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Challenging a paradigm: Skin sensitivity to sodium lauryl sulfate is independent of atopic diathesis

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Abbreviations

AD	atopic dermatitis
EAS	Erlangen Atopy Score
FLG	Filaggrin
LOF	loss-of-function
SLS	sodium lauryl sulfate
TEWL	transepidermal water loss

What is already known about this topic?

Irritant contact dermatitis and atopic skin diathesis share an impaired skin barrier function as pathophysiological pattern. Sodium lauryl sulfate (SLS) is tested at 0.25% aq. as irritant control in patch testing. Hence, results might be affected by atopic skin diathesis.

What does this study add?

Challenging a long-standing paradigm, we found no association of increased reactivity to SLS patch tests in individuals with atopic skin diathesis, atopic dermatitis, allergic rhinitis, or allergic asthma in a large patient cohort. Thus, irritant control testing with SLS, which is useful in interpreting doubtful allergen patch test results, does not depend on individual atopy status.

Abstract

Background: Sodium lauryl sulfate (SLS) is the best-studied detergent in irritant contact dermatitis. In atopic dermatitis, the two major pathophysiological abnormalities concern skin barrier function and regulation of cutaneous immune responses. The probability of atopic skin diathesis can be assessed by comprehensive analysis of patient history as well as clinical and laboratory findings resulting in the Erlangen Atopy Score (EAS).

Objective: To investigate the impact of (i) atopic skin diathesis according to the EAS, and (ii) the physician-assessed diagnoses “atopic dermatitis”, “allergic rhinitis”, and “allergic asthma” on SLS skin reactions.

Patients and Methods: Retrospective analysis of data from 2,030 consecutive patients patch-tested with SLS (0.25% aq.) from two tertiary referral centers in Germany, from 2008 to 2014.

Results: Patients with a high probability of atopic skin diathesis showed no significant increase in positive SLS reactions compared to patients without atopic skin diathesis (14.2 vs. 16.8%). The grading of positive SLS skin reactions (1-4) revealed no differences in patients with or without atopic skin diathesis. Further, diagnoses of atopic dermatitis, allergic rhinitis, or allergic asthma had no impact on positive SLS skin reactions in multivariate logistic regression analysis.

Conclusions: We found no association of increased skin irritability to SLS with atopic skin diathesis, atopic dermatitis, allergic rhinitis, or allergic asthma in a large patient cohort. It therefore seems that the test of skin irritability with SLS, which is common practice in many centers so far, does not allow to predict the susceptibility to irritant eczematous inflammation in atopic vs. non-atopic individuals.

Introduction

The skin barrier is a fascinating but complex interplay of cells, intercellular components and soluble agents. It is formed by corneocytes, corneodesmosomes, corneocyte envelope-bound ceramides producing the cornified envelope, bound water and lipids.¹ Impairment of the skin barrier is a major pathophysiological hallmark in atopic dermatitis (AD) besides several other skin diseases, but also in allergic rhinitis, allergic asthma, and food allergies.² The best known genetic factor in AD is a loss-of-function (LOF) mutation in filaggrin gene (*FLG*) which is found in approximately 10-20% of atopic individuals.³ In addition, the LOF mutation in *FLG* was associated with atopy and increased susceptibility to chronic irritant contact dermatitis in a case-control study.⁴ However, since most AD patients do not harbour a *FLG* mutation, and even 60% of the carriers do not develop any skin disease, the *FLG* mutation is an important risk factor but neither sufficient nor necessary to result in manifestation of AD.^{3,5} The skin of heterozygous *FLG* mutation carriers is in many ways fundamentally different from normal skin, showing xerosis, scales, keratosis pilaris and palmar hyperlinearity, i.e. characteristics of ichthyosis vulgaris.³ Other skin barrier-modulating factors e.g. environmental influences such as urban life, diet (“fast food”), and obesity were found to be just as relevant.⁶ Besides the impaired skin barrier, the second hallmark of AD is cutaneous inflammation which is present even in uninvolved skin of atopic individuals.⁷ Both AD hallmarks, barrier dysfunction and inflammation, are closely linked and mutually reinforcing.⁵ The increased inflammation process negatively affects the differentiation of keratinocytes and decreases the tight-junction proteins.^{8,9} Patients with AD and even with atopic diathesis display skin barrier disruptions which resemble the effects of sodium lauryl sulfate (SLS) exposure in higher concentrations.¹⁰

