

Prevalence of foot eczema and associated occupational and non-occupational factors in patients with hand eczema

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Summary

Background. Foot eczema often occurs in combination with hand eczema. However, in contrast to the situation with hand eczema, knowledge about foot eczema is scarce, especially in occupational settings.

Objective. To evaluate the prevalence of foot eczema and associated factors in patients with hand eczema taking part in a tertiary individual prevention programme for occupational skin diseases.

Patients/materials/methods. In a retrospective cohort study, the medical records of 843 patients taking part in the tertiary individual prevention programme were evaluated.

Results. Seven hundred and twenty-three patients (85.8%) suffered from hand eczema. Among these, 201 patients (27.8%) had concomitant foot eczema, mainly atopic foot eczema (60.4%). An occupational irritant component was possible in 38 patients with foot eczema (18.9%). In the majority of patients, the same morphological features were found on the hands and feet (71.1%). The presence of foot eczema was significantly associated with male sex [odds ratio (OR) 1.78, 95% confidence interval (CI) 1.29–2.49], atopic hand eczema (OR 1.60, 95% CI 1.15–2.22), hyperhidrosis (OR 1.73, 95% CI 1.33–2.43), and the wearing of safety shoes/boots at work (OR 2.04, 95% CI 1.46–2.87). Tobacco smoking was associated with foot eczema (OR 1.79, 95% CI 1.25–2.57), in particular with the vesicular subtype.

Conclusions. Foot eczema is common in patients with hand eczema, and is related to both occupational and non-occupational factors.

Key words: foot eczema; irritant contact dermatitis; occupational; tobacco smoking.

In many occupations, it is mainly the hands that are exposed to skin hazards. Therefore, occupational skin diseases are primarily located on the hands, with hand eczema (HE) being the most common skin disease

acquired at work (1). Frequently, HE is accompanied by foot eczema (FE) (2, 3). The point prevalence of concomitant HE and FE in an average industrial city was estimated to be 5.4% (4). However, unlike the situation with HE, knowledge regarding the prevalence of FE and associated factors is scarce, especially in occupational settings. Individual predispositions may interact with exogenous factors, for example those related to occupational footwear. Behavioural and lifestyle factors, such as tobacco smoking, may modify the disease.

Like classifications of HE (5, 6), subtypes of FE are often differentiated by their aetiology and morphology.

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However, no common classification system exists. The main entities proposed for FE are atopic FE and irritant or allergic contact dermatitis of the feet. They appear either alone or in combination. Morphological subtypes include vesicular and hyperkeratotic FE. However, discriminating between these subtypes often remains difficult. Moreover, differential diagnoses such as fungal infection and psoriasis of the feet should be excluded (7).

Gaining insights into risk factors for FE may help to improve the treatment and prevention of this often overseen skin disease, and help to differentiate between environmental and endogenous causes. Therefore, the aim of this retrospective study was to evaluate the prevalence of FE and associated factors in patients with HE taking part in an inpatient/outpatient tertiary individual prevention (TIP) programme for occupational skin diseases (8, 9). The different morphological subtypes of FE and self-reported smoking behaviour were taken into consideration.

Patients and Methods

In a retrospective cohort study, the medical records of all 843 consecutive patients who took part in the TIP programme in the two dermatological centres of the Institute for Interdisciplinary Dermatologic Prevention and Rehabilitation (iDerm) at the University of Osnabrück and at the Trauma Hospital Hamburg, Germany, between January 2008 and December 2009 were evaluated. Beforehand, ethical approval was obtained from the ethics committee of the University of Osnabrück. Participants in the TIP programme are largely representative of the population of patients in Germany with severe types of skin disease suspected to be of occupational origin who did not sufficiently respond to secondary outpatient prevention measures (8, 9). The patients had been seen by trained dermatologists, who had taken a detailed history, performed skin examinations and assessed the aetiology of the presented skin diseases during the inpatient phase of the TIP programme. The diagnosis, location and morphology of eczema, and demographic information, including age, sex, profession, and self-reported smoking behaviour, had been recorded. Hyperhidrosis of palms and/or soles had been diagnosed on the basis of the patient's history and the clinical observations, and atopy was defined as the current or past presence of flexural eczema and/or an Erlanger atopy score of ≥ 10 (10). An atopic eczema component was diagnosed in patients with atopy according to the above definition and evidence for an at least partially seasonal or undulating temporal course of the eczema without clear association with exposure to relevant irritants or allergens. Irritant

