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Short communication

Epidemiology of contact allergy in adults

Background: We aimed to determine the prevalence of contact sensitization in the general population and to investigate associations with important sociodemographic and medical characteristics.
Methods: Within a population-based nested, case-control study in Germany, we performed patch tests with 25 standard allergens in 1141 adults (50.4% female, age median 50 years). Additional information was obtained by a dermatologic examination, a standardized interview, and blood analysis.
Results: At least one positive reaction was exhibited by 40.0% of the subjects, with reactions most frequently observed to fragrance mix (15.9%), nickel (13.1%), thimerosal (4.7%), and balsam of Peru (3.8%). Women were sensitized more often than men (50.2% *vs* 29.9%, OR 2.36, CI 1.84–3.03), and this was also significant for fragrance mix, nickel, turpentine, cobalt chloride, and thimerosal. Contact sensitization was more frequent in subjects who reported adverse skin reactions (53.8% vs. 32.6%; OR 2.41, CI 1.85–3.14), and this was particularly true for sensitization to nickel (45.5% *vs* 8.8%, OR 8.64, CI 5.67–13.17) and fragrance mix (29.0% *vs* 14.0%, OR 2.51, CI 1.60–3.91) and the corresponding intolerance of fashion jewelry and fragrances. Contact sensitization decreased with increasing degree of occupational training (unskilled 45.9%, apprenticeship 40.1%, technical college 40.4%, and school of engineering 12.5%; $P=0.023$; trend test $P=0.042$). Significant associations of contact sensitization and presence of allergen-specific IgE antibodies, atopic eczema, or psoriasis were not observed. Frequency estimates for the general adult population based on these findings were 28.0% for overall contact sensitization and 11.4% for fragrance mix, 9.9% for nickel, and 3.2% for thimerosal.
Conclusions: It is concluded that contact allergy is influenced by socio-demographic parameters and plays an important role in the general population.

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Contact allergy and sensitization are frequent, but population-based data on their epidemiology are scarce. One of the best estimates for an adult general population (aged 15–69 years) came from the Glostrup Allergy Study in Denmark, which revealed a prevalence of overall sensitization of 15.2% (1). These researches recently revealed that between 1990 and 1998 the prevalence of overall contact sensitization increased from 15.9% to 18.6% in 290 and 469 subjects, respectively, aged 15–41 years (2).

We aimed to determine the prevalence of contact sensitization in the general German population and to investigate associations with important sociodemographic and medical characteristics. We therefore patch-tested a selected population-based sample of adults and determined the association of allergic contact sensitization with sex, occupational education, data from the medical history, manifestations of atopy, and chronic inflammatory skin diseases. From these data, frequency estimates for the general population were calculated, and the findings compared with results from patient databases.

Material and methods

Study design and subjects

We here report on a nested, case-control study. The subjects were recruited from the third MONICA survey, which was performed in Augsburg, Germany, during the years 1994 and 1995. The objective and protocol of the MONICA surveys, which started in 1984 at this location, have been published earlier (3, 4). The study base of the MONICA surveys consisted of all registered residents of the city of Augsburg aged 25–74 years. A random cross-sectional sample stratified for age and sex was drawn in 1994/5 ($n=4178$). In the sera of these subjects, allergen-specific IgE antibodies to common aeroallergens (grass and birch pollen, house-dust mite, cat, and *Cladosporium*) were determined by the radioallergosorbent test

(RAST). We aimed to recruit 1600 subjects out of this random sample of 4178 individuals. Half of these subjects should exhibit a positive RAST result, and within each group 50% should have given at least one positive answer to the questions on asthma attacks, allergic rhinitis, and skin irritation. To account for nonresponders, a gross sample of 2539 subjects was approached. The case-control study was performed between September 1997 and December 1998. Finally, 1537 subjects participated (60.5%), of whom 50.2% exhibited a positive RAST result, and 53.9% of this group and 43.1% of those with negative RAST result reported symptoms of allergy. After excluding irritative and questionable results, a total of 1141 valid tests were included in the further analysis. This group had an age median of 51 years (28–78 years), and the four age categories (28–39, 40–49, 50–59, and 60–78) showed an almost equal distribution (24.1%, 22.5%, 25.1%, and 28.2%, respectively).

A written, informed consent form was obtained from all participants prior to the beginning of the study.

Outcome assessment

Dermatologic examination and patch test. All subjects received a full dermatologic examination by physicians of the Department of Dermatology and Allergy, Technical University Munich. On this occasion, actual cases of atopic eczema and psoriasis were identified on a clinical basis.

