Association between occupation and contact allergy to the fragrance mix: a multifactorial analysis of national surveillance data

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Abstract

***Objectives*—To assess the role of potential (occupational) risk factors for fragrance contact allergy (FCA). Most studies assessing the range of contact sensitisation in various clinical populations found the fragrance mix, a good screening tool for the detection of FCA in general, to be one of the leading allergens. The role of occupational exposure to fragrances is, however, yet unclear.**

***Methods*—Firstly, crude analyses of the prevalence of FCA in various occupational fields including all 57 779 patients patch tested in the participating centres of the Information Network of Departments of Dermatology (IVDK) between January 1992 and December 1998. Secondly, a multifactorial Poisson regression analysis of these patients, including several potential risk factors.**

***Results*—(*a*) The proportion of patients with FCA varied greatly between different occupational groups from 2.5% to 17.4%, (*b*) the highest occupational risk of FCA was associated with work as a masseur or physiotherapist, metal furnace operator, potter or glass maker etc, or geriatric nurse, (*c*) non-occupational factors that influenced risk of FCA included atopy, female sex, several sites, in particular the axillae, and increasing age.**

***Conclusions*—Occupations with a high risk of FCA were identified as targets of preventive action—that is, the substitution of scented products with fragrance free materials with which to work (skin disinfectants, cleaning solutions, personal care products) wherever possible.**

(*Occup Environ Med* 2001;**58**:392–398)

Keywords: contact allergy; occupational risk factors; fragrances

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Accepted 1 March 2001

Considering the ubiquitous occurrence of fragrance materials, the risk of side effects is small.[1] However, in clinical populations (patch test patients) the fragrance mix, eight common fragrances, is one of the leading contact allergens world wide.[2] On a population level, about 1% seem to have fragrance contact allergy (FCA), according to the Danish Glostrup allergy study.[3] Thus, FCA is an important public health issue.

Previous studies evaluating factors associated with a given contact sensitisation by multifactorial analysis have hinted at the usefulness of this approach to obtain estimates of the degree of association between certain risk factors while controlling for other, confounding factors.[4 5] However, the association between certain occupations (as markers of respective occupational exposure) and a particular contact sensitisation—namely, FCA—has not yet been considered. In view of various sources of contact to scented materials in different work environments, such an analysis could contribute to occupational risk assessment, disentangling occupational and non-occupational factors. The present epidemiological study reports on the risk of FCA associated with different occupations, controlling for a different distribution of various potential confounding factors in these occupations, and attempts to provide insight into the needs for future in depth research for improving prevention of contact sensitisation to fragrances.

Methods

The Information Network of Departments of Dermatology (IVDK) surveys the epidemiology of contact allergy and has been described in detail,[6–8] including its approach to the epidemiology of occupational contact dermatitis.[9] Basically, all patch test results and a standardised history of all patients patch tested in the participating centres are recorded and transferred to the data centre in Göttingen at regular intervals for pooled analysis. Thus, the IVDK assesses clinical epidemiology: analyses based on data of patients referred for the evaluation of suspected contact allergy, as opposed to population based epidemiological approaches. Data management and analysis are performed with the program package SAS (Version 8.1, SAS Institute, Cary, NC).

In the present analysis, contact allergy to the fragrance mix is considered. The fragrance mix contains eight perfume compounds (oak moss, isoeugenol, eugenol, cinnamic aldehyde, geraniol, hydroxycitronellal, cinnamic alcohol, α-amylcinnamic aldehyde, 1% each) in petrolatum as the test vehicle and is supplied by Hermal/Trolab, Reinbek, Germany. It is regarded as a relatively good screening test for FCA in general. All patients patch tested in the participating centres of the IVDK between January 1992 and December 1998 were included in this analysis.

