Evidence of increased skin irritation after wet work: impact of water exposure and occlusion

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doi:10.1111/j.1600-0536.2012.02063.x

Summary

Background. Exposure to humid environments/water and prolonged glove occlusion are both believed to cause irritant contact dermatitis.

Objectives. To study the effects of different forms of wet work, especially the differences between water exposure and occlusion, by using an experimental model simulating occupational wet work.

Methods. The responses to water exposure and occlusion over multiple daily exposure periods for 7 days were compared in 73 volunteers. After the 1 week exposure, the sites were irritated with sodium lauryl sulfate (SLS). Comparison was performed via visual inspection and bioengineering methods.

Results. Whereas occlusion did not induce measurable alterations in skin physiology, water exposure for more than 3 hr daily caused a significant increase in transepidermal water loss (TEWL) as compared with the control areas. SLS irritation of the previously occluded and the water-exposed sites induced higher TEWL and clinical scores in a time-dependent fashion as compared with the control areas, with more pronounced reactions in the water-exposed sites than in the occluded sites.

Conclusion. Both previous occlusion and water exposure were capable of inducing higher susceptibility to SLS irritation. Skin hydration by occlusion had a different biological effect than water exposure. Short occlusions seem to harm the skin less than water exposure for the same duration.

Key words: barrier disturbance; glove occlusion; irritation; water contact; wet work.

Introduction

Employees performing wet work, working in a humid environment (i.e. water contact) or experiencing occlusion by wearing impermeable gloves (1–4) have a significantly increased risk of suffering irritant contact eczema of the hands (4–8).

Unprotected exposure to water (5, 9) and prolonged occlusion (10) are both known to induce a variety of skin changes that seem to affect the morphology (10–12) and function of the epidermal barrier (13–16). Both forms of exposure are often found simultaneously in the same profession; the extent to which the barrier-disturbing effects are similar or even additive is unknown. To separate the influence of occlusion from the influence of water (e.g. humidity exposure) and to compare the two exposures, this study used an experimental approach whereby the
skin sites of human subjects were continuously exposed to humidity (i.e. water exposure) and occlusion for varying time periods, simulating actual work exposure. The aims of the study were as follows: (i) to develop an experimental design that allows for a comparison of the effects of different forms of wet exposure; (ii) to study the influence of the different forms of wet exposure on the skin by using intra-individual comparisons (exposure to water and occlusion by moisture-resistant glove material); and (iii) to evaluate the extent to which varying exposure durations influence the condition of the skin.

In addition, we examined the extent to which the additive effects of the combined ‘glove occlusion followed by work in wet environments’ influence the skin, especially the barrier function, as compared with ‘occlusion alone’ for the same exposure duration.

Methods

Characterization of participants and experimental procedure

All investigations were performed in accordance with the ethical principles for medical research involving human subjects documented in the World Medical Association Declaration of Helsinki; ethical approval was obtained from the local ethics committee (Medical Faculty, Ruhr-University of Bochum, Reg. No: 3470-09). Written consent was obtained from all participants.

Participants

In total, 73 volunteers without symptomatic skin changes were recruited from university employees and students. The subjects included atopic individuals. Individuals were excluded from participation if they were pregnant or breastfeeding, undergoing treatment with substances that might influence the effect of the test substances, such as immunosuppressants, or suffering from endocrine or immune system diseases. During the study, participants were not allowed to apply detergents, emollients or moisturizers to their arms, and they were also asked to avoid exposure to natural or artificial ultraviolet radiation.

Design of a method for wet work (occlusion and continuous water exposure)

In this study, the term ‘wet work’ was used for both exposure forms (occlusion and water exposure). Previous studies have shown that the forearms provide reliable results for experimental testing (15, 17), even though irritant contact dermatitis is normally located on the hands.

Participants were randomized into four groups.

Group A (2 hr of daily exposure to water and occlusion for 7 consecutive days): n = 20 (15 females, 5 males; mean age 37.5 ± 10.35 years, range 22–56 years).

Group B (3 hr of daily exposure to water and occlusion for 7 consecutive days): n = 20 (12 females, 8 males; mean age 35.0 ± 9.04 years, range 19–47 years).

Group C (4 hr of daily exposure to water and occlusion for 7 consecutive days): n = 21 (16 females, 5 males; mean age 38.4 ± 9.62 years, range 23–55 years).

Group D (combined exposure – 6 hr of occlusion versus 3 hr of occlusion followed by 3 hr of water exposure daily for 7 consecutive days: n = 12 (8 females, 4 males; mean age 31.33 ± 10.64 years, range 19–49 years).

