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Cutaneous Sensitivity to Ultraviolett Light and Chemical Irritants*

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Summary. This investigation examines the relationship between the sun sensitivity of human skin and its response to chemical irritants. Forty-four Caucasoid subjects with normal back skin were studied. The minimal erythema dose (MED) was determined with the sunburning spectrum of a high-pressure mercury lamp. Cutaneous irritability was quantified using a series of seven irritants of different chemical structure, solubility, and concentrations. The response was either expressed as a threshold value of exposure time (ammonium hydroxide, sodium hydroxide) or was graded after a standard exposure in intensity of whealing (dimethyl sulphoxide) or erythema (sodium lauryl sulphate, quaternium 1, croton oil, kerosene).

A significant correlation between the MED and the response to all seven primary irritants was found. The relationship was better for water-soluble irritants than for lipid-soluble ones. Despite marked individual variations the determination of the MED is suggested as a valuable tool in identifying hyperirritable skin. Skin typing based on complexion and sunburn history proved to be less reliable.

Key words: Light sensitivity – Cutaneous irritability – Chamber testing – DMSO test – Alkali resistance – Skin type – Duhring chambers

Zusammenfassung. Das Ziel dieser Studie war die Untersuchung des Zusammenhanges zwischen der Sonnenempfindlichkeit menschlicher Haut und deren Reaktion auf chemische Irritantien. 44 weiße Probanden mit normaler Rückenhaut wurden getestet. Die minimale Erythemdosis (MED) wurde mit dem Sonnenbrandspektrum einer Quecksilberhochdrucklampe bestimmt. Die Hautirritabilität wurde quantifiziert durch eine Serie von sieben gut bekannten chemischen Irritantien von unterschiedlicher chemischer Struktur, Löslichkeit und Konzentration. Die Reaktion wurde entweder als Schwellenwert der Expositionszeit ausgedrückt (Ammoniaklösung, Natronlauge) oder nach einer

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Standardexposition bewertet hinsichtlich der Intensität der urticariellen Reaktion (Dimethylsulfoxid) bzw. des Erythems (Natriumlaurylsulfat, Quaternium 1, Krotonöl, Kerosin).

Es wurde eine signifikante Korrelation zwischen der MED und allen sieben chemischen Irritantien festgestellt. Die Beziehung war enger für wasserlösliche Irritantien als für lipidlösliche. Trotz starker individueller Abweichungen wird die Bestimmung der MED empfohlen für die Erkennung von empfindlicher Haut. Die Hauttypisierung aufgrund äußerer Kriterien und der Sonnenbrandvorgeschichte erwies sich als weniger zuverlässig.

Schlüsselwörter: Lichtempfindlichkeit – Hautirritabilität – Kammer-Test – DMSO-Test – Alkali-Resistenz – Haut-Typ – Duhring-Kammern

Confusion exists about the relationship of the skin's sensitivity against ultraviolet light and chemical irritants. The common belief is that skin which burns easily in the sun is also less resistant to various other external stimuli. This view lacks solid scientific evidence. Only few investigational studies have been reported. Miescher after determining the threshold reactions to an artificial light source and various chemical irritants concluded that in some individuals there was a positive relationship to some chemicals [14]. Leder found a positive relationship between light sensitivity and the reactivity to benzene in general but pointed out that large individual deviations exist [11]. On the other hand, Klaschka reviewing the subject recently, expressed his disbelief in any association between light and chemical sensitivity of the skin [9].

Epidemiologic data, however, suggest that fair skinned, easily sunburnt persons of Celtic extraction are more prone to develop irritant dermatitis in various industries in comparison to their dark-complexioned colleagues [15, 20].

When developing various biometric probes to quantify skin functions in vivo we were struck by the wide scatter of normalcy [3, 4]. Skin complexion and sunburn history seemed to be significant when ranking a subject on the sensitivity scale for chemical irritants. If sun-sensitive individuals also had a low tolerance to various chemical irritants in general, the relatively simple determination of the erythema threshold to ultraviolet radiation could turn out to be a useful tool for identifying hyperirritable skin.

