

Relevance of multiparametric skin bioengineering in a prospectively-followed cohort of junior hairdressers

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There is conflicting evidence concerning predictors of individual susceptibility to develop irritant contact dermatitis in wet work. A cohort of initially 92 hairdresser apprentices was prospectively followed for 3 years. The association between anamnestic and clinical findings, and multiparametric skin bioengineering data (transepidermal water loss [TEWL], microcirculation, capacitance, pH, sebum, temperature) was investigated. The observation intervals were 3 months in the 1st year of training and 12 months thereafter. Of the 92 apprentices, 6 had already developed hand dermatitis on 1st examination, 20 dropped out or had occupational exposure longer than 7 weeks prior to investigation. Of the remaining 66 participants considered here, 19 (29%) developed moderate or severe dermatitis ("cases"), 32 minimal skin changes, 15 none within the observation period. Average incidence rate of hand dermatitis was 21.1 cases per 100 person years. Atopy score was not associated with the development of dermatitis, nor were the investigated basal bioengineering parameters, including TEWL, in a multivariable model. However, there was a significant increase in TEWL within the 1st year of training in presumptive "cases". The aim to develop an objective and predictive instrumentary for pre-employment counselling in wet work, by a combination of (a) clinical and (b) relevant non-invasive bioengineering parameters, has not yet been accomplished. Skin-provocation tests employing bioengineering seem to be required. Notwithstanding, work-related monitoring of basal biophysical skin-functions may become useful in the secondary prevention of occupational dermatitis.

Key words: skin bioengineering methods; occupational contact dermatitis; predictors; transepidermal water loss; hairdressers. © Munksgaard, 2000.

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Irritant contact dermatitis is a considerable hazard in wet work occupations, particularly in the hairdressing trade. It is usually the result of a complex disease process with a multifactorial pathogenesis, to which constitutional as well as exogenous factors may contribute. There is conflicting evidence as to predisposing factors for individual susceptibility to develop contact dermatitis. Many studies have claimed that pre-exposure non-invasive cutaneous bioengineering, especially transepidermal water loss (TEWL) as an indicator of epidermal barrier function, can discriminate between hyper-reactivity and normal skin reactivity (1–3). However, there was also doubt (4, 5). In an epidemiologic study in the Singapore metal industry, pre-employment measurement of baseline TEWL (dorsal hands) was considered predictive for the devel-

opment of contact dermatitis in wet work (6). However, conditions of measurements were poorly standardized. A later study, performed by the same group, in nurses and hairdressers, did not reproduce the results (7), though in hairdressers, an increased incidence rate above a certain TEWL threshold ($>15 \text{ g/m}^2 \text{ h}$) was suspected, but relative risk of elevated TEWL could not be demonstrated to be statistically significant. Again, the very sensitive measurements could not be performed under completely standardized circumstances, according to the guidelines (8), and only 1 biophysical parameter (TEWL) was investigated.

To determine the prospective value of baseline skin bioengineering conclusively, we designed a prospective cohort study in a high-risk occupation, measuring a combination of biophysical par-

ameters (transepidermal water loss [TEWL], microcirculation [LDF], pH, sebum, temperature) under standardized circumstances in an air-conditioned laboratory. Furthermore, anamnestic and clinical parameters, including those relevant for the Erlangen atopy score (9), were obtained. The aim of the study was to identify individuals at risk by combining relevant non-invasive bioengineering data and clinical findings, in order to proceed further to an objective screening tool for effective pre-employment counselling in wet work.

