

Predictive washing test for evaluation of individual eczema risk

W. GEHRING¹, M. GLOOR¹ AND P. KLEESZ²

¹Dermatological Clinic of the Municipal Clinics Karlsruhe, Germany

²Research Center of Berufsgenossenschaft Nahrungsmittel und Gaststätten, Germany

It was the aim of our studies to estimate predictively the individual eczema risk for persons due to repetitive contact with washing-active substances, by a barrier function test on clinically healthy skin over 2 weeks. Within the scope of the study 3 groups with different atopy scores were compared. As washing solutions, 0.1 m SLS and a slightly acid soap-free washing emulsion were used in comparison to tap water. Prior to the 1st washing procedure, on days 3, 5, 8, 10, and 12, the transepidermal water loss, the horny layer moisture, and the skin blood flow were measured as parameters of barrier function, as well as the inflammatory reaction. The results prove that the atopy score has only limited validity as a predictive method for the acceptance of washing-active substances. The repetitive washing test, however, seems to be more adequate for evaluating the individual barrier function as well as the eczema risk. Irritation by a washing procedure may be greatly influenced by choice of the washing solution.

Key words: repetitive washing test; atopy score; eczema risk; irritant contact dermatitis; sodium lauryl sulfate; prevention; individual variability; individual susceptibility; bioengineering methods.
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Any washing procedure may lead to a disturbance of the barrier function, which can be documented as an increase in transepidermal water loss (TEWL) and as a reduction in horny layer moisture (1). Repetitive washings result in a cumulative irritant effect (2) that leads, differing individually, to an irritant (toxic) contact dermatitis, which itself favors a later allergic contact dermatitis (3). Clinical experience shows the wide array of variation for the development of an irritant contact dermatitis, because not everybody working in a humid environment actually develops the disease. It was the aim of our studies to evaluate predictively the individual eczema risk by application of a barrier function test in healthy skin, based on repetitive washings over a period of 2 weeks. In this study 3 groups with different atopy scores were compared.

Materials and Methods

Groups of test persons

The studies were performed on 3 separate groups, which were defined according to the atopy score. The atopy score is based on a point score of clini-

cal and anamnestic criteria, which allow a conclusion regarding an atopic constitution (4). For allocation to the different groups total IgE was not taken into account.

Group I: atopy score up to 5 points
atopy very unlikely

In this group, 12 women within a range of 25–54 years of age and four men within an age-range of 28–53 years, were included. The average age of the women was 37.2 years while the men's average age was 35.3 years. In the entire group the average age was 36.7 years.

Group II: atopy score 6–10 points
atopy not to be excluded

This group was represented by 14 women, ranging from 20–58 years of age, of an average age of 32.4 years. Also, 1 man of the age of 26 years took part. Total average age was 31.9.

Group III: atopy score greater than 11
atopy very likely

This group comprised 9 females of the age of 20–49 years and one male of the age of 26. The average age of the women was 31 years. Hence, in the entire group an average age of 30.5 years resulted.

All volunteers had been informed precisely about the way the study was to be conducted and had given their expressed agreement to take part. Especially, they were informed that the repetitive washings might lead to skin irritation and that, for this reason, they could quit the study at any time.

Washing solutions

As washing solutions, in comparison to tap water, 0.1 m sodium lauryl sulfate (SLS) and a soap-free washing emulsion at a slightly acid pH* were used. The soap-free washing emulsion was diluted ready-to-use at a 1:8 ratio. Pretests with a dirt paste showed that at a dilution ratio of 1:8 both, the soap-free syndet and 0.1 m SLS had the same washing efficiency. The declaration of the soap-free washing emulsion is given according to INCI in Table 1.

The irritant potential of SLS is dependent on the degree of purity and increases with increasing purity. According to the guidelines on SLS-exposure tests (5), we have used high purity SLS (99%) from Merck (D-64271 Darmstadt, FRG).

Washing procedure

The standardized washings were performed on the volar side of the upper and lower arms. Thus, 4 test areas in total were available. In order to exclude anatomical differences, a rotation of the test areas was done from volunteer to volunteer. 1 area always remained untreated as a control area, 3 test areas were treated as described above.