Methods

Light Testing

A high-pressure mercury lamp (Ultra-Vitalux, G 176, Osram) was used to evaluate the light sensitivity. This lamp emits virtually no ultraviolet (UV) light in the UV-C range, and shows an intensity peak in the UV-B (315 nm) and in the UV-A (380 nm) range. At a skin distance of 15 cm the following radiation intensities were measured: UV-B: 360 $\mu W/cm^2$; UV-A: 8.300 $\mu W/cm^2$. Skin areas of 0.5×1 cm were irradiated with exposure times starting at 10 s and being raised by 20 % increments up to 154 s. Reactions were read 24 h after irradiation. The MED was defined as the exposure time that produced a slight but well-defined erythema.

Testing with Irritants

Ammonium Hydroxide. The minimal blistering time (MBT) of ammonium hydroxide (NH_4OH) was determined as previously described [3]. Briefly, a 1:1 aqueous solution of concentrated NH_4OH is filled into the well of a plastic block (6-mm diameter) and the exposure time is determined for raising a complete subcorneal blister.

Alkali Resistance Test. The resistance to sodium hydroxide (NaOH) was determined using the method as described by Locher [10]. This method is more accurate than the original Burckhardt technique. For further differentiation we reduced the exposure intervals from 5 to 2.5 min.

DMSO. The whealing response to dimethyl sulphoxide (DMSO) was quantified as outlined in detail elsewhere [4]. Aqueous dilutions of DMSO (90%, 95%) and undiluted were applied for 5 min to the skin via plastic blocks (8-mm diameter wells). The whealing was graded 10 min later on a four-point scale (1+ slight, 2+ moderate, 3+ severe, 4+ very severe).

Chamber Testing Materials

Sodium lauryl sulphate (SLS; Sigma Chemicals, München, FRG), 0.25%, 1.0%, 2.50%; Quaternium 1 (Q1, Hyamine 3500; Röhm & Haas, Frankfurt, FRG), 0.25%, 1.0%, 1.75%; Croton oil (CO; Meht KG, Hamburg, FRG), 2.5%, 5%, 10.0%; Kerosine (KER; Fluka AG, Buchs, Switzerland), 40.0%, 60.0%, 80.0%.

The solvent for the detergents (Q1 and SLS) was distilled water, mineral oil was used for the other two irritants.

Application and Reading

A volume of 0.1 ml was applied to the skin occlusively for 20 h, utilizing Duhring chambers [3]. The reactions were read 1 h after removal on the following scales: Erythema: 0 none; 1+ slight; 2+ moderate; 3+ severe; 4+ very severe. Vesiculation, pustules: 0 none; 1+ tiny, just perceptible lesions (<25% of the test area); 2+ well recognizable lesions (<50% of the test area); 3+ confluent lesions (<75% of the test area); 4+ large bulla (100% of the test area).

Test Persons and Location. Testing was performed on 44 white volunteers (21 men, 23 women; ages 18–66 years). Twenty-three subjects were healthy young students. The remaining were hospitalized because of the following reasons: allergy testing (11), stasis ulcers (four), nevi and plantar warts (three), furunculosis (one), Raynaud syndrome (one), syphilis (one). Subjects with an intense recent tan were avoided. All tests were carried out during cool seasons of the year (October to February). Testing with both light and irritants was performed on the paravertebral mid-portion of the back. None of the patients were in the acute stage of the disease, all of them had normal skin on the back and at least 80% of the remaining body.

Skin Typing. All subjects were typed on a I–VI scale according to their complexion, sunburn history, and tanning ability [12].

