

INVESTIGATIVE REPORT

Allergy and Irritation: An Adverse Association in Patients with Atopic Eczema

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The pathomechanism of atopic eczema is complex. Two of the most important exogenous factors for atopic eczema are allergenic and irritant substances. In this study we investigate the combined effect of topical aeroallergens and irritation on the skin of atopic individuals. We performed patch testing with several aeroallergens (atopy patch test) and with an irritant, sodium lauryl sulphate, on clinically unaffected skin of 30 sensitized patients with atopic eczema. Application was conducted alone and as a consecutive application. Healthy volunteers served as controls. Evaluation was made by measurement of transepidermal water loss 2 h after removal of the patches. In atopic patients, we found increased levels of transepidermal water loss induced by the aeroallergens as well as by sodium lauryl sulphate. The most impressive barrier disruption was seen after application of house dust mite, followed by cat dander and grass pollen. However, the consecutive application of aeroallergens and sodium lauryl sulphate led to a highly pronounced increase in transepidermal water loss. Hence, in sensitized atopic subjects the combined effect of aeroallergens and detergents may cause severe skin problems, and this may be relevant in daily practice. **Key words:** atopic eczema; atopy patch test; cat dander; consecutive application; grass pollen; house dust mite; irritant contact dermatitis; sodium lauryl sulphate.

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In human skin, disruption of the epidermal water barrier can be induced by detergents such as sodium lauryl sulphate (SLS) (1–3). A recent study has shown that topical aeroallergens affect the epidermal barrier of sensitized atopics (4). This is important, because it can lead to exacerbation of skin problems from house dust mite and cat dander. In daily practice, however, contact with aeroallergens and skin irritants, e.g. SLS, does not occur separately in atopic patients but rather in combination. The question is whether a skin barrier disrupted by aeroallergens is more susceptible to detergents and vice versa. So far, the interaction between these two factors has not been assessed in experimental studies.

The aim of this study was to investigate the single and concomitant effect of aeroallergens and irritants when applied topically on the skin of sensitized atopic subjects.

PATIENTS AND METHODS

Study population

Forty volunteers (22 women and 18 men, aged between 18 and 60 years) participated in the study; 30 of them were patients with atopic eczema recruited from the Department of Dermatology, University of Marburg. Informed consent was obtained from all participants, and the study was approved by the ethics committee of the University Hospital of Marburg.

The patients had an atopy score according to Diepgen et al. (5, 6) of >10, with only slight eczema at the time of testing. All patients had a history of atopic dermatitis, atopic rhinoconjunctivitis and/or atopic asthma with a positive prick test and a specific IgE RAST level of ≥ 2 to at least one of the following substances: house dust mite (dermatophagoides pteronyssinus, $n=24$), cat dander ($n=14$), grass pollen ($n=25$) or birch pollen ($n=13$).

Ten healthy volunteers with no sign of atopy (atopy score according to Diepgen et al. (5, 6) of <4) and with negative prick tests to the above-mentioned allergens served as controls.

Test procedure

The tested aeroallergens were house dust mite, grass and birch pollen and cat dander, which were obtained from HAL Ltd. (Düsseldorf, Germany) and used in concentrations of 20,000 and 50,000 AU/ml in petrolatum. These concentrations are not comparable with those used in the standardization study of Darsow et al. (7, 8). We performed a pilot study and tested each allergen in 10 sensitized atopic individuals with both concentrations. We saw significantly stronger reactions with 50,000 AU/ml compared to 20,000 AU/ml in the patients, whereas no reactions were seen in controls. For further testing, 50,000 AU/ml was chosen. All were patch-tested on the back with the four aeroallergens in large Finn Chambers[®] (inner diameter 12 mm, Epitest Ltd., Hyrlä, Finland) on Scanpore[®] tape in accordance with the schedule in Table I. The first patch tests were applied for 24 h, removed and new patch tests applied ("consecutive application"). Irritation testing was done according to the guidelines of sodium lauryl sulphate exposure tests by the Standardization Group of the European Society of Contact Dermatitis (9). Skin reactions were evaluated by transepidermal water loss (TEWL) with a TEWAMETER TM210 (Courage & Khazaka, Cologne, Germany) with the patient lying face down on a couch. Measurements were performed before application of test chambers (basal values) and 2 h after patch removal. During the TEWL measurements, the probe was hand-held with the

Table I. Test design; rows 1–3 with 4 patches (for each aeroallergen one patch), rows 4–6 with only one patch