On the 1st day of the study, the washings were performed in the laboratory guided by the laboratory technicians, and the volunteers were advised how to perform the standardized washings. Using a single-use pipet, 5 ml of water and the 2 tenside solutions were applied to the test areas consecutively, followed by hand movements similar to regular washing movements over 1 min in order to disperse the solutions. Prior to application of each new washing solution, the hands had to be cleaned carefully with pure water. On the following days, the test persons were advised to proceed with the washings according to the advice given by the laboratory technicians on the 1st day. The test persons were strictly advised not to wash beyond the bend of the elbow, in order to prevent the test solutions flowing into each other. The washing procedure was repeated on 12 consecutive days, 5× daily, in the same manner.

* Sebamed® flüssig exclusiv. Sebapharma GmbH & Co. Bingerstr. 80, D-56154 Boppard-Bad Salzig, Germany.

A disadvantage of this procedure was that, due to organizational reasons, the washings could not be performed in a standardized manner within the laboratory over the entire test period. Hence, it cannot clearly be ruled out that irregularities may occur in the use of the washing solutions. For this reason, volunteers had been very carefully selected with regard to likely compliance.

Determination of irritation and barrier function

Prior to the 1st washing procedure, at days 3, 5, 8, 10, and 12, TEWL (6) was determined, as well as horny layer moisture by capacitance measurements (7), while the skin blood-flow situation was monitored using a laser Doppler flowmeter (8). For determination of TEWL, a Tewameter TM 210 (Courage and Khazaka) was applied; for measuring the horny layer moisture, we used a Corneometer CM 820 (Courage and Khazaka), as well as a Periflux Pf2 for laser Doppler flowmetry (LDF).

The TEWL is a very sensitive measuring parameter, which is under the influence of a number of parameters (9). Therefore, our measurements were performed in a partly air-conditioned room, within a measuring box used as draught shield, and after a previous adaptation period for the volunteers of 30 min. Within the scope of the capacitance measurements, it was taken care that the measuring head was always applied to less hairy skin areas (10).

Statistical evaluation

Within each group, the washing solutions were compared against each other, applying the

Table 1. Declaration of the soap-free washing emulsion according to INCI

aqua
sodium laureth-6 carboxylate
decyl polyglucose
disodium laureth sulfosuccinate
potassium cocoyl hydrolyzed collagen
PEG-7 glyceryl cocoate
PEG-120 methyl glucose dioleate
sodium lactate
ethyl linoleate
tocopherol
tocopheryl acetate
squalane
lactic acid
magnesium sulfate
PEG-200 hydrogenated glyceryl palmitate
phenoxyethanol
benzyl alcohol
parfum
sorbic acid
methylparaben
ethylparaben

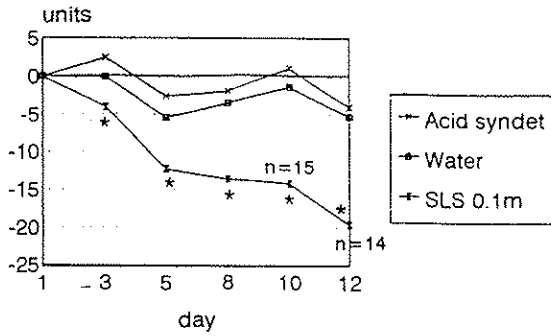
Wilcoxon pair difference test for combined random samples. By application of the Wilcoxon test, a parameter-free procedure is given which is un-critical in terms of data distribution. The groups were compared using the χ^2 test. Calculations were done using the statistics program *PC-Statistik* (Heise/Germany).