Wet work treatment (occlusion and water exposure) for 2, 3 and 4 hr (groups A, B, and C – phase 1)

In phase 1 (Figs. 1 and 2) of the study, two application areas (3 × 5 cm) were marked on each volar forearm. One arm was exposed to wet work (occlusion and water exposure), and the other arm was left untreated (left/right randomization of the arms). The two areas on the arm exposed to wet work were permuted (occlusion and water exposure). To avoid an anatomical selection bias, the same anatomical regions (distal and proximal) were

![Fig. 1. Experimental procedure: Two application areas were marked on each arm. One arm was exposed to wet work (occlusion and water exposure). The areas in the same anatomical regions of the other arm served as a control, and were left untouched during the first week of the experiment (phase 1).](image-url)
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Fig. 2. Study design. Phase 1: occlusion and water exposure, or combined exposure, were performed daily for 2, 3, 4 or 6 hr on 7 consecutive days. Each group of volunteers was wet work-exposed for a different duration. Healthy skin was water-exposed and occluded in the same individual. Readings and measurements were performed on day 1 (baseline), day 2 and day 8 24 hr after the last exposure. Phase 2: after the measurements on day 8, sodium lauryl sulfate (SLS) (0.5%) patches were placed on each of six areas for 24 hr (on the previously wet work-exposed arm and on the control arm). Evaluation was performed 2 hr after the removal of the patches on day 9 and again on day 10. TEWL, transepidermal water loss.

used in the treatment forearm as in the untreated arm, so that comparisons of the same anatomical regions could be performed (Fig. 1). One area was exposed to water-soaked cotton patches, simulating water exposure, and the second area was occluded with polyvinyl glove material, simulating occlusion by glove. The test sites were treated repeatedly for 7 consecutive days during the 1-week experiment, with different exposure periods (2, 3 and 4 hr).

Permanent occlusion (6 hr) as compared with combined exposure (3 hr of occlusion followed by 3 hr of water exposure) (group D)

Two application areas were marked on both forearms. One area of the forearm was occluded by polyvinyl material for 6 hr daily for 1 week, and the second area was occluded with polyvinyl glove material, simulating occlusion by glove. The test sites were treated repeatedly for 7 consecutive days during the 1-week experiment, with different exposure periods (2, 3 and 4 hr).

Sodium lauryl sulfate (SLS) challenge of the wet work-exposed and non-exposed control areas – phase 2

Because we had hypothesized that the stratum corneum would be more susceptible to irritation after various time periods of wet work exposure, we decided to challenge the formerly wet-exposed areas (occlusion and water exposure) and the control areas with SLS irritation to detect differences in the susceptibility to SLS irritation (see Discussion).

In phase 2 of the study, after the 1 week exposure, the marked areas of both volar forearms (the previously wet work-exposed areas and the non-exposed areas of the control arm) were irritated with SLS (50 μl, 0.5% SLS, purity ≥ 99%; Sigma-Aldrich, St. Louis, MO, USA), following the guidelines for SLS testing of the Standardization Group of the European Society of Contact Dermatitis (ESCD) (18). Large Finn Chambers® (diameter 12 mm; Epitest Ltd Oy, Tuusula, Finland) were positioned for 24 hr (day 8, 22–24 hr after the last wet work exposure) and fixed with adhesive tape (Scanpor®). Evaluations with bioengineering methods and visual scoring were performed before (day 8) the SLS testing, after 24 hr (2 hr after the SLS patches were taken off, day 9) and after 48 hr (day 10) (Fig. 2) on the previously wet-exposed and non-wet-exposed forearms.

Occlusion

Occlusion with gloves was simulated with 3 × 5 cm polyvinyl glove material (Peha-soft Vinyl, powder-free; Paul Hartmann AG, Heidenheim, Germany) fixed at the borders with Fixomull® Stretch (BSN Medical GmbH-Polyester, Hamburg, Germany).

Water exposure

The patch model was standardized in preliminary studies (n = 16). We modified the method of water-soaked patches published by Kligerman (19) with cotton patches (100% Cotton, NOBA; Verbandsmittel Danz GmbH u Co KG, Wetter, Germany) and by fixing a sponge (polyurethane: Stinnes-Intertec, Landau, Germany; 3 × 5 cm, 1 cm in thickness) to the top of the cotton patches by adhesion (Fixomull® Stretch; BSN Medical GmbH). The sponge was rehydrated every 20 min with a 2 ml syringe (Inject-Luer Solo; Braun Melsungen AG, Melsungen, Germany) with 1 ml of tap water to achieve a constantly moist cotton surface. Tap water was stored in a bottle and maintained at room temperature. Additionally, in a preliminary study, we tested whether a dry cotton patch was capable of inducing any changes to the bioengineering characteristics of the skin when applied for 3–6 hr daily for 1 week; we found that the dry patch did not induce such changes (data not shown).

Evaluation

Visual inspection (clinical score) and evaluation of the skin barrier and inflammation were performed with bioengineering methods [transepidermal water loss (TEWL), skin hydration and erythema (Colorimetry CR 300, a-parameter)], in a defined area in the middle of the exposure area.

In phase 1 of the study, the evaluations and baseline measurements were performed on days 1, 2 and 8 at
least 24 hr after the last wet exposure. In phase 2 of the study on day 9, measurements of the irritated skin were performed 2 hr after removal of the 24 hr SLS 0.5% patches, and these measurements were repeated on day 10 (48 hr after SLS irritation) (Fig. 2).