SLS is a detergent commonly used in cosmetics, toothpastes, and soaps due to its cleansing properties as an anionic surfactant. In dermatological research, SLS has been widely used to study irritant contact dermatitis. Pioneering works on irritant skin reactions and differences between various chemicals, gender, and other cofactors date back to the 1970s and early 1980s.^{11,12} Although multiple studies addressed the impact of SLS on many known skin parameters such as natural moisturizing factor, keratin filaments, corneocyte morphology, immune cell invasion, cytokine profiles etc., the pathophysiology of SLS-induced skin reactions is not fully understood yet.¹³⁻¹⁵ Sophisticated experimental studies elucidated how SLS may destabilize the integrity of

the skin barrier, e.g. by increasing the pH of the stratum corneum, denaturing keratins, degrading lipid processing enzymes, and lowering expression of serine proteases, thus eventually impairing keratinocyte differentiation.¹⁶⁻¹⁹ Thus, besides the amount of percutaneous penetration of irritants, complex biologic responses are involved in SLS-induced skin reactions. Although contact time, concentration, and vehicle of the SLS application impact on the skin reaction, most studies showed significant variation in these parameters. Further, most studies were conducted with SLS concentrations ranging from 0.5-1.0% although these concentrations are neither used in day-to-day detergents nor in medical diagnostics such as patch testing.

Patients with SLS-positive patch tests display increased erythematous patch test reactions to allergens compared to SLS-negative patients.^{20,21} Aiming to improve specificity of patch tests, SLS was introduced as irritant control (SLS 0.25% aq.) into the baseline series in dermatology clinics following the German Contact Dermatitis Research Group (DKG) guidelines.²² Indeed, data of the Information Network of Departments of Dermatology (IVDK) revealed that patients with positive SLS reactions tend to react with more irritant but not allergic positive patch test reactions to other test substances, which may appear as erythematous or weak (false) positive reactions.²³ Further, SLS patch test reactions were frequently investigated for confounders by the MOAHLFA index with multivariate analyses (MOAHLFA is an acronym of the seven items male sex, occupational dermatitis, atopic dermatitis, hand dermatitis, leg dermatitis, face dermatitis, age > 40 years²⁴). Male sex and age over 40 years were identified to increase the risk of positive (irritant) patch test reactions to SLS 0.25% aq.²⁵

In epicutaneous patch testing, AD patients are often excluded because of concerns about flare-up reactions or difficulties in interpreting the results. However, many AD patients need patch-testing to diagnose or rule out additional allergic contact dermatitis. Especially atopic patients often have occupational irritative or allergic contact dermatitis.^{26,27} The “Erlangen Atopy Score” (EAS) was established in the 1990s to estimate the likelihood of atopic skin diathesis.²⁸ Various items concerning medical history, atopic signs and symptoms, and lab results are included in the EAS, thus exceeding the commonly used criteria by Hanifin and Rajka for diagnosing AD.²⁹ However, this score exclusively indicates an atopic skin diathesis; it does not diagnose active AD. Hence, a low EAS does not necessarily rule out AD.

Interestingly, no different frequencies of SLS reactions in patients with and without a history of AD were found in a large patch test cohort of 26,879 patients.²⁰ Older studies with small patient samples yielded different results.^{30,31} In further studies with lower patient numbers, no increased skin susceptibility to irritants such as SLS was observed in individuals with allergic asthma, elevated total IgE levels or a history of AD.²⁰ These findings remain unexplained since penetration of SLS through uninvolved skin of AD patients was increased compared to normal skin.¹³ Since diagnosis criteria of AD were limited to clinical signs and varied significantly between the aforementioned studies, we hypothesized that the extensive EAS may be a more sensitive tool to identify patients at risk for irritant skin reactions by SLS, in total number and in magnitude of the skin reactions.