contact dermatitis was diagnosed on the basis of significant exposure to known irritants and a related temporal course of the disease. All patients had been patch tested with the German baseline series of contact allergens and, when required, with additional substances. Allergic contact dermatitis was diagnosed in patients with a positive patch test reaction to at least one allergen with ascertained exposure that was considered to be relevant for the current eczema. According to the description of the clinical picture and the medical history, three morphological subtypes of eczema were differentiated, for both HE and FE. Vesicular eczema was characterized by vesicles with or without hyperkeratosis. Hyperkeratotic eczema was defined as eczema with visible hyperkeratosis with and without fissures, but without any signs or history of vesicles. The third clinical subtype was eczema with erythema and desquamation but without any signs or history of either vesicles or hyperkeratosis.

Statistical testing was performed with SPSS™ 22.0 for Windows™ (SPSS Inc, Chicago, IL, USA). Descriptive statistics are reported as means and standard deviations (SDs) for continuous variables, and as (relative) frequencies for categorical variables. Associations between categorical variables were assessed with the chi-square (χ^2) test. Whenever appropriate, associations were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). To analyse associations between categorical and continuous variables, unifactorial analysis of variance was used. To further explore potential confounding effects of selected variables, binary logistic regression analysis was performed, with FE as the dependent variable. Differences were considered to be significant if the *p*-value obtained was ≤ 0.05 .

Results

Study population

The medical records revealed that the majority of the 843 patients suffered from HE with or without FE ($n = 723$, 85.8%). Only in a few patients isolated FE was the reason for admission ($n = 7$, 0.8%). Other primary diagnoses in patients without HE included psoriasis ($n = 70$, 8.3%), isolated facial eczema ($n = 3$, 0.4%), atopic dermatitis of other body parts ($n = 8$, 0.9%), and other rare dermatoses ($n = 7$, 0.8%). Twenty-five patients (3%) had a history of hand eczema without current symptoms. Two hundred and seventy-three patients (32.4%) had dermatoses of the feet. The most common diagnosis among these patients was FE ($n = 208$, 76.2%). Other diagnoses were psoriasis of the feet ($n = 29$, 10.6%), fungal infection ($n = 31$, 11.4%), pitted keratolysis ($n = 2$, 0.7%), plantar

hyperkeratosis ($n = 2$, 0.7%), and chronic lichen simplex ($n = 1$, 0.4%).

Only those suffering from HE when admitted to the TIP programme were further investigated ($n = 723$). The mean age was 42.7 ± 12.34 years. Slightly more women than men ($n = 420$; 58.1%) were present. The largest cohorts came from the healthcare sector ($n = 269$; 37.2%), the metal industry ($n = 135$, 18.7%), the hairdressing trade ($n = 79$, 10.9%), cleaning/food handling professions ($n = 47$, 6.5%), and the construction industry ($n = 44$, 6.1%). Two hundred and thirty-two patients (32.1%) worked in professions in which the wearing of safety shoes or boots was mandatory. The majority of this subgroup were men ($n = 215$, 92.7%, $p < 0.001$). Two hundred and thirty-seven patients (32.8%) reported or showed increased sweating of the palms and/or soles, in particular when wearing gloves or occlusive footwear. Atopy was diagnosed in 414 patients (57.3%). The majority of patients had an irritant HE component (77.9%), followed by an atopic (57.3%) and allergic (27.0%) HE component. In 71.6%, the HE consisted aetiologically of an overlap subtype. Vesicular HE was seen in 405 patients (56.0%), hyperkeratotic HE without vesicles in 80 patients (11.0%), and non-vesicular and non-hyperkeratotic HE with erythema and desquamation in 238 patients (32.9%). Two hundred and eighty-eight patients were self-reported non-smokers (39.8%), 335 were smokers (46.7%), and 42 were ex-smokers (5.8%). For 58 patients (8.0%), the information regarding smoking status was missing. In most of the smokers ($n = 326$, 97.3%), the self-reported daily cigarette consumption at admission was recorded. One hundred and twenty-six patients (38.7%) were heavy smokers who admitted consuming > 15 cigarettes per day.