During the several years of documentation since the beginning of the IVDK project in

Table 1 Crude prevalences of FCA above average, defined as "at least a weak positive reaction (+)" and "at least a positive reaction (++)" at 72 hours in different occupations

ISCO-88	*Job title/group*	*n*	*‰**	*+ to +++ (%)*	*++ to +++ (%)*
2230, 3231	Geriatric nurse	322	1.209	17.4	6.2
3226	Masseur, physiotherapist	287	2.921	16.4	5.9
8120	Metal furnace operator, melter, caster, drawer	119	1.097	16.0	5.9
7320	Potter, glass maker, or blower	70	0.879	15.7	8.6
5141	Cosmetologist	139	12.981	14.4	2.9
5121†	Household worker (including housewife)	6820	NC	13.9	4.7
6110, 6120, (6200, 9211)	Agricultural labourer	333	3.187	13.8	4.2
5220, 5230, 9110	Salesperson	1013	0.616	13.3	4.5
2300	Teaching professional	1498	1.583	13.1	3.9
7311	Precision mechanic	153	1.593	13.1	3.9
7430, (5200)	Textile worker or salesperson	408	1.936	13.0	5.1
3131, 7344, 8224	Photographer, laboratory worker	108	3.375	13.0	1.9
1000, 4000, and others	Office worker	7779	1.043	12.2	4.2
5123	Waiter, bartender, etc	471	1.404	12.1	3.6
4211, 4212	Cashier	125	1.119	12.0	4.8
(5220, 5230), 6113	Florist, gardener	468	1.578	12.0	4.9
9151, 9322, 9333	Package and transport labourer	488	0.389	11.9	3.7
7311, 7343, 7346	Printer, typesetter, and related	187	1.076	11.8	4.8
7213	Sheet metal worker	78	0.629	11.5	3.8
2142–2147	Engineer	1279	0.716	11.5	4.1
Average of all people with occupation		37592	1.337	11.4	3.9

*Of all workers employed in the respective occupation(s) (average) according to the "Bundesanstalt für Arbeit" (Federal Labour Office, http://www.arbeitsamt.de) official statistics.
†ISCO-88 only includes (domestic) occupations with formal employment.
NC=not calculable (number of "informal" household workers unknown).
ISCO-88 number in parentheses: only part of category applicable.

1989, a patient may have been recorded more than once due to several consultations, and is identified as a different "case" each time. If there were multiple consultations of one patient, the case with the strongest reaction to the fragrance mix was selected for the present analysis. The anamnestic profile included the site of current dermatitis, information on previous or current atopic dermatitis, age, sex, the year in which the patch test was performed, and the current occupation. Occupations are registered within the IVDK primarily with the code numbers of the Federal Statistical Bureau (maximum: three digit precision).[10] For the purpose of the present analysis, single occupations were aggregated to occupational groups if considered appropriate from the point of view of a presumably homogenous occupational exposure profile to contact with scented materials. In this paper, key international code numbers[11] are given to enable international comparisons, despite some general limitations of the validity of work exposures described this way.[12] Numbers of major and minor groups were padded with trailing

Table 2 Crude prevalences of FCA below average, defined as "at least a weak positive reaction (+)" and "at least a positive reaction (++)" at 72 hours

ISCO-88	*Job title/group*	*n*	*‰**	*+ to +++ (%)*	*++ to +++ (%)*
Average of all people with occupation		37592	1.337	11.4	3.9
3230	Nurse, midwife	2929	2.227	11.4	4.0
4142	Mail and related clerk	219	1.372	11.0	4.6
3221, 3223	Medical assistant	538	4.315	10.8	3.2
7137, 7240, 8282, 8283	Electrician	503	0.538	10.3	3.2
2221	Physician	525	3.608	10.3	3.4
3111, 3116, 8150, 8220	Chemical industry technician or labourer	399	1.017	10.3	2.8
(5220), 8300	Driver, filling station attendant	517	0.501	10.3	2.1
2224	Pharmacist	108	1.183	10.2	3.7
7212	Welder, solderer	90	0.829	10.0	5.6
—	Missing job title	4629		9.8	3.9
7143, (9130, 9142)	Cleaner	1152	1.352	9.5	3.0
8231	Rubber manufacturer	42	0.846	9.5	7.1
7411	Butcher, fishmonger	227	1.801	9.3	4.0
8211	Metal worker (cutting)	326	1.298	9.2	2.8
2222, 3225, (7310)	Dentist, dental assistant, or technician	681	9.351	9.0	3.1
5122, 7414	Cook, food preserver	710	1.404	8.9	3.4
7231–7233	Mechanic	1460	1.165	8.6	3.2
8142, 8143	Paper maker	82	0.659	8.5	4.9
7141, 7142	Painter, varnisher	307	1.024	8.5	2.9
7222, 7136	Locksmith	740	0.568	8.4	3.8
2450, 3470	Artist, professional sports	215	1.858	8.4	2.8
7412	Baker, confectioner	399	3.240	8.0	2.8
5141	Hairdresser	866	5.094	7.9	2.3
7440, 8265, 8266	Leather goods manufacturer	105	2.105	7.6	2.9
7224, 8223	Metal finisher	81	1.528	7.4	3.7
0000, 3450, 5160, 9152	Security service	546	1.524	7.0	2.7
6141, 9212	Logger, forest worker	30	0.549	6.7	0
7121–3, 7131–5, 9312–3	Construction labourer	872	0.596	6.1	2.2
7124, 7331, 7420, 8141	Carpenter, joiner, and other woodworker	450	0.879	5.8	0.9
8110, 9311	Miner	102	1.005	4.9	2.0
8232	Plastic material manufacturer	108	0.574	4.6	0.9
6120, 6151–3	Animal keeper	80	1.570	2.5	0

