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Associations between tobacco smoking status and patch test results—A cross-sectional pilot study from the Information Network of Departments of Dermatology (IVDK)

Sonja Molin[1,2] | Richard Brans[3,4] | Andrea Bauer[5] | Detlef Becker[6] | Burkhard Kreft[7] | Vera Mahler[8,9†] | Christoph Skudlik[3,4] | Rudolf Stadler[10] | Christiane Szliska[11] | Elke Weisshaar[12] | Johannes Geier[13]

[1]Division of Dermatology, Queen's University, Kingston, Ontario, Canada

[2]Department of Dermatology and Allergy, Ludwig Maximilian University, Munich, Germany

[3]Institute for Interdisciplinary Dermatologic Prevention and Rehabilitation (iDerm) at the Osnabrück University, Osnabrück, Germany

[4]Department of Dermatology, Environmental Medicine, and Health Theory, Osnabrück University, Osnabrück, Germany

[5]Department of Dermatology, University Allergy Center, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany

[6]Department of Dermatology, University of Mainz, Mainz, Germany

[7]Department of Dermatology and Venereology, Martin Luther University Halle-Wittenberg, Halle, Germany

[8]Department of Dermatology, Erlangen University Hospital, Erlangen, Germany

[9]Paul-Ehrlich-Institut, Langen, Germany

[10]University Clinic for Dermatology, Johannes Wesling Medical Centre, University of Bochum, Minden, Germany

[11]Department of Dermatology, Bethesda Hospital, Freudenberg, Germany

[12]Division of Occupational Dermatology, Department of Dermatology, University Hospital Heidelberg, Ruprecht Karl University Heidelberg, Heidelberg, Germany

[13]Information Network of Departments of Dermatology (IVDK), Institute at the University Medical Centre Göttingen, Göttingen, Germany

Correspondence
Richard Brans, Department of Dermatology, Environmental Medicine and Health Theory, Osnabrück University, Am Finkenhügel 7a, D-49076 Osnabrück, Germany.
Email: rbrans@uos.de

Abstract

Background: Earlier studies suggested a potential association between tobacco smoking and nickel sensitization, but little is known about other contact allergens.

Objectives: To investigate the association of smoking status and contact sensitizations as well as subtypes of dermatitis, and to analyse the sensitization profiles of tobacco smokers.

Patients and Methods: Within the Information Network of Departments of Dermatology (IVDK), we performed a cross-sectional multicentre pilot study comprising 1091 patch-tested patients from 9 departments, comparing 541 patients with a history of cigarette smoking (281 current and 260 former smokers) with 550 never-smokers.

Sonja Molin and Richard Brans shared first authorship.

† The views expressed in this article are the personal views of the author and may not be understood or quoted as being made on behalf of or reflecting the position of the respective national competent authority, the European Medicines Agency, or one of its committees or working parties.

Results: We could not confirm the previously reported association between nickel sensitization and tobacco smoking. Moreover, sensitizations to other allergens, including colophony, fragrance mix I, *Myroxylon pereirae* and formaldehyde, were not increased in cigarette smokers compared with never smokers. Hand dermatitis (50.6% vs. 33.6%) and occupational cause (36.2% vs. 22.5%) were significantly more frequent among cigarette smokers compared with never-smokers as shown by non-overlapping 95% confidence intervals.

Conclusions: Although our study does not allow a firm conclusion on whether smoking status contributes to certain contact sensitizations, it confirms an association of smoking with hand dermatitis and occupational cause.

KEYWORDS
allergic contact dermatitis, hand dermatitis, occupational, patch testing, tobacco smoking

1 | INTRODUCTION

Nearly one-quarter of the adult population worldwide smokes tobacco which is mainly attributable to smoking of cigarettes.[1] In general, more men than women are smokers, but this difference is less pronounced in high-income countries than in low-income countries.[2,3] Tobacco smoking has multiple effects on the skin, either through direct contact or indirectly via the bloodstream.[4] It has been demonstrated that smoking induces pro-inflammatory cytokines such as tumour necrosis factor α (TNF-α), interleukin (IL)-1β and IL-6 while it decreases the level of anti-inflammatory cytokines such as IL-10.[4,5] Moreover, it may cause tissue damage by induction of oxidative stress.[4]