Concomitant HE and FE

Among the 723 patients with HE, 201 patients (27.8%) suffered from concomitant FE. One hundred and twenty patients had vesicular FE (59.7%), 28 patients had hyperkeratotic FE without vesicles (13.9%), and 53 patients (26.4%) had non-vesicular and non-hyperkeratotic FE consisting of erythema and desquamation of the feet. In the majority of patients, the same morphological subtype was found on the hands and feet ($n = 143$, 71.1%). FE was primarily located on the plantar aspects of the feet ($n = 158$, 78.6%). An atopic component was diagnosed in 121 patients (60.4%). An irritant component resulting from hyperhidrosis was considered to be likely in 84 patients (41.8%). An occupational component resulting from a combination of hyperhidrosis and the wearing of safety shoes/boots at work was suspected in 38 patients

with FE (18.9%). Current allergic contact dermatitis of the feet was diagnosed in only 4 patients (2.0%), 3 of whom had sensitization to chromate, 2 to thiuram disulfides and mercaptobenzothiazoles, and 1 to phenol formaldehyde resin. In 2 patients, former allergic contact dermatitis of the feet was suspected. However, an additional shoe series was tested in only 27% of patients with FE. In 21 patients with FE (10.4%), a fungal infection of the feet was diagnosed and considered to be superimposed on eczema. Patients with FE were slightly older than those without FE (mean age $\pm$ SD: 44.11 ± 10.26 years versus 42.10 ± 13.02 years, $p = 0.051$). The highest prevalence of FE was seen in patients working in the construction industry (17/44, 38.6%), and the lowest prevalence in hairdressers (11/79, 13.9%). Univariate data analysis showed that FE was significantly associated with male sex ($p = 0.001$), atopic HE ($p = 0.006$), hyperhidrosis of the palms and/or soles ($p = 0.002$), and wearing of safety shoes/boots at work ($p < 0.001$), especially in combination with hyperhidrosis ($p < 0.001$) (Table 1). In the subgroup of patients with HE who were either self-reported smokers or non-smokers at admission ($n = 623$), similar associations between key variables and having FE were found as in the whole cohort (Table 2). In addition, self-reported tobacco smoking was significantly associated with FE ($p = 0.002$). In particular, heavy smokers (> 15 cigarettes per day) were significantly more common among patients with FE (56/110, 50.9%) than among those without FE (70/216, 32.4%, OR 2.16, 95% CI 1.35–3.46, $p = 0.001$). A logistic regression analysis in this subgroup showed that the associations between key variables and having FE remained relatively unchanged (Table 2).

Morphological subtypes of FE

Vesicular FE. Vesicular FE was significantly associated with younger age ($p = 0.024$), an atopic HE component ($p = 0.030$), and vesicular HE ($p < 0.001$) (Table 3). It was also more common in patients with atopy and with hyperhidrosis, in particular in combination with the wearing of safety shoes/boots. However, these associations were not significant. Vesicular FE was significantly less common in patients with hyperkeratotic HE or HE with erythema and desquamation. In contrast to the other two morphological subtypes, vesicular FE was significantly associated with tobacco smoking ($p = 0.002$) (Table 4).

Hyperkeratotic FE. Hyperkeratotic FE was significantly associated with older age ($p = 0.001$) and concomitant hyperkeratotic HE ($p < 0.001$) (Table 3). Atopy ($p = 0.020$), an atopic HE component ($p = 0.012$),

Table 1. The relationship between potential risk factors and the prevalence of concomitant foot eczema (FE) in all patients with hand eczema (HE)

	HE with FE, n = 201	HE without FE, n = 522	OR ^a (95% CI)	p-value
Male sex, no. (%)	105 (52.2)	198 (37.9)	1.78 (1.29–2.49)	0.001
Age (years), mean ± SD	44.11 ± 10.26	42.10 ± 13.02	1.01 (1.00–1.03)	0.051
Hyperhidrosis, no. (%)	84 (41.8)	153 (29.3)	1.73 (1.33–2.43)	0.002
Safety shoes, no. (%)	88 (43.8)	144 (27.6)	2.04 (1.46–2.87)	<0.001
Hyperhidrosis + safety shoes, no. (%)	40 (19.9)	32 (6.1)	3.80 (2.31–6.26)	<0.001
Atopy, no. (%)	122 (60.7)	292 (55.9)	1.22 (0.87–1.70)	0.275
Component of HE, no. (%)				
Irritant contact dermatitis	143 (71.1)	420 (80.5)	0.60 (0.41–0.87)	0.009
Atopic HE	118 (58.7)	246 (47.1)	1.60 (1.15–2.22)	0.006
Allergic contact dermatitis	45 (22.4)	150 (28.7)	0.72 (0.49–1.05)	0.093