All measurements were conducted in air-conditioned rooms (room temperature, 20–22°C; relative humidity, 30–45%). The room temperature and humidity data were recorded during the measurements, following the guidelines of the Standardization Group of the ESCD (20). All measurements were performed in autumn and spring 2009/2010 after a rest of 30 min for equilibration.

**TEWL measurements**

Quantitative measurements of TEWL as an indicator of the integrity of the epidermal water diffusion barrier were conducted with the Tewameter TM 210 (Courage and Khazaka, Cologne, Germany), in accordance with the published guidelines (20). TEWL was calculated automatically and expressed in g/m²/h. The Tewameter probe was used in a holding device to avoid heating of the probe. The probe was rested on the skin, and TEWL was continuously recorded for a 3 min period. Mean values were obtained from two successive recordings for every test site. TEWL values were analysed in the form of differences obtained from two successive recordings for every test site. TEWL values were analysed in the form of differences obtained from two successive recordings for every test site. TEWL values were analysed in the form of differences obtained from two successive recordings for every test site.

Hydration of the stratum corneum was measured with a Corneometer CM 820, PH900/SM810 (Courage and Khasaka), according to the published guidelines (22). Horny layer moisture measurements recorded as arbitrary units (0–99 arbitrary units) are based on the measuring principle of capacitance (measuring surface, 49 mm²; measurement frequency, 0.9–1.2 MHz; accuracy, ± 3%).

**Clinical examination**

A subjective assessment of the degree of irritation was made in accordance with the ESCD guideline on the clinical scoring of acute SLS irritant reactions (18, 23): 0, no reaction; 0.5, slight scaling or very weak erythema and smooth surface; 1, weak erythema, possibly slight infiltration, slight roughness, slight scaling, mild oedema, and fine fissures; 2, erythema, more roughness, scaling, oedema, and fissures; and 3, pronounced erythema, extensive scaling, pronounced oedema, possibly vesicles, bullae, pustules and/or pronounced crusting. Readings were performed by a dermatologist in a blinded fashion on days 1, 2, 8, 9, and 10.

**Statistical analysis**

The differences between the measurements of the water-exposed and control areas on different locations of the same arms are dependent observations, and the data are not Gaussian-distributed at baseline (checked with the Shapiro–Wilks test at a 10% level); therefore, non-parametric statistical analyses were performed (24). The two-sided Wilcoxon signed rank sum test for matched pairs was used to compare the differences between the water-exposed arms and the control arms for all four groups after 7 days of wet exposure $\Delta x$ ($\Delta x_{\text{baseline}}$) and after the SLS irritation (day 9 and day 10 to baseline) for each of the four groups. The values are shown as medians with first and second quartiles in parentheses. The results are presented in box plots. The bottom line of the box represents the first quartile (Q1), and the top line represents the third quartile (Q3). A line is drawn across the box at the median, and the positive sign indicates the mean of the data. The whiskers are the lines that extend from the top and bottom of the box to the lowest and highest observations that are still inside the region defined by the following limits: (i) lower limits, Q1 – 1.5 (Q3–Q1); and (ii) upper limits, Q3 + 1.5 (Q3–Q1). Outliers are points outside the lower and upper limits and are plotted as asterisks. $P$-values < 0.05 were considered to be statistically significant.

For all analyses, SAS™ version 9.2 was used (SAS Institute Inc., Cary, NC, USA).

**Results**

**Differences between occlusion and water exposure with regard to exposure period**

The barrier function (assessed by TEWL) and the clinical score were the main parameters used to discriminate intra-individually between the wet-exposed areas and the control sites. A specific pattern of reaction was detected in all treatment groups, showing that the skin reacted in a time-dependent manner to the two different forms of wet exposure. The skin showed a more pronounced reaction to the water exposure: during phase 1, the water-exposed areas already showed a significant increase in TEWL (as...
Fig. 3. Comparison of the increases in transepidermal water loss (ΔTEWL) (ΔTEWL_{D8 – D1 baseline}) after 1 week of water exposure with different durations (groups A–C). The water-exposed areas, as compared with the control areas (same anatomical areas), showed a statistically significant TEWL increase after 3 and 4 hr, whereas the 2-hr exposure did not seem to alter the barrier.

Fig. 4. After 1 week of water exposure of different durations, the susceptibility to sodium lauryl sulfate (SLS) was amplified significantly as shown by the increase in transepidermal water loss (ΔTEWL) (ΔTEWL_{D10 – D1 baseline}) (a) and the increase in clinical score (b) for all exposure durations.

compared with baseline) when exposed for more than 3 hr (Fig. 3). In all treatment groups, the sites that had been water-exposed before irritation in phase 2 showed a significant additive skin response (indicated by both TEWL and clinical score) to SLS irritation (Fig. 4a, b).