Materials and Methods

Study design

A cohort of all 92 hairdresser apprentices from the Osnabrück vocational training school was prospectively followed for a full educational cycle (3 years, 1992–1995), after informed consent was obtained. The response was 100%. The study was approved by the Ethical Committee of the University of Osnabrück. The 1st examination took place after the official start of training in August 1992. Strict pre-employment investigation was not possible for logistical reasons; some trainees had already been working prior to official enrollment in vocational training. Of the 92 apprentices, 6 already had hand dermatitis on 1st examination, 20 dropped out or had started work longer than 48 days prior to investigation and were also excluded; for 86% of the remaining 66 participants, 1st examination took place within 20 days of 1st professional exposure. The observation intervals were 3 months in the 1st year of training, and 12 months thereafter (Fig. 1). Within the 1st year of training, the investigations took place in the Dermatology Department of the University of Osnabrück, where clinical examination and cutaneous bioengineering were conducted. In the 2nd and 3rd year

of training only clinical examinations were performed. Dropout follow-up was performed by telephone interviews.

Clinical investigation

History-taking and examination were performed by physicians in specialist training for occupational dermatology or dermatologists.

(1) On the 1st investigation, the complete dermatological history was taken, using a questionnaire. Emphasis was laid on atopy criteria, history of flexural eczema, past hand eczema, allergic rhinitis or asthma. Permission was obtained to inquire from local dermatologists whether pre-employment consultations or testing had occurred (consent was always given; involved local dermatologists then were very cooperative concerning details). Furthermore, leisure activities, main tasks at work and protection habits were recorded.

(2) A physical examination of the skin was performed, including hands, forearms, flexures, thighs (for keratosis pilaris) and specific areas of interest according to the history. Dermographism was routinely tested for on the upper back. The physical findings were documented in a standardized form.

(3) On the consecutive examinations, mainly the hands and forearms were investigated clinically, unless symptoms were reported elsewhere. Prior to this, the history since the last examination was taken (skin symptoms, skin tests, sick-leave, physicians involved, etc.) and recent leisure activities, main tasks at work and protection habits were recorded.

Bioengineering

The investigations took place in the air-conditioned laboratory of the Dermatology Department at steady-state conditions (ambient temperature 20–21°C, rel. humidity 40–45%). Participants were requested not to use soap or creams/emollients in the areas of investigation 24 h prior to each examination. Measurements were made after at least 15 min of acclimatization of the participants and, if existing, according to the guidelines of the standardization group of the European Society of Contact Dermatitis (8 (10, though published after the measurements)). Measurements were performed only in clinically healthy skin. The following baseline bioengineering parameters were obtained: transepidermal water loss (TEWL), capacitance (RSM=relative skin moisture), microcirculation (LDF=laser Doppler flow), pH, sebum, temperature (Table 1). Measurements were made at 6 locations: R/L volar forearm 17 cm from wrist, R/L center of dorsum of hand, R/L palm

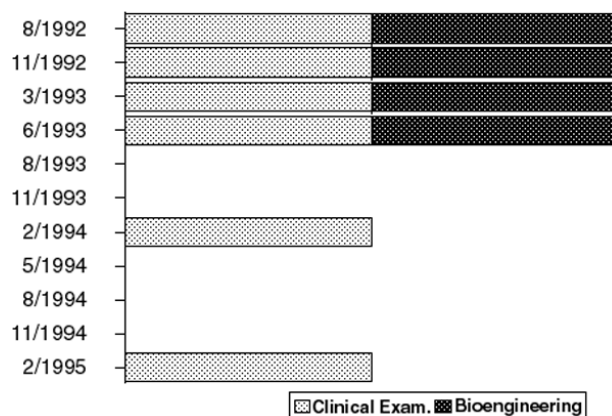


Fig. 1. Schedule of prospective cohort study in apprentice hairdressers ($n=66$).

Table 1. Bioengineering methods employed, measurements were performed after a minimum 15 min acclimatization period in an air-conditioned laboratory (20–21°C, 40–45% RH)

Procedure	Parameter	Units	Device
evaporimetry	transepidermal water loss (baseline) (TEWL)	g/m ² h	EP 1, Servo Med, Sweden
laser Doppler flowmetry (LDF)	dermal microcirculation	arbitr.	Periflux PF3, Perimed, Sweden
thermometry	temperature (IR radiation)	°C	Thermophil system M 220, Ultracust, Germany
capacitance	rel. skin moisture (RSM)	arbitr.	Corneometer C 820, Courage & Khazaka, Germany
acidimetry	pH	–	pH meter 611, Orion Research, MA, USA
sebumetry	superficial sebum	g/cm ²	Sebumeter SM 810, Courage & Khazaka, Germany

(thenar). TEWL was measured in a perspex incubator using the ServoMed gold-plated protection cover (steel grid) and a rubber stopper as an insulating probeholder; for LDF, the Perimed adhesive probeholder was used; capacitance was measured in triplicate, the median was then taken as the RSM value.

