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How irritant is alcohol?

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Conflicts of interest
None declared.

Summary

Background Alcohol-based hand rubs are used worldwide to prevent transmission of nosocomial pathogens.

Objectives To investigate skin irritation caused by alcohols alone and in combination with detergent washing.

Methods Single and repetitive patch testing with 60–100% alcohols [ethanol, 1-propanol, 2-propanol (synonyms: isopropyl alcohol, isopropanol)], a positive control [0·5% sodium lauryl sulphate (SLS)] and negative controls (empty chamber and water) were performed. Wash tests were performed with 80% ethanol and 0·5% SLS on the forearms with each agent alone and with both agents in a tandem design. Skin hydration, erythema and barrier disruption [measured as transepidermal water loss (TEWL)] were evaluated (always 15 volunteers).

Results We found no significant change in skin barrier or erythema induced by the alcohols in the patch tests, whereas skin hydration decreased significantly. Application of alcohols to previously irritated skin did not show a stronger skin barrier disruption than application of SLS alone. Wash tests demonstrated that alcohol application caused significantly less skin irritation than washing with a detergent (TEWL, $P < 0·001$; skin hydration, $P < 0·05$; erythema, $P < 0·05$). Even on previously irritated skin, ethanol did not enhance irritation. By contrast, a protective effect of ethanol used after skin washing was observed (TEWL, $P < 0·05$; skin hydration, $P < 0·05$; erythema, $P < 0·05$).

Conclusions Alcohol-based hand rubs cause less skin irritation than hand washing and are therefore preferred for hand hygiene from the dermatological point of view. An alcohol-based hand rub may even decrease rather than increase skin irritation after a hand wash due to a mechanical partial elimination of the detergent.

Millions of healthcare workers perform hand disinfection with alcohol-based hand rubs several times daily. Their efficacy for control of nosocomial infection led to widespread U.S. government endorsement.[1] The assumption of poor skin tolerance, however, remains a major reason for low compliance rates.[2] 'Hand hygiene' may lead to irritation and hand eczema. The prevalence of eczematous hand lesions in medical staff remains between 20% and 40%.[3,4] The nursing and related professions (employees in the healthcare system) have up to a six times increased risk for occupational dermatitis.[5,6] Irritant contact dermatitis is frequently observed in these occupations and is widely accepted as unavoidable. Even a mild interdigital eczema can be an important sign for future hand eczema on which microbes can grow more easily.[7,8] Irritant skin changes in healthcare employees are undoubtedly caused by frequent wet work and contact with detergents.[9] Nevertheless, 'hand hygiene' procedures are often quoted as important pathogenetic factors for the development of hand dermatitis.[10–12]

When the irritant effect of alcohol on the skin has been evaluated, most authors found low toxicity.[13–16] By contrast, many healthcare workers complain about unacceptable skin irritation caused by alcohol-based hand rubs. Even in the *Guideline for Hand Hygiene in Healthcare Settings* of the Centers for Disease Control,[1] skin tolerability of alcohol-based hand rubs is stated as potentially problematic: 'Although alcohols are among the safest antiseptics available, they can cause dryness and irritation'.

The assumed irritation due to alcohol-based hand antiseptics may hold up their wide use, especially in the U.S.A.[7] This study, therefore, evaluates the irritant potencies of the relevant types of alcohols alone and in sequence with use of a detergent in a highly standardized test design (patch test) as well as in a more realistic standardized wash test.

Materials and methods

Study population and design

A total of 105 healthy volunteers without skin diseases (49 women and 56 men, age range 18–52 years, mean ± SD 32 ± 8·2) participated. Atopic individuals were excluded. Written informed consent was obtained, and the study was approved by the ethical committee of the University of California San Francisco (CA, U.S.A.) and the University of Marburg (Germany). The study was performed in a multicentre design in San Francisco, U.S.A., and Marburg, Germany. Subjects were instructed not to apply topical 'leave-on' products such as lotions or creams to the test sites for 1 week prior to study. Before the measurements began, the volunteers rested in the test room for acclimatization for at least 30 min.

Test procedure

Two different tests were performed: the repetitive occlusive patch test (Fig. 1) and the wash test.

Repetitive occlusive patch test

The repetitive occlusive patch test consists of two occlusive applications of substances on the same test area (tandem application), each lasting 24 h. Sixty microlitres of the test solution was pipetted in large Finn Chambers® (Epitest, Helsinki, Finland; inner diameter 12 mm) and applied for 24 h on the back. After removal of the patch, the test area was marked and a further patch (with the same agent or with another agent) was subsequently applied on the same area for another 24 h. The removal of the second patch was performed at 48 h; evaluation was conducted before the first application (0 h) and after 72 h (hence, substance-nonspecific alterations of measurements due to occlusion could be minimized[17]). Each group consisted of 15 volunteers, and an empty chamber and a distilled water chamber were used as controls. Alcohols (> 99% purity) were supplied by Bode Chemie GmbH & Co. KG (Hamburg, Germany); sodium lauryl sulphate (SLS, > 99% purity) was supplied by Sigma Chemicals (St Louis, MO, U.S.A. and Munich, Germany).

Part 1 consisted of repetitive applications of the same patch: ethanol, 1-propanol or 2-propanol (synonyms: isopropyl alcohol, isopropanol), each in the concentration of 60%, 70%, 80%, 90% and 100% (ethanol 99%).

Part 2 consisted of repetitive applications of alcohol patches (ethanol 80%, 1-propanol 60% and 2-propanol 70%, analogous to the concentrations used in commonly used alcohol-based hand rubs,[18] followed by SLS 0·5% patches and vice versa. SLS 0·5% and an empty chamber served as controls.

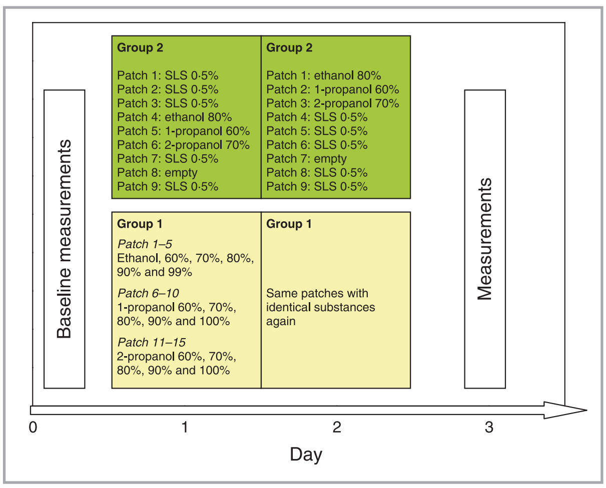

Fig 1. Test design of the repetitive patch tests (each group consists of 15 volunteers): group 1 with twice 24-h application of the same alcohol patch; group 2 with alternating application of alcohol and detergent. SLS, sodium lauryl sulphate.

Wash test

Procedure 1: SLS wash test. This standardized wash test was performed on the forearm: a foam roller (Lehnartz, Remscheid, Germany) was soaked with SLS 0·5% and moved 10 times within 1 min up and down on the volar forearm. Then, the roller was soaked again with test solution and the whole procedure was repeated for altogether five times. At the end, the forearm was rinsed with clear tap water and dried carefully with a paper towel. For each washing procedure 50 mL of test solution was used. In two groups (see below) tap water was used instead of SLS.

Procedure 2: disinfection test. For simulation of hand disinfection with an alcohol-based hand rub, the procedure was basically identical to the SLS wash test, except that alcohol was allowed to air dry on the skin between each treatment.

Procedure 3: combination of hand washing and disinfection. In this procedure the forearm was washed and dried first and disinfected thereafter. Therefore, a surgical hand disinfection was mimicked.

The described procedures were performed twice daily for 7 days with evaluation on day 0 (baseline: before the first procedure), on day 8 and after 2 days of skin recovery on day 10. In each test group, a comparison between two different procedures (each of them on one forearm) was performed by a randomized assignment of a procedure to one forearm.

The following groups were tested: (i) ethanol 80% alone (procedure 2) vs. SLS 0·5% alone (procedure 1); (ii) ethanol 80% alone (procedure 2) vs. SLS 0·5% followed by ethanol 80% (procedure 3); (iii) SLS 0·5% (procedure 1) alone vs. SLS 0·5% followed by ethanol 80% (procedure 3); (iv) SLS 0·5% (procedure 1) followed by tap water (procedure 1) vs. SLS

0·5% followed by ethanol 80% (procedure 3); and (v) ethanol 80% alone (procedure 2) vs. tap water alone (procedure 1).

Biometrics

Bioengineering measurements of transepidermal water loss (TEWL), skin hydration and erythema were performed. TEWL was evaluated with a Tewameter TM210 (Courage & Khazaka, Cologne, Germany; Acaderm, Menlo Park, CA, U.S.A.). During the TEWL measurements, the probe was hand held by use of an insulating glove until a stable TEWL value was established (~1 min). Air convection was prevented by reducing movements and talking in the test room. Temperature and humidity were recorded (20–22 °C, 40–55% relative humidity). The results were evaluated according to the guidelines for TEWL measurement by the Standardization Group of the European Society of Contact Dermatitis.[19] Each TEWL test value consisted of the mean of two single measurements.

Skin hydration was evaluated with a Corneometer CM 920 (Courage & Khazaka; Acaderm); each test value was attained by taking the mean of five single measurements.[20] Erythema was measured with a Chromameter CR 300 (Minolta, Osaka, Japan); during measurement the light in the test room was dimmed, and each test value was attained by taking the mean of five single measurements.[21]

Subjective sensations

After the washing procedure each volunteer estimated his/her subjective sensations of dryness, itching and burning on a visual analogue scale ranging from 0 to 10. The full length of the scale was defined as the subjective maximum sensation; each participant marked the degree of his/her individual sensation on the scale. We measured the length between 0 and the marked point for each sensation.

Statistics

Statistical analysis was performed using SPSS software version 11.5 (SPSS, Chicago, IL, U.S.A.). The results of the bioengineering measurements were calculated regarding their symmetrical distribution with the Kolmogorov–Smirnov test. Because they showed a symmetrical distribution, the values are shown as mean ± SD. Differences between the bioengineering values of each test procedure were calculated regarding significance by means of the paired, two-sided Student's t-test. Statistical significance was accepted when $P \leq 0{\cdot}05$.

Results

Patch tests

Alcohols alone

We noticed a significantly decreased skin hydration induced by alcohols compared with the empty chamber and the water chamber (Fig. 2). This decrease tended to be stronger with ethanol and 1-propanol than with 2-propanol. Remarkably, decreased hydration seemed less pronounced at higher alcohol concentrations. No significant change from the negative controls was seen regarding erythema (chromameter values) and skin barrier (TEWL values) at all patches (data not shown).