Footnotes as table 1.

zeros to present four digit numbers throughout. To describe the proportion of workers in the respective occupational groups examined in the IVDK centres relative to the total number of people employed in these occupations in Germany, the mean numbers of employed people (in the period considered) were retrieved from the Federal Labour Office (http://www.arbeitsamt.de) and are shown in tables 1 and 2.

As a first step, the proportions of people who reacted with at least a weakly positive (+) reaction, and at least a positive (++) reaction to the fragrance mix on the 3rd day of the patch test were identified and aggregated on the level of current occupations and occupational groups. Results are shown in table 1 for those occupations with prevalence of FCA above average, and in table 2 for those occupations with prevalence of FCA below average.

Secondly, the association between seniority (duration of occupational exposure, categorised in the quartiles of the actual distribution) and prevalence of FCA was analysed for selected occupations and occupational groups. For this purpose, the proportions of people with FCA within the quartiles of the respective seniorities were determined.

Thirdly, Poisson regression analysis was performed. The model included all 52 occupations and occupational groups, 14 sites, age, sex, year of patch test, and atopic dermatitis (past or present, derived from the patient's history). The site of current contact dermatitis was classified according to similar previous analyses[4 13] and clinical knowledge of particular patterns of allergic contact dermatitis to fragrances.[1 14] Age was categorised according to the quartiles of the age distribution in our sample.

Table 3 Results of a Poisson regression analysis of patients tested with the fragrance mix between January 1992 and December 1998, considering two alternative outcomes—part I: non-occupational factors

Attribute	Prevalence (%)	At least + (11.5%)		At least ++ (4.0%)	
		PR	95% CI	PR	95% CI
Age:					
≤30	26.7	1.00	Reference	1.00	Reference
>30–44	23.8	1.42	1.31 to 1.53	1.61	1.40 to 1.84
>44–58	25.6	1.67	1.55 to 1.80	1.90	1.66 to 2.16
>58	23.9	1.93	1.77 to 2.10	2.07	1.79 to 2.39
Sex (female)	64.5	1.29	1.21 to 1.37	1.18	1.07 to 1.31
Main site:*					
Trunk	2.9	1.00	Reference	1.00	Reference
Hands	29.9	1.24	1.07 to 1.46	1.28	0.98 to 1.67
Arm	3.8	1.23	1.01 to 1.49	1.19	0.86 to 1.65
Face	15.2	1.20	1.03 to 1.42	1.13	0.86 to 1.48
Neck	1.4	1.39	1.10 to 1.75	1.31	0.88 to 1.94
Feet	2.8	1.26	1.02 to 1.55	1.19	0.84 to 1.68
Leg	8.7	1.59	1.36 to 1.89	1.50	1.14 to 1.99
Axilla	0.9	2.77	2.20 to 3.46	2.73	1.87 to 4.00
Other site	8.9	0.66	0.55 to 0.80	0.48	0.35 to 0.67
Atopic dermatitis, past or present	18.1	1.15	1.07 to 1.22	1.14	1.02 to 1.28
Year of patch test:					
1992	10.1	1.00	Reference	1.00	Reference
1993	13.5	1.46	1.30 to 1.63	1.39	1.15 to 1.67
1994	15.4	1.71	1.54 to 1.91	1.43	1.19 to 1.71
1995	15.0	1.30	1.16 to 1.45	1.13	0.94 to 1.37
1996	15.6	1.33	1.19 to 1.49	1.16	0.96 to 1.39
1997	15.1	1.43	1.28 to 1.60	1.41	1.18 to 1.68
1998	15.2	1.58	1.42 to 1.76	1.40	1.17 to 1.68

*Additionally controlled for several more sites—none of these associated with a significantly increased or decreased risk.