Fig. 5. (a) After the irritation by sodium lauryl sulfate (SLS), the pre-occluded areas showed exposure time-dependent increases of both transepidermal water loss (ΔTEWL) (ΔTEWL_{D10 – D1 baseline}) and clinical score as compared with the irritated control areas. In contrast to the water exposure, the susceptibility to SLS was amplified after > 3 hr. In contrast to the areas with water exposure, the occluded areas did not show a significant influence on barrier function in phase 1 of the study, showing that occlusion seems to have less influence on barrier function.

Occlusion exposure showed a different pattern. Even the longest occlusion time of 6 hr daily did not seem to affect the skin significantly, and did not lead to measurably disturbed barrier functions in phase 1 of the study.

After the application of SLS 0.5% (which was performed 1 day after the last occlusion exposure), significant increases in both TEWL and clinical score (Fig. 5a, b) were seen.

Details of phase 1 of the study

Water exposure (Table 1, Fig. 3). Group A (2 hr of exposure). The epidermal barrier function, assessed as ΔTEWL (ΔTEWL_{D8 – D1 baseline}), showed no significant increase during the exposure treatment as compared with the untreated control arm (identical anatomical region) (\( p = 0.5744 \)). Group B (3 hr of exposure, \( p = 0.0035^{**} \)) and group C (4 hr of exposure, \( p = 0.0444^{*} \)) showed
Table 1. Phase 1 (after 7 days of water exposure)

<table>
<thead>
<tr>
<th>Group A (n = 20)</th>
<th>Water-exposed arm</th>
<th>Control arm (no intervention)</th>
<th>p-value Wilcoxon matched pairs test (two-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔTEWL_{D8–D1}</td>
<td>0.70 (−0.20 to 1.40)</td>
<td>0.70 (−0.40 to 1.40)</td>
<td>0.5744</td>
</tr>
<tr>
<td>Δ Erythema_{D8–D1}</td>
<td>−0.18 (−0.69 to 0.46)</td>
<td>−0.48 (−1.02 to 0.59)</td>
<td>0.5153</td>
</tr>
<tr>
<td>Δ Capacitance_{D8–D1}</td>
<td>1.00 (−4.00 to 2.00)</td>
<td>−1.00 (−3.00 to 2.00)</td>
<td>0.7398</td>
</tr>
<tr>
<td>Group B (n = 20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL_{D8–D1}</td>
<td>1.20 (0.30 to 2.25)</td>
<td>0.10 (−0.60 to 0.85)</td>
<td>0.0035**</td>
</tr>
<tr>
<td>Δ Erythema_{D8–D1}</td>
<td>0.12 (−0.15 to 0.99)</td>
<td>0.05 (−0.68 to 0.67)</td>
<td>0.4806</td>
</tr>
<tr>
<td>Δ Capacitance_{D8–D1}</td>
<td>−1.50 (−6.50 to 2.50)</td>
<td>−2.50 (−6.50 to 3.00)</td>
<td>0.8260</td>
</tr>
<tr>
<td>Group C (n = 21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL_{D8–D1}</td>
<td>0.70 (−0.20 to 3.30)</td>
<td>0.70 (−0.30 to 1.70)</td>
<td>0.0444*</td>
</tr>
<tr>
<td>Δ Erythema_{D8–D1}</td>
<td>0.33 (−0.58 to 0.97)</td>
<td>0.07 (−0.50 to 0.94)</td>
<td>0.8934</td>
</tr>
<tr>
<td>Δ Capacitance_{D8–D1}</td>
<td>−1.00 (−5.00 to 3.00)</td>
<td>1.00 (−5.00 to 3.00)</td>
<td>0.6007</td>
</tr>
</tbody>
</table>

Significance: *< 0.05; **< 0.01; ***< 0.001.

TEWL, transepidermal water loss.

ΔTEWL_{D8–D1}(g/m²/hr): TEWL_{D8} – TEWL_{D1}baseline.
ΔErythema_{D8–D1}: a* values: a^*_{D8} – a^*_1baseline.
ΔCapacitance_{D8–D1} (arbitrary units): capacitance_{D8} – capacitance_{D1}baseline.

In accordance with previous findings, the 1 week occlusion for various time periods did not influence either barrier function or other physiological parameters of healthy skin. No significant increase in TEWL as compared with either baseline or the non-treated control arm was detected (2 hr, p = 0.9636; 3 hr, p = 0.2650, p = 0.0817; 4 hr, p = 0.0817; data not shown). No differences in erythema, electrical capacitance, or clinical score.

Oclusion. Groups A–C. In accordance with previous findings, the 1 week occlusion for various time periods did not influence either barrier function or other physiological parameters of healthy skin. No significant increase in TEWL as compared with either baseline or the non-treated control arm was detected (2 hr, p = 0.9636; 3 hr, p = 0.2650, p = 0.0817; 4 hr, p = 0.0817; data not shown). No differences in erythema, electrical capacitance...
or clinical score were found. Additionally, group D had been occluded for 6 hr (see group D; Fig. 6a, Table 3).