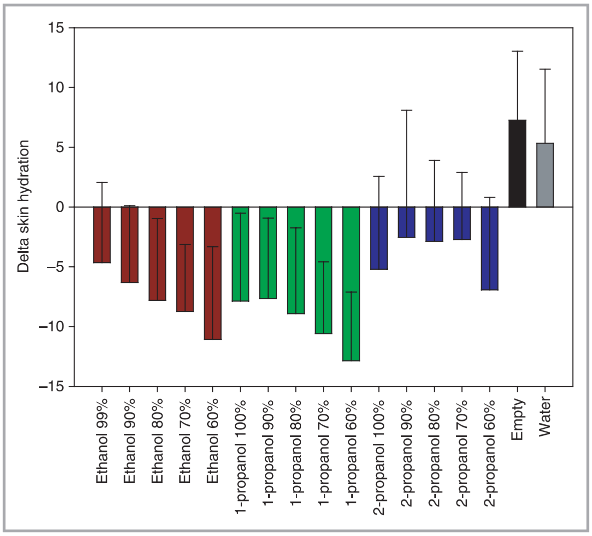

Fig 2. Mean ± SD changes in skin hydration compared with basal value after repeated application (twice, each for 24 h) of ethanol (red), 1-propanol (green) and 2-propanol (blue) at different concentrations and two control chambers in a patch test design. Differences between the alcohols and the water or empty chamber were significant at $P < 0{\cdot}05$.

Alcohols and sodium lauryl sulphate

When SLS 0·5% was applied in a tandem test design with the alcohols or controls, no significant change was found for Δskin hydration (Δ = difference between SLS + alcohol and SLS + empty chamber) for any sequence. A different picture was observed for TEWL and erythema. The highest ΔTEWL and Δerythema were found with a tandem application of SLS (Table 1). A single SLS application followed by an empty chamber (control) significantly increased TEWL. Replacement of the empty chamber with any of the three alcohols revealed a similar ΔTEWL. When SLS was applied in the second patch after a preceding empty chamber (control) or a preceding patch with any of the three alcohols, ΔTEWL was also in a similar range.

Wash tests

Ethanol 80% vs. sodium lauryl sulphate 0·5%

As shown in Table 2, there was a significant increase of barrier disruption, a lower skin hydration and a greater erythema at the forearm washed with the detergent compared with the disinfected forearm at the end of the treatment period (day 8). Although a stabilization of the skin physiology was seen 2 days later, the SLS-treated side was still more affected

Table 1 Changes in transepidermal water loss (TEWL), skin hydration and erythema (mean ± SD) after tandem application of various hand hygiene agents in a repetitive occlusive patch test design

Type of treatment	ΔTEWL	ΔSkin hydration	ΔErythema
SLS 0·5% followed by empty chamber (control)	23·0 ± 8·6	−5·6 ± 9·0	5·2 ± 2·3
SLS 0·5% followed by SLS 0·5%	40·9 ± 12·5**	−1·6 ± 10·7	7·4 ± 3·2*
SLS 0·5% followed by ethanol 80%	22·6 ± 8·6	−4·8 ± 11·7	4·7 ± 2·5
SLS 0·5% followed by 1-propanol 60%	24·5 ± 11·3	−0·4 ± 18·9	4·9 ± 2·5
SLS 0·5% followed by 2-propanol 70%	18·2 ± 8·9*	−0·4 ± 10·1	3·6 ± 1·4*
Empty chamber followed by SLS 0·5% (control)	16·2 ± 9·3	−3·2 ± 15·8	4·9 ± 2·1
Ethanol 80% followed by SLS 0·5%	17·3 ± 11·1	−3·6 ± 7·8	3·1 ± 2·2
1-propanol 60% followed by SLS 0·5%	15·1 ± 7·5	−4·4 ± 10·1	3·6 ± 2·6
2-propanol 70% followed by SLS 0·5%	14·3 ± 8·5	−0·1 ± 11·8	2·8 ± 1·9*

SLS, sodium lauryl sulphate. Difference from control is significant at $*P < 0.05$ or $**P < 0.001$.