Results

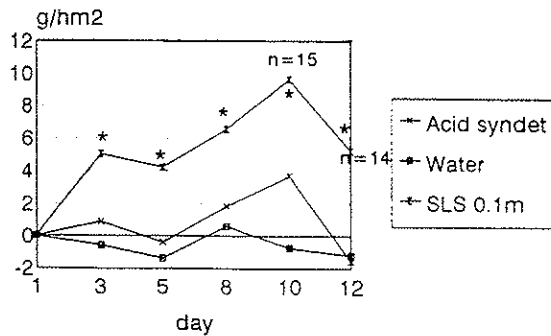
Group I

Over the treatment interval of 12 days, a statistically significant irritation by SLS could be detected, which was documented as an increase in TEWL, a loss of horny layer moisture, as well as

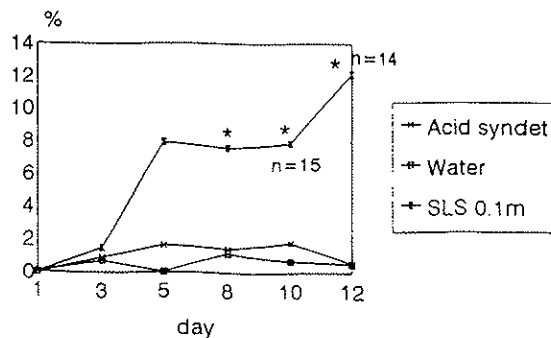
Capacitance measurement



TEWL



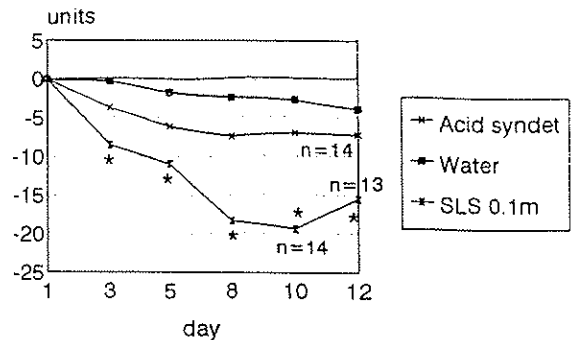
LDF



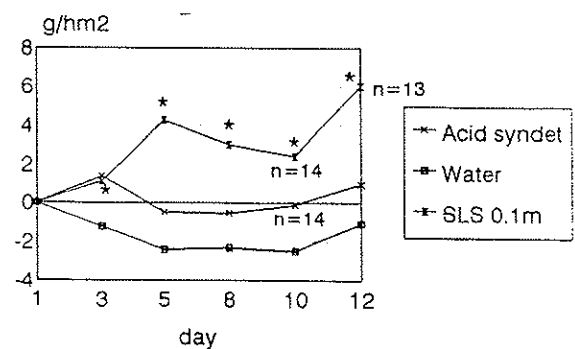
n = 16
* = p<0,01; + = p<0,05

Fig. 1. Repetitive washing in group I (atopy score up to 5 points).