Patients and methods

This retrospective analysis was based on patient data collected by the IVDK. The IVDK is a network of departments of dermatology in Germany, Switzerland, and Austria, dedicated to the epidemiology of contact allergy. Its structure and routine operating procedures are described in detail elsewhere.³² Briefly, patients' history, clinical data, and test results of all patients patch tested in the participating centers are recorded in local databases and, after anonymization, transmitted to the IVDK central office at the University of Göttingen twice a year. Data are subject to standardized quality control, added to the central IVDK database, and analyzed according to international standards.³³ For correlation of contact dermatitis with atopic diathesis, the EAS is optionally recorded as part of the standardized IVDK patient history in selected clinics. The study cohort in this manuscript comprised of 1,582 patients consecutively tested in Erlangen, Germany, and 448 patients tested in Marburg, Germany, from August 2008 to December 2014. This retrospective study has been reviewed and approved by the local ethics committee at the University Medical Center Göttingen.

The EAS includes 24 criteria in the categories family history for atopy, AD, clinical signs suggestive for atopy, and laboratory tests (Tab. S1). This score was proposed in 1991 and is frequently used in atopy studies.²⁸ Each item is rated with 0.5 to 3 points. If symptoms are unclear or weak, awarding partial points is recommended for some items. The final score results in a value between 0 and 41.5 points (Tab. S1a). Based on this score, an atopic skin diathesis can be probable

or improbable.³⁴ Patients with a total score ≤ 7 have no or are unlikely to have atopic skin disposition and only very rarely develop AD, while patients with a score ≥ 10 have a distinctive atopic skin disposition and are prone to clinically manifest AD (Tab. S1b). Eight to nine points constitute an undetermined atopic skin diathesis. Thus, all patients with a final EAS of 8-9 points were excluded from analyses of EAS subgroups in this manuscript.

In addition to EAS, the IVDK collects information on patients' history regarding physician-diagnosed atopic diseases (allergic rhinitis, allergic asthma, AD) as described.^{32,35} These clinics are also members of the German Contact Dermatitis Research Group (DKG), therefore standardized test protocols and procedures are used, following national and international guidelines. Exclusively patients with exposure to 0.25% SLS aq. for 48 hours were included in this study to exclude bias due to different test protocols (exposure of 0.25% SLS aq. for shorter intervals results in significantly decreased numbers of SLS reactions²³). SLS reactions were coded according to a modified Tupker scale.³⁶ The test preparation SLS 0.25% aq. was purchased from Hermal, Reinbek, Germany, and from 2014 on from SmartPractice Europe, Reinbek, Germany. Small Finn Chambers on Scanpor were used (SmartPractice Europe, 8 mm inner diameter). Positive SLS reactions were graded into four categories according to erythema, scaling and infiltration from weak (SLS 1) to severe (SLS 4).²⁵

Statistics

Data was managed and analysed using the software package SAS®, version 9.4 (SAS Institute, Cary, NC, USA). Statistical tests involved were Chi²-test and Fisher's exact test, where appropriate. A P value of < 0.05 was regarded as significant. To estimate the impact of EAS on SLS reactivity, controlled for other potentially influencing parameters, a multivariate logistic regression analysis was calculated with a positive reaction to SLS as target variable (dependent variable). Explanatory variables (independent variables) were the potentially important items: male sex, occupational dermatitis, AD, hand dermatitis, age ≥ 40 years, allergic rhinitis, allergic asthma, EAS ≥ 10 , and test in winter (October-March).

Results

2,030 patients were evaluated with the Erlangen atopy score (EAS) before patch testing was performed including SLS 0.25% aq. as irritant control. 1,693 patients (83.4%) showed no reaction to SLS while 337 patients (16.6%) showed a positive reaction to SLS. Analysing six different EAS subgroups (EAS points 0-3, 4-7, 8-9, 10-14, 15-19, >20), 79.4-86.0% of each EAS group showed no reaction to SLS while 14.4-20.6% did react to SLS (Fig. 1). Comparing the percentage of positive SLS reactions within the six EAS groups, no significant difference was found. Thus, SLS negative (SLS 0) and SLS positive (SLS 1-3) reactions are generally not associated with the score level of the EAS.