Table 2 Changes in transepidermal water loss (TEWL), skin hydration and erythema (mean ± SD) after tandem wash tests with hand hygiene agents; procedures were performed on the forearms (side A and side B), and Δ-values (difference from basal values on day 0) are shown

Substance/procedure		ΔTEWL		ΔSkin hydration		ΔErythema	
		Day 8	Day 10	Day 8	Day 10	Day 8	Day 10
Side A	Ethanol 80%	3·9 ± 4·0**	1·5 ± 1·1**	−6·8 ± 5·8*	−3·2 ± 6·1	0·6 ± 0·6*	0·1 ± 0·4*
Side B	SLS 0·5%	9·7 ± 5·6**	6·7 ± 2·1**	−10·1 ± 6·1*	−5·8 ± 7·2	1·8 ± 1·6*	0·9 ± 1·1*
Side A	Ethanol 80%	2·4 ± 1·0**	1·1 ± 3·4**	−7·7 ± 3·5*	−3·5 ± 3·6*	0·6 ± 0·3*	0·1 ± 0·4
Side B	SLS 0·5% followed by ethanol 80%	8·0 ± 4·0**	4·1 ± 2·0**	−11·7 ± 5·2*	−6·4 ± 6·1*	1·0 ± 6·5*	0·4 ± 0·5
Side A	SLS 0·5%	9·9 ± 5·1*	6·8 ± 3·4*	−10·6 ± 4·6*	−5·9 ± 5·6*	2·1 ± 1·2**	1·0 ± 0·9*
Side B	SLS 0·5% followed by ethanol 80%	6·9 ± 3·3*	4·7 ± 2·3*	−6·6 ± 5·8*	−2·8 ± 6·3*	1·2 ± 0·9**	0·5 ± 0·6*
Side A	SLS 0·5% followed by water	7·9 ± 9·1	4·9 ± 5·8	−7·2 ± 6·3	−5·4 ± 5·1	1·7 ± 1·5	0·8 ± 0·5
Side B	SLS 0·5% followed by ethanol 80%	8·6 ± 6·4	5·2 ± 4·3	−9·6 ± 5·8	−4·5 ± 5·7	1·6 ± 1·4	0·6 ± 0·6
Side A	Ethanol 80%	1·6 ± 2·1	0·6 ± 1·3	−3·5 ± 8·2	−1·9 ± 8·5	0·1 ± 0·6	−0·2 ± 0·9
Side B	Water	1·5 ± 2·0	1·2 ± 1·7	−1·1 ± 7·5	−0·1 ± 9·7	0·2 ± 0·8	−0·2 ± 1·5

SLS, sodium lauryl sulphate. The difference between side A and side B is significant at $*P < 0.05$ or $**P < 0.001$.

(Fig. 3a). Subjective sensation was overall slight but on day 8 was greater regarding dryness, itching and burning at the SLS-treated side.

Ethanol 80% vs. sodium lauryl sulphate 0·5% followed by ethanol 80%

The combination of washing and disinfection caused significantly greater impairment of all evaluated physiological skin parameters (increased barrier disruption, decreased skin hydration and increased erythema) than disinfection alone. This effect was also apparent on day 10 but with diminished values (Fig. 3b). Subjective sensations were stronger on the SLS/ethanol side, especially regarding dryness and itching.

Sodium lauryl sulphate (SLS) 0·5% vs. SLS 0·5% followed by ethanol 80%

The skin physiology evaluated by water barrier disruption, skin hydration and erythema was clearly affected by washing with SLS. When the skin was disinfected with ethanol after washing, all skin physiological parameters were significantly less influenced by the combination than by the washing procedure alone. Therefore, the skin was less irritated by washing and disinfection compared with washing alone (Fig. 3c). By contrast, there were moderate subjective sensations, especially on the SLS/ethanol side, regarding burning and dryness.

Sodium lauryl sulphate (SLS) 0·5% followed by water vs. SLS 0·5% followed by ethanol 80%

Both procedures led to comparable skin physiology changes. A tendency towards a pronounced decrease of skin hydration was seen with the combination of SLS with ethanol but this did not reach the level of significance. However, there were no significant differences between both forearms at 8 or 10 days (Table 2). Although there were only moderate subjective sensations, the number of burning sensations at the SLS/ethanol side was higher.