Patch tests were performed as recommended by the ICDRG (5) and the German Contact Dermatitis Group. A standard panel of 25 allergens was tested, and Finn chambers and substances were delivered by Hermal, Reinbek, Germany. The tests were applied for 48 h on the upper back, and the participants were asked to remove the patches after that time and to come back after a total of 72 h, when the readings were performed by the investigating physicians. For the final analysis, only definitive positive (+−+++) and negative (0) results were considered, whereas irritative and questionable (+?) results were excluded.

Sociodemographic parameters and medical history. As part of the case-control study, a computer-assisted standardized interview was performed. Beside data on age and sex, the highest degree of occupational training as proxy for socioeconomic status was obtained in four categories (unskilled, apprenticeship, technical college, and school of engineering) according to the protocol of earlier WHO-MONICA studies (3). The subjects were also asked whether they had experienced adverse skin reactions (such as itch, redness, or dermatitis) to certain products, and, if so, whether they could link these to specific things such as fashion jewelry or fragrances. In addition, all participants were asked whether they had ever undergone a patch test and whether contact allergy was diagnosed on the basis of positive reactions.

Statistical analyses. Beside descriptive parameters, we report P values of chi-square (trend) tests or odds ratios (OR) and 95% confidence intervals (CI) as parameters of association and stability. To estimate population-based frequencies, we extrapolated the findings of this nested study ($n=1537$) to the representative study base of the MONICA survey ($n=4178$) by taking the weighted distribution of our selection criteria (RAST/symptoms) into account.

Results

A total of 1141 valid patch tests was analyzed, and 40.0% of the subjects exhibited at least one positive reaction. The highest frequencies of positive reactions were seen to fragrance mix (15.9%), nickel (13.1%), and thimerosal (4.7%). Women were sensitized significantly more often than men (50.2% *vs* 29.9%; OR 2.36, CI 1.84–3.03). With respect to single allergens, the sex differences were significant for fragrance mix, nickel, turpentine, cobalt chloride, and thimerosal. Detailed data are given in Table 1.

The analysis with respect to age categories (28–39, 40–49, 50–59 and 60–78) revealed a trend of decreasing sensitization with age (43.6%, 42.0%, 36.7%, and 37.9%, respectively) ($P_{\text{trend}}=0.09$) and a significant decrease for sensitization to nickel with age (23.4%, 13.3%, 8.8%, and 9.0%, respectively) ($P_{\text{trend}}<0.0001$). In contrast, the sensitization to fragrance mix seemed to increase with age (11.8%, 12.8%, 20.4%, and 19.1%, respectively) ($P_{\text{trend}}=0.003$).

Exactly 32.3% of subjects gave a history of adverse skin reactions to certain substances. In detail, 11.7% reported intolerance of fashion jewelry, 10.4% claimed that fragrances would cause skin reactions, and 5.4% identified occupational substances. Roughly half of the subjects (48.2%) had ever undergone an allergy test, and 27.2% reported that a patch test was performed. Of those who had undergone a patch test earlier, 42.5% were diagnosed with contact allergy, which equals 11.5% of the total study group.

A positive patch test in this study was obtained in 53.8% of those, who gave a history of adverse skin reactions, in contrast to 32.6% positive reactions in those without such a history (OR 2.41, CI 1.85–3.14). Of those who were ever diagnosed with contact allergy after patch testing, 65.1% exhibited a positive reaction in this study, as opposed to 36.8% positive reactions in those who denied earlier patch testing and a diagnosis of contact allergy (OR 3.21, CI 2.15–4.80). Significant associations were also obtained in comparing a history of intolerance of fashion jewelry with actual reactions to nickel. A positive patch-test reaction was shown by 45.5% with such a history, in contrast to 8.8% who denied intolerance of fashion jewelry (OR 8.64, CI 5.67–13.17). Similarly, those who reported intolerance of fragrances were sensitized significantly more often to fragrance mix (29.0%) than those without reported adverse effects (14.0%, OR 2.51, CI 1.60–3.91).

A statistically significant decreasing trend of contact sensitization with increasing level of occupational degree over four categories was observed (unskilled, 45.9%; apprenticeship, 40.1%; technical college, 40.4%; and school of engineering, 12.5%; $P=0.023$; trend test $P=0.042$).

Twenty-five cases of atopic eczema (2.2%) and 43 subjects with psoriasis (3.8%) were identified by clinical examination. The overall prevalence of contact sