

Predictive testing of metalworking fluids: a comparison of 2 cumulative human irritation models and correlation with epidemiological data

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Metalworking fluids (MWF) have been reported as being an important cause of irritant contact dermatitis in metal workers. Our purpose was to determine whether the irritancy of different MWF assessed by 2 different types of predictive human in vivo tests could be compared with epidemiological data. 3 water-based MWF were tested in the same panel of subjects. Reactions were assessed by a visual score (VS), evaporimetry to evaluate the transepidermal water loss (TEWL) and chromametry to quantify erythema. *Test 1*: MWF were applied with Finn Chambers on the volunteers' mid-back, removed after 1 day of exposure, and reapplied for a further 2 days. *Test 2*: Cumulative irritant contact dermatitis was induced using a repetitive irritation test for 2 weeks (omitting weekends) for 6 h per day. We observed an increase in VS, TEWL, and erythema for all MWF, with the same irritancy ranking in both test models. Differentiation of the substances was better in the D1/D3 test. The experimental results partially correlated with the epidemiological data. Considering the shorter application time and the better discrimination of irritancy, we prefer the D1/D3 model as a predictive test of MWF irritancy. Our results might aid development of a standardized test to reduce cumulative skin irritation in metal workers.

Key words: metalworking fluid; contact dermatitis; predictive testing; transepidermal water loss; colorimetry; prevention; occupational. © Munksgaard, 1997.

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Although computerized tooling operations are increasing, metalworking fluids (MWF) remain one of the most important causes of hand dermatitis in the metal industry (1). Irritant contact dermatitis (ICD) seems to be more frequent than allergic contact dermatitis (ACD) due to MWF (2–6), of which the water-based fluids are known to have a higher irritating and sensitizing potential than neat oils (2, 6–10). It should be kept in mind that metalworkers have a high incidence of occupational skin diseases (11, 12) and the risk for hand dermatitis is closely linked to MWF exposure (12). The prevalence of hand dermatitis may reach 30% if high MWF exposure occurs (13). A Swiss study (14) showed that 10% of Swiss metal worker trainees experienced minor signs of skin irritation (erythema, induration, flaking) 8 to 10 months after the beginning of the apprenticeship. Transepidermal water loss (TEWL), which is an adequate tool for monitoring metal workers exposed to mineral oils and MWF (15), increased continuously within

3 months of first examination, and the observed increase was significantly influenced only by exposure to water-soluble MWF. Replacement of irritant MWF by less toxic products is therefore an important measure in the prevention of MWF-associated hand dermatitis. In recent studies, the irritancy of different MWF on the skin was investigated comparatively by non-invasive measuring methods (16, 17). However, since the results of irritancy assessments have not been correlated to epidemiological data from field studies of workers exposed to the tested products, the practical value of laboratory irritancy assessments remained open.

The aim of the present study was to evaluate the irritancy of 3 different MWF by means of 2 different types of predictive tests in relation to epidemiological data. Based on the irritancy rating of 3 MWF by a prospective epidemiological field study in metalworking trainees, we performed a comparative study of 2 predictive tests for MWF irritancy in order to identify a sensitive and specific

test that could be recommended for future testing. Furthermore, unused MWF and those out of the machining process were tested to determine differences in irritancy and to aid in the decision as to whether, new or used products should be used for MWF irritancy testing.

Patients and Methods

Field study

In the ongoing Prospective Metal Workers' Eczema Study (PROMETES) performed in cooperation between the Departments of Dermatology and Social and Preventive Medicine, University of Zurich, 205 metal worker trainees were non-selectively recruited in the trainees workshops of 22 different metal working factories. They underwent an initial skin examination, including a standardized interview and a clinical examination of the skin. Dermal exposure assessment was based on expert interviews and job diaries (18). The trainees were reexamined 8 to 10 months after they had started their apprenticeship and all signs of early stage of hand eczema (erythema, induration, flaking) were registered. MWF from 3 trainee workshops were selected for predictive testing. MWF A was from a workshop with 36% of work-related skin changes, MWF B from a workshop with 12% of skin changes, and MWF C from a workshop with 0% of skin changes. Informations on exposure to irritants, leisure time exposure, skin protection/hygiene and number of school days per week in 3 workshops are presented in Table 1.

Study population

15 healthy volunteer subjects, 6 male and 9 female without any skin diseases, entered the study after informed consent in accordance with the Helsinki declarations. The study had passed review by the

Ethical Commission of the University Hospital Zurich. The age of the subjects was between 25 and 38 years with a mean age of 29.7. The study subjects were not allowed to shower, bathe or to use any detergents or creams on their backs during the days of investigation.

Test substances

The water-based MWF are delivered by the producers as concentrates, which have to be diluted with water. More detailed specifications cannot be given for commercial reasons. We tested the MWF (A, B, C) at factory use concentrations of 3%-5% (pH 8.7-9.2) and the same MWF in use (A*, B*, C*).

MWF A: pH: 8.85 (A), 8.05 (A*),
mineral oil: 62%,
MWF B: pH: 8.70 (B), 7.89 (B*),
mineral oil: 57%,
MWF C: pH: 9.20 (C), 8.60 (C*),
mineral oil: 45%,
Sodium lauryl sulfate (SLS highest grade, dissolved in water 0.1%), distilled water.

Test procedure

2 different tests were carried out in the same panel of subjects during October and November of 1995 with the same 3 water-based MWFs (A, B, C).

Test 1. This test model was based on the study of Hüner et al. (17). Application area was the paravertebral skin of the mid-back, and the test fields were randomized. Test fields were treated with 0.05 ml of MWF applied with large Finn Chambers (12 mm diameter, filling volume 0.05 ml; Epitest Ltd., Hyrlä, Finland) and fixed with overlapping sheets of Fixomull stretch tape (Beiersdorf, Hamburg, Germany). The chambers were removed after 1 day (24h) of exposure. 3h after removal the test

Table 1. Field study. Exposure and skin protection in the trainees of the 3 workshops, using MWF A, B, or C (number of trainees: 44)

% skin changes	Workshop, MWF A in use		Workshop, MWF B in use		Workshop, MWF C in use	
	36		12		0	
	mean	SD	mean	SD	mean	SD
exposure to MWF (water-based) ¹	538.1	93.5	533.2	91.5	533.7	57.2
exposure to MWF (oil-based) ¹	321.3	79.8	251.4	113.3	748.1	62.3
exposure to metal dust ¹	142.2	61.5	251.4	113.3	264.9	23.6
exposure to cleaning agents ¹	79.5	33.6	115.0	39.2	264.9	23.6
exposure to friction pressure ¹	189.4	92.4	248.1	117.7	264.9	23.6
exposure to irritants during leisure time ¹	1.3	1.1	5.9	7.3	2.7	3.1
score for quality of skin protection/hygiene ³	1.9	0.5	2.3	0.5	2.1	0.4
no. days/week in school	1.8	0.3	1.9	0.3	1.5	0.0

¹Total number of hours since start of training. ²Number of hours/week (average of the last 4 weeks). ³Score composed of 'application of protective creams', 'number of hand washes', 'kind of cleaner', 'post-exposure skin care'; 1=good; 2=sufficient; 3=insufficient.

reactions were evaluated and new chambers were reapplied to the original sites, for a further 2 days (48 h), to induce a cumulative irritant reaction. Measurements were performed again after the 2nd exposure at 3 days (72 h).

Test 2. Cumulative irritant contact dermatitis was induced using a repetitive irritation test for 2 weeks. Testing MWF A, B, C and samples of the same MWFs from the machining process (A*, B*, C*), the volunteers were treated by the same kind of application as in test 1 from Monday to Friday in the 1st week and after the weekend from Monday to Thursday (in each case at the same time of day ± 1 h) for 6 h per day. Water and SLS applications were tested as controls. Measurements were performed before the first application, at day (D) 5 and again at D 12.

Measurements

Visual score (VS): The test sites were evaluated each day by the same investigator according to the following scale: 0 (none) to 5 (very severe with epidermal defects) as modified from Willis et al. (19).

Transepidermal water loss (TEWL) was measured with the Tewameter (Courage & Khazaka, Cologne, Germany). TEWL measurements were performed before application of the test substances at the beginning, at D1 and at D3 (test 1), and in test 2 at D 5 and D 12 following the recommendations for measurement of TEWL as described in detail by Pinnagoda et al. (20).

Measurements of skin colour were taken with the Chroma-Meter CR-200 (Minolta, Osaka, Japan) according to the recommendations of Elsner (21). Each value is the average of 3 individual measurements.

Statistics

Statistical computations were performed with a statistical package (SPSS for the Macintosh, SPSS, Chicago, IL) on an Apple Macintosh computer using an analysis of variance (procedure ONE-WAY). All values are expressed as mean $\pm$ standard error of the mean (SEM). Differences are established at the 0.05 significance level. Differences between medians of unused and used MWF were checked for significance using the Wilcoxon *U*-test for the non-parametric visual score, and the student *t*-test for paired comparison of TEWL and Chromameter values.

Results

Figs. 1a and 1b show the mean values of the VS as well as the standard errors of the mean in both

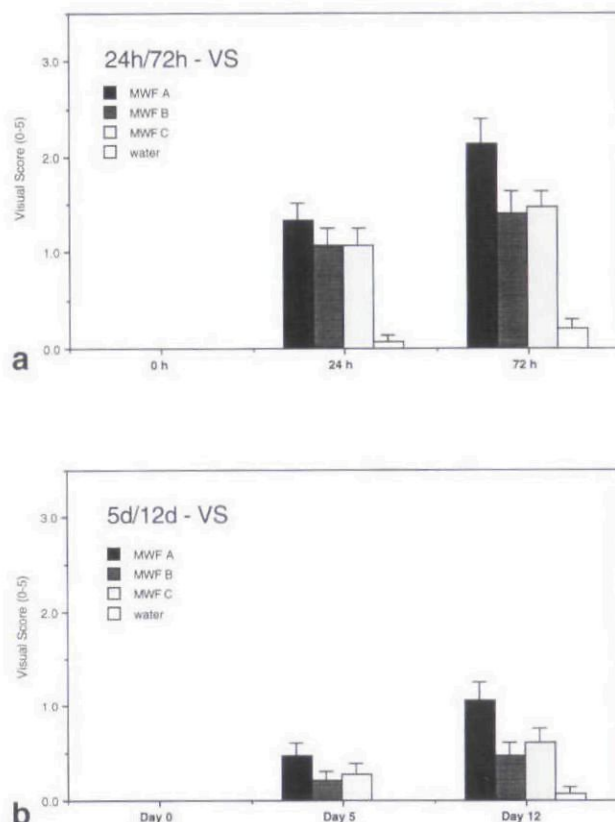


Fig. 1. The effect of different MWF on visual score. Results are given as mean $\pm$ standard error of the mean (SEM). The following irritancy ranking of test substances is seen in both test models: MWF A > MWF C > MWF B > water.

test models. After D1/D3 exposure, the VS of all MWF test sites increased significantly higher than that of controls. Even MWF C, which was used in the workshop with 0% of work related skin changes, showed irritant potential. The values in test 2 were much lower than in the D3 study period and, after 5 days of irritation, only the VS of MWF A were significantly higher than those treated with water, which remained fairly constant throughout the study period. The analysis of variance in this test model showed a worse differentiation of the substances, i. e., fewer significant differences were observed at the 0.05 significance level (Table 2). As was to be expected, the results of the chromametry showed similar results to the VS (Figs. 2). The differentiation of the test substances was much better in the D1/D3 test. According to the mild inflammation, there were no significant differences in chromametry in test 2 (Table 2). All values of VS and chromametry were much lower in test 2 than in the D3 study period. Fig. 3 shows the mean TEWL of test sites as well as the standard errors of the mean over the D3 and D12 study period. The TEWL increase was significantly different between control and MWF A, and be-

Table 2. Discriminative power of the visual score, transepidermal water loss (TEWL), and chromametry in the 2 test models.