Ethanol 80% vs. water

Forearm disinfection with ethanol led to similar changes in skin physiology as did washing with water alone. There was a

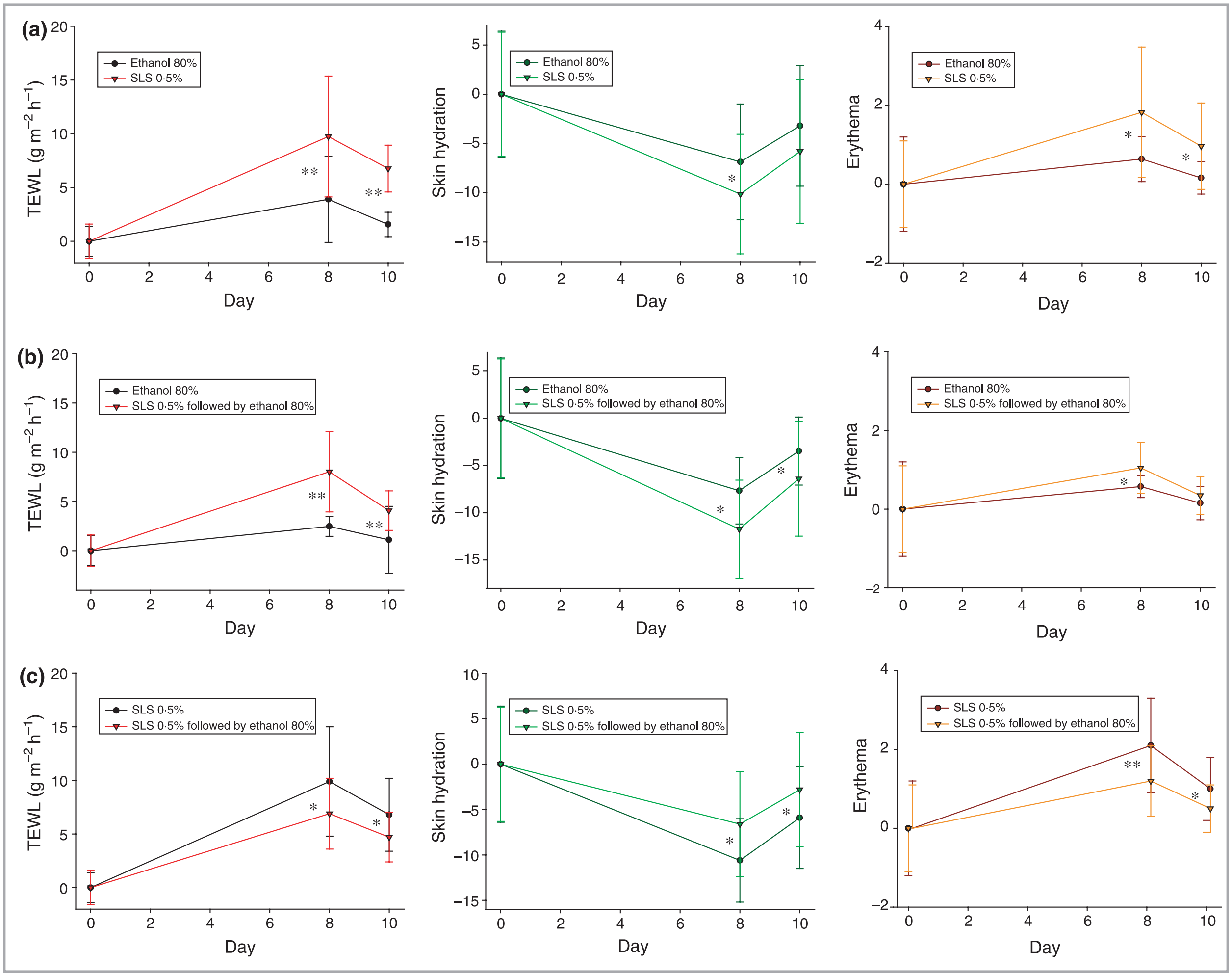

Fig 3. Bioengineering changes (mean ± SD) caused by wash procedure with (a) ethanol 80% vs. sodium lauryl sulphate (SLS) 0·5%, (b) ethanol 80% vs. SLS 0·5% followed by ethanol 80%, or (c) SLS 0·5% vs. SLS 0·5% followed by ethanol 80%. Differences between both procedures were significant at *$P < 0{\cdot}05$ or **$P < 0{\cdot}001$, with SLS inducing a stronger irritation (a), SLS/ethanol inducing a stronger irritation (b) and SLS alone inducing a stronger irritation (c).