To improve clarity of our analyses, we determined two subgroups of patients according to the score level of the EAS. 1,215 patients (59.9%) were found with low probability of a relevant atopic skin diathesis ($EAS \leq 7$), while 521 patients (25.7%) were identified with a high probability of atopic skin diathesis ($EAS \geq 10$). Patients with an intermediate EAS of 8-9 points (294/2,030, 14.5%) were excluded from further analysis for EAS subgroups due to the undetermined information on atopic skin diathesis (Tab. S1b). Patients with a high probability of atopic skin diathesis showed neither significant differences in the total numbers (74/521 patients, 14.2% vs. 204/1,215, 16.8%) nor in the level of positive SLS patch test reactions when compared to individuals without atopic skin diathesis (Tab. 1).

Epidemiological characteristics of all patients showed a commonly seen distribution in patch-test cohorts (Tab. 2), with male patients being under-represented (36.3%), while individuals above 40 years were over-represented (65.9%). We hypothesized that other patient characteristics may differ in the subgroups of patients with low and high EAS (≤ 7 vs. ≥ 10 points), such as former or current presence of AD. In order to quantify important factors possibly interfering with the frequency of SLS reactions, we analysed the two subgroups using the MOAHLFA index (Tab. 2). Interestingly, age ≥ 40 as well as leg dermatitis were significantly over-represented in the $EAS \leq 7$ cohort. In contrast, in the $EAS \geq 10$ cohort, occupational dermatitis, hand dermatitis, and AD were significantly over-represented (Chi²-test; $p < 0.001$). Sex and face dermatitis were evenly distributed between groups.

In addition to the analysis of MOAHLFA items according to high or low probability of atopic skin diathesis, we also investigated MOAHLFA items of SLS positive and negative individuals, respectively (Tab. 3). Among patients reacting to SLS, there were significantly more men and patients aged ≥ 40 years, but significantly less patients with occupational dermatitis, hand dermatitis, and AD. Some of the items which were not evenly distributed in these subgroups of patients may interact with each other, for instance occupational dermatitis and hand dermatitis. To quantify the independent impact of each of these factors as well as other important parameters, most prominently the EAS on SLS reactivity, we calculated a multivariate logistic regression analysis. Calculations were done with a positive reaction to SLS as target variable (dependent variable), and an EAS ≥ 10 , as well as AD, allergic rhinitis, allergic asthma, and additional important items as explanatory variables (independent variables). It turned out that only male sex (OR = 1.55) and age ≥ 40 years (OR = 1.85) significantly increased the risk for a positive SLS reaction, while hand dermatitis had a significant “protective effect” (OR = 0.58) in this respect. All other investigated items including EAS ≥ 10 as well as past or present AD had no significant influence on SLS reactivity. Additional data analyses (details not shown) revealed patients with hand dermatitis being significantly more frequently diagnosed with chronic irritant contact dermatitis than the remaining cohort (158/691 = 22.9% [95%-CI; 19.8-26.2%] vs. 59/1,339 = 4.4% [95%-CI; 3.4-5.6%]).

Discussion

We analysed patch test results for SLS 0.25% aq., the irritant control of the DKG baseline series, in correlation to the EAS, a rather extensive score to rate probability of atopic skin diathesis. The EAS relies on clinical examination, family history and comprehensive information from the patient's past medical history as well as optional laboratory tests assessing the individual atopic diathesis. Although the EAS has been evaluated as a probability score for atopic skin diathesis, patients with an individual EAS > 20 usually present with clinically active AD in our experience. Therefore, we hypothesized an increased intensity of SLS reactions in patients with high EAS, which should be a more sensitive and reliable marker for current skin barrier dysfunction than recording the widely-used parameter "past or present AD".