Statistics. Correlation coefficients were calculated according to Pearson when parametric data were evaluated (MED, MBT, NaOH time) and a nonparametric rank correlation design after Spearman was used for the scoring data (DMSO and chamber tests) [18]. When several concentrations of one irritant were used, the correlation with the MED was calculated separately with the score obtained by each concentration and with the sum of the scores.

Results

The results are illustrated in Figs 1–6. The correlation coefficients and level of significance are given in Table 1. Based on the results of the MEDs, four groups of different light sensitivity were formed: I ($n = 11$) 10–25 s; II ($n = 16$) 26–40 s; III

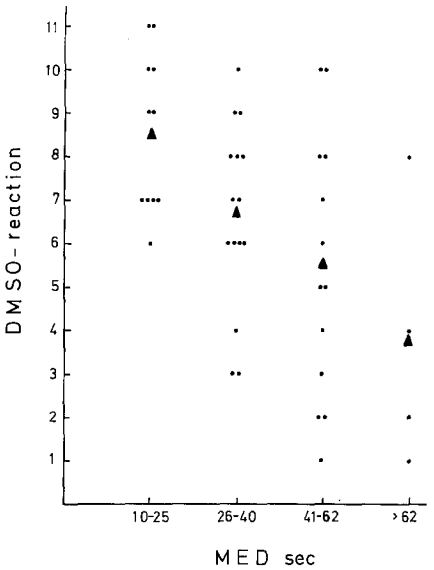

Fig. 1. Relationship between the whealing response to *DMSO* and the *MED* of UV light in 44 white subjects. Sum of scores to 90%, 95%, and 100% *DMSO* (●); mean values (▲) of the four groups of different light sensitivity

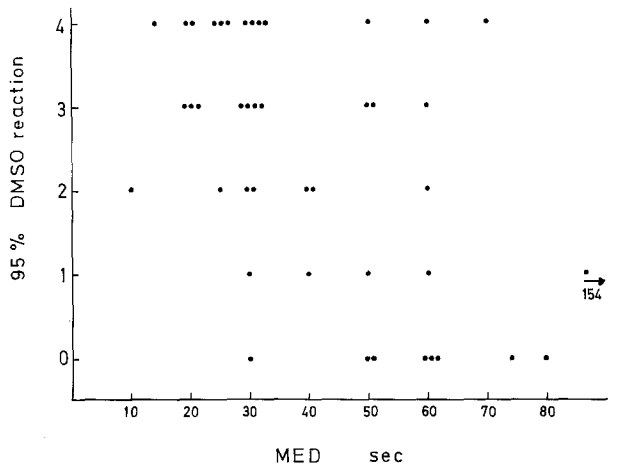

Fig. 2. Individual data of Fig. 1. The whealing response to 95% *DMSO* in relation to the *MED*

($n = 13$) 41 – 62 s; IV ($n = 4$) 62 – 154 s. The intensity of the DMSO reaction decreased with increasing MED and vice versa (Figs. 1, 2). This inverse relationship between the DMSO reaction and the MED was significant for each test concentration as well as for the total score (Table 1).

However, marked individual deviations were found. The total score of the DMSO reaction in group III ranged from 1 + to 10 + (mean 5.5 +) and one subject in the group with the lowest light sensitivity reacted to DMSO as strongly as the majority of the subjects with the highest UV sensitivity.

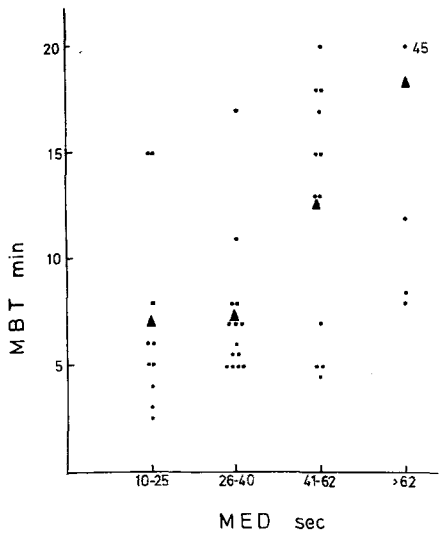

Fig. 3. Relationship between the *MBT* of NH_4OH and *MED* of UV light in 44 white subjects