Associations between tobacco smoking and hand dermatitis have been conflicting.[6–12] Some studies suggested that tobacco smokers have a higher likelihood to develop hand dermatitis and others demonstrated an association between tobacco smoking and severity of hand dermatitis. For instance, a prospective cohort study in 303 metalwork trainees showed that the development of hand dermatitis during the training was significantly associated with cigarette smoking.[13] In a cross-sectional population-based study from the Netherlands, tobacco smoking was associated with severity of hand dermatitis.[10] Similarly, it was shown in a prospective follow-up study in 1608 patients with occupational hand dermatitis that the severity of hand dermatitis was increased among smokers, and they had a poorer prognosis compared with non-smokers.[14] Notably, allergic contact dermatitis was found to be significantly more frequent among the smoking patients with occupational hand dermatitis.[14] Another study among 153 patients with chronic hand dermatitis demonstrated an association between tobacco smoking and hand dermatitis characterised by concomitant allergic and irritant contact dermatitis.[15] Others reported that smoking is associated with contact sensitizations in women[16] and contact sensitization to nickel.[17,18] Contact allergens including nickel, menthol, colophony, cocoa, licorice, *Myroxlyon pereirae*, or formaldehyde can be found in tobacco or filter and paper of cigarettes.[4,19] Thus, the reported link between sensitization to nickel and smoking might be related to the presence of nickel in the tobacco plant through uptake from the soil or chemicals used on the plants.[17] Little is known, however, about whether contact sensitization to other allergens is associated with tobacco smoking and studies on this topic are lacking. Therefore, the aim of this pilot study was to examine associations between tobacco smoking status and contact sensitizations in dermatitis patients undergoing patch-testing.

2 | METHODS

2.1 | Clinical sample

In a cross-sectional multicentre pilot study, patients undergoing patch testing with the baseline series of the German Contact Dermatitis Research Group (DKG) at nine centres participating in the Information Network of Departments of Dermatology (IVDK) were asked about their smoking status after obtaining written informed consent. The IVDK consists of 56 departments of dermatology in Germany, Switzerland, and Austria and is dedicated to the epidemiology of contact allergy. Its structure and routine operating procedures are described elsewhere in detail.[20] Demographic and clinical data from patch test patients at the participating centres including history, diagnosis, and patch test results are recorded in local databases and transmitted pseudonymised to the IVDK central office twice a year. The data undergo standardised quality control and are analysed according to international standards. All nine centres participating in this pilot study are located in Germany and consist of the departments in Dresden, Erlangen, Freudenberg, Halle/Saale, Heidelberg, Mainz, Minden, Munich and Osnabrück. Time frame for recruiting was July 2015 to June 2016. The study was reviewed and approved by the local ethics committee and was carried out in accordance with the principles of the Declaration of Helsinki.

2.2 | Patch testing

Patch testing and evaluation of reactions was done according to the guidelines of the DKG[21–23] and the European Society of

Contact Dermatitis (ESCD).[24] Patch test exposure time was 2 days in 896 patients (76.5%) and 1 day in 276 patients (23.5%). The shorter exposure time was in line with the then valid DKG guideline recommendations and practiced by some of the centres.[21] In 1034 patients (88.2%), Finn-Chambers-on-Scanpor, and in 138 patients (11.8%) allergEAZE chambers (both Smart Practice Europe, Greven, Germany) were used. Patch test reactions at day (D)3 were considered for evaluation. If a reading was done at D4 instead of D3, this reading was selected. Readings were coded as +, ++ or +++, that is, erythema, infiltration, papules and/or vesicles in the test field were rated as positive in dichotomized analyses. Except for Compositae Mix II, which was obtained from Chemotechnique Diagnostics (Vellinge, Sweden), all patch test preparations for the baseline series were purchased from SmartPractice Europe (Greven, Germany).

2.3 | Questionnaire

The short questionnaire contained questions about current and past smoking habits (Figure S1). The questions aimed at identifying current or former smokers (smokers who had stopped smoking) versus never smokers as well as the type of the tobacco preparation and the duration of usage.

2.4 | Data analyses

As reaction frequencies to single allergens can be influenced by age and sex and as both were not distributed equally in the compared patient cohorts, reaction rates were standardised for sex and age (32.5% women <40 years of age, 32.5% women ≥40 years of age, 17.5% men <40 years of age, 17.5% men ≥40 years of age) using previously published methods.[25] Data was analysed using the statistical analysis software SAS©, version 9.4 (SAS Institute, Cary, NC). Differences in population characteristics between the patient groups were tested for statistical significance with non-overlapping 95% confidence intervals (CI). Statistical significance ($P < 0.05$) in sensitization frequencies was determined by non-overlapping 95% CI of standardised reaction rates. To identify factors independently associated with sensitizations to selected contact allergens that may occur in cigarettes, we performed logistic regression analyses with positive patch test reactions to nickel sulphate, colophony, fragrance mix I, *Myroxylon pereirae*, and formaldehyde as target variables, and five dichotomized independent variables. These were female sex, age ≥40 years, hand dermatitis, cosmetics as suspected allergen source, and being a cigarette smoker (member of the study group) vs. a never smoker (member of the control group). The detected significant differences in population characteristics between cigarette smokers and never smokers were taken into account when selecting these independent variables. Results are presented as odds ratios (ORs) with 95% CI (profile likelihood method).