The frequency of SLS patch test reactions did not differ significantly in patients with positive atopic skin diathesis (EAS $\geq$ 10) compared to patients with a low probability of atopic skin diathesis (EAS $\leq$ 7). Surprisingly, not even the intensity of SLS reactions (1-4) was elevated in patients with high EAS. As expected, patients with AD were significantly over-represented in the EAS $\geq$ 10 cohort (59.3% vs. 7.0%), suggesting a convincing correlation of high EAS with actual skin disease. However, most earlier studies reported that past or present AD in the patients' history did not correlate with SLS reactions in patch testing.^{20,25} At the time of patch testing, patients did not necessarily have any AD symptoms. Current patch test guidelines discourage from testing patients with active AD due to potential flare-up reactions of the skin disease and difficulties in obtaining ambiguous patch test results. Further, while these patients may have suffered from eczema at some point in their lives, the pathophysiology of atopy may not have been established conclusively. Therefore, our approach correlating EAS with SLS reactions seemed to be a more sophisticated and detailed method to investigate effects of atopic skin diathesis on SLS reactions in a large cohort.

Increased transepidermal water-loss (TEWL) after 0.5% SLS aq. application was reported exclusively in patients with active AD without visual differences of the SLS reaction³⁰, while other studies reported increased TEWL levels even in inactive AD.^{7,10,37} Although these results point towards a compromised barrier function in these individuals, neither atopic skin diathesis nor former or present atopic diseases influenced SLS skin reactions on a qualitative and quantitative

level in our study cohort. However, increased permeability is not necessarily associated with a clinical or subclinical correlate of skin inflammation. The loss of function mutations of the filaggrin gene in roughly 20% of AD patients in Western Europe may explain increased permeability for SLS in patients with a history of AD.⁴ Thus, our data suggests that SLS skin reactions are largely independent of skin permeability or impairment of skin barrier function. Besides skin disease, former reports suggested that SLS skin reactions are independent of other atopic diseases such as allergic rhinitis and allergic asthma.^{20,38} We confirmed this finding in our study cohort, since these items were assessed separately from the EAS in our patients. Unfortunately, we collected no individual information on the different scoring items of the EAS, except for the final score. We therefore may have missed individual symptoms or features of the EAS which might indeed be associated with SLS skin reactivity. Further, different irritants, SLS concentrations, durations of exposition, or atopic dermatitis criteria may have yielded different results.³⁹ And it is well recognized that reproducibility of irritative skin reactions either by serial testing of the same compound or prediction of an irritant skin reaction to another irritant chemical differs widely.^{20,40,41}

In summary, atopic skin diathesis *per se* is no risk factor for an increased frequency or severity of SLS skin reactions, contradicting our initial working hypothesis that patients with atopic diathesis tend to more frequent and/ or more severe SLS skin reactions. This is in-line with the findings from a previous study in 205 metalworker trainees which found by comparison of TEWL values before and after irritation with SLS, dimethylsulfoxide (DMSO), or sodium hydroxide (NaOH) that skin atopy is not associated with increased skin irritability.⁴²

In another study with inactive AD and control patients, repeated application of SLS 0.5% aq. over four days twice daily for 30 min under occlusion resulted in a significant decrease of natural moisturizing factor (NMF) levels in all individuals as well as increased skin permeability in all study participants.³⁷ In contrast, our study cohort tested with SLS 0.25% aq. for 48 hours of uninterrupted exposure displayed positive reactions in 16.6% of our patients only, independently of atopic skin diathesis. Although inclusion of SLS as irritant control may be helpful for interpretation of patch-test results^{20,25}, a convincing pathophysiological explanation for this medically relevant discrimination has yet to be found. It has also been suggested that the interpretation of SLS patch tests is potential source of error.⁴³