CI, confidence interval; OR, odds ratio; SD, standard deviation.

^a χ^2 test (except for logistic regression analysis used for age).**Table 2.** The relationship between potential risk factors and the prevalence of concomitant foot eczema (FE) in smokers and non-smokers with hand eczema (HE)

	HE with FE, n = 175	HE without FE, n = 448	OR ^a (95% CI)	p-value	Adjusted OR ^b (95% CI)	p-value
Hyperhidrosis + safety shoes, no. (%)	37 (21.1)	28 (6.3)	4.02 (2.37–6.81)	<0.001	3.26 (1.80–5.91)	<0.001
Male sex, no. (%)	90 (51.4)	161 (35.9)	1.89 (1.32–2.69)	<0.001	1.58 (1.05–2.39)	0.035
Age (years), mean ± SD	43.55 ± 10.37	41.26 ± 13.01	1.02 (1.00–1.03)	0.038	1.02 (1.00–1.04)	0.019
Component of HE, no. (%)						
Irritant contact dermatitis	126 (72.0)	361 (80.6)	0.62 (0.41–0.93)	0.023	0.65 (0.42–1.00)	0.049
Atopic hand eczema	109 (62.3)	219 (48.9)	1.72 (1.21–2.47)	0.003	2.07 (1.40–3.06)	<0.001
Allergic contact dermatitis	43 (24.6)	133 (29.7)	0.77 (0.52–1.15)	0.235	0.84 (0.55–1.29)	0.430
Smokers	112 (64.0)	223 (49.8)	1.79 (1.25–2.57)	0.002	1.81 (1.24–2.64)	0.002

CI, confidence interval; OR, odds ratio; SD, standard deviation.

^a χ^2 test (except for logistic regression analysis used for age).^bLogistic regression analysis adjusted for hyperhidrosis + safety shoes, sex, age, morphology and component of HE, and smoking.

vesicular HE ($p < 0.001$) and tobacco smoking ($p = 0.041$) were significantly less common in patients with hyperkeratotic FE than in patients with other FE subtypes. Men were more common among patients with hyperkeratotic FE than among patients with other types of FE. However, this association was not significant.

FE with erythema and desquamation. FE with erythema and desquamation was significantly associated with concomitant HE with erythema and desquamation ($p < 0.001$) (Table 3). Concomitant vesicular HE ($p < 0.001$) was significantly less common in this subgroup. There were no significant associations with age, sex, atopy, hyperhidrosis, the wearing of safety shoes, any of the aetiological HE components, or tobacco smoking.

Discussion

Not much is known about the prevalence of FE and associated factors in patients with HE, especially in

occupational settings. In line with previous findings (8, 9), the present study has shown that the majority of patients taking part in the TIP programme suffer from HE. Here, we show for the first time that approximately one-third of these patients have concomitant FE. The most common aetiological component was atopic FE. However, an irritant component was possible in up to 42% of patients with FE, and an occupational irritant component resulting from profuse sweating in safety footwear in ~20% of patients with FE. In these patients, the German legal criteria for a work-related disease can be fulfilled if there are more reasons in favour of an occupational cause than reasons in favour of rejecting such an association.