Meteorologic data

Meteorologic data on ambient temperature (T) and relative humidity (RH) on the days of examination were obtained from the German Meteorological Service (DWD; Deutscher Wetterdienst), Department of Medical Meteorology, Freiburg, Germany. There is a local DWD weather station in Osnabrück. Daily mean values, received from this local weather station, were considered adequate. Absolute humidity (AH) was calculated from T and RH according to Uter (11).

Relevant variables and statistical analyses

Operational definitions for atopic skin changes and signs were previously outlined (12), and were used for calculation of the atopy score according to Diepgen (9). For skin changes of the hands, operational definitions were based on 11 morphology/spread and 6 site/severity categories with a 4-point ordinal scale each, which was published in detail elsewhere (12). For statistical analysis, the case definition was modelled in a 3-point ordinal scale (“no”, “minimal”, “moderate or severe” skin changes). Actual dermatitis occurred only in the 3rd group; for this at least 1 morphology or site had to be registered as “moderate” or “severe” (e.g., erythema, erosions, fissures, exudation, etc). The “minimal” category comprised only occasional mild scaling or limited slight erythema without other symptoms (12). If at any stage of the investigation a participant on medical investigation

had moderate or severe skin changes he was identified a “case” of hand dermatitis.

For the calculation of incidence rates, expressed as the amount of new cases per 100 person years, observation time was accumulated from the date of 1st investigation to the date of last (medical) follow-up investigation or until the occurrence of at least moderate skin changes, i.e., when becoming a “case”. If a participant did not attend at the scheduled date of follow-up-investigation, he would be represented in the calculations only till the last investigation which he did attend.

For work-related monitoring in the “case” group, the 1st measurement (e.g. TEWL₁) was compared to the last measurement in the same body area before developing skin changes (e.g. TEWL_X); in non-diseased participants, the 1st and the last bioengineering measurements were taken. % difference (pTWL, pRSM, pLDF, p-pH, pTemp, pSeb) was then calculated in comparison to the 1st measurement (e.g., pTEWL = [(TEWL_X–TEWL₁) / TEWL₁] *100).

Besides descriptive statistical analysis, data evaluation focussed on the estimation of predictors associated with the later development of hand eczema. The unadjusted predictive value of various bioengineering parameters for the outcome was estimated using bivariate 2-tailed non-parametric tests (Mann-Whitney-*U* or Kruskal-Wallis). In a consecutive multiple logistic regression analysis, those variables were included in a parsimonious model that are commonly believed most relevant. For this latter analysis, the subgroups with no skin changes and with minimal skin changes were amalgamated (“non-diseased”) and compared with the remaining subgroup with moderate or severe skin changes (“cases”). Odds ratios (OR) and approximate 95% confidence intervals were calculated.

Correlations between the various bioengineering parameters were calculated using the 2-tailed Spearman rank correlation test.

For statistical analyses, the statistical software

package SAS (version 6.12, SAS Institute Inc. Cary, NC, USA) was employed.

Results

Cohort

Of the 92 junior apprentices, 6 already presented with hand dermatitis at the 1st examination and were excluded from the study, 20 dropped out after the 1st investigation or were already occupationally exposed for longer than 48 days (7 weeks) prior to investigation and were also excluded. Of the remaining 66 participants, 19 (29%) developed moderate ($n=11$) or severe ($n=8$) occupational dermatitis ("cases"), 32 (49%) developed minimal skin changes, and 15 (23%) apprentices no skin changes within the observation period.