3 | RESULTS

3.1 | Clinical sample and cigarette consumption

A total number of 1220 questionnaires was collected at the nine participating centres. Patch test data was not available for 48 patients, hence only 1172 questionnaires were being evaluated. Exactly 550 patients had never smoked, 622 were current or former smokers, with 593 being cigarette smokers. For 541 of the 593 cigarette smokers detailed data on their smoking status was available which allowed us to calculate their pack-years. We, therefore, focussed our analysis on these 541 cigarette smokers of which 281 were current and 260 were former smokers. The average number of daily consumption varied from 0.1 to 70 (median 12.5) cigarettes with an average range of years of smoking between 0 and 58 (median 20) and average pack-years between 0 and 115 (median 13.5).

3.2 | Characteristics of subgroups

We found significant differences between cigarette smokers (current and former) and never smokers using the MOAHLFA-index[26] (Table 1). Male sex (48.2% vs. 30.9%), occupational cause (36.2% vs. 22.5%), and hand dermatitis (50.6% vs. 33.6%) were significantly more common among cigarette smokers compared with the patients who had never smoked, while facial dermatitis was significantly more common in the never smokers (16.2%) compared with the smokers (9.8%). Comparison of exposure profiles of both groups revealed additional differences (Table 1). Culprit allergens were significantly more often suspected to be cosmetics or skin care products in never-smokers, whereas gloves were significantly more often suspected to be the culprit allergen source in the group of smokers.

A comparison of the MOAHLFA indices of the current and former cigarette smokers is presented in Table 2. Occupational cause (49.1% vs. 22.3%) and hand dermatitis (61.9% vs. 38.5%) were significantly more common among the current smokers compared with the former smokers. In contrast, the former smokers were diagnosed significantly more often with leg dermatitis (13.1% vs. 5.3%) and had more often an age ≥40 years (87.3% vs. 68.3%) compared with the current smokers.

3.3 | Comparison of patch test results

Comparisons of patch test results with the DKG baseline series of cigarette smokers and never smokers as well as of current and former cigarette smokers are presented in Tables 3 and 4. The only significant differences were seen with ylang-ylang (I + II) oil, to which more never smokers than smokers had a positive reaction (2.8% vs. 0.6%), and oil of turpentine, to which more of the current smokers had a positive reaction when compared with former smokers (2.8% vs. 0.2%).

Sensitization frequencies to allergens like nickel, colophony, fragrances, *Myroxylon pereirae*, and formaldehyde in the defined patient

TABLE 1 Comparison of MOAHLFA-indices and selected clinical data of cigarette smokers and never smokers.

	Cigarette smokers (current and former); $n = 541$		Never smokers; $n = 550$	
	n	% [95% CI]	*n*	% [95% CI]
Male	261	**48.2 [44.0–52.6]**	170	**30.9 [27.1–35.0]**
Occupational cause	196	**36.2 [32.2–40.4]**	124	**22.5 [19.1–26.3]**
Atopic dermatitis	137	25.3 [21.7–29.2]	156	28.4 [24.6–32.3]
Hand dermatitis	274	**50.6 [46.4–54.9]**	185	**33.6 [29.7–37.8]**
Leg dermatitis	49	9.1 [6.8–11.8]	58	10.5 [8.1–13.4]
Face dermatitis	53	**9.8 [7.4–12.6]**	89	**16.2 [13.2–19.5]**
Age ≥40 years	419	77.4 [73.7–80.9]	403	73.3 [69.4–76.9]
Atopic background				
• Allergic rhinitis	135	25.0 [21.4–28.8]	163	29.6 [25.9–33.7]
• Allergic asthma	60	11.1 [8.6–14.0]	64	11.6 [9.1–14.6]
Suspected allergen source				
• **Cosmetics, skin care products**	**156**	**28.8 [25.1–32.9]**	**204**	**37.1 [33.0–41.3]**
• **Gloves**	**131**	**24.2 [20.7–28.1]**	**76**	**13.8 [11.0–17.0]**
Reason for patch testing				
• Exclusion of contact allergy	194	35.9 [31.8–40.1]	208	37.8 [33.8–42.0]
Final main diagnosis				
• Allergic contact dermatitis	145	26.8 [23.1–30.8]	141	25.6 [22.0–29.5]
• Irritant contact dermatitis	74	13.7 [10.9–16.9]	63	11.5 [8.9–14.4]

Note: Significant differences are presented in bold.
Abbreviation: CI, confidence interval.