The adjusted prevalence ratios (PRs) (95 % confidence intervals (95% CIs)) were derived from the estimates of the Poisson model to measure the strength of association estimated by the profile likelihood method. The implicit assumption when using a Poisson model for the counts of people with FCA refers to the equality of mean and variance of the response variable. In the case of overdispersion or underdispersion in the response variable (relative to the assumption of the standard Poisson model) the 95% CI underestimates or overestimates the nominal 95% CI, which has to be taken into account in the interpretation.

Results

In the period mentioned, 57 779 of the 64 185 patients examined in the 32 participating centres were patch tested with the fragrance mix contained in the standard series. Multiple consultations were noted in 1454 (2.5%) of 57 779 patients, rarely (n=71) more than twice. Demographic characteristics of the whole patch test population, including time trends of certain features, have been published recently.[15] The MOAHLFA index[16] of the present large subset of this group is male 35.5%; occupational dermatitis 15.3%; atopic dermatitis 18.1%; hand dermatitis 29.9%; leg dermatitis 8.7%; face dermatitis 15.2%; and age 40 and more 57.1%.

Altogether 592 additional people had been tested with the standard series, but with omission of the fragrance mix—that is, about 1% of all patients tested with the standard series. To consider potential bias by selective omission of the fragrance mix associated with certain occupations, the respective proportions were analysed. These varied unsystematically between 0.6% and 1.5%.

The crude prevalences of FCA in our groups of patients with contact dermatitis working in different occupations varied considerably between the extremes, ranging from 2.5% to 17.4% (table 1 *v* 2). A group of 15 596 patients altogether with undetermined exposure—mainly old age pensioners and students—was not considered in this particular analysis. When interpreting the proportions found, and the rank order, the small group sizes should be taken into account. The ranking in tables 1 and 2, which is based on the proportion of at least a weakly positive reaction, reflects the order based on stronger reactivity relatively well, again bearing in mind the even smaller number of at least a++ positive reaction in some occupational groups. There are vast differences in the proportions of workers in the respective groups who consulted IVDK centres. This indicates selection processes (see discussion).

Seniority, the number of years spent in the occupation, and its relation to FCA has been analysed. Information on the duration of work in the current occupation had been given in 62.9% of all 57 779 cases. Considerable variation of the distribution of seniority is noted: some occupations are associated with a relatively short latency period until presentation

Table 4 Results of a Poisson regression analysis of patients tested with the fragrance mix between January 1992 and December 1998, considering two alternative outcomes—part II: occupational factors