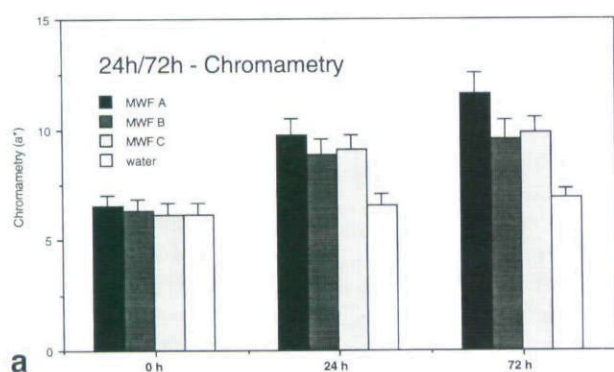
24 h/72 h-test					5 d/12 d-test					
visual score	D1	water	MWF B	MWF C	MWF A	D5	water	MWF B	MWF C	MWF A
	D3	water	MWF B	MWF C	MWF A	D12	water	MWF B	MWF C	MWF A
TEWL	D1	water	MWF B	MWF C	MWF A	D5	water	MWF B	MWF C	MWF A
	D3	water	MWF B	MWF C	MWF A	D12	water	MWF B	MWF C	MWF A
chromametry	D1	water	MWF B	MWF C	MWF A	D5	water	MWF B	MWF C	MWF A
							no significant differences			
	D3	water	MWF B	MWF C	MWF A	D12	water	MWF B	MWF C	MWF A
							no significant differences			

The substances are ordered with respect to their means. Substances which are significantly different at the 0.05 level in the analysis of variance are connected by underlining.

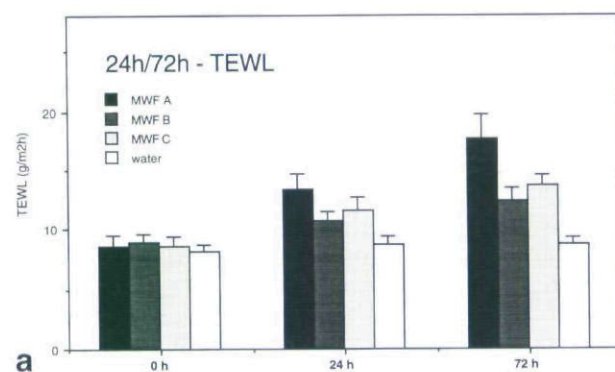
tween control and MWF C at D1 and D5, respectively. After 3 days of exposure, we observed a further increase of TEWL, which was also significantly higher than test sites treated with water.

Similar findings were observed in test 2: MWF A scored higher than the others with nearly the same increase in both test models.

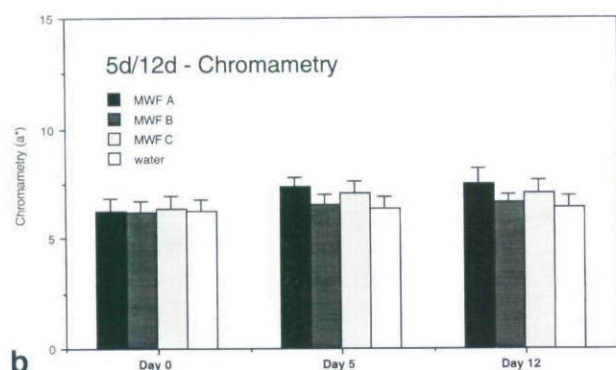
The ranking for the test substances at D1 and



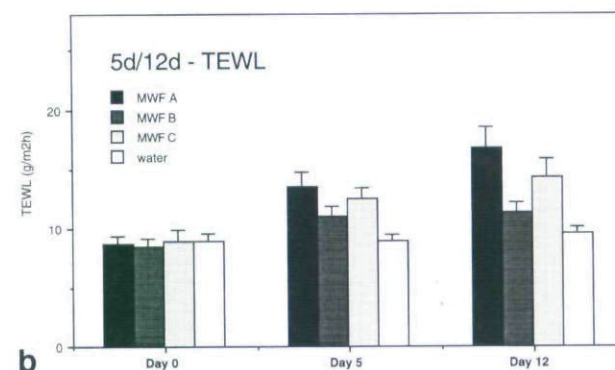
a



a



b



b

Fig. 2. The effect of different MWF on chromametry. Results are given as mean $\pm$ SEM. The following irritancy ranking of test substances is seen in both test models: MWF A > MWF C > MWF B > water.