**Comparison of 6 hr of occlusion and combined exposure (3 hr of occlusion followed by 3 hr of water exposure).** Group D (Fig 6a, Table 3). Neither the 6 hr occluded areas nor the areas with combined exposure showed significant differences in either clinical score or other bioengineering parameters.

Electrical capacitance and erythema did not change significantly during phase 1 of the study. No significant differences were observed between the arms.

**Phase 2 – SLS challenge**

**Water exposure** (Fig. 4a, b, Table 2). In phase 2, the formerly water-exposed areas and the control areas had been irritated by SLS 0.5%. On comparison of the formerly water-exposed areas with the control areas, all of the water-exposed areas showed a significantly greater increase in TEWL on days 9 and 10 ($\Delta$TEWL$_{D9} = $ TEWL$_{D9} - $ TEWL$_{D1baseline};$ $\Delta$TEWL$_{D10} = $ TEWL$_{D10} - $ TEWL$_{D1baseline}$), with the exception of the areas exposed for 2 hr, which showed a significant increase only on day 10 ($p = 0.0006^{***}$), and not on day 9 ($p = 0.0623$). The increase in TEWL was more pronounced after 48 hr (day 10) than after 24 hr (day 9).

In agreement with the TEWL results, the clinical scores of the water-exposed areas showed significant differences on day 9 or 10 when compared with the corresponding control areas.

**Occlusion. Groups A–C** (Fig. 5a, b). After 2 hr of occlusion, there was no indication of increased susceptibility to SLS irritation. Both TEWL and clinical score were similar to those for the control areas. After 3 hr of pre-occlusion, statistically significant increases in TEWL on day 9 ($p = 0.0064^{***}$) and clinical score on day 10 ($p = 0.0399^*$) were observed as compared with the control sites. Six hours (group D) of pre-occlusion induced significant increases in TEWL (on days 9 and 10) and in clinical scores.

**Electrical capacitance and erythema index** (data not shown). Electrical capacitance and erythema did not change significantly during phase 2 of the study. No significant differences were observed between the arms.

**Comparison of 6 hr of occlusion with combined exposure (3 h of occlusion followed by 3 h of water exposure)** (Fig. 6b, Table 4).

Group D. Both exposed areas showed a statistically significant increase in TEWL after the SLS challenge, whereas erythema and capacitance did not differ from those in controls [6 hr of occlusion, $\Delta$TEWL$_{D9}, p = 0.0044,$ $\Delta$TEWL$_{D10}, p = 0.0044;$ combined exposure (3 hr of occlusion followed by 3 hr of water exposure), $\Delta$TEWL$_{D9}, p = 0.0012, \Delta$TEWL$_{D10}, p = 0.0012$]. Additionally, the clinical scores on day 10 showed a significant difference in the degree of irritation as compared with the control area for the 6 hr occlusion ($p = 0.0039$), but not for the combined exposure ($p = 0.1563$).

**Discussion**

It is well known and corroborated by epidemiological studies that prolonged contact with moisture (water) and occlusion are major risk factors in the development of irritant contact dermatitis, even without the influence of other irritating substances. Furthermore, wet work is known to be a common exposure characterizing most cases of occupational dermatosis (3, 4, 25). Both activities that cause exposure to water, detergents or other skin-irritating substances and activities that need to be performed with moisture-resistant occlusive gloves are considered to be harmful for the skin. The harmful effects of wearing occlusive gloves may be attributable to the skin-irritating effect of occlusion-induced perspiration (25). Previous studies and the German Technical Standards for Hazardous Substances (1) summarize these activities under the term ‘wet work’ (3, 4). This term is a simplified definition that is also used to regulate the duration of wet work exposure in Germany. The exposure to humidity and the wearing of occlusive gloves are regarded here as similar hazards, and the duration of these forms of exposure are added to determine total exposure.

This basic definition does take into consideration that, under occupational conditions, wet work is not ‘water only’, but a combined exposure to water, water-soluble irritants, and moist hands resulting from glove use. A number of questions regarding exposure to humidity (e.g. water contact) and/or occlusion that are important from an occupational health and safety perspective are still unanswered. Wearing protective gloves has been proposed worldwide as a measure (16, 25–27) to prevent exposure to water and other hazardous substances. The extent to which the benefit of the ‘skin-protective’ effect of glove use by preventing exposure to water outweighs the ‘skin-irritating’ effect of occlusion-induced perspiration (4) is unknown, as is the association between the benefit and the duration of exposure. To our knowledge, no experimental data are available that compare the skin hazards resulting from to water exposure with those induced by occlusion alone.
Table 2. Phase 2: sodium lauryl sulfate (SLS, 0.5%) irritation of the previously wet work-exposed areas and control areas