Current job	*Prevalence (%)*	*At least + (11.5%)*		*At least ++ (4.0%)*	
		PR	*95% CI*	*PR*	*95% CI*
Engineer	2.2	1.00	Reference	1.00	Reference
Metal furnace operator, etc	0.2	1.42	0.85 to 2.23	1.41	0.64 to 3.11
Masseur, physiotherapist	0.5	1.37	0.98 to 1.90	1.45	0.84 to 2.51
Geriatric nurse	0.6	1.28	0.93 to 1.73	1.31	0.78 to 2.20
Potter, glass maker, etc	0.1	1.19	0.58 to 2.14	1.66	0.66 to 4.17
Precision mechanic	0.3	1.14	0.69 to 1.78	0.97	0.42 to 2.26
Photographer, etc	0.2	1.07	0.59 to 1.78	0.45	0.11 to 1.84
Cosmetologist	0.2	1.07	0.65 to 1.67	0.63	0.23 to 1.75
Salesperson	1.8	1.02	0.80 to 1.29	1.01	0.67 to 1.50
Printer, etc	0.3	1.01	0.63 to 1.54	1.14	0.56 to 2.31
Electrician	0.9	0.99	0.71 to 1.34	0.94	0.48 to 1.47
Teaching professional	2.6	0.98	0.79 to 1.22	0.86	0.59 to 1.25
Agricultural labourer	0.6	0.97	0.69 to 1.35	0.85	0.47 to 1.54
Package and transport	0.9	0.97	0.71 to 1.31	0.83	0.48 to 1.41
Sheet metal worker	0.1	0.97	0.46 to 1.79	0.88	0.28 to 2.82
Florist, gardener	0.8	0.96	0.70 to 1.30	1.13	0.69 to 1.85
Office worker	13.5	0.95	0.80 to 1.14	0.95	0.71 to 1.27
Waiter, bartender, etc.	0.8	0.94	0.69 to 1.28	0.81	0.47 to 1.40
Nurse, midwife	5.1	0.92	0.76 to 1.13	0.95	0.68 to 1.33
Household worker	11.8	0.89	0.75 to 1.08	0.91	0.68 to 1.24
Welder, solderer	0.2	0.89	0.42 to 1.64	1.33	0.53 to 3.34
Textile worker, etc	0.7	0.89	0.64 to 1.23	1.12	0.67 to 1.87
Driver, filling station attendant	0.9	0.88	0.64 to 1.19	0.49	0.26 to 0.95
Mail and related clerk	0.4	0.86	0.55 to 1.30	1.03	0.52 to 2.03
Missing job title	7.9	0.85	0.70 to 1.03	0.95	0.69 to 1.30
Chemical industry	0.7	0.85	0.59 to 1.20	0.66	0.35 to 1.27
Cashier	0.2	0.84	0.48 to 1.39	0.99	0.42 to 2.31
Metal worker (cutting)	0.6	0.84	0.56 to 1.23	0.67	0.33 to 1.35
Medical assistant	0.9	0.82	0.60 to 1.11	0.71	0.41 to 1.23
Physician	0.9	0.81	0.59 to 1.10	0.76	0.45 to 1.30
Rubber manufacturer	0.1	0.80	0.25 to 1.89	1.63	0.51 to 5.23
Pharmacist	0.2	0.78	0.40 to 1.37	0.83	0.30 to 2.31
Mechanic	2.5	0.78	0.61 to 0.99	0.78	0.52 to 1.15
Locksmith	1.3	0.78	0.57 to 1.04	0.94	0.59 to 1.48
Painter, varnisher	0.5	0.77	0.49 to 1.14	0.72	0.36 to 1.46
Butcher, fishmonger	0.4	0.76	0.46 to 1.17	0.94	0.46 to 1.91
Dentist, etc	1.2	0.76	0.56 to 1.02	0.76	0.45 to 1.26
Baker, confectioner	0.7	0.74	0.50 to 1.07	0.74	0.39 to 1.42
Cook, food preserver	1.2	0.72	0.53 to 0.96	0.79	0.49 to 1.28
Artist, professional sport	0.4	0.70	0.42 to 1.11	0.67	0.29 to 1.56
Cleaner	2.0	0.67	0.52 to 0.86	0.62	0.40 to 0.96
Paper maker	0.1	0.67	0.28 to 1.32	1.06	0.38 to 2.93
Hairdresser	1.5	0.66	0.49 to 0.89	0.59	0.35 to 0.99
Security service	1.0	0.63	0.44 to 0.89	0.69	0.39 to 1.23
Logger, forest worker	0.1	0.61	0.10 to 1.91	—	—
Metal finisher	0.1	0.61	0.24 to 1.27	0.83	0.26 to 2.65
Leather goods manufacturer	0.2	0.60	0.27 to 1.15	0.63	0.20 to 2.03
Construction labourer	1.5	0.54	0.39 to 0.74	0.52	0.31 to 0.88
Carpenter, etc	0.8	0.53	0.34 to 0.79	0.23	0.08 to 0.62
Plastic material manufacturer	0.2	0.37	0.13 to 0.82	0.20	0.03 to 1.48
Miner	0.2	0.35	0.11 to 0.84	0.49	0.12 to 1.99
Animal keeper	0.1	0.19	0.03 to 0.61	—	—

with dermatitis—namely, geriatric nurses, hairdressers, cosmetologists, bakers and confectioners, cashiers, cleaners, loggers and forest workers, and package and transport labourers with a median of 6 years or less, whereas others have a much longer latency period of, for example, 15 years and more (median)—namely, miners, agricultural labourers, teaching professionals, sheet metal workers, and household workers. The distribution of FCA proportions among the respective quartiles of years in an occupation does not show a consistent pattern for both outcomes considered; mostly the proportion of FCA increases with increasing seniority.