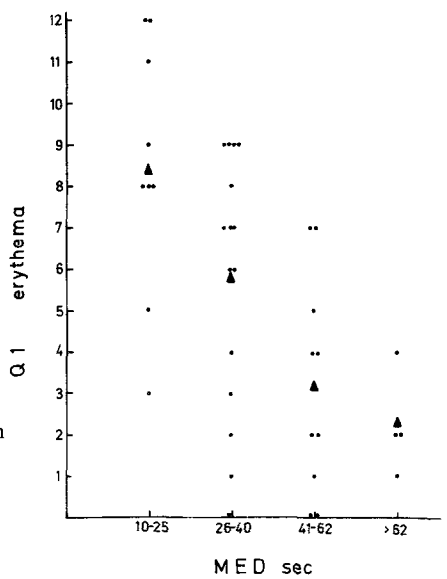

Fig. 4. Relationship between the erythematous response to Quaternium 1 (*Q 1*) and the *MED*. Sum of scores to 0.25, 1.0, and 1.75% *Q 1* (●); mean values (▲) of the four groups of different light sensitivity

The same was found with other irritants. The correlation was best between the MED and the sum of erythema scores of Q 1. The correlation was weakest with KER. Low, but still significant, correlation coefficients were obtained for all but one test concentration (80%), as well as for the total score.

The MBT and the alkali resistance time were the only parameters that showed a direct and not an inverse correlation with the MED. The reason is that low values of the former two indicate a high sensitivity to NH_4OH and NaOH just as in the case with the MED and the UV sensitivity. For illustrative reasons in Fig. 6

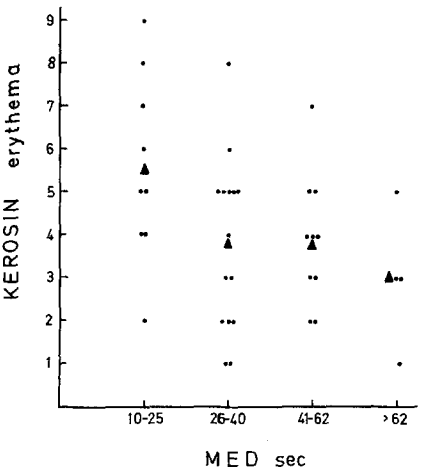

Fig. 5. Relationship between the erythematous response to kerosine and the *MED*. Sum of scores to 40, 60 and 80% kerosine; mean values (▲) of the four groups of different light sensitivity

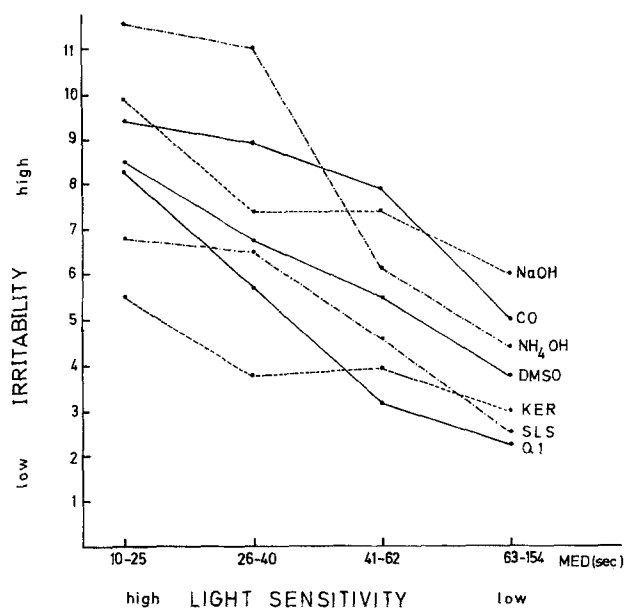

Fig. 6. Summarizing graph of the positive relationship between light sensitivity and chemical irritability of the skin. Shown are the mean values of 44 subjects (sum of erythema scores to three different concentrations of *SLS, CO, KER, Q1;* sum of whealing scores to *DMSO;* reciprocal threshold exposure times of NH_4OH and NaOH)