TABLE 2 MOAHLFA-indices of former cigarette smokers versus current smokers.

	Current smokers; $n = 281$		Former smokers; $n = 260$	
	n	% [95% CI]	*n*	% [95% CI]
Male	130	46.3 [40.3–52.3]	131	50.4 [44.1–56.6]
Occupational cause	138	**49.1 [43.1–55.1]**	58	**22.3 [17.4–27.9]**
Atopic dermatitis	85	30.2 [24.9–36.0]	52	20.0 [15.3–25.4]
Hand dermatitis	174	**61.9 [56.0–67.6]**	100	**38.5 [32.5–44.7]**
Leg dermatitis	15	**5.3 [3.0–8.7]**	34	**13.1 [9.2–17.8]**
Face dermatitis	18	6.4 [3.8–9.9]	35	13.5 [9.6–18.2]
Age ≥40 years	192	**68.3 [62.5–73.7]**	227	**87.3 [82.6–91.1]**

Note: Significant differences are presented in bold.
Abbreviation: CI, confidence interval.

populations may not only be influenced by distributions of age and sex, but also by localization of dermatitis, suspected allergen source and possibly by various other items. Several of these factors are not distributed equally in the study group (and the control group) and may hence act as confounders. Therefore, we performed logistic regression analyses with positive patch test reactions to nickel sulphate, colophony, fragrance mix I, *Myroxylon pereirae*, and formaldehyde as target variables, and five dichotomized independent variables. Apart from female sex, age ≥40 years and being a current or past cigarette smoker (member of the study group) or a never-smoker (member of the control group), they were selected based on the detected other significant differences in population characteristics between cigarette smokers and never smokers and included, hand dermatitis, and cosmetics as suspected allergen source(Table 5). Gloves and occupational causes were not included as they are associated with hand dermatitis whereas face dermatitis was not included as it is associated with cosmetics as a suspected allergen source. The following significant effects were seen: Female sex was associated with sensitization to nickel (OR 5.8) and formaldehyde (OR 4.8), age ≥40 years was associated with sensitization to *Myroxylon pereirae* (OR 2.2), and hand dermatitis was associated with formaldehyde sensitization (OR 6.7). Cigarette smoking was not significantly associated with sensitization to any of the five allergens.

A similar analysis was performed to find out whether being a heavy smoker might be associated with sensitization to any of the four allergens mentioned above. In the study group, there were

TABLE 3 Comparison of patch test results with the DKG baseline series of current or past cigarette smokers and never smokers.

Substance	Test concentration	Cigarette smokers ($n = 541$)			Never smokers ($n = 550$)		
		Number of patients tested	Patients with positive reactions	Age- and sex-standardised % positive [95% CI]	Number of patients tested	Patients with positive reactions	Age- and sex-standardised % positive [95% CI]
Metals							
Nickel sulphate	5% pet.	492	74	18.1 [13.8–22.5]	500	74	14.6 [11.1–18.1]
Cobalt chloride	1% pet.	510	25	6.5 [3.6–9.5]	509	26	5.4 [3.1–7.7]
Potassium dichromate	0.5% pet.	511	23	4.4 [2.2–6.6]	508	25	5.4 [3.1–7.8]
Fragrances							
Fragrance mix I	8% pet.	508	37	7.1 [4.3–9.9]	508	45	8.5 [5.8–11.2]
Myroxylon pereirae	25% pet.	513	37	6.0 [3.8–8.3]	511	39	6.3 [4.2–8.5]
Fragrance mix II	14% pet.	510	13	2.1 [0.7–3.4]	509	20	4.0 [2.1–5.9]
Jasmine absolute	5% pet.	515	5	1.2 [0.0–2.5]	511	7	1.3 [0.2–2.5]
Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC)	5% pet.	513	5	0.7 [0.1–1.3]	511	7	1.3 [0.2–2.5]
Ylang-ylang (I + II) oil INCI: Cananga Odora Flower Oil	10% pet.	**515**	**4**	**0.6 [0.0–1.1]**	**511**	**14**	**2.8 [1.2–4.4]**
Sandalwood oil INCI: Santalum Album Oil	10% pet.	515	3	0.3 [0.0–0.7]	512	4	0.8 [0.0–1.6]
Preservatives							
Methylisothiazolinone	0.05% aq.	513	31	5.6 [3.2–7.9]	512	21	4.1 [2.2–6.1]
Methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI)	0.01% aq.	511	22	4.0 [1.9–6.1]	497	17	4.3 [2.1–6.5]
Formaldehyde	1% aq.	510	8	1.9 [0.3–3.5]	509	3	0.4 [0.0–0.8]
Methyldibromo glutaronitrile	0.3% pet.	136	7	5.8 [0.8–10.9]	145	5	2.7 [0.1–5.2]
Methyldibromo glutaronitrile	0.2% pet.	372	7	1.9 [0.1–3.7]	364	4	0.7 [0.0–1.4]
Iodopropynyl butylcarbamate	0.2% pet.	515	3	0.5 [0.0–1.2]	512	3	0.4 [0.0–0.8]
Paraben mix	16% pet.	514	1	0.5 [0.0–1.6]	511	0	0.0 [0.0–0.0]
Rubber additives							
Thiuram mix	1% pet.	513	17	2.6 [1.1–4.1]	510	8	1.3 [0.3–2.2]
N-Isopropyl-*N*′-phenyl-*p*-phenylenediamine	0.1% pet.	515	6	0.6 [0.1–1.1]	512	3	0.9 [0.0–2.0]
Mercaptobenzothiazole	2% pet.	373	2	0.3 [0.0–0.6]	366	1	0.2 [0.0–0.6]
Mercaptobenzothiazole	1% pet.	137	0	0.0 [0.0–0.0]	147	0	0.0 [0.0–0.0]
Zinc diethyldithiocarbamate	1% pet.	514	1	0.2 [0.0–0.5]	511	1	0.2 [0.0–0.5]
Mercapto mix (without MBT)	1% pet.	514	0	0.0 [0.0–0.0]	511	0	0.0 [0.0–0.0]
Resins/glues							
Colophony	20% pet.	510	20	3.9 [1.8–6.0]	511	23	4.9 [2.7–7.1]
Epoxy resin	1% pet.	488	10	2.2 [0.5–3.9]	496	10	2.4 [0.8–4.0]
Other							
Propolis	10% pet.	513	20	2.7 [1.4–3.9]	512	18	3.8 [1.9–5.8]
Lanolin alcohols	30% pet.	514	8	1.9 [0.3–3.5]	512	6	1.5 [0.2–2.8]
Oil of turpentine	10% pet.	514	9	1.8 [0.4–3.3]	512	4	0.8 [0.0–1.7]
Compositae mix II	5% pet.	514	8	1.5 [0.2–2.8]	512	2	0.3 [0.0–0.8]
Sorbitan sesquioleate	20% pet.	507	4	0.9 [0.0–2.0]	476	8	1.9 [0.4–3.4]
Cetearyl alcohol	20% pet.	514	1	0.2 [0.0–0.5]	512	2	0.2 [0.0–0.6]

Note: Significant differences are presented in bold.

Abbreviations: Aq., aqua; CI, confidence interval; DKG, German Contact Dermatitis Research Group; MBT, mercaptobenzothiazole; pet., petrolatum.

136 heavy smokers with more than 26 pack years. As 97% of these heavy smokers were at the age of 40 years or more, we limited the control group for this analysis to never-smokers aged 40 years or more ($n = 403$). Again, positive patch test reactions to nickel sulphate, colophony, fragrance mix I, *Myroxylon pereirae*, and formaldehyde served as target (dependent) variables, and female sex, hand dermatitis, cosmetics as suspected allergen source, and being a heavy smoker or a never-smoker as dichotomized independent variables (Table S1). Female sex was significantly associated with sensitization to nickel (OR 8.8), while heavy smoking was not associated with sensitization to any of the five allergens.

4 | DISCUSSION

The results of this cross-sectional multicentre pilot study did not reveal any firm associations between smoking status and contact sensitizations. It was, however, confirmed that tobacco smoking is associated with other characteristics of patients undergoing patch testing.