<table>
<thead>
<tr>
<th>Group</th>
<th>Previously wet work-exposed arm and SLS</th>
<th>Control arm and SLS</th>
<th>p-value Wilcoxon matched pairs test (two-sided)</th>
<th>Previously wet work-exposed arm and SLS</th>
<th>Control arm and SLS</th>
<th>p-value Wilcoxon matched pairs test (two-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n = 20)</td>
<td>2 hr of occlusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D9 - D1&lt;/sub&gt;</td>
<td>11.70 (9.40–14.05)</td>
<td>11.10 (6.95–14.85)</td>
<td>0.7841</td>
<td>12.70 (9.15–18.30)</td>
<td>10.35 (7.20–14.50)</td>
<td>0.0623</td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D10 - D1&lt;/sub&gt;</td>
<td>16.00 (10.95–20.25)</td>
<td>13.40 (9.45–17.70)</td>
<td>0.2342</td>
<td>19.80 (15.00–28.80)</td>
<td>12.30 (8.70–17.90)</td>
<td>0.0006**</td>
</tr>
<tr>
<td>Clinical score&lt;sub&gt;D9&lt;/sub&gt;</td>
<td>0.50 (0.50–1.50)</td>
<td>0.50 (0.00–0.50)</td>
<td>0.0923</td>
<td>0.50 (0.50–0.50)</td>
<td>0.50 (0.00–0.50)</td>
<td>0.0000</td>
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<tr>
<td>Clinical score&lt;sub&gt;D10&lt;/sub&gt;</td>
<td>1.00 (0.50–1.50)</td>
<td>1.00 (0.50–1.00)</td>
<td>0.0753</td>
<td>1.50 (0.50–1.50)</td>
<td>1.00 (0.50–1.50)</td>
<td>0.2045</td>
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<tr>
<td>Group B (n = 20)</td>
<td>3 hr of occlusion</td>
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<td></td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D9 - D1&lt;/sub&gt;</td>
<td>22.80 (16.20–29.90)</td>
<td>16.30 (9.10–26.45)</td>
<td>0.0064**</td>
<td>26.15 (18.35–46.35)</td>
<td>19.60 (9.90–7.75)</td>
<td>0.0002**</td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D10 - D1&lt;/sub&gt;</td>
<td>27.75 (15.90–40.75)</td>
<td>22.60 (11.40–35.30)</td>
<td>0.0954</td>
<td>38.45 (23.55–48.55)</td>
<td>25.25 (12.30–37.75)</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Clinical score&lt;sub&gt;D9&lt;/sub&gt;</td>
<td>1.00 (1.00–1.75)</td>
<td>1.00 (0.50–1.50)</td>
<td>0.0524</td>
<td>1.25 (1.00–2.00)</td>
<td>1.00 (0.50–1.50)</td>
<td>0.0092**</td>
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<tr>
<td>Clinical score&lt;sub&gt;D10&lt;/sub&gt;</td>
<td>1.50 (1.00–2.00)</td>
<td>1.00 (1.00–2.00)</td>
<td>0.0399*</td>
<td>2.00 (1.00–2.00)</td>
<td>1.00 (0.75–2.00)</td>
<td>0.0038**</td>
</tr>
<tr>
<td>Group C (n = 20)</td>
<td>4 hr of occlusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D9 - D1&lt;/sub&gt;</td>
<td>20.40 (13.80–27.00)</td>
<td>12.10 (7.90–16.30)</td>
<td>&lt;0.0001***</td>
<td>19.80 (11.30–24.60)</td>
<td>14.10 (7.80–16.20)</td>
<td>0.0103*</td>
</tr>
<tr>
<td>ΔTEWL&lt;sub&gt;D10 - D1&lt;/sub&gt;</td>
<td>24.50 (14.00–30.00)</td>
<td>14.30 (8.80–23.10)</td>
<td>0.0033**</td>
<td>25.00 (15.20–33.40)</td>
<td>20.70 (9.90–27.00)</td>
<td>0.0215*</td>
</tr>
<tr>
<td>Clinical score&lt;sub&gt;D9&lt;/sub&gt;</td>
<td>1.00 (0.50–1.50)</td>
<td>0.50 (0.00–1.00)</td>
<td>0.0078*</td>
<td>1.00 (0.50–1.50)</td>
<td>0.50 (0.00–1.00)</td>
<td>0.0156*</td>
</tr>
<tr>
<td>Clinical score&lt;sub&gt;D10&lt;/sub&gt;</td>
<td>1.50 (1.00–2.00)</td>
<td>1.00 (0.50–1.00)</td>
<td>0.0025*</td>
<td>1.00 (1.00–2.00)</td>
<td>1.00 (0.50–1.00)</td>
<td>0.0184*</td>
</tr>
</tbody>
</table>

Significance: * < 0.05; ** < 0.01; *** < 0.001.

TEWL, transepidermal water loss.

Median values; first and second quartiles are in parentheses. The SLS irritation on day 8 was performed 24 hr after the last wet exposure (water and occlusion). Values of TEWL of day 9 were assessed 2 hr after the SLS patch was taken off.