tendency on day 8 and 10 towards a pronounced decrease of skin hydration caused by ethanol, but these changes were not significant. At day 10 (3 days after completion of the washing) the values were nearly normal. Subjective sensations were not different between the two sides.

Discussion

Ethanol, 1-propanol and 2-propanol lead to only minor skin barrier changes (comparable with those with water or the empty chamber) and no changes in erythema independent of the concentration tested. This is a first indication that these substances are not important irritants when the contact duration is limited, and supports previous findings.[14,15] In contrast, detergents can (depending on their type and concentration) induce relevant barrier disruption and inflammation even after a single patch test.[22] A decrease of skin hydration can also be observed after the application of alcohols even in the occlusive patch test design, with the strongest decrease with 1-propanol, followed by ethanol; the smallest decrease was observed with 2-propanol. With a single 24-h application, decreased skin hydration was not detected (data not shown). There is a tendency towards a greater decrease of skin hydration perceivable at the lower concentrations of ethanol and 1-propanol. These differences are small; we currently have no explanation for this phenomenon. However, our results demonstrate the ability of epicutaneously applied alcoholic substances to reduce skin hydration, as described earlier.[23–26] It was not possible to induce detectable irritation (barrier disruption or erythema).

Because this test design is exaggerated (long-term occlusive testing) and its relevance for the daily work of healthcare employees unclear, the washing/disinfection study was performed. When ethanol 80% was repetitively applied in a more realistic use test design over 1 week, only a minimal barrier disruption was induced, comparable with that induced by tap water. This barrier disruption might be due to scrubbing (moving the roller over the skin) rather than to an inherent feature of ethanol. We did not detect an increase in erythema, in accordance with results from studies in which no or only minor irritant potency is described after application of an alcohol-based hand rub,[13–16,27–32] which can be further reduced by addition of emollients.[33,34] In our model skin hydration was moderately reduced by ethanol treatment, slightly more than by tap water. By contrast to ethanol, the detergent SLS induced a much stronger barrier disruption and a pronounced skin hydration decrease, despite the fact that the concentration of the detergent was low (0·5%), which was emphasized by the moderate increase of erythema. In our view ethanol has only a low irritancy which is clinically relevant only regarding its potential for reducing skin hydration.

The most interesting question remains the ability of alcohol-based hand rubs to induce skin damage when applied on previously irritated skin as described previously.[15] The hands of healthcare workers are often previously irritated because of wet work and the occlusive milieu of gloves.[4,5] Because alcohol-based hand rubs are sometimes used after hand washing (classic procedure of surgical hand antisepsis), the combination of washing with a detergent and disinfection may be a crucial point in occupationally induced hand dermatitis.

First, we investigated the influence of a repetitive tandem application on skin physiology with patch tests. Consequently, ethanol, 1-propanol and 2-propanol were applied before or after an SLS patch. Remarkably, no increase of irritation was induced when the alcohol (regardless of which) was applied after the SLS patch. This demonstrates that the detergent-induced skin irritation, detected by barrier disruption, decrease of skin hydration and increase of erythema, was not exacerbated by these alcohols. Even after the combined application, skin hydration was not different from that following use of the detergent alone. When the application order was reversed (first an alcohol patch then the SLS patch), the degree of irritation remained the same. Hence, no alcohol impaired the skin physiology such that the following detergent induced a greater irritation. In this feature, all three types of alcohols are different from several other (including physical) irritants, which enhanced skin reaction induced by a detergent in a tandem patch test design as shown previously.[35–38] We confirmed the finding of Kappes *et al.*, who demonstrated that 1-propanol did not enhance the cumulative skin irritation when used after SLS,[39] and we can furthermore extend their results to 2-propanol and ethanol.