Row	Day 1	Day 2	Day 3
1	4 × aeroallergens	4 × aeroallergens	Removal of patch and evaluation
2	4 × aeroallergens	4 × SLS	
3	4 × SLS	4 × aeroallergens	
4	Petrolatum	SLS	
5	SLS	Petrolatum	
6	SLS	SLS	

use of an insulating glove until a stable TEWL value was established (~1 min). Air convection was prevented by use of a protective measuring chamber and by reducing movements and speaking in the test-room. The test results were evaluated by two experienced persons in accordance with the guidelines for TEWL measurement by the Standardization Group of the European Society of Contact Dermatitis (10). Each TEWL test value was the average of three single measurements. Before measurement, the volunteers rested for at least 0.5 h in the test-room, a fully air-conditioned room (climatization without air movement by Thermotexx[®]) with a stable temperature between 20°C and 22°C and relative humidity between 35% and 62%.

Biostatistical methods

Data were calculated with SPSS for Windows[®]. TEWL values were shown as median, as there was no symmetrical distribution according to the Kolmogorov-Smirnov test. Delta TEWL results were often slightly increased and occasionally showed a very strong increase. Hence the distribution showed a shift to the left. Differences between the test groups were calculated by means of the Mann-Whitney U test. Differences within a test group (e.g. SLS vs. aeroallergen) were calculated by means of the Wilcoxon test. The data for each group of aeroallergen-positive volunteers were evaluated and compared separately with the control group.

RESULTS

The medians of TEWL values are listed in Table II. There were visible atopy patch reactions in 38% to 64% of the sensitized subjects ($n=30$). In these individuals, a

significant increase was observed in TEWL, and was highest in individuals sensitized and tested with house dust mite and grass pollen, less severe with cat dander and only moderate (but still significant) with birch pollen. There was no relationship between patch-test positivity and RAST test in the patients.

Application of aeroallergens to healthy, non-sensitized volunteers revealed neither clinical changes nor significant changes in TEWL, regardless of which aeroallergen has been applied. All volunteers showed an increase in TEWL after SLS application (alone or consecutive application).

The application of SLS and petrolatum (and vice versa) led to a similar significant increase of TEWL in the group of atopics compared to the healthy control group. However, the consecutive application of aeroallergens and SLS (rows 2 and 3) led to a significantly stronger disruption of the epidermal barrier in the group of sensitized atopics compared to the control group (Fig. 1).

The sequence of applications (aeroallergen/SLS or SLS/aeroallergen) was not relevant for the test outcome in the atopic group, whereas in the control group the sequence aeroallergen/SLS showed a tendency to stronger reactions compared to the sequence SLS/aeroallergen. Among the atopics, however, the SLS-induced increase of TEWL was higher after SLS once (rows 4 and 5) or twice (row 6), and also stronger than after application of the aeroallergens alone (row 1). To elucidate the differences between the various aeroallergen groups and the controls, the TEWL values after aeroallergen and SLS application are shown in Fig. 1.

DISCUSSION

In sensitized atopic patients, topical application of a type 1 allergen or classical aeroallergens can give rise to a cutaneous response morphologically similar to atopic eczema (7, 8). This so-called “atopy patch test” has been shown to be sufficient in detecting relevant allergens in subjects with atopic dermatitis and the test’s specificity regarding the clinical relevance is better than prick

Table II. Transepidermal water loss (TEWL) ($\text{g/m}^2 \text{ h}$) in the different groups and schema of applications. Values (except the basal value) are displayed as medium Δ -values (TEWL test basal-value)

		Baseline	SLS (row 6)	Aeroallergen (row 1)	Aeroallergen/SLS (row 2)	SLS/Aeroallergen (row 3)	Petrolatum/SLS (row 4)	SLS/Petrolatum (row 5)
Control group	Mite	8.0	17.9	0.3	18.1	16.1	10.1	11.1
	Grass			0.4	20.1	10.0		
	Birch			0.5	14.5	7.5		
	Cat			0.3	11.2	8.4		
Atopy group	Mite	8.4	14.6	7.1*	22.2 [#]	22.0 [#]	12.4	11.3
	Grass	9.5	12.9	8.8*	18.7 [#]	20.9 [#]	11.9	10.7
	Birch	9.5	17.7	2.6*	14.8	11.9 [#]	14.1	10.7
	Cat	9.3	17.6	4.5*	14.5 [#]	23.3 [#]	12.6	9.9

Mite=house dust mite allergen; grass=grass pollen allergen; birch=birch pollen allergen; cat=cat dander allergen.

*Difference of TEWL between basal value and value after aeroallergen application is significant ($p<0.01$).

[#]Difference of TEWL between combination aeroallergen/SLS to petrolatum/SLS (or vice versa) is significant ($p<0.05$).