Poisson regression analysis showed several factors which were associated with a significantly increased risk of FCA (table 3 and 4). Although the role of occupational exposure to fragrances is the focus of the present paper, the other factors are nevertheless of interest and are thus shown. With increasing age, the risk of FCA increased monotonically up to a PR of 1.93 (95% CI 1.77 to 2.10) for the broader and 2.07 (1.79 to 2.39) for the more conservative case definition, respectively, in the oldest age quartile. Female sex was associated with a slightly, yet significantly increased risk. Many sites of dermatitis considered here are significant risk factors indicative of FCA, in particular dermatitis involving the axilla, compared with the reference site trunk. Scalp, elbow, and popliteal flexures, generalised pattern, and "missing site" were additional site categories not included in table 3 and were not associated with a significantly increased or decreased risk in this analysis.

Previous or current atopic dermatitis was a significant, albeit very weak risk factor for both outcomes. Except for the year 1992, the year of patch test had no significant influence on the prevalence of positive fragrance mix test results. Interestingly, variation in time was more marked for at least a weak positive reaction than for the more conservatively defined outcome.

Significant variation in risk of FCA between the occupational groups was found for both outcomes ($p<0.0001$ for at least a weak positive reaction and $p=0.004$ for at least a positive reaction). Several occupations were associated with an increased risk of FCA (based on at least a weak positive reaction) in this analysis—namely, masseur or physiotherapist, metal furnace operator, geriatric nurse, potter or glass maker etc, precision mechanic, photographer etc, cosmetologist, salesperson, and printer etc, with PRs above 1, compared with the reference group chosen (engineers), which is largely in accordance with results of the unadjusted analysis (tables 1 and 2). It should be noted, however, that although the ranking of risk estimates is definite, the actual estimates depend on the definition of the reference group, which is arbitrary (see discussion). In this case, an occupational group with a prevalence of FCA very close to the mean has been chosen.

A check of the underlying distributional assumption of the Poisson regression model showed evidence for some underdispersion in both models, more pronounced for the more restrictive case definition (scaled deviance of 0.631 and 0.407 in the two models, respectively). This means that the computed 95% CIs are too wide and represent a conservative upper bound for the true precision of the adjusted PR. We refrained, however, from incorporating the underdispersion into the model (by a suitable scaling factor), as such a late adjustment for underdispersion gives too optimistic an impression of the precision of estimates.

Discussion

Fragrances are ubiquitous substances and there are numerous chances of contact both in work and in private environments.[1] The fragrance mix is a mixture of eight single fragrance materials still used commonly[17] which for decades have been identified as potential allergens.[14] At the same time, the mix is considered to be a relatively good screening

tool for the detection of FCA in general,[18] not only of contact allergy to one of its constituents. In populations who have had clinical patch tests it is usually the most common contact allergen after nickel.[1] On the population level, FCA will be rarer than in a population selected for morbidity of suspected allergic contact dermatitis. As a consequence, the positive predictive values of positive patch test results of the fragrance mix will be lower, which can seriously limit the validity of analyses such as ours if using a sample based on a population as opposed to a clinical sample.

The number of workers from a certain occupational group consulting one of the IVDK centres for diagnostic patch testing relative to the mean number of people employed in these occupations in Germany varied considerably between the different occupational groups (tables 1 and 2). There are probably many reasons for this.

- The risk of contact dermatitis varies considerably between occupations and thus renders people more or less likely to consult one of the IVDK centres.
- Some occupations are associated with a well known high risk of sensitisation to a relatively well defined set of allergens—for example, the hairdressing trade—which may enable adequate diagnosis already on the level of primary dermatological care. This could introduce some bias in underrepresentation in the IVDK centres by selective non-referral for patch testing.
- Access to healthcare institutions may generally be easier for some workers (including those working in the healthcare sector) than for others.

However, the contribution of these factors to overall or specific occupation selection cannot be measured well. Thus, our analysis could not incorporate such factors effectively and the interpretation of our findings based on a sample unrepresentative of the whole population has to be cautious, paying due attention to the potentially biasing effect of selection.

This unprecedented analysis of clinical surveillance data on contact allergies puts the role of occupation—as a surrogate for more specific occupational exposures—on the development of FCA into the perspective of other risk factors for this particular type of contact allergy by controlling for them in a multivariable analysis.

A first, unadjusted analysis (tables 1 and 2) showed a threefold range of prevalence of FCA, if some smaller occupational groups were disregarded. However, it is well known that occupations may differ greatly in distribution of sex and age, comparing, for example, hairdressers (predominantly young women) and construction workers (predominantly men). Thus, the proportion of FCA in different occupations could be determined more by these factors—or the actual exposures they represent—than by occupational exposure, and estimates of association may be confounded by such factors. Standardisation for age and sex[19] may circumvent this problem to a certain degree, but additional factors—such as atopy or time of patch testing—may also act as confounders, if they are both associated with the outcome and one of the explanatory factors of interest. This was the reason for performing a multivariable analysis.