reciprocal values of the MBT and of the alkali resistance time were used. All values were transformed by forming the quotient with the highest measured value of the least sensitive subject (e.g., MBT = 3 min; MBT = $\frac{45}{3}$ = 15). Applying this procedure, the close association between light sensitivity and chemical irritability of the skin becomes evident in Fig. 6.

Table 1. Correlation coefficients between MED, skin type, and the response to seven primary irritants

	MBT	NaOH	Type	DMSO			
				90%	95%	100%	TS
MED	R = 0.440 $P < 0.002$	R = 0.523 $P < 0.001$	r = 0.554 $P < 0.001$	r = −0.406 $P < 0.003$	r = −0.498 $P < 0.001$	r = −0.344 $P < 0.012$	r = −0.493 $P < 0.001$
Type	r = 0.10 $P > 0.254$*	r = 0.243 $P > 0.052$*	–	r = −0.365 $P < 0.006$	r = −0.418 $P < 0.002$	r = −0.208 $P > 0.083$*	r = −0.421 $P < 0.002$

	SLS				Q 1			
	0.25%	1.00%	2.50%	TS	0.25%	1.00%	1.75%	TS
MED	r = −0.629 $P < 0.001$	r = −0.273 $P < 0.040$	r = −0.472 $P < 0.001$	r = −0.513 $P < 0.001$	r = −0.516 $P < 0.001$	r = −0.537 $P < 0.001$	r = −0.530 $P < 0.001$	r = −0.597 $P < 0.001$
Type	r = −0.226 $P > 0.065$*	r = −0.207 $P > 0.084$*	r = −0.265 $P < 0.037$	r = −0.244 $P > 0.052$*	r = −0.262 $P < 0.039$	r = −0.331 $P < 0.016$	r = −0.386 $P < 0.006$	r = −0.365 $P < 0.009$

	CO				KER			
	2.50%	5.00%	10.00%	TS	40.00%	60.00%	80.00%	TS
MED	r = −0.356 $P < 0.010$	r = −0.287 $P < 0.032$	r = −0.389 $P < 0.005$	r = −0.384 $P < 0.006$	r = −0.317 $P < 0.020$	r = −0.372 $P < 0.008$	r = −0.219 $P > 0.093$*	r = −0.348 $P < 0.016$
Type	r = −0.509 $P < 0.001$	r = −0.364 $P < 0.006$	r = −0.413 $P < 0.002$	r = −0.499 $P < 0.001$	r = −0.266 $P < 0.037$	r = −0.383 $P < 0.004$	r = −0.252 $P > 0.053$*	r = −0.360 $P < 0.010$

Calculation after Pearson (R) and after Spearman (r). TS total erythema score of all three test concentrations. Significance was obtained for $P < 0.05$ (* not significant). MBT = minimal blistering time of ammonium hydroxide. NaOH = sodium hydroxide. DMSO = dimethyl sulfoxide. SLS = sodium lauryl sulfate. Q 1 = Quaternium 1. CO = croton oil. KER = kerosine

When skin typing was used to estimate the cutaneous light sensitivity instead of determining the MED the correlation with the chemical vulnerability was much weaker (Table 1). Correlations failed significance in five parameters (MBT, NaOH, 100% DMSO, SLS, 80% KER). Skin type correlated best with the MED ($P < 0.001$). Skin types ranged from I ($n = 4$) to IV ($n = 8$) with the majority being III ($n = 17$).

No major differences were found when the parameters pustules and vesiculation were considered.