ΔTEWL<sub>D9 - D1</sub> (g/m²/hr): TEWL<sub>D9</sub> – TEWL<sub>D1</sub>baseline).

ΔTEWL<sub>D10 - D1</sub> (g/m²/hr): TEWL<sub>D10</sub> – TEWL<sub>D1</sub>baseline).
water exposure

For intra-individual comparison of the effects of water exposure with the effects of occlusion, a modified water-soak patch (cotton glove material) test was adapted. The patches were applied in corresponding periods.

The effects of direct water exposure (8) and occlusion-induced perspiration (28) are complex. Water exposure can modify the physiological functions of the skin. Water-associated irritancy may partially result from occlusion or from occlusion as an additive factor (8). The water-induced changes to the epidermal barrier are not believed to be direct effects of water. Rather, these changes are thought to result from a secondary alteration to the horny layer (12) by hydration, with a three-fold to four-fold increase in the stratum corneum thickness, the creation of large pools of water in the intercellular spaces, and disruption of the intercellular lipid structures (11). Furthermore, the influence on epidermal DNA synthesis (29) and other immunological mechanisms, such as the release of cytokines, may also play a role in the irritancy of water (30–32). Multiple techniques have been used in experimental settings to study water exposure. One technique is to study water under occlusion (12), either by water cup occlusion or by the use of large Finn Chambers® (33) on the skin. Occlusive studies have produced most of the experimental data on water irritancy (8). However, in these procedures, the influence of occlusion cannot be separated from the influence of water (8). The other methods used to study the effect of water on the skin are immersion of the skin (9) or the use of water-soaked patches (19). Ramsing and Agner (9) studied the effect of water on experimentally irritated skin, and showed that immersion for 15 min twice daily for 2 weeks caused a significant increase in skin blood flow, whereas clinical evaluation did not show a difference. Kligman (19) occluded normal skin with water-soaked patches for 2 weeks (with changes every 2 days), and induced an inflammatory reaction of the skin.

Effect of occlusion

Previous experimental studies mainly focused on occlusion, and showed that the short-term exposure of healthy skin to occlusion (occlusion for 4, 6 or 8 hr for 7 consecutive days and occlusion for 72 consecutive hours) did not induce measurable alterations in skin physiology (9, 13–15, 27, 34) or in the lipid profiles of the epidermal barrier (15). Only long-term experimental exposure has shown that occlusion via closed chambers (35) or via prolonged glove occlusion (6 hr/day for 14 days)(13) induces an elevation in TEWL, indicating a negative effect on skin barrier function. However, when pre-irritation of the skin of the hand or back (9, 13, 14, 36, 37) was followed by occlusion (37) or water immersion (9), differences in skin physiology were shown, mainly characterized by changes in TEWL (33), with decreased healing of SLS-damaged skin (15).

Comparison of water exposure and occlusion

The comparison of water exposure and occlusion in our experimental setting showed that, in phase 1, water exposure induced measurable barrier alterations, causing mild but significant increases in TEWL values after 3 and 4 hr of daily exposure. In contrast, the areas that were occluded by glove material did not show any alterations in TEWL as compared with the control areas. Additionally, no differences were found for capacitance or redness ($a^*$)
as assessed with the Chromameter. In phase 2 of our experiment (1 day after the last wet exposure), the SLS-induced irritation (24 hr patch test) was amplified when wet work (either occlusion or water exposure) had been performed in advance, with distinct response patterns being seen for the different exposure forms. When the healthy skin was occluded, no significant disruption of the permeability barrier could be detected, at least with the exposure duration of 2–6 hr daily. This finding is similar to those of most of the published bioengineering studies (9, 13–15, 27, 34).

After challenge of the previously occluded skin with SLS, the skin showed an amplified irritant reaction, as shown by increases in TEWL and visual scores. Immunological reasons may explain the increased irritability caused by occlusion as shown by TEWL and clinical score. Occlusion may induce subtle subclinical inflammatory reactions, leading to the release of preformed cytokines, which then either aggravate the reaction to SLS or impact on the penetration of SLS. Either mechanism could cause an enhancement of the irritation because of slight structural alterations of the barrier (38), a mechanism that was previously shown in diseased skin (39).

Another study (15) analysed the effect of SLS on previously occluded skin (8 hr for 7 consecutive days and occlusion for 72 consecutive hours). No significant differences regarding the susceptibility to SLS irritation were found in the occluded areas as compared with the non-occluded control area. The difference between this finding and our results may be attributable to the application of SLS having been already performed 4 hr after the last occlusion (as compared with 24 hr in our procedure). Furthermore, a higher concentration of SLS had been used (1% versus 0.5%) to induce irritation. One could speculate that the induction of stronger clinical irritation may suppress subtle differences regarding increased SLS penetration or subclinical local inflammatory responses that were already present.