In the "cases" group, 11 hairdressers ($n=3$ formerly severe dermatitis) were still working by the end of the study. Of these participants, 2 (formerly moderate dermatitis) had no skin changes on final examination, 4 had only minimal residues. 6 "cases" had left the occupation because of derma-

titis, and 2 for other reasons. The main characteristics of the cohort are summarized in Table 2.

Incidence rates

Overall incidence rate of hand dermatitis was 21.1 cases per 100 person-years. Considering only the 1st year of training, with extreme wet-work exposure due to activities like shampooing up to $50 \times$ daily, the incidence rate was 31.7 cases per 100 person-years. Incidence rates were not significantly different in participants with elevated "pre-exposure" transepidermal water loss (Table 3).

Anamnestic and clinical parameters

A past history of flexural eczema contributes significantly to the risk of developing dermatitis; past hand dermatitis showed an odds ratio of 4.9, which was not significant (Table 4). Interestingly, the 6 participants (9.1% of study population) with past flexural eczema and the 4 participants with past hand dermatitis (6.1% of study population)

Table 2. Characteristics of the cohort on 1st examination; the bioengineering parameters included in the table are the results of the "pre-exposure" measurements; where applicable, the 25% and 75% percentiles are represented

Parameter	<i>n</i>	(%)	Median	25%–75% percentile
age	66		17.1	16.4–18.3
female	64	97		
male	2	3		
past flexural eczema	6	9.1		
past hand eczema	4	6.1		
allergic rhinitis	5	7.5		
atopy score	66	100	6	3.0–9.5
TEWL forearm R			5.0	4.0–7.0
TEWL dors. hand R			8.5	6.0–10.0
temp. forearm R			31.6	30.7–32.0
temp. dors. hand R			30.1	28.9–31.6
RSM forearm R			68.5	61.0–73.0
RSM dors. hand R			75.0	70.0–84.0
LDF forearm R			6.8	5.0–9.0
LDF dors. hand R			7.4	5.4–10.0
pH dors. hand R	65	99	5.1	4.7–5.3
sebum dors. hand R	46	70	1.0	1.0–2.0

Table 3. Incidence rates of hand dermatitis; incidence rates were not influenced significantly in individuals with raised "pre-exposure" transepidermal water loss

Parameter	Cases	Incidence rate: cases per 100 person-years
1st year	14	31.71
2nd and 3rd year	5	8.70
overall	19	21.10
TEWL on 1st examination (split by median)		
back of left hand	TEWL <median	12
(median=9 g/m ² h)	TEWL ≥median	7
left forearm	TEWL <median	6
(median=6 g/m ² h)	TEWL ≥median	13

Table 4. Odds ratios for hand dermatitis (ever) in a multivariable model (*asterisk*= $p<0.05$). For bioengineering variables the “pre-exposure” values were used for the calculations

Parameter	<i>n</i>	Odds ratio	Confidence limits
past flexural eczema	6	22.51*	2.90–481.47
past hand eczema	4	4.88	0.52–56.65
TEWL forearm R	66	0.61	0.15–2.38
TEWL dorsum hand R	66	0.49	0.13–1.72
RSM dorsum hand R	66	0.55	0.15–1.85

were not, even partially, identical. They were all free of acute symptoms when initially examined.

A number of anamnestic and clinical features documented in the 1st investigation were summarized in the atopy score according to Diepgen (9). If tested versus the outcome (dermatitis/no dermatitis), there were no significant differences in the distribution of the atopy score in these 2 outcome groups ($p=0.09$). If atopy score was tested versus past flexural eczema, again there were no significant differences in the distribution ($p=0.12$).

Bioengineering parameters

The basal bioengineering parameters correlate significantly in right/left comparison in all 3 body areas investigated. Furthermore, different parameters that measure a common feature like blood perfusion (LDF and skin temperature) show significant correlations. However, there was no significant association between any of the basal bioengineering parameters investigated and the outcome ($p>0.05$) (for distribution see Fig. 2). The same holds true if analysed in a multivariable model, including the 2 commonly-believed most relevant factors (TEWL of forearm and of dorsum of hand): bioengineering variables had no significant effect on the model (Table 4). The Lemeshow and Hosmer goodness-of-fit test was $p=0.93$ (13).

