Irritancy Testing in Occupational Dermatology: Comparison between Two Quick Tests and the Acute Irritation Induced by Sodium Lauryl Sulphate

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To reduce the incidence of irritant contact dermatitis, the development of screening methods to identify subjects with increased susceptibility to irritants is essential. In a pilot study on the comparison between two quick, non-invasive irritancy tests (dimethyl sulfoxide (DMSO) and sodium hydroxide (NaOH)) with the time-consuming patch testing with sodium lauryl sulphate (SLS), no correlation between the "quick tests" and SLS patch testing was observed. In the present paper the results of irritancy testing in 181 metal worker trainees are presented. Experimental irritant contact dermatitis reactions were induced on the medial third of the volar forearm using SLS 0.5%, applied for 23 h and as "quick tests" DMSO 90% and 95% and a solution of 0.2 mol/l NaOH applied for 5 min. Assessment of skin irritability was made by visual scoring and measurement of transepidermal water loss. Except for a statistically significant relationship between the irritations by DMSO 90% and 95%, correlations between the different techniques were weak or non-existent. This is most probably due to different pathophysiological pathways for the irritant reactions. We therefore propose to use a spectrum of different tests in occupational dermatology for predicting the individual's risk of irritant contact dermatitis. *Key words: skin irritancy; irritant contact dermatitis; bioengineering methods; transepidermal water loss (TEWL).*

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Several assays for the examination of individual skin vulnerability have been proposed for predicting the risk of irritant contact dermatitis (1–3). Hinnen et al. (4) performed a pilot study on the correlation between patch testing with sodium lauryl sulphate (SLS) (5) and two less time-consuming tests for the determination of individual susceptibility to irritants (2, 6): experimental irritation with sodium hydroxide (NaOH) and with dimethyl sulfoxide (DMSO) (7). Visual scoring and measuring of transepidermal water loss (TEWL) were used to determine skin vulnerability. The pilot study showed a lack of agreement between the three tests. To verify these findings in a high-risk group for occupational contact dermatitis, we performed the present field study on 181 metal worker trainees.

PATIENTS AND METHODS

Study population

Two hundred and five healthy metal worker trainees, within their first 3 months of vocational training, without any skin diseases, participated in the study after informed consent. The study was performed as part of the PROMETES field study (**Pro**spective **met**al worker eczema **s**tudy) taking place in 22 metal processing factories in Switzerland. A mobile caravan equipped with skin bioengineering devices and with facilities for applying irritation tests and performing clinical examinations was used as study location.

All participants with incomplete data ($n=20$) and those with TEWL values >25 g/m²/h ($n=4$) before irritation were excluded. A final study population of 181 participants between 15 and 25 years (median $=16$), 179 males and 2 females, was taken into statistical evaluation.

Induction of irritation

Quick tests. The quick tests were performed using 50 µl of DMSO aqueous solution at concentrations of 90% and 95% and 0.1 ml of NaOH at a concentration of 0.2 mol/l aqueous solution (modified alkali resistance test) (both DMSO and NaOH from Fluka Chemie AG, Buchs, Switzerland). They were performed simultaneously at exactly defined application areas (21×32 mm) on the medial third of the volar forearm and left there for 5 min by means of plastic blocks. *SLS-test.* The SLS irritation test was initiated the same day on the same forearm using 50 µl of an aqueous solution of SLS (high purity; Sigma, St. Louis, MO) at a concentration of 0.5%, applied to the skin in large Finn chambers (inner diameter 1.2 cm, Epitest Ltd., Hyrlä, Finland) for 23 h. A control site (application of a 0.9% aqueous solution of NaCl, also in Finn chambers) was chosen at the same forearm, close to the SLS application site.

Measurements

All measurements were carried out as in the pilot study (4):
Visual scoring. Visual scoring was performed before and after irritation according to Frosch & Kligman (5). For the visual scoring of the DMSO test, slightly different criteria were used: instead of fissures we scored *wheals:* (1+) slightly elevated, solid wheal, (2+) elevated, solid, tense wheal.
Transepidermal water loss (TEWL). TEWL was measured with an evaporimeter (Tewameter, Courage & Khazaka, Cologne, Germany) (8) 1 h after removal of the SLS patch test and 5 to 10 min after the "quick irritants" NaOH and DMSO had been carefully wiped off, respectively. TEWL was then converted to a standard temperature of 30° C (TEWLtemp) (9). The effect of the challenge tests on TEWL was expressed by calculating Delta-TEWL-values (TEWL after irritation-TEWL before irritation). The experiments were performed in the fall of 1994.

Statistics

Visual score data and Delta-TEWLtemp-values were statistically analyzed with the statistical package SPSS for Macintosh. Simple linear correlations between the different methods were checked by computing Pearson correlation coefficients and confidence intervals for the regression lines.

RESULTS

Visual score. The mean visual score values of the quick tests (DMSO 90%, DMSO 95% and NaOH 0.2 mol/l) ranged between 0.02 and 0.04 and did not differ significantly.

In contrast, the SLS-irritated skin displayed with 0.24 a tenfold higher mean visual score than the quick tests. Physiological NaCl solution, being applied for negative control to SLS patch testing, produced a mean visual score of 0.04,

indicating that part of the SLS irritation may be due to the skin moistening provoked by occlusion (Table I). In visual scoring the irritation potency of the agents tested was SLS > > DMSO 95% > DMSO 90% > NaOH. Although different visual scoring systems were used, the visual scores can be regarded as comparable since neither scaling nor fissures nor wheals but only erythema were induced. Significant correlations in visual scoring ($p < 0.01$) were calculated between DMSO 90% and DMSO 95%, and between SLS and DMSO 90% (Table II).