Additionally, in phase 2 of our study, only the skin occluded for 2 hr failed to show any significant differences in susceptibility to SLS as compared with the non-treated sites. Although the pretreated areas showed increases in TEWL and clinical score as compared with the non-treated areas, the increases did not show a clear linear, dose–response relationship, because 4 and 6 hr of wet work did not consistently cause stronger increases in TEWL than 3 hr of wet work. This finding could be explained by the well-known interindividual variation in skin response to irritation and the interindividual susceptibility to both SLS and wet work. This biological diversity might be responsible for the lack of a clear dose (time)–response relationship. Future studies will use intraindividual comparisons of varying exposure durations of occlusion to allow for the detection of a dose–response relationship of the reaction of the barrier.

An additional approach involved the tandem application of a 3 hr occlusion followed by a 3 hr water exposure as compared with a 6 hr permanent occlusion. The skin sites that were exposed to either the long-term occlusion

### Table 4. Phase 2: sodium lauryl sulfate (SLS, 0.5%) irritation of the pretreated areas (combined exposure; 6 hr of occlusion versus 3 hr of occlusion followed by 3 hr of water exposure)

<table>
<thead>
<tr>
<th>Group D (n = 12)</th>
<th>Previously wet work-exposed arm and SLS</th>
<th>Control arm and SLS</th>
<th>p-value Wilcoxon matched pairs test (two-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 hr of occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL₀₋₀</td>
<td>18.15 (14.73–26.08)</td>
<td>13.75 (8.83–19.78)</td>
<td>0.0010**</td>
</tr>
<tr>
<td>ΔTEWL₁₀₋₀</td>
<td>24.60 (14.13–33.63)</td>
<td>13.95 (7.60–25.58)</td>
<td>0.0034**</td>
</tr>
<tr>
<td>Clinical score₀</td>
<td>1.00 (0.50–1.00)</td>
<td>0.50 (0.50–0.75)</td>
<td>0.0625</td>
</tr>
<tr>
<td>Clinical score₁₀</td>
<td>1.25 (1.00–2.00)</td>
<td>1.00 (0.50–1.00)</td>
<td>0.0039**</td>
</tr>
<tr>
<td></td>
<td>3 hr of occlusion + 3 hr of water exposure and SLS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔTEWL₀₋₀</td>
<td>19.25 (15.00–26.80)</td>
<td>18.03 (12.48–24.05)</td>
<td>0.0342*</td>
</tr>
<tr>
<td>ΔTEWL₁₀₋₀</td>
<td>25.80 (19.25–40.03)</td>
<td>18.68 (13.28–25.68)</td>
<td>0.0024**</td>
</tr>
<tr>
<td>Clinical score₀</td>
<td>1.00 (0.50–1.00)</td>
<td>0.75 (0.50–1.00)</td>
<td>0.7813</td>
</tr>
<tr>
<td>Clinical score₁₀</td>
<td>1.00 (1.00–1.50)</td>
<td>1.00 (0.50–1.25)</td>
<td>0.1563</td>
</tr>
</tbody>
</table>

Significance: * < 0.05; ** < 0.01; *** < 0.001.

TEWL, transepidermal water loss.
Median values; first and second quartile are in parentheses.
The SLS irritation on day 8 was performed 24 hr after the last wet exposure (water and occlusion).
Values of TEWL of day 9 were assessed 2 hr after the SLS patch was taken off.
ΔTEWL₀₋₀ (g/m²/hr): TEWL₀₋₀ – TEWL₀baseline.
ΔTEWL₁₀₋₀ (g/m²/hr): TEWL₁₀₋₀ – TEWL₁₀baseline.
or the tandem exposure both showed significant differences in TEWL as compared with the irritated control sites. However, on comparison of the TEWL increases in the two procedures, no statistically significant differences could be detected. Because we had hypothesized that the stratum corneum would be more susceptible to water exposure after an occlusion period, as had been shown in a study where occlusion followed by mechanical irritation induced stronger impairment of the barrier function (33), the present study suggests that occlusion followed by water exposure did not lead to more pronounced inflammatory reactions than occlusion alone under the given circumstances. This approach has its limitations, because the duration of occlusion of the tandem application was in the range of 3 hr, which was previously shown to only slightly influence barrier properties. A longer duration of occlusion followed by water exposure might increase the reactivity of the skin to irritation. Furthermore, only 12 subjects participated in this study. Thus, this exposure procedure requires further study.

In conclusion, we showed that, 24 hr after the 1 week occlusion, the skin still showed higher susceptibility to SLS irritation than the control areas, as illustrated by amplified barrier disturbance. The findings suggest that, after water exposure or the use of occlusive gloves, the irritant effect of detergent might be aggravated, and the skin seems to be more prone to react to stress. However, these findings are also limited to SLS as the irritant, and cannot be generalized to the dermatological effects of other chemical irritants.

We compared the different forms of wet work-induced barrier disruption, and showed that skin hydration by occlusion has a different biological effect on the skin than water exposure. The study further provides experimental evidence that the ‘skin-protective’ effect of glove use by preventing exposure to water might be greater than the supposed ‘skin-irritating’ effect of occlusion-induced perspiration.

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