Further, our data confirmed earlier findings showing a significantly increased risk in logistic regression analyses of a positive SLS reaction in men and in patients ≥ 40 years of age.^{20,25,44} Several other parameters may influence susceptibility to irritation, such as concomitant disease other than atopy, menstrual cycle, ethnicity, application site, and climatic conditions.⁴⁴ With regards to climatic conditions, we found no difference in SLS testing during the cooler months versus the warmer months in our logistic regression analysis (SLS testing during October-March vs. April-September). Our finding of an independent “protective effect” of hand dermatitis on the frequency of SLS positive patients (OR 0.58; CI = 0.40-0.83) was unexpected. Former studies analysing exclusively TEWL after SLS 0.5% aq. found increased values in a small cohort of hand dermatitis patients with active skin disease.⁴⁵ Of note, our patients with hand dermatitis were more frequently diagnosed with chronic irritant contact dermatitis than the remaining patient cohort. Hand dermatitis is more often induced or sustained by external, irritant factors whereas manifestation of eczema at other body sites may rather be caused by intrinsic factors (e.g. stasis dermatitis, seborrheic eczema, nummular eczema, xerotic eczema, AD). In addition, hand dermatitis is the most common manifestation of occupational dermatitis.⁴⁶ Interestingly, occupational dermatitis was determined a risk factor for positive SLS reactions in former studies but not in this cohort.²⁰ Patients with hand dermatitis work under hand occlusion (gloves), wet working conditions, with disinfecting agents, or skin barrier disrupting detergents (nurses, kitchen workers, craftsmen, and others). We conclude that the irritant exposure of the hands is the major cause of the disease, but this is not reflected by SLS reactivity since SLS is not primarily a marker for increased skin irritability in general but only a marker for increased susceptibility at the time of patch testing. Although the exact pathophysiology of SLS skin reactions remains unclear and without association to atopic diseases, we speculate that positive SLS reactions may still indicate a rather internal (genetic?) disposition towards other forms of eczema than exclusively externally caused eczema types.

Conclusion

Although an impaired skin barrier may lead to elevated absorption of irritants and allergens into the skin, we found no association of increased skin irritability to SLS with atopic skin diathesis, AD, allergic rhinitis, or allergic asthma in a large patient cohort with more than 2,000 patients.

SLS skin reactions can neither be associated with skin barrier dysfunction nor with consistent polarization of the immune system in atopy. Thus, the current assumption of SLS being an irritant compound in general needs to be challenged in further studies. In daily clinical practice, dermatologists should avoid to explain positive SLS reactions as predisposition towards higher skin sensitivity.

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Tables

	all patients (n=2030)		Patients with EAS ≤ 7 (n=1215)		Patients with EAS ≥ 10 (n=521)	
reaction	n	%	n	%	n	%
sls0	1693	83.4	1011	83.2	447	85.8
sls1	282	13.9	171	14.1	60	11.5
sls2	47	2.3	26	2.1	14	2.7
sls3	8	0.4	7	0.6	0	0.0
sls4	0	0.0	0	0.0	0	0.0

Tab. 1: Distribution of SLS reactions including the level of positive reactions within the total patient population, and subgroups EAS ≤ 7 and EAS ≥ 10 .

Percentage of positive reactions did not differ significantly between the subgroups of patients with Erlangen Atopy Score (EAS) ≤ 7 and EAS ≥ 10 (Fisher's exact test, $p = 0.14$). SLS 4 reactions did not occur. Patients with EAS 8-9 were excluded for subgroup analysis.

	All patients (n=2030)		Patients with EAS ≤ 7 (n=1215)		Patients with EAS ≥ 10 (n=521)		Chi ² test
	n	%	n	%	n	%	p-value
Male	736	36.3	462	38.0	180	34.5	0.17
Occupational dermatitis	514	25.3	261	21.5	164	31.5	< 0.0001
Atopic dermatitis	473	23.3	85	7.0	309	59.3	< 0.0001
Hand dermatitis	691	34.0	347	28.6	225	43.2	< 0.0001
Leg dermatitis	134	6.6	106	8.7	12	2.3	< 0.0001
Face dermatitis	418	20.6	241	19.8	116	22.3	0.25
Age ≥ 40 years	1337	65.9	867	71.4	290	55.7	< 0.0001

Tab. 2: Total patient population, and subgroups EAS ≤ 7 and EAS ≥ 10 analysed using the MOAHLFA index.