To date, it remains unclear whether tobacco smoking increases the risk for contact sensitizations. Two cross-sectional studies in cohorts from the general population in Denmark revealed an association between tobacco smoking and sensitization to nickel. This was shown by Thyssen et al. who patch-tested a random sample of 3460 Danish adults.[17] Similarly, Linneberg et al. demonstrated that a smoking history of more than 15 pack years was associated with contact allergy in general, sensitization to nickel and allergic nickel contact dermatitis in 1056 individuals from Denmark aged 15–69 years.[18] In contrast, Meijer et al. did not find an association between tobacco smoking and sensitization to nickel or cobalt in 520 young Swedish men.[27] Zimmer et al.[8] published a review in 2018 on the association of tobacco smoking with contact dermatitis and hand dermatitis. They concluded that although seven out of eight articles found an association between smoking and contact dermatitis or nickel sensitization, it is impossible to make a definitive statement on a possible link due to limitations of the existing studies (e.g., small study number, study design, inconsistent patch testing, inconsistent timing of patch test reading, etc.). In the present pilot study, which was not done in individuals from the general population, but in patients with dermatitis undergoing patch testing, no association between cigarette smoking and sensitization to nickel was observed. In addition, we did not find any significant associations between cigarette smoking and contact sensitizations to colophony, fragrances, *Myroxylon pereirae*, or formaldehyde, which could be present in cigarettes.[4,19] The results of our logistic regression analyses reproduced well-known effects like association of female sex with nickel sensitization or higher age with sensitization to *Myroxylon pereirae*, which might be interpreted as an indicator of plausibility of our data.[28,29] We were, however, unable to detect any associations of cigarette smoking or being a heavy smoker and sensitization to any of these five allergens.

Concerning contact sensitizations, only two significant group differences were found in the present study. Cigarette smokers were less frequently sensitised to ylang-ylang (I + II) oil when compared with never smokers (0.6% vs. 2.8%; Table 3), and current cigarette smokers were more frequently sensitised to oil of turpentine when compared with former smokers (2.8% vs. 0.2%; Table 4). The relevance of these results is unclear. It is unlikely that cigarette smoking has a protective effect on sensitization to ylang-ylang oil, an essential oil commonly used in the fragrance industry. Probably, other factors were responsible for this finding. As can be seen from Tables 1 and 2, there were significantly more women and more patients with suspected cosmetic intolerance among the patch-tested never-smokers. Both factors may have increased the likelihood of ylang-ylang oil sensitization; at least for female sex this has been proven lately.[30] Oil of turpentine contains terpenes like α-pinene which are commonly found in tobacco and is also used as an ink diluter added to printing ink for cigarette packages.[31] It is possible that skin contact to turpentine is increased among cigarette smokers, hence leading to higher sensitization rates. The group of patients who were current cigarette smokers had a longer overall duration of smoking and thus exposure time to turpentine compared with the former smokers and this might have contributed to the difference. It is also possible that the increased sensitization to oil of turpentine is a result of workplace exposures given that occupational cause and hand dermatitis were not only significantly more frequent among cigarette smokers compared with never smokers, but also among the current cigarette smokers compared with former smokers.

Tobacco smoking has been shown to induce proinflammatory mechanisms and oxidative stress which may explain a higher likelihood of developing hand dermatitis.[4,5] However, studies assessing associations between hand dermatitis and tobacco smoking provided partly conflicting results.[6–12,15] The most recent systematic review and meta-analysis found low-quality evidence that tobacco smoking is associated with a higher prevalence of hand dermatitis but highlighted that at this point no final conclusions about this specific association can be drawn.[9] In many occupations, the hands are exposed to irritants and allergens. Therefore, hand dermatitis is common in patients with occupational dermatitis explaining the link between both of them.[32,33] It is well known that tobacco smokers are more common among individuals with little education and low income and those who perform blue-collar work.[34–38] As these occupations are often accompanied by manual work, wet work and exposure to other skin hazards, this may sufficiently explain the association between cigarette smoking, hand dermatitis and occupational cause in the present study. This is reflected by the higher percentage of gloves as suspected allergen source in cigarette smokers.

Atopic dermatitis was significantly more common in current cigarette smokers than in former smokers (30.2% vs. 20%). Even though this difference did not reach statistical significance, it may align with findings from the literature. A systematic review and meta-analysis on the association of smoking with atopic dermatitis showed that active smoking as well as passive smoke exposure are associated with an increased prevalence of atopic dermatitis.[39] A recent analysis looking at disease characteristics and comorbidities in smoking and non-smoking atopic dermatitis patients from Germany found tobacco

TABLE 4 Comparison of patch test results with the DKG baseline series of current and former cigarette smokers.