It is well known that atopy and atopic dermatitis are the main endogenous risk factors for HE (11). As reported previously, the majority of patients with HE taking part in the TIP programme have an atopic background (8). This was also true for those with concomitant FE. Although atopy itself, defined as the current or past presence of flexural eczema and/or an Erlanger atopy score of ≥ 10 (10),

Table 3. The relationship between potential risk factors and the prevalence of different morphological subtypes of concomitant foot eczema (FE) in patients with hand eczema (HE)

	VES FE, n = 120 (59.7%)	Other FE, n = 81 (40.3%)	OR ^a (95% CI), p-value	HK FE, n = 28 (13.9%)	Other FE, n = 173 (86.1%)	OR ^a (95% CI), p-value	E × D FE, n = 53 (26.4%)	Other FE, n = 148 (73.6%)	OR ^a (95% CI), p-value
Male sex, no. (%)	61 (50.8)	44 (54.3)	0.87 (0.51–1.53), 0.667	16 (57.1)	89 (54.4)	1.26 (0.56–2.78), 0.684	28 (52.8)	77 (52.0)	1.03 (0.53–1.93), 1.000
Age (years), mean ± SD	42.78 ± 10.43	46.09 ± 9.73	0.97 (0.94–1.00), 0.024	50.18 ± 5.89	43.13 ± 10.484	1.10 (1.04–1.16), 0.001	43.92 ± 10.67	44.18 ± 10.14	1.00 (0.97–1.03), 0.879
Atopy, no. (%)	79 (65.8)	43 (53.1)	1.70 (0.96–3.03), 0.078	11 (39.3)	111 (64.2)	0.36 (0.16–0.82), 0.020	32 (60.4)	90 (60.8)	0.98 (0.52–1.87), 1.000
Hyperhidrosis, no. (%)	56 (46.7)	28 (34.6)	1.66 (0.92–2.96), 0.109	7 (25.0)	77 (44.5)	0.42 (0.17–1.03), 0.063	21 (39.6)	63 (42.6)	0.89 (0.47–1.68), 0.748
Safety shoes, no. (%)	54 (45.0)	34 (42.0)	1.13 (0.64–2.00), 0.684	11 (39.3)	77 (44.5)	0.81 (0.36–1.82), 0.684	23 (43.4)	65 (43.9)	0.98 (0.52–1.84), 1.000
Hyperhidrosis + safety shoes, no. (%)	28 (23.3)	10 (12.3)	2.16 (0.99–4.74), 0.066	2 (7.1)	36 (20.8)	0.29 (0.07–1.29), 0.118	8 (15.4)	30 (20.1)	0.72 (0.31–1.69), 0.540
Component of HE, no. (%)									
ICD	85 (70.8)	58 (71.6)	0.96 (0.52–1.80), 1.000	20 (71.4)	123 (71.1)	1.02 (0.42–2.46), 1.000	38 (71.7)	105 (70.9)	1.04 (0.52–2.08), 1.000
AHE	78 (65.0)	40 (49.4)	1.90 (1.07–3.38), 0.030	10 (35.7)	108 (62.4)	0.33 (0.15–0.77), 0.012	30 (56.6)	88 (59.5)	0.89 (0.47–1.68), 0.747
ACD	24 (20.0)	21 (25.9)	0.71 (0.37–1.40), 0.389	9 (32.1)	36 (20.8)	1.80 (0.75–4.32), 0.221	12 (22.6)	33 (22.3)	1.02 (0.48–2.16), 1.000
Morphology of HE, no. (%)									
VES	106 (88.3)	30 (37.0)	12.87 (6.28–26.36), <0.001	8 (28.6)	128 (74.0)	0.14 (0.06–0.34), <0.001	22 (41.5)	114 (77.0)	0.21 (0.11–0.41), <0.001
HK	7 (5.8)	20 (24.7)	0.19 (0.08–0.47), <0.001	13 (46.4)	14 (8.1)	9.84 (3.92–24.75), <0.001	7 (13.2)	20 (13.5)	0.97 (0.39–2.45), 1.000
E × D	7 (5.8)	31 (38.3)	0.10 (0.04–0.24), <0.001	7 (25.0)	31 (17.9)	1.53 (0.60–3.91), 0.434	24 (45.3)	14 (9.4)	7.92 (3.66–17.14), <0.001

ACD, allergic contact dermatitis; AHE, atopic hand eczema; CI, confidence interval; E × D, subtype with erythema and desquamation; HK, hyperkeratotic subtype; ICD, irritant contact dermatitis; OR, odds ratio; SD, standard deviation; VES, vesicular subtype.

^a χ^2 test (except for logistic regression analysis used for age).