The relevant question remains, however, if the detergent-induced irritation can be exacerbated by a subsequent application of ethanol. Surprisingly, all skin physiological parameters evaluated were less impaired by the combination of SLS with ethanol compared with SLS alone. This suggests that application of ethanol after hand washing may reduce irritant skin changes caused by washing. Similar results were shown in a short test protocol by Pedersen *et al.*[40] They used commercial products in an intensive repetitive application test over 2 days and also detected diminished irritation induced by the combination of washing and disinfection compared with washing alone. It was uncertain whether this protective effect was due to different amounts of detergents applied, or to the glycerol which was added to the disinfection solution.[40] In our study, we demonstrated that the combination of SLS washing with subsequent ethanol treatment induced similar skin irritation as the combination of SLS washing with subsequent water treatment. Hence, the protective effect is most likely to be caused by a washout of detergent molecules which are on and in the stratum corneum and which may lead to a prolonged skin irritation.[41] This washout can be achieved with similar results by ethanol or water treatment. The important finding of this study is that alcohols used in hand rubs did not induce further skin irritation. Contrarily, disinfection may even reduce irritation caused by detergents, which might be an important element in the concept of early prevention.[42]

Why do so many healthcare employees believe that alcohol-based hand rinses are strong irritants and that these substances lead to hand dermatitis? One reason is the fact that alcoholic solutions induce burning sensations (sensory irritation) at previously irritated skin. This was observed by our volunteers especially in the groups in which SLS treatment was followed by ethanol. In these groups, irritation was induced by SLS and the subsequently applied ethanol could possibly penetrate more easily to sensory nerve endings. However, despite the fact that the application caused sensory discomfort, the physiology of the skin was not altered. Healthcare employees, however, will blame the alcohol-based product for this discomfort and not the underlying disturbed barrier function.[12,43] The consequences are obvious: the probably harmless disinfection procedure will be neglected and increasingly replaced by further hand washing. This does not lead to immediate discomfort, but will exacerbate the skin condition in a vicious circle.[44] Burning after the use of alcohol-based hand rubs should probably be recognized as a sign for an already disturbed skin barrier and for an impending hand dermatitis. Chew and Maibach summarize the extensive recent literature on irritation that may be beyond this mechanism.[45] Based on our results, the influence of longer and exaggerated (20 times every day) use of alcohols and different aspects of tandem effects, as well as the effect on individuals with an increased risk of hand dermatitis (e.g. atopic individuals) should be investigated in detail.

Our study is of relevance for all medical staff, because it demonstrates the good skin compatibility of three alcohols frequently used in alcohol-based hand rubs and underlines the known problematic skin compatibility of detergents and hand washing. Promotion and education (most effectively during clinical training) may individually be necessary to encourage the use of alcohol-based hand rubs.[25,42,46] Moreover, the visibly improved skin condition after the regular use of alcoholic hand disinfection may encourage healthcare employees to change their behaviour.[2,15,25,27,31]

The advantages of alcohol-based hand disinfection compared with hand washing regarding its bactericidal efficacy are obvious. Because there is evidence that hand washing before disinfection may decrease rather than increase bactericidal efficacy of the combined procedure, reduction of hand washing may be recommended not only from the skin physiological point of view but also for hygienic reasons.[47,48]

We do not wish to overgeneralize the results and understand the difficulties of extrapolating from 100 volunteers to millions of users. Yet the data provided by these highly controlled observations offer the foundation for epidemiological investigations and further investigations such as methods of decreasing sensory irritation.[49,50]

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