Substance	Test concentration	Current cigarette smokers ($n = 281$)			Former cigarette smokers ($n = 260$)		
		Number of patients tested	Patients with positive reactions	Age- and sex-standardised % positive [95% CI]	Number of patients tested	Patients with positive reactions	Age- and sex-standardised % positive [95% CI]
Metals							
Nickel sulphate	5% pet.	256	48	20.5 [15.0–26.1]	236	26	16.1 [8.4–23.9]
Cobalt chloride	1% pet.	269	15	5.8 [2.6–9.0]	241	10	9.5 [2.6–16.4]
Potassium dichromate	0.5% pet.	270	13	4.0 [1.7–6.4]	241	10	6.1 [0.7–11.5]
Fragrances							
Fragrance mix I	8% pet.	269	22	8.5 [4.7–12.4]	239	15	3.6 [1.7–5.5]
Myroxylon pereirae	25% pet.	271	17	5.8 [2.8–8.8]	242	20	5.7 [2.6–8.8]
Fragrance mix II	14% pet.	270	4	1.1 [0.0–2.1]	240	9	4.0 [0.0–8.2]
Jasmine absolute	5% pet.	273	4	1.3 [0.0–2.5]	242	1	2.0 [0.0–6.0]
Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC)	5% pet.	272	1	0.2 [0.0–0.6]	241	4	1.2 [0.0–2.3]
Ylang-ylang (I + II) oil INCI: Cananga Odora Flower Oil	10% pet.	273	3	1.0 [0.0–2.0]	242	1	0.2 [0.0–0.5]
Sandalwood oil INCI: Santalum Album Oil	10% pet.	273	2	0.5 [0.0–1.3]	242	1	0.2 [0.0–0.5]
Preservatives							
Methylisothiazolinone	0.05% aq.	273	21	7.2 [3.9–10.5]	240	10	3.4 [0.7–6.2]
Methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI)	0.01% aq.	272	13	4.4 [1.8–7.1]	239	9	3.8 [0.0–8.0]
Formaldehyde	1% aq.	269	5	2.3 [0.1–4.6]	241	3	0.8 [0.0–1.8]
Methyldibromo glutaronitrile	0.3% pet.	69	5	7.2 [0.3–14.1]	67	2	2.4 [0.0–5.7]
Methyldibromo glutaronitrile	0.2% pet.	199	4	2.3 [0.0–4.8]	173	3	0.9 [0.0–2.0]
Iodopropynyl butylcarbamate	0.2% pet.	272	0	0.0 [0.0–1.3]	243	3	1.6 [0.0–4.0]
Paraben mix	16% pet.	272	0	0.0 [0.0–1.3]	242	1	1.9 [0.0–5.7]
Rubber additives							
Thiuram mix	1% pet.	272	15	4.0 [2.0–6.1]	241	2	2.1 [0.0–5.8]
N-Isopropyl-*N*′-phenyl-p-phenylenediamine	0.1% pet.	273	4	0.9 [0.0–1.9]	242	2	0.3 [0.0–0.8]
Mercaptobenzothiazole	2% pet.	199	1	0.3 [0.0–0.9]	174	1	0.2 [0.0–0.7]
Mercaptobenzothiazole	1% pet.	70	0	0.0 [0.0–5.1]	67	0	0.0 [0.0–0.0]
Zinc diethyldithiocarbamate	1% pet.	272	1	0.3 [0.0–1.0]	242	0	0.0 [0.0–1.5]
Mercapto mix (without MBT)	1% pet.	272	0	0.0 [0.0–1.3]	242	0	0.0 [0.0–1.5]
Resins/glues							
Colophony	20% pet.	271	11	4.4 [1.5–7.3]	239	9	2.3 [0.7–3.8]
Epoxy resin	1% pet.	256	2	1.0 [0.0–2.6]	232	8	3.9 [0.0–8.2]
Other							
Propolis	10% pet.	272	9	2.5 [0.9–4.2]	241	11	2.6 [1.0–4.2]
Lanolin alcohols	30% pet.	272	4	1.5 [0.0–3.1]	242	4	2.9 [0.0–6.8]
Oil of turpentine	**10% pet.**	**272**	**8**	**2.8 [0.7–4.9]**	**242**	**1**	**0.2 [0.0–0.5]**
Compositae Mix II	5% pet.	272	6	2.3 [0.4–4.3]	242	2	0.3 [0.0–0.8]
Sorbitan sesquioleate	20% pet.	267	2	0.5 [0.0–1.3]	240	2	2.1 [0.0–5.8]
Cetearyl alcohol	20% pet.	272	1	0.3 [0.0–1.0]	242	0	0.0 [0.0–0.0]

Note: Significant differences are presented in bold.