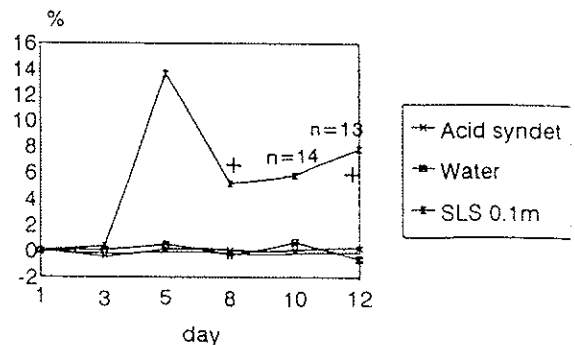
Capacitance measurement



TEWL



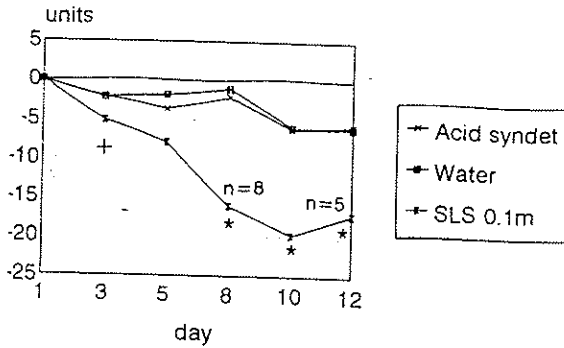
LDF



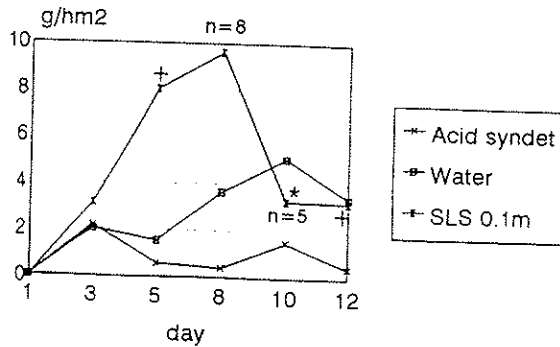
n = 15
* = p<0,01; + = p<0,05

Fig. 2. Repetitive washing in group II (atopy score 6-10 points).

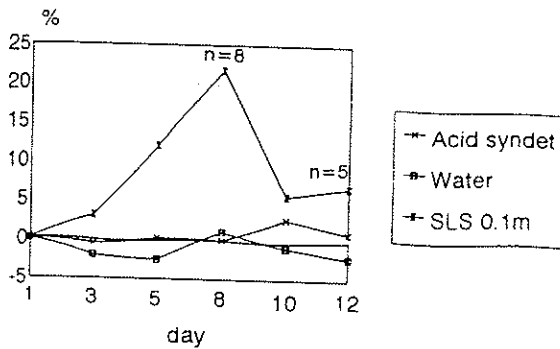
Capacitance measurement



TEWL



LDF



n = 10
* = p < 0,01; + = p < 0,05

Fig. 3. Repetitive washing in group III (atopy score greater than 11 points).

an increase in corial blood flow (Fig. 1). In the entire group, the irritation maximum, monitored via TEWL, was reached on day (D) 10. On D 12, the mean value was lower. This result is an indication of a hardening effect on the washing with SLS. The analysis of the individual courses of

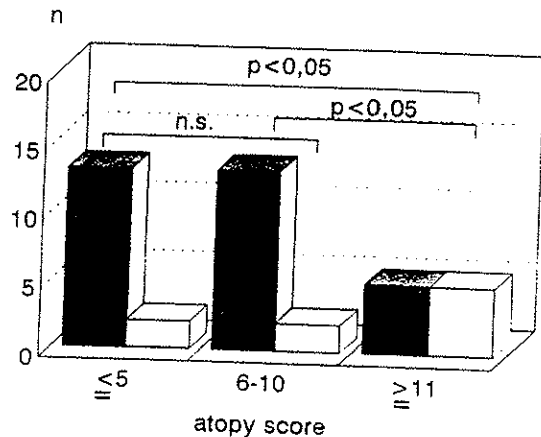
treatment shows that part of the volunteers did not react at all to washing with SLS, and that in the other volunteers, a hardening effect was recognizable at different points in time between D 3 and D 10. 1 volunteer discontinued the washings with SLS due to severe inflammatory reactions on D 10, another volunteer quit on D 12. Washing with water and the soap-free syndet did not lead to a reaction.

A distinct hardening effect was to be seen in 6 volunteers, using the TEWL and LDF. The TEWL rose from 11.77 g/m²h to 25.02 g/m²h (p=0.0284) and dropped again to 13.28 g/m²h (p=0.0153). The same course was confirmed by using the LDF. After an increase from 9.4% to 17.4%, we saw a drop to 11.2 (p=0.0191).

Group II

Comparably to group I, washing with SLS, when compared to water, led to a statistically significant increase in TEWL and to a decrease in horny moisture (Fig. 2). In group II, too, a hardening effect was detectable in 6 test persons upon washing, which was probably best monitored by TEWL. The initial value of 8 g/m²h rose to 17.5 g/m²h (p=0.0091) upon washing with SLS, and dropped to 10.0 g/m²h (p=0.0035). 1 volunteer quit washing with SLS and the acid syndet on D 10; another discontinued washing with SLS just before D 12.