Table 4. The relationship between tobacco smoking and the prevalence of different morphological subtypes of concomitant foot eczema (FE) in patients with hand eczema

	VES FE, n/n _{total} (%)	Other FE, n/n _{total} (%)	OR ^a (95% CI), p-value	HK FE, n/n _{total} (%)	Other FE, n/n _{total} (%)	OR ^a (95% CI), p-value	E x D FE, n/n _{total} (%)	Other FE, n/n _{total} (%)	OR ^a (95% CI), p-value
Smokers	80/110 (72.7)	32/65 (49.2)	2.75 (1.45–5.23), 0.002	11/25 (44.0)	101/150 (67.3)	0.38 (0.16–0.90), 0.041	21/40 (52.5)	91/135 (67.4)	0.53 (0.26–1.10), 0.094
Heavy smoking, > 15 cigarettes/day	40/78 (51.3)	16/32 (50.0)	1.05 (0.46–2.40), 1.000	6/11 (54.5)	50/99 (50.5)	1.18 (0.34–4.11), 1.000	10/21 (47.6)	46/89 (51.7)	0.85 (0.33–2.20), 0.811

CI, confidence interval; E x D, subtype with erythema and desquamation; HK, hyperkeratotic subtype; OR, odds ratio; VES, vesicular subtype.

^a χ^2 test.

did not significantly increase the risk of having FE, an atopic HE component was significantly associated with having FE. Involvement of the hands and/or feet is a frequent finding in children with atopic dermatitis (12). However, not much is known about the prevalence of FE in adult patients with atopic dermatitis. FE was not associated with either irritant or allergic contact dermatitis of the hands, suggesting that the feet and hands are rarely exposed to the same allergens and irritants, especially in occupational settings.

Another significant endogenous risk factor for concomitant FE was hyperhidrosis. Both the palms and soles contain a high density of eccrine sweat glands. Sweating induces a moist or wet environment, causing maceration and irritation of the skin. Moreover, it favours fungal, bacterial and viral skin infections (13). Sweating can be aggravated by occlusive footwear, especially during warmer periods. The materials of shoes and boots, as well as of socks, have an impact on water evaporation from the skin surface. Long durations of wear and physical exercise may increase the warmth and humidity within footwear. In addition, poorly fitting footwear may cause friction and pressure on the skin. This may be enhanced by excessive movements and carrying of heavy loads, as occurs, for example, in the construction industry. In many occupations, safety shoes or boots are mandatory. Their water evaporation capacity varies greatly. As safety shoes/boots are usually worn continuously for up to 10 hr/day, they may have a substantial impact on the skin of the feet. The presented results show that wearing of safety shoes/boots at work is significantly associated with FE in patients with HE, especially in those with concomitant hyperhidrosis. This suggests that irritation related to profuse sweating in safety shoes/boots may induce occupational FE.

The significantly higher prevalence of men among patients with FE in this study may be related to a significantly higher number of men than women wearing safety shoes/boots at work. In accordance with this, the highest prevalence of FE was seen in patients working in the male-dominated construction industry, in which safety shoes/boots are mandatory. Landeck et al. reported that, in a large cohort of patients undergoing patch testing, male sex was significantly associated with skin changes of the feet as compared with those tested for other body sites (52.4% versus 37.2%) (14). In general, allergic contact dermatitis is less commonly located on the feet than on the hands (14). The reported prevalence of patients with foot dermatitis from patch test clinics shows a wide variation, and ranges between 3.0% and 14.0% (7, 14–16). In this study, current or former allergic contact dermatitis of the feet was rarely diagnosed. It has to be noted that an

additional shoe series was applied in only 27% of patients with FE. Although the most common shoe allergens are already covered in the baseline series, this may have led to an underestimation of the true number of patients with allergic contact dermatitis of the feet.

It has been established that tobacco smoking has a negative impact on skin diseases such as palmoplantar pustulosis and psoriasis, which may be related to tobacco-induced proinflammatory cutaneous effects. Moreover, it has been linked with delayed wound healing, wrinkling, and premature skin ageing (17). Several studies have suggested a positive association between tobacco smoking and the prevalence of HE in the general population (18–21). However, others could not confirm this finding (22, 23). In a recent cross-sectional population-based study, only individuals smoking >15 cigarettes per day had an increased risk for HE (24). A few studies have addressed associations between tobacco smoking and occupational HE, with contradictory results (19, 25–27). In a study from Sweden, only in a subgroup of heavily smoking hairdressers was the risk of HE slightly increased (18). Previously, we have shown that tobacco smoking is associated with the severity of occupational HE and a worse prognosis in those taking part in the TIP programme (28). We are not aware of any study evaluating associations between tobacco smoking and FE. Here, we show for the first time that concomitant FE in patients with HE is significantly associated with self-reported tobacco smoking, in particular in those smoking >15 cigarettes per day.