Abbreviations: Aq., aqua; CI, confidence interval; DKG, German Contact Dermatitis Research Group; MBT, mercaptobenzothiazole; pet., petrolatum.

TABLE 5 Logistic regression analyses with positive patch test reactions to nickel sulphate, colophony, fragrance mix I, *Myroxylon pereirae* and formaldehyde as dependent variables, and five dichotomized independent variables.

Independent variable	Nickel sulphate 5% pet. OR [95% CI]	Colophony 20% pet. OR [95% CI]	Fragrance mix I 8% pet. OR [95% CI]	*Myroxylon pereirae* 25% pet. OR [95% CI]	Formaldehyde 1% aq. OR [95% CI]
Cigarette smoker	1.39 [0.96–2.01]	0.89 [0.47–1.67]	0.86 [0.54–1.38]	0.96 [0.59–1.57]	2.20 [0.61–10.35]
Female sex	**5.78 [3.58–9.80]**	1.44 [0.75–2.89]	1.42 [0.87–2.36]	0.97 [0.60–1.60]	**4.80 [1.20–32.10]**
Age ≥40 years	0.88 [0.58–1.35]	0.81 [0.41–1.70]	1.25 [0.73–2.24]	**2.24 [1.17–4.74]**	1.85 [0.46–12.44]
Hand dermatitis	0.94 [0.64–1.38]	0.96 [0.49–1.83]	1.12 [0.68–1.80]	0.84 [0.50–1.39]	**6.70 [1.64–45.20]**
Cosmetics and skin care products as suspected allergen source	0.94 [0.64–1.38]	0.54 [0.25–1.08]	1.30 [0.80–2.07]	1.15 [0.70–1.88]	0.49 [0.07–1.98]

Note: Significant differences are presented in bold.
Abbreviations: Aq., aqua; CI, confidence interval; OR, odds ratio; pet., petrolatum.

smoking to be a risk factor for increased pruritus, less well-controlled atopic dermatitis and more intense lesions.[40] Similarly, tobacco smoking was associated with severe atopic dermatitis in a cross-sectional study from Finland.[41]

Limitations of our study are the relatively small sample size of the patient subgroups. Our study was intended to be a pilot project and hence was only conducted at a selection of departments participating in the IVDK. Larger prospective studies are warranted to allow gender-stratified analyses and to add more insight into whether contact sensitization and hand dermatitis are associated with tobacco smoking, including adjusting for socioeconomic status.

In conclusion, our study showed that cigarette smoking is associated with hand dermatitis and occupational cause in patients undergoing patch testing. However, we did not find any contact sensitization which is plausibly and significantly associated with cigarette smoking. Future studies with larger cohorts will be needed to corroborate these findings further.

AUTHOR CONTRIBUTIONS

Sonja Molin: Conceptualization; methodology; writing – review and editing; writing – original draft; investigation. **Richard Brans:** Writing – original draft; writing – review and editing; investigation. **Andrea Bauer:** Investigation; writing – review and editing. **Detlef Becker:** Investigation; writing – review and editing. **Burkhard Kreft:** Investigation; writing – review and editing. **Vera Mahler:** Investigation; writing – review and editing. **Christoph Skudlik:** Investigation; writing – review and editing. **Rudolf Stadler:** Investigation; writing – review and editing. **Christiane Szliska:** Investigation; writing – review and editing. **Elke Weisshaar:** Investigation; writing – review and editing. **Johannes Geier:** Conceptualization; investigation; writing – original draft; methodology; writing – review and editing; formal analysis; data curation; resources.

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CONFLICT OF INTEREST STATEMENT

The IVDK, maintained by the IVDK e.V., of which J.G. is an employee, is sponsored by the chemical, cosmetic and fragrance industry (associations) as well as by public funds. For details, see http://ivdk.org/en/sponsors/.

DATA AVAILABILITY STATEMENT

Sharing of original data is not possible due to legal data protection restrictions.

ORCID

Sonja Molin https://orcid.org/0000-0002-9383-034X
Richard Brans https://orcid.org/0000-0002-1245-024X
Andrea Bauer https://orcid.org/0000-0002-4411-3088
Detlef Becker https://orcid.org/0000-0003-1679-3095
Burkhard Kreft https://orcid.org/0009-0004-0373-7283
Vera Mahler https://orcid.org/0000-0001-6471-1811
Christoph Skudlik https://orcid.org/0000-0002-5670-8396
Rudolf Stadler https://orcid.org/0000-0003-2683-6028
Elke Weisshaar https://orcid.org/0000-0002-7016-0224
Johannes Geier https://orcid.org/0000-0002-5047-8948

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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