- Repetitive washing with SLS - Experimentally induced eczema according to the atopy score



n.s. = not significant

■ no visible eczema
□ visible eczema

Fig. 4. Comparison of groups.

Group III

Within this group, the reaction to washing with SLS was very varied. $\frac{1}{2}$ of the 10 volunteers quit washing due to severe inflammatory reactions on D 5 or D 8 at the latest. The remaining 5 volunteers tolerated washing with SLS over the entire study interval without showing any reactions (Fig. 3). It should be noted that all volunteers who quit washing with SLS continued washing with water or the acid syndet without any measurable or clinically detectable reaction. No hardening effect was observed within this group.

Comparison of groups

Fig. 4 represents a comparison of eczema risk in the 3 groups. The risk of developing an eczema by repetitive washing with SLS is statistically significantly higher in group 3 (atopy Score >11) than in groups 1 and 2. Group 2 and 1 cannot be distinguished from each other.

Discussion

The repetitive washing study over 12 days using different washing solutions was performed with the aim of gaining information on the individual barrier function of each individual test person, which would enable us to draw conclusions regarding possible individual eczema reactivity. An open washing procedure, as opposed to an occlusive repetitive application of tensides (11), was chosen in order to simulate more realistically the situation in humid working environments.

For our studies, the test persons were separated into 3 groups with respect to their atopy score. In group I, atopy is considered to be very unlikely, in group II, it is not to be ruled out, and in group III, atopy is very likely. When the 3 groups were compared with each other, group III, as expected, showed a higher risk of developing an eczema by repetitive washing with SLS. There was a striking range of variability within the separate groups. Contrary to our expectations, 2 volunteers discontinued washing with SLS even in group I, due to severe eczema reactions. The discrepancy with the expectations in group III is clear. Only $\frac{1}{2}$ of this volunteers' group reacted to washing with SLS by developing eczema in such a way that the test had to be quit. The other $\frac{1}{2}$ continued washing with SLS without any clinical or measurable irritation being detected. By this, the validity of the atopy score is relatively set back as a predictive means for estimating a given eczema risk. This observation does not come as a surprise. Seidenari et al. (12) already referred to the fact that a group of 'atopics' does not

represent a homogenous type. In the course of their studies, they did not find an increased proneness to irritation in cases of respiratory atopy.

Only in 1 case within group II, was washing with the soap-free syndet discontinued. In all other cases, all test persons in the 3 groups tolerated the soap-free syndet without any reactions. Remarkably, all test persons who had quit washing with SLS, continued washing with the acid syndet without any sign of irritation. This observation is especially surprising in group III and proves the possibility of counteracting an irritation by washing-active substances if a suitable cleaning agent is chosen.

Grunewald et al. (13) gave a hint towards repair mechanisms within the epidermal barrier upon washing with SLS. Tupker et al. (14) recognized a hardening effect in single test persons upon irritation with SDS, di-sodium lauryl 3-ethoxysulfosuccinate, and Shellsol K. Our present study confirms the hardening effect in groups I and II. However, great variations in individual expression and in the point of time when it occurred are seen. Within group III, no training effect was noted. Either irritations were seen early on or the washing was tolerated linearly over the entire study period.

Summarizing, we draw the following conclusions.

In contrast to groups I and II, as expected, a higher eczema risk is found in group III. However, there are great differences in the individual reaction scheme. Thus, even in group III, 50% of the test persons tolerated intensive washings with SLS without any signs of irritation. Hence, the significance of the atopy score for predictively judging the individual eczema risk becomes limited.

The repetitive washing test allows conclusions regarding the individual barrier function and seems to be a suitable procedure for evaluating individual eczema risk upon contact with washing-active substances.

The irritation by a washing procedure may be controlled by choosing the appropriate washing solution. In our studies, we succeeded in avoiding irritation by using an acid, soap-free syndet in almost all cases.

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Address:

W. Gehring
Hautklinik am Städtischen Klinikum Karlsruhe GmbH
Moltkestrasse 120
D-76133 Karlsruhe
Germany