Age ≥ 40 and leg dermatitis were significantly over-represented in the EAS ≤ 7 cohort. In contrast, under-represented items were occupational dermatitis, hand dermatitis, and atopic dermatitis (Chi²-test; $p < 0.001$).

	All patients (n=2030)		SLS 0 (n=1693)		SLS 1-3 (n=337)		Chi ² test
	n	%	n	%	n	%	p-value
Male	736	36.3	593	35.0	143	42.4	0.01
Occupational dermatitis	514	25.3	446	26.3	68	20.2	0.02
Atopic dermatitis	473	23.3	415	24.5	58	17.2	0.004
Hand dermatitis	691	34.0	603	35.6	88	26.1	0.0008
Leg dermatitis	134	6.6	107	6.3	27	8.0	0.25
Face dermatitis	418	20.6	342	20.2	76	22.6	0.33
Age 40+ years	1337	65.9	1071	63.3	266	78.9	< 0.0001

Tab. 3: Total patient population, and negative (SLS 0) and positive (SLS 1-3) subgroup analysed using the MOAHLFA index.

Among patients reacting to SLS, there were significantly more men and patients aged 40+, but significantly less patients with occupational dermatitis, hand dermatitis, and atopic dermatitis.

Explanatory variable	Odds ratio [profile-likelihood confidence interval]
Male sex	1.545 [1.177 - 2.025]*
Occupational dermatitis	1.032 [0.690 - 1.531]
Atopic dermatitis (past or present)	0.770 [0.505 - 1.160]
Hand dermatitis	0.577 [0.398 - 0.826]*
Age $\geq$ 40 years	1.849 [1.349 - 2.565]*
Allergic rhinitis	0.920 [0.621 - 1.342]
Allergic asthma	0.897 [0.514 - 1.511]
EAS $\geq$ 10	1.158 [0.793 - 1.680]
Test in winter (October – March)	1.162 [0.895 - 1.512]

Tab. 4: Multivariate logistic regression analyses with positive reaction to SLS (SLS 1-3) as target variable.

*Male sex and age over 40 years means a significantly higher risk of positive SLS reaction, while hand dermatitis means a significantly reduced risk of a positive SLS reaction.