Delta-TEWL. The mean Delta-TEWL values induced by the quick tests were 2.61 and 3.48 for DMSO 90% and 95%, respectively, and 10.43 for NaOH. SLS led to a Delta-TEWL of 5.76. After subtracting the NaCl Delta-TEWL of 0.93, SLS patch testing results in an actual Delta-TEWL of 4.83. Thus the irritation potency of the agents tested considering TEWL

Table I. *Values of TEWL and of visual scoring in 181 metal worker trainees, before and after challenge testing, as well as Delta-TEWL values*

TEWL values are converted to a standard skin temperature of 30°C.

	TEWL		Visual score	
	Mean	SD	Mean	SD
DMSO 90%:				
Before	9.64	3.05		
After	12.25	3.07	0.03	0.16
Delta-TEWL	2.61	0.02		
DMSO 95%:				
Before	9.64	3.05		
After	13.12	3.42	0.04	0.21
Delta-TEWL	3.48	0.37		
NaOH 0.2 mol/l:				
Before	9.64	3.05		
After	20.07	6.21	0.02	0.16
Delta-TEWL	10.43	3.16		
SLS 0.5%:				
Before	10.61	3.19		
After	16.37	5.57	0.24	0.55
Delta-TEWL	5.76	2.38		
NaCl 0.9% (control):				
Before	10.61	3.19		
After	11.54	3.44	0.04	0.21
Delta-TEWL	0.93	0.25		

SD = standard deviation.

Table II. *Correlation matrix of the visual scores (VS) between the DMSO 90%-, the DMSO 95%-test and SLS-patch testing*

The VS values of the NaCl-irritated skin were subtracted from those of SLS-irritated skin, in order to exclude irritative effects of the occlusive tape, as reflected by the NaCl VS, from calculation.

	NaOH	DMSO 90%	DMSO 95%	SLS
NaOH	1			
DMSO 90%	−0.02	1		
DMSO 95%	−0.02	0.46**	1	
SLS	0.03	0.23**	0.14	1

* significance level = 0.05; ** significance level = 0.01.

measurements is NaOH > SLS > DMSO 95% > DMSO 90%. Statistically significant correlations in TEWL ($p < 0.01$) were calculated between the TEWL values of the two concentrations of DMSO. A low, but statistically significant correlation was found between the irritation with NaOH and SLS patch testing (Table III).

DISCUSSION

The DMSO test was suggested by Frosch as a quick and reliable test to assess the barrier function of the skin (10). TEWL and other non-invasive skin bioengineering methods after irritation with DMSO at a concentration of 100% were later reexamined by Agner & Serup in 6 healthy volunteers, showing DMSO testing to be a relevant model for experimental skin inflammation (7). In a pilot study, Hinnen et al. (4) observed that the irritant reactions to DMSO 90%, 95% and 100% correlated significantly in visual scoring but not in TEWL. In our study testings with DMSO 90% and DMSO 95% were found to correlate significantly both in visual scoring and TEWL. This correlation seems logical. The difference to the TEWL-findings in the pilot study is most probably due to the larger (181 in the present vs. 20 in the pilot study) and thus more representative study population. In the present study, DMSO at a concentration of 100% was not used due to its strong irritancy and the previously observed high correlation to the other DMSO solutions.

The irritation test with NaOH 0.2 mol/l, as performed in our study, is a modification of the alkali resistance test by Burckhardt (6), proposed by Wilhelm et al. as a short and simple technique to induce subclinical experimental irritation of the skin in order to identify subjects with increased sensitivity to irritants. In their study on 10 subjects, Wilhelm et al. calculated a highly significant correlation of the NaOH-test with 24 h SLS patch testing (2). These findings could neither be corroborated in the pilot study by Hinnen et al. (20 subjects) nor by the data of the present study (181 subjects), showing that there is probably only a weak correlation between NaOH and SLS testing. Thus these two tests are not exchangeable. In comparison to the pilot study the DMSO tests and SLS patch testing showed distinctly lower visual score values, whereas NaOH scored slightly higher. Contrary effects could be observed in the TEWL-data, displaying distinctly higher values and standard deviations. These effects are most probably due to the fact that the present study was performed in

Table III. *Correlation matrix of the Delta-TEWL values between the quick tests with DMSO 90%, DMSO 95%, NaOH and SLS patch testing*

The TEWL values of the NaCl-irritated skin were subtracted from the Delta-TEWL values of SLS-irritated skin, in order to exclude moisturizing effects of the occlusive tape, as reflected by the NaCl Delta-TEWL, from calculation.

	DMSO 90%	DMSO 95%	SLS
NaOH	1		
DMSO 90%	0.09	1	
DMSO 95%	0.08	0.69**	1
SLS	−0.2**	−0.06	0.11

Note: NaOH column header spans leftmost data column (value 1), subsequent columns DMSO 90%, DMSO 95%, SLS.

* significance level = 0.05; ** significance level = 0.01.

a field situation during the autumn months, whereas the pilot study took place in the laboratory in early spring. Other possible reasons might be variations in the study population. Whereas the participants of the pilot study were mainly medical students and hospital employees, the present study was performed on metal worker trainees with a possibly predamaged skin barrier at the lower forearms.

Our results, however, are for the most part in agreement with those of the pilot study and corroborate its message that the three investigated tests are not equivalent for determining individual susceptibility to chemical irritants and thus cannot be replaced by another. Except for a statistically significant relationship between the irritations by DMSO 90% and 95%, the correlations are weak or non-existent between the different techniques. Since it is likely that the examined methods of skin irritancy assessment reflect different pathophysiological pathways for irritant reactions, we propose to use a spectrum of different tests in occupational dermatology for predicting the individual's risk of irritant contact dermatitis.

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