The results of the Poisson regression analysis clearly show that there is roughly a threefold variation in risk of FCA between high and low risk occupations, after controlling for other important risk factors. The absolute values of point estimates (PRs) should not be taken at face value, because they depend on the definition of the reference group, which is arbitrary, especially with a nominally scaled attribute, which has no natural end point as a potential reference. However, the ranking and the degree of variation in risk can be regarded as valid. In this case, we opted for a reference group with about average prevalence of FCA for both outcomes. As a consequence, risk, measured as PRs is distributed around this reference. Still, we found significant variation of prevalance (risk) of FCA between occupations when adjusting for the other, potentially confounding factors. In conclusion, we think that it is justified to identify the four occupations with highest risk for both outcomes as targets of further in depth research and prevention (see later).

Weak positive reactions to the fragrance mix may be irritant rather than allergic in some cases. Therefore, a separate analysis, with the same set of explanatory variables, was performed with a more conservatively defined outcome—at least a positive reaction. A comparison between risk estimates for these two outcomes is reassuring in that no important differences were noted: risk estimates are mostly similar—taking into account their limited precision—with a few exceptions such as textile workers, drivers and filling station attendants, and carpenters etc (table 4).

Aimed testing of an allergen may introduce heavy bias, if the reason for aimed testing—for example, working in a certain occupation—is included in the set of explanatory variables. However, in the fragrance mix there is no such effect, as this mix is tested routinely in the standard series, which is an essential part of the patch test programme for every patient, irrespective of occupation. Likewise there is no detectable downward bias due to aimed omission of the mix from the individual patch test panels related to the occupation of the patient.

Looking at the four occupations which are associated with the highest risk of FCA, harmful occupational exposures can be pinpointed to certain, more or less specific work materials in two of these. In the case of masseurs and physiotherapists, the range of work exposures has recently been reviewed.[20] The authors emphasised the role of irritation by friction and cumulative exposure to emulsifiers and certain lipids, which may enhance penetration of allergens, not to mention the importance of primary irritant dermatitis as a percursor for second stage allergic contact dermatitis to fragrances,[1] which abound in massage lotions and related products.

Geriatric nurses are people who work taking personal care of elderly people in the home or

in institutions. In either case they perform various tasks which include, among others, (*a*) contact with wetness and irritants such as washing solutions, (*b*) frequent disinfection of the hands, and (*c*) appliance of body care products and external drugs.[21] All three categories of products are usually perfumed. Thus, the exposure pattern is similar to that of masseurs and physiotherapists, except for the lack of friction, and the risk of primary irritant contact dermatitis is also high. Interestingly, nurses working in patient care (international standard classification of occupations (ISCO)-88: 3230) have a lower prevalence of FCA—possibly (partly) due to some dilution bias introduced by relative overconsultation (already discussed). Specific reasons for this difference are difficult to assess by analysing surveillance data, but should be elucidated by—for example, a cross sectional epidemiological study focusing on relevant exposures.

By contrast, the high risk found for metal furnace operators, casters, etc is surprising and cannot be easily explained on the grounds of our data. Five of the 19 positive reactions (from weak to strong) occurred in a group of only 24 patients tested in Dortmund, thus, a local or regional factor—such as the use of a heavily scented body lotion—as previously reported for a group of coal miners in Nottinghamshire,[22] may possibly have contributed to the effect found. Similarly, scented compounds have not yet been identified as playing a major part in occupational dermatitis of potters, glass makers, and blowers.[23]

On the other hand, several occupations were found to be associated with a low risk of FCA. At least some of these share similarities which may be relevant to the risk of FCA (table 2). Firstly, construction labourers, and carpenters and joiners, two large groups, are blue collar jobs traditionally chosen by men. Although the risk of irritant contact dermatitis as a potential precursor of contact sensitisation and subsequent allergic contact dermatitis is certainly not low, there is much less contact with scented material beyond an everyday level as—for example, protective emollients, which may be scented, are usually applied by a few in these occupations only. Hairdressing, by contrast, is traditionally chosen by women with a lower class background, at least in Germany. It is characterised by very heavy, largely unprotected exposure to wet work and also to a multitude of heavily scented work products, which many hairdressers apply to themselves as well. Therefore, it is surprising that hairdressers do not have an increased risk of FCA. One speculative explanation could be the heavy exposure to competing, even more aggressive allergens well known in this occupation, which cause allergic contact dermatitis and induce presentation for patch testing before FCA develops (note that the current, and not a previous employment, was used to classify occupation).