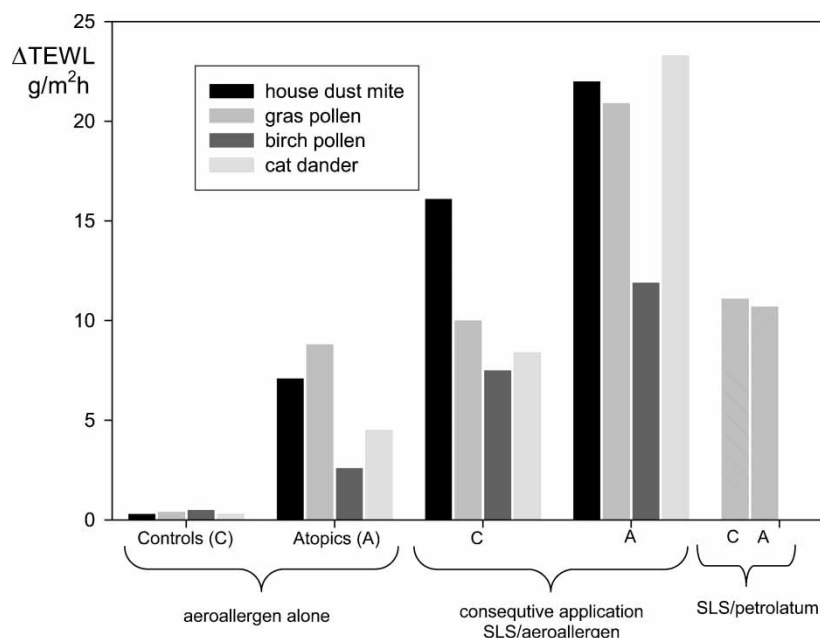


Fig. 1. Delta transepidermal water loss (Δ TEWL) values (difference to the basal value) after aeroallergens alone or consecutive application of aeroallergen and SLS.

or intracutaneous testing (11). Activation of dendritic cells seems to be a crucial pathogenetic factor and the reaction is IgE-mediated (13, 15, 16) with release of proinflammatory mediators and induction of allergen-specific T-cell clones (17–19). The eczema development includes skin barrier disruption, composition of the cellular infiltrate (20–22) and cytokine release (23, 24) similar to atopic eczema.

Until now, pretreatment with a detergent before an atopy patch test has only been performed to enhance the penetration of allergens (25). We found no changes in skin barrier function after application of aeroallergens on the skin of healthy volunteers, indicating that aeroallergens do not usually disrupt the intact epidermal barrier. By contrast, the application of aeroallergens to sensitized atopics leads to an increase of TEWL as an indicator of barrier disruption, thereby supporting the data of Gfesser et al. (4). The observed barrier disruption in our study was dependent on the aeroallergen used: While there was a strong increase in TEWL after house dust mite and grass pollen allergens, the barrier disruption caused by cat dander and especially birch pollen was less pronounced. This is in line with earlier findings (11) and may be due to the different size of the molecules and degree of sensitization. Individuals who showed a strong barrier disruption after atopy patch test often reported a seasonal aggravation of their atopic eczema (26).

In the control group, application of an aeroallergen to the skin pretreated with 0.5% SLS did not worsen the barrier disruption compared to a consecutive application with SLS/petrolatum. This indicates that in healthy

volunteers aeroallergens have no significant influence on the intensity of the cutaneous response to primary irritants.

However, different results were obtained in the group of patients with atopic eczema: the consecutive application with SLS/aeroallergen led to a significantly stronger reaction than SLS/petrolatum. This is understandable because application of petrolatum usually leads to a diminished barrier disruption caused by SLS (27, 28). By contrast, aeroallergens in petrolatum can induce a barrier disruption, so that the combination with SLS increases this disruption probably because of better penetration of the aeroallergens. This would support the notion that atopic skin with a disturbed barrier function is more susceptible for induction of specific immune responses. Such a specific reaction may, in turn, lead to further impairment of the skin barrier and worsening of pre-existing eczema.

In daily life, taking showers or bathing in a tub during the pollen season can exert a calamitous effect on the skin of atopic individuals, as this provides an adverse association of aeroallergen and irritant exposure. Therefore, when taking a shower, an irritant effect can be diminished by quick showering and reduced use of soap and detergents.

In conclusion, consecutive application of SLS and aeroallergens in sensitized atopic eczema patients leads to a more severe barrier disruption than a separate application of each component. This interrelation between allergy and irritation (which may be dependent on the severity of the dermatitis (29)) is a further factor that can induce eczema. Hence, in the pathogenesis of atopic eczema, endogenous factors and irritation and (aero)allergens may act together, giving rise to a vicious circle.

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