The most common morphological subtype was vesicular FE. It has been reported that hyperhidrosis aggravates pompholyx, an often chronic relapsing form of vesiculobullous palmoplantar eczema (29, 30). Here, vesicular FE was associated with hyperhidrosis, in particular when safety shoes/boots were worn at work. However, this finding was not significant ($p = 0.066$). In the present study, vesicular FE was the only morphological subtype that was significantly associated with tobacco smoking. This may indicate that tobacco smoking, in particular, is a risk factor for vesicular eczema. Recently, it was reported that, among metal workers with irritant hand dermatitis, smokers had significantly higher score values for vesicles on the hands than non-smokers (27). Moreover, chronic vesicular palmoplantar eczema is less likely to respond to bath psoralen combined with ultraviolet A therapy in smokers than in non-smokers (3). Notably, in the present study, heavy smokers (>15 cigarettes per day) were equally common among patients with all three morphological subtypes of FE. It is well known that hyperkeratotic HE is associated with male sex and older age (5, 31, 32). Similarly, in our study, patients with hyperkeratotic FE

were significantly older than patients with other subtypes of FE. However, the positive association with male sex was not significant. A negative association was found between hyperkeratotic FE and atopy or an atopic HE component, suggesting that hyperkeratotic FE is not a typical clinical feature of atopic dermatitis. It has to be considered that the main differential diagnosis of hyperkeratotic FE is plantar psoriasis. In the present study, patients with current psoriasis lesions elsewhere or a history of psoriasis were excluded. However, it is sometimes difficult to differentiate between hyperkeratotic eczema and psoriasis of the hands and feet, both clinically and histologically. The cohort of patients with non-vesicular and non-hyperkeratotic FE characterized by erythema and desquamation was more heterogeneous than the cohorts with the other two clinical subtypes. No relevant associations with any of the evaluated potential risk factors were detected. Furthermore, all three morphological subtypes of FE were equally common among the different occupations (data not shown).

There are several strengths and limitations of our study. The medical records of a large cohort of well-documented patients with occupational skin diseases were evaluated to assess the prevalence of FE and associated factors in patients with HE. Age, sex, atopy, hyperhidrosis, smoking status and occupational backgrounds were considered. The patients had been continuously monitored by trained dermatologists taking thorough histories, assessing the aetiology of the presented skin diseases, and documenting the morphological features. The univariate analysis revealed significant associations between FE and potential risk factors. These associations remained relatively unchanged after adjustment for confounders by logistic regression analysis. However, the retrospective study design has limitations in accuracy, in particular with regard to the differentiation of specific morphological subtypes of both HE and FE. Moreover, no validated score was applied to assess the severity of disease. It is possible that the presented findings are only representative for severe HE, as patients taking part in the TIP programme usually suffer from severe skin diseases. Further studies are needed to evaluate correlations between the severity of HE and the prevalence of FE, and between the severity of FE and associated factors. The information regarding smoking was self-reported and therefore potentially unreliable in some cases. Furthermore, no conclusion with regard to the relationship between duration of smoking and FE can be drawn. Moreover, the associations that we have found may, in principle, represent the effects of other unmeasured individual factors and confounders. The evaluation of the different morphological subtypes of FE was hampered by the study size. Further

studies in larger cohorts are necessary to confirm these findings.

In conclusion, concomitant FE is common in patients with HE taking part in a TIP programme for severe occupational skin diseases, and may frequently be related to the workplace. FE is significantly associated with male

sex, atopic HE, hyperhidrosis, and the wearing of safety shoes/boots. Tobacco smoking is highly associated with FE, especially with the vesicular subtype. These results suggest that wearing breathable, well-fitting footwear may promote healthy feet, especially in individuals at risk. Moreover, smoking cessation should be encouraged.

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