Discussion

In view of earlier work it was surprising to find such a good correlation between UV light sensitivity and the reactivity to a group of extremely different chemical irritants. Miescher [13] reported an association between the thresholds to UV light und to the irritants chrysarobin and hydrochloric acid, but pointed out the lack of such a relationship with CO, lime, and "pinen" (constituent of turpentine). Leder [11] found a positive correlation between UV sensitivity and irritability to benzene. He noted a wide scatter in his large test panel of 208 persons but emphasized that all extremely light sensitive subjects had a very low threshold to benzene. The same was found for the other extreme. After producing a hyperkeratosis by repeated UV radiation ("Lichtschwiele") both thresholds for UV and for benzene increased. Leder [11] used a Kromayer lamp which is rich in shortwave UV-C. Miescher [13] described no details of radiation but supposedly employed the same light source. Both studies lack statistical analysis.

The quality of the light source profoundly influences the threshold of the MED. As Kaidbey et al. [8] recently demonstrated scattering and absorption in the horny layer and epidermis are much greater with UV-C in comparison to the longer wave lengths of UV-B; UV-B penetrates deeper into the epidermis and superficial dermis than UV-C and causes a more intense inflammation, particularly with supra-threshold doses. Since UV-C is virtually absent in atmospheric sunlight, light testing with a UV-B source such as used in this study seems preferable and more representative for the actual sun sensitivity of an individual. Furthermore, a good correlation with the erythema thresholds obtained by a solar simulator could be established in the meantime (Xenon arc 150 W, Solar Light Co., Philadelphia PA, USA).

The major skin barrier against external harmful stimuli of any type is the horny layer. With respect to UV light this was discovered by Miescher [13]. The regional differences of the MED as reported by Olson et al. [16] are in fairly good argreement with measurements of horny-layer thickness in these areas [6]. Kaidbey et al. [8] pointed out that in Caucasoid skin the horny layer is the main filter against UV radiation, whereas in black skin the heavily melanized epidermis provides additional protection. As demonstrated elsewhere [2] the MBT of NH_4 OH correlates directly with the number of cell layers and is thus an indirect measurement of the horny-layer thickness. The same relationship has been assumed for the alkali resistance test [10]. Our results therefore indicate that the major factor in determining the sensitivity to light and chemical irritants is the thickness *and* integrity of the horny layer.

In analogy to the light-protective effect of melanin it is an interesting hypothesis to speculate on a similar action for chemical irritants. Melanin is a polymer with the ability to oxidate and reducte. It has been shown to bind chlorpromazin [1] and may act as a biologic electron exchange polymer to minimize the impact of incident photons on other cell constituents [5]. It therefore does not seem impossible that in darkly pigmented individuals the melanin may ameliorate the destructive action of an irritant by direct or indirect interference with the chemical itself or its cytotoxic products, for example, free radicals.

Generally, polar water-soluble irritants penetrate the horny layer at a lower rate than nonpolar lipid-soluble ones [19]. The irritant reaction of lipid-soluble agents is less dependent on the horny layer. This may be one of the reasons why the correlation with the MED was lower with CO and KER in comparison to aqueous chemicals. The test concentration of the agent may be critical for obtaining a significant relationship (Table 1). If the concentration is too high individual differentiation becomes less evident due to severe reactions in almost everybody (100% DMSO, 80% KER), and if the concentration is very low there are too few responders (0.25% and 1.0% SLS). Other factors which may account for discrepancies between the reactions to UV light and chemical irritants are probably due to differences in inflammatory mediators [7, 17].

Nevertheless, no matter what type of chemical is applied to the skin, an extremely light-sensitive individual of Celtic origin is prone to hyperreact in contrast to a dark-complexioned tough "sun lover". Determination of the MED by an objective method will be more reliable than just skin typing based on history and physical findings, as our results have shown. The quick and noninvasive DMSO test will further narrow down the range of skin reactivity that is to be expected.

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