Fig. 3. The effect of different MWF on transepidermal water loss (TEWL). Results are given as mean $\pm$ SEM. The following irritancy ranking of test substances is seen in both test models: MWF A > MWF C > MWF B > water.

D3 was MWF A>MWF C>MWF B for the VS, the TEWL and the chromametry values. We found the same ranking for the test substances in test 2. However, the analysis of variance showed a better differentiation of the substances over the 3 day study period, i.e., more significant differences were observed at the 0.05 level (Table 2).

A comparison of unused MWF and those out of the machining process in test 2 is summarized in Table 3. We observed significant differences between MWF A and A* only. The values of the unused MWF (A) in TEWL by D12 ($p \leq 0.05$) and in the chromametry by D5 and D12 ($p \leq 0.01$) were significantly higher than those of MWF A*. As shown in Fig. 4, all MWF caused more barrier disruption than application of water, but the potential of irritancy was higher for SLS 0.1%.

Discussion

In spite of the irritant potential of MWF, predictive skin risk testing is done only sporadically and in different ways, by MWF suppliers (22). Some Swiss suppliers of MWF products do not perform any sensitization testing nor any cumulative irritation testing before marketing new MWF, and if so only a part of the products are tested (22). Although, in recent studies, the irritant effect of MWF has been examined quantitatively by non-invasive measuring methods (14–17, 23–25), no standard procedures exist for predictive skin irri-

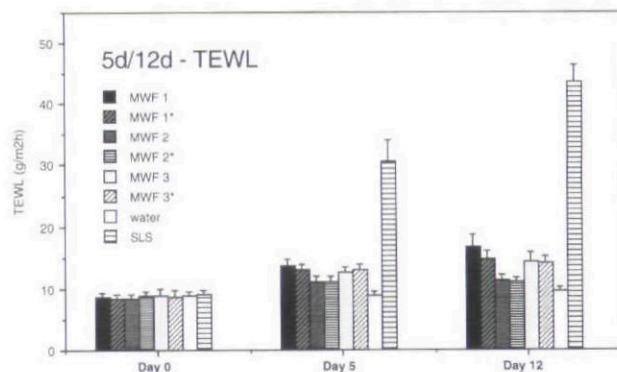


Fig. 4. The effect of unused and used (*) MWF, water and SLS 0.1% on transepidermal water loss (TEWL). Results are given as mean $\pm$ SEM.

tancy testing of MWF so far. De Boer et al. (16) showed that MWF are generally only mildly irritant in their test procedure. In the test model of Hüner et al. (17), 2 out of 3 MWF caused a significant increase in TEWL after a 1 day occlusive application and after cumulative exposure.

In the present study, we observed in both test models an increase in VS, TEWL, and chromametry for all MWF tested, compared with water used as control. The same irritancy ranking of the substances was detected in both tests. Our experimental results partially correlate with the data of PROMETES. Workers who were exposed to MWF A, which showed the highest increase in VS, TEWL and chromametry in both tests, developed ICD more often than those exposed to MWF B and MWF C, though the exposure to MWF C was the highest. In both test models, the ranking between the MWF with no development of ICD in workshop (C) and the MWF with 12% of ICD (B) was in reverse order to the epidemiological data.

A reason for this finding could be that physical and chemical confounders, like the extent of MWF exposure and microtrauma, and the use of after-work emollients or machine cleaning chemicals in the factories, may influence the outcome even if the irritancy potential of the MWFs is low. The exposure to irritants such as MWFs and cleaning agents was higher in the workshop that used MWF C (Table 1).

In spite of the results in our test, the measurements in PROMETES showed more skin changes in the workshop that used MWF B. Still, a coarse classification of MWF seems to be possible using the predictive tests shown, while the assessment of mildly irritating products remains problematic.

As in the studies of De Boer et al. (16) and Hüner et al. (17), modified patch tests were used. It may be questioned if cumulative irritation is better predicted by a modified patch test than by a more

Table 3. Discriminative power of the visual score, transepidermal water loss (TEWL), and chromametry in new and used MWF.