We could also detect no significant association between any of the bioengineering parameters investigated and the atopy score. Furthermore, persons with past flexural or hand eczema did not show any significantly different distribution of basal bioengineering parameters.

Meteorological influences

Local meteorologic data (mean relative and absolute humidity, ambient temperature) at the time of the examinations were correlated with the bioengineering parameters, including TEWL and RSM; however, there was no consistent correlation. We could not detect seasonal variations in the various bioengineering parameters during a comparatively mild winter in the period of the measurements (ab-

solute humidity on the days of investigation even in winter (November 1992 and March 1993) stayed well above 9 ml/l; mean for last investigation was 15 ml/l).

Work-related monitoring

For work-related monitoring in the “cases” group, the 1st measurement was compared to the last

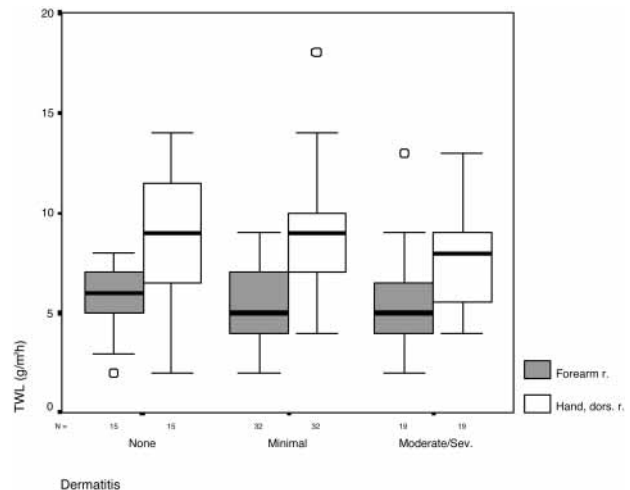


Fig. 2. Box plot of “pre-employment” TEWL (1st examination) in the 3 outcome groups (development of dermatitis). Horizontal line in box: median; upper and lower border of box: 25 versus 75% percentile. No significant differences in the 3 outcome groups, neither for the hand nor for the forearm measurements ($p=0.15$ [hand]; $p=0.53$ [forearm]; Kruskal-Wallis test). ○=outliers.

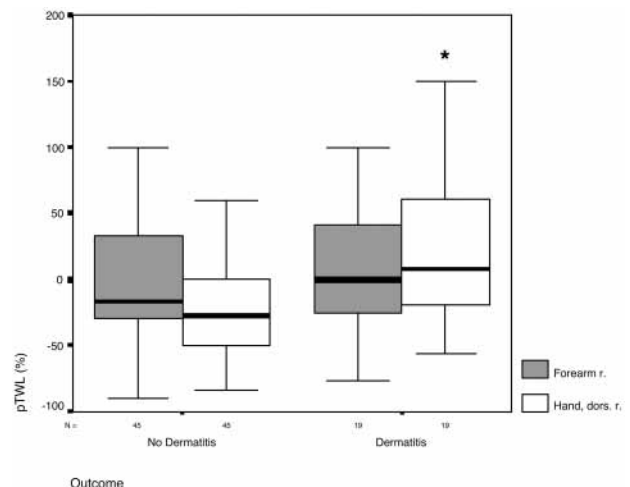


Fig. 3. Box plot comparing TEWL at the 1st and last eligible investigation in a primarily exposed (dorsum of right hand) and a less exposed area (right forearm). On the *dorsum* of the right hand the % difference (pTEWL) was significant ($p=0.03$; *asterisk*). The same applies for the comparison of the *left* forearm and the *left* dorsum of hand: only on the *dorsum* of the left hand was there a significant % difference in the 2 groups (“dermatitis” versus “no dermatitis”), reflecting subclinical changes before a person develops clinically detectable hand dermatitis.