The main risk factor of general importance is age, which reflects increasing risk with cumulative lifetime exposure to fragrances. As age is highly correlated with years in occupations (albeit with a different underlying age distribution in different occupations) it will have confounded the respective analysis. It is thus surprising that a steady increase in prevalence of FCA is not always found with increasing seniority in such an analysis. This may point to cohort effects—cohorts are defined in this case as people taking up a given occupation in the same period—with a similar exposure which has presumably increased over time, whereas people with a longer occupational history may have reached higher, more administrative positions which lessened their exposure. Of course, selection processes—as a variation of the healthy worker effect—may also play a part in biasing estimates of frequency of FCA downwards for those remaining at work until they eventually get sick and present for patch testing.

Age is, in the Poisson regression analysis, not confounded by stasis dermatitis, which occurs mostly in the older age groups, as this factor has separately been taken into account (45.9% and 23.6% stasis dermatitis, respectively, in the oldest and second oldest age groups). For the site of dermatitis, a roughly threefold risk is found in patients with dermatitis of the axilla, most likely due to the application of deodorants and antiperspirants in this region with several predisposing factors.[14] Leg (stasis) dermatitis is a well known risk factor for the acquisition of contact sensitisation to many ingredients of topical drugs and ointments applied to that region.[5] Also, hand and face dermatitis were associated with an increased risk of FCA, compared with the reference region chosen, which is in line with previous clinical experience[1]—both sites can be regarded as more heavily exposed to emollients and similar products than other regions of the body.

In conclusion, for those occupations identified to be associated with an increased risk, exposure to fragrances should be reduced for primary prevention of FCA—for example, by using truly fragrance free products whenever possible[2]—to lessen the burden of occupational exposure. Due to the ubiquity and complexity of fragrances, this approach calls for a concerted action of the fragrance industry and its research institution (IFRA), manufacturers of work materials and skin care products containing fragrances used occupationally, and occupational physicians monitoring the application of these alternative products at the workplace. In those occupations where relevant contact to fragrances is less obvious, studies should aim to pinpoint relevant exposures.

Centres of the IVDK contributing to this analysis (in alphabetical order): Aachen (H Dickel), Augsburg (O Hirschsteiner, A Ludwig), Berlin Benjamin-Franklin (B Tebbe, R Treudler), Berlin Charité (B Laubstein, J Grabbe, T Zuberbier), Berlin UKRV (J Grabbe, T Zuberbier), Dortmund (PJ Frosch, B Pilz, C Pirker), Dresden (G Richter), Duisburg (J Schaller), Erlangen (K-P Peters, M Fartasch), Essen (H-M Ockenfels, U Hillen), Göttingen (Th Fuchs, J Geier), Graz (W Aberer, B Kränke), Halle (G Gaber, D Lübbe), Hamburg (M Kiehn, D Vieluf), Heidelberg (A Schulze-Dirks, M Hartmann), Homburg/Saar (P Koch), Jena (M Gebhardt, A Bauer), Kiel (J Brasch), Lübeck (J Kreusch, J Grabbe), Magdeburg (U Jappe, E Weisshaar), Mainz (D Becker), Marburg (I Effendy), München LMU (F Enders, B Przybilla, F Rueff), München Schwabing (M Agathos), München TU (J Rakoski), Nürnberg (I Müller), Osnabrück (W

Uter), Rostock (H Heise), Tübingen (G Lischka), Ulm (H Gall†), and Wuppertal (O Mainusch, J Raguz).

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References should be numbered consecutively in the order in which they are first mentioned in the text by Arabic numerals on the line in square brackets on each occasion the reference is cited (Manson[1] confirmed other reports[2][3][4][5]). In future references to papers submitted to *Occup Environ Med* should include: the names of all authors if there are three or less or, if there are more, the first three followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter. Titles not in *Index Medicus* should be given in full.

Examples of common forms of references are:

1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomed journals. *JAMA* 1993;**269**:2282-6.
2 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histmaine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med 1976*;**294**:687-90.
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