any SSR-exposed site. The data show the number of sites with a PLE response at a given SSR dose, regardless of the number of exposures. The theoretical maximum for each site is the number of patients ( $N=25$ ). This means that 1 (4%) of 25 buttock sites responded with 0.25-minimal erythemal dose (MED) exposures and that 12 (48%) of 25 arm and/or back sites responded with 1.5-MED exposures. Arm and/or back skin was more responsive than buttock skin despite having lower inflammatory doses.



**Figure 4.** Three exposures are generally necessary to provoke polymorphic light eruption (PLE). The results show the cumulative percentage of patients with positive reactions on buttock and arm and/or back skin with the minimum solar-simulated radiation (SSR) dose used. At least 3 exposures were necessary to provoke PLE in at least 50% of patients. There is no difference between previously exposed and previously unexposed skin. Not all patients reacted on both sites. Two important caveats: (1) 1 patient was included who showed PLE on the buttock minimal erythemal dose test site after a single exposure; (2) the cumulative value does not reach 68% because patients required different numbers of exposures on different sites and some patients reacted on one site but not on the other.

increasing number of daily exposures. **Figure 4** shows the cumulative success rate for both sites, regardless of the dose used. The data show that 3 exposures are necessary to obtain a success rate of more than 50%. However, **Figure 3** also shows that it is possible to provoke PLE with a single SSR exposure on buttock skin (1 patient with macular lesions) and on arm and/or back skin (2 patients with papular lesions).

#### COMMENT

A summary of articles published since 1980 on the experimental provocation of PLE is provided in Table 1. This shows a very diverse range of UVR spectra, doses, and induction protocols, and sometimes it is difficult to determine the exact radiation protocol. In general, the doses given, whether single or repeated, have been greater than 1 MED. Only our group<sup>25</sup> has previously used SSR

in a suberythematous protocol. Furthermore, in some cases the doses would have been phototoxic, causing a severe erythematous reaction.

In general, studies with UV-A have been more successful than those with UV-B. Solar UVR is mostly UV-A (approximately 95%), yet the approximate 5% UV-B causes more than 80% of the sunburn. Patients often report PLE without sunburn, which has led clinicians to believe that the disease may be triggered with suberythematous UV-A exposure. Yet, success with UV-A dose-response studies has been with doses that were certainly erythematous (eg, 60-100 J/cm<sup>2</sup> in Holzle et al<sup>14</sup> and >50 J/cm<sup>2</sup> in 20 of 22 patients in McFadden and Larsen<sup>15</sup>). In this context, such studies do not reproduce the natural situation.

We have successfully reproduced PLE in a small group of PLE patients using environmentally and physiologically relevant UVR exposures. This was done with comparable rates of success on previously exposed and unexposed skin. The erythematous response after 2 exposures on the buttock was much greater than that on the arm and/or back, as shown in Figure 2, almost certainly because buttock MED was lower than the MED of sites that had a history of exposure. In other words, our protocol was less inflammatory on the arm and back than on the buttock.

Polymorphic light eruption can be induced by suberythematous exposures, as shown in Figure 3. Figure 2 shows PLE in association with very shallow erythema dose-response curves, especially on the arm and back. These observations are consistent with patient reports that PLE may evolve without concomitant sunburn. Overall, our data show that erythema and PLE are independent clinical outcomes, suggesting that they have different chromophores. DNA is thought to be the major chromophore for erythema,<sup>33</sup> but as yet we have no candidate chromophores for PLE.

The most frequent outcome was pruritus and erythema in combination with papular or papulovesicular lesions, which accounted for 88% of the positive reactions. The remaining 12% involved pruritus, erythema, and macules that persisted for at least 12 hours after the last exposure. The lesions were sometimes sparsely scattered over the irradiated area, which means that test areas should not be too small. Thus, we believe that our 4 × 4-cm test area for each dose is appropriate. Larger areas are not necessary: Neumann et al<sup>16</sup> have shown that whole body UV-A exposure was no more effective than the exposure of smaller previously involved skin sites.

Our success rate was 68% (17/25), which is good compared with most of the reports in Table 1. There was little difference between the success rates on previously affected sites (13/17; 76%) and previously unaffected sites (12/17; 71%). Most studies have attempted to induce PLE on previously sun-exposed sites.<sup>12,14,15,18,31</sup> Only 2 other studies<sup>14,18</sup> attempted, without clear success, to induce PLE on previously unaffected (ie, non-sun-exposed) sites. Our results clearly show that successful provocation of PLE is not dependent on skin site.

Polymorphic light eruption usually requires several consecutive exposures to sunlight. We thus tried to simulate the natural conditions with repeated daily exposures of 0.25, 0.5, 0.75, 1.0, 1.25, and 1.5 just percep-

tible MEDs. Unfortunately, the total number of exposures was limited because most patients were not willing to cooperate for more than 4 consecutive exposures. The influence of number of exposures is shown in Figure 4. This shows that at least 3 exposures are necessary to obtain a success rate of at least 50% on previously exposed and previously unexposed skin.

The SSR dose (cumulative physical dose) required to induce PLE ranged from 1.7 to 25 J/cm<sup>2</sup> (mean MED, 4.9 J/cm<sup>2</sup>; range, 2.6-10.1 J/cm<sup>2</sup>), and there was no evident correlation between outcome and cumulative physical dose. In a recent study,<sup>5</sup> members of our group used single exposure doses of 0.6, 1, or 2 MED to induce immunosuppression in PLE patients and in age- and skin type-matched controls. Exposure to 1 MED suppressed contact hypersensitivity response by 78% in controls but induced significantly less suppression (44%) in PLE patients (*P* < .01). Suppression was also less in PLE patients than in controls after 0.6 MED (31% vs 43%), but this did not reach significance (*P* = .50). In contrast, suppression was almost complete (93%) in both PLE patients and controls after exposure to 2 MED, suggesting that PLE patients have a resistance to immunosuppression after low to moderate doses of UVR, but resistance to immunosuppression can be overcome if higher UVR doses are given.

It is possible that more exposures would have increased our success rate. On the other hand, the clinical symptoms of PLE are likely to represent a balance between the induction of the putative photoantigen and the UVR-induced suppression of the immunologic response to the antigen. Such a balance is likely to be highly dependent on individual immunologic and UVR exposure parameters. Polymorphic light eruption was provoked after a single exposure in 3 (18%) of 17 patients, and in 1 of these cases the PLE was evident after the MED series. This contrasts with the findings of other authors,<sup>15,25,27,28,30,31</sup> who reported good results from a single exposure with a wide range of sources and doses.

In conclusion, we have shown that PLE can be readily induced when the natural causes of the disease are simulated. The lack of consistent results from studies of the PLE action spectrum further supports the use of SSR. We have also shown, for the first time, that the condition can be just as readily provoked on previously unexposed sites. This indicates that the putative photoantigen can be induced *de novo*. Finally, we believe that a standard protocol for the induction and assessment of PLE would benefit research and clinical practice, and we advocate that researchers in this field work toward this end.

*Accepted for publication June 25, 2003.*

*This study was supported by a personal training award from the Guy's & St Thomas' Charitable Foundation, London, England (Dr van de Pas), and a project grant from the Claneil Foundation Inc, Plymouth Meeting, Pa.*

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