measurement in the same body area before the individual developed clinically detectable dermatitis. If the dynamics of bioengineering measurements in the various examinations are being analysed in the group of presumptive "cases", a significant % increase in TEWL only in the occupationally primarily exposed areas (dorsum of hands; $p=0.03^*$ [R], $p=0.01^*$ [L]) was detected, whereas the much less exposed areas (volar forearms; $p=0.47$ [R], $p=0.23$ [L]) did not show any significant differences from the "non-diseased" (Fig. 3). The fact that the median % difference (pTEWL, s. Fig. 3) was negative reflects the fact that TEWL values on last measurement were frequently lower than on 1st measurement. The remaining bioengineering parameters (pRSM, pLDF, p-pH, pTemp, pSeb), analysed in the same fashion, did not reveal significant differences in the 2 outcome groups ("cases" versus "non-diseased").

Discussion

Morbidity

In this study, we have observed considerable morbidity among junior hairdressers, the cumulative incidence of dermatitis being 29%. These figures are similar to a cohort of 74 hairdresser apprentices recently studied in Holland (7). The latter is the only epidemiological study in which a biophysical parameter (TEWL) was studied in hairdressers. Obviously, for epidemiological parameters, clinical case definition is crucial; the authors have used a comparatively restrictive case definition. Average incidence rate was higher (32.8 per 100 person-years) in the Dutch study, but then, the observation period was only 1 year. If, in our study, we calculate the incidence rate only for the 1st year, it is 31.7 per 100 person-years. This is due to the initially extreme wet work exposure in the trade (14).

For socio-economic reasons, a considerable proportion (58%) of apprentices remained at work in spite of (mostly moderate) dermatitis. In 6 cases, dermatitis improved by the end of the observation period, which may partly be attributed to hardening (15), or increased awareness of disease resulting in improved protection. Furthermore, wet exposure decreases in later stages of training compared to the 1st year, because with increasing skill more dry tasks are performed (14).

Concerning clinical predictors in this study, only past flexural eczema was a significant risk factor in a multivariable model, whereas the atopy score (12) was not associated with increased susceptibility to develop dermatitis. In the metal industry, Elsner et al. (10) recently could not identify the atopy score as an indicator in 205 male workers.

Obviously, in our study, the comparatively small study size has to be taken into consideration, as well as the fact that 6 participants were excluded due to hand dermatitis, which had already developed within the comparatively short interval of occupational exposure before our investigation took place. One of these participants had a history of childhood hand eczema, no participant had current or past atopic dermatitis. Obviously, a selective drop-out of persons with presumable constitutional risk ("healthy worker-effect") would hamper the evaluation of potential associations. After the beginning of this investigation, the POSH study, comprising 2352 prospectively-followed hairdresser apprentices in 15 vocational training schools in Northern Germany was started, focussing on clinical phenomena. Clinical data from the present study were integrated in the framework of the POSH study. The relevance of clinical parameters for the development of hand dermatitis in hairdresser apprentices is presented in detail elsewhere (14, 17). In this large cohort, an atopy score greater than 7 was associated with a marginally increased relative risk ever to develop hand dermatitis (14).

Seasonal influences

Previous studies have demonstrated seasonal influences on the incidence of irritant contact dermatitis (18), and low absolute ambient humidity in winter has recently been identified as a relevant additional risk factor in wet work (11). Skin bioengineering studies mostly report an increased reactivity to irritants in winter (19); the effect, however, is generally not considered large. In our study, we did not use irritation tests; basal biophysical parameters (incl. TEWL, RSM) were not influenced by seasonal factors. This is likely due to relatively mild ambient conditions in November 1992 and March 1993, as documented by the local meteorological data, which we included in the study, and the fact that measurements were performed at steady state in an air-conditioned laboratory.