		MWF 1		MWF 2		MWF 3	
		new	used	new	used	new	used
VS	mean	0.46	0.46	0.20	0.20	0.27	0.27
	SEM	0.13	0.13	0.10	0.13	0.12	0.12
D5	sign.	ns		ns		ns	
	mean	1.06	1.06	0.47	0.47	0.60	0.73
D12	SEM	0.18	0.15	0.13	0.13	0.16	0.15
	sign.	ns		ns		ns	
TEWL	mean	13.56	12.91	11.02	11.05	12.53	12.97
	SEM	1.24	1.04	0.86	0.78	0.94	0.90
D5	sign.	ns		ns		ns	
	mean	16.77	14.73	11.35	11.05	14.34	14.02
D12	SEM	1.79	1.21	0.86	0.71	1.49	1.18
	sign.	*		ns		ns	
CHR	mean	7.37	6.59	6.54	6.60	7.06	7.01
	SEM	0.43	0.50	0.46	0.50	0.56	0.50
D5	sign.	**		ns		ns	
	mean	7.49	6.61	6.66	6.57	7.07	6.87
D12	SEM	0.69	0.54	0.39	0.37	0.60	0.52
	sign.	**		ns		ns	

Significances of differences are marked as follows: * $p \leq 0.05$,

** $p \leq 0.01$, *** $p \leq 0.001$, ns = not significant.

realistic type of test. Hannuksela and Hannuksela (26) showed that chamber test results predicted poorly the result of an open wash test. Since they did not investigate product irritancy, but differences in irritability between application procedures and atotics versus non-atotics, their results do not contribute to our problem. Although in our investigation the 2 week exposure with repetitive and cumulative contact with MWF seems to be nearer to real-life exposure than the short time model, the analysis of variance (one-way) showed a better differentiation of the MWF in the single D1 patch test with repeated application to D3 in VS, TEWL and chromametry than the other model. Considering the shorter application time and the better discrimination of irritancy, we prefer the 1st model as a routine procedure for the predictive testing of MWF irritancy and propose the visual score and the TEWL for measurements, since chromametry adds objectivity and quantification, but no new information in addition to the VS.

Water-soluble MWFs are emulsions, which are usually supplied to factories as concentrates to be diluted with water. They are complicated mixtures and act like alkalies. Several components of MWF may be irritants (2). Considering a possible increased strength of MWF in use by evaporation of water, we expected differences in irritancy between unused and used MWF.

During the machining process, the fluid may become more concentrated and some components may reach an irritant concentration or the pH may rise which leads to further irritancy of the fluid (2, 27). Microtrauma from metal chips in the fluid may increase the barrier disruption. The proneness to bacterial contamination is very important for medical and economic reasons. Bacteria are known to cause problems of odour, emulsion breakdown, and metal corrosion due to a decreased pH (28, 29). We were surprised that only fresh MWF A was significantly different to MWF A* regarding irritancy. The values for fresh MWF B and MWF C did not differ from the MWF in use. One reason for our results may be that mechanical trauma from metal chips, as happens in the practical use situation, did not play an important rôle in these patch tests.

Rycroft (28) showed that there is no support for the hypothesis that the indigenous microflora of soluble oil emulsions directly contributes to dermatitis. While metabolic products of bacteria in MWF may act as primary irritants or contact sensitizers (28), there was no indication for this finding in our test. Regarding the irritancy due to alkalinity the differences between MWF A and MWF A* could be explainable.

Random samples we took in one of the partici-

pating factories showed a continuous decrease of pH. In use, the alkalinity decreased from pH 8.95 to pH 8.20 after 2 months and resulted in a pH of 7.89 after 6 months. However, the relevance of a decreased pH alone for the test reactions we observed is less certain. We conclude that in contrast to allergy patch testing, new products should be used for MWF irritancy testing.

The prognosis of contact dermatitis in metal workers is variable (29–32). Because of their high-risk workplace, primary and secondary measures in irritant contact dermatitis are necessary. The efficacy of skin care products to protect from MWF irritation still remains speculative; they even may aggravate skin irritation (23–25). Gloves as an alternative preventive measure carry the risk of accidents. Therefore, the substitution of noxious products by less aggressive MWF is an important measure to reduce the incidence of ICD in metal workers. The selection of MWF based on a standardized predictive methodology for irritant potential is desirable, to help reduce the development of chronic irritant contact dermatitis in exposed workers.

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