Figure

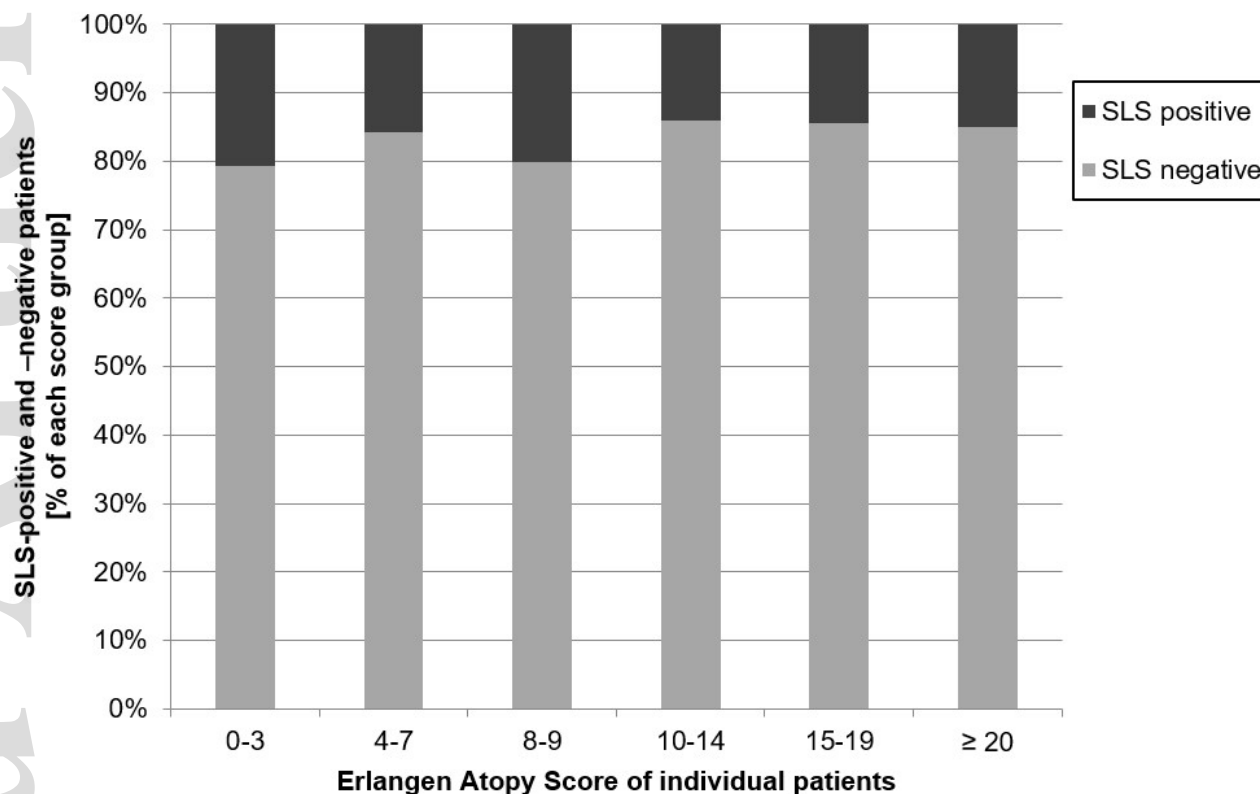


Fig. 1: Subgroups of the Erlangen atopy score (EAS) display no relevant differences in skin reactivity to SLS (0.25% aq.).

Proportions of SLS negative (SLS 0) or SLS positive (SLS 1-3) reactions do not differ significantly in subgroups of patients with different EAS (Chi² test, 5 degrees of freedom, $p = 0.16$).

Supplement

Tab. S1a: Atopy criteria for the Erlangen Atopy Score (EAS)

Attending physician does the assessment. If symptoms are unclear or weak, awarding partial points is recommended.

Family assessment for atopy (first grade relatives):	
Flexural dermatitis	max. 2 points
Allergic rhinitis/asthma	max. 0,5 points
personal history of atopic diseases:	
Allergic rhinitis	1 point
Allergic asthma	1 point
Cradle cap	1 point
Itch on uncompromised skin when sweating	3 points
Wool intolerance	3 points
Metal intolerance	1 point
Photophobia	1 point
Minimal atopic eczema (examination/medical history):	
Xerosis	3 points
Earlobe fissures	2 points
Dyshidrosis or podopompholyx	2 points
Pityriasis alba	2 points
Pulpitis sicca	2 points
Dermatitis of the mamilla	2 points
Cheilitis sicca / perleche	1 point
Atopic characteristics:	
Hyperlinear palms	max. 2 points
Hertoghe sign	max. 2 points
„Dirty neck“	max. 2 points
Keratosis pilaris	max. 1 point
Dermal neurovegetative Symptoms:	
White dermographism	max. 3 points
Acrocyanosis	1 point
Laboratory results:	
IgE (serum) $\geq$ 150 U/ml	1 point
IgE (serum) $\geq$ 400 U/ml	2 points
Positive immunocap assay	1 point

Tab. S1b: Evaluation of the atopic skin diathesis based on the Erlangen Atopy Score (EAS)

The EAS divides patients into six groups. Percentage of patients found with atopic dermatitis is presented for patients within each EAS group.

Erlangen Atopy Score	Patients with atopic dermatitis	Evaluation
0-3	0 %	no atopic skin diathesis
4-7	5 %	improbable atopic skin diathesis
8-9	34 %	unknown atopic skin diathesis
10-14	78 %	atopic skin diathesis
15-19	97 %	atopic skin diathesis
≥ 20	100 %	atopic skin diathesis