Bioengineering as a predictor

There was abundant evidence from past laboratory investigations indicating a predictive value of 1 or more biophysical parameters, like TEWL, pH, RSM, LDF (1-3, 5, 19). However, other authors have found only a poor or no correlation between pre- and post-exposure TEWL (4, 5). Prospective epidemiologic studies are the most valid study design to answer the question. In an epidemiologic study in the Singapore metal industry, pre-employment measurements of baseline TEWL (dorsal

hands) were considered predictive for the development of contact dermatitis in wet work (6). However, conditions of measurements were poorly standardized. A later study, performed by the same group, in nurses and hairdressers did not reproduce the results (7), though in hairdressers, an increased incidence rate above a basal TEWL > 15 g/m² h was observed, but relative risk was not significantly raised. Again, the very sensitive measurements could not be performed under completely standardized circumstances according to the guidelines (8) and only 1 parameter (TEWL) was investigated. In our study, for the 1st time, a combination of biophysical parameters under fully standardized circumstances were measured in an epidemiological setting. However, our results do not support the hypothesis that an increased basal trans-epidermal water loss or other basal biophysical parameters, not even in combination, indicate an elevated risk for developing dermatitis. Our findings are consistent with the above-mentioned Dutch study (7), though the incidence rate in our study did not show any significant variation in groups of different basal TEWL.

Due to the high incidence of dermatitis, the study should have had the power to detect relevant effects – had there been any. Criticism could be directed at the interval between the beginning of work exposure and 1st examination. For logistical reasons, it was not possible to carry out a strict pre-exposure investigation; on careful examination, it turned out that most of the participants had previously been involved in occasional or regular hairdressing activities. In 86% of the 66 participants, this was not more than 20 days; if it turned out to be more than 48 days, apprentices were not admitted to the study. Undoubtedly, an initial exposure phase has effects on the biophysical skin properties. However, this effect could be interpreted as a kind of work-induced provocation test. Thus, differences in skin irritability should become detectable even more easily. That this is not only a theoretical thought, can be proven by the fact that, on repetitive measuring over a sustained observation period, we could distinguish between “cases” and “non-diseased” on the basis of biophysical data. This finding indirectly advocates skin provocation tests for prediction of irritant susceptibility.

Laboratory investigations previously claimed to distinguish atopics from non-atopics by means of base-line bioengineering (5, 20). In the present study, we could not detect a correlation between basal bioengineering parameters and clinical parameters such as atopy score or flexural eczema. Thus, if we consider at least the latter participants atopics, we cannot by means of basal non-invasive

bioengineering techniques discriminate between atopics and non-atopics, nor can we detect other constitutional risk factors (“skin sensitivity”, if independent from atopy). These findings are in agreement with the results of a recently performed epidemiologic study in 205 Swiss metal workers, where neither constitutional factors nor outcome were associated with basal biophysical parameters (16, 21). We will therefore have to close the chapter concerning the predictive value of pre-exposure base-line bioengineering. Provocation tests seem to be required and legitimized. Most recently, it has been shown, that in field studies, a combination of various irritation tests employing bioengineering provides a certain predictive sensitivity, though still lacking specificity (21). Further epidemiological evidence is needed, because an objective, standardized and reproducible screening procedure for pre-employment counselling in wet work is not yet available.

Work-related monitoring

Several authors (22, 23) have claimed that the repetitive measurement of TEWL at selected exposed areas (dorsum of hand) may be important for early detection of subclinical skin irritation, wet work thus acting as a continuous moderate irritation test. This could also be demonstrated in our study comparing primarily-exposed (hands) and much less exposed skin areas (forearms); the effect was shown to be symmetrical. The fact that the median % difference was negative (Fig. 3) reflects the phenomenon that TEWL values on last measurement were frequently lower than on 1st measurement. As we could exclude seasonal influences, this might be explained by a latent hardening process (15), more pronounced in the mainly exposed areas (dorsum of hands), and to a certain extent also in the much less exposed volar forearms.

Interestingly, only TEWL turned out to be predictive (no relevance of RSM, LDF, temperature, pH, sebum). Thus, work-related monitoring of only this parameter (TEWL) may be useful for secondary prevention of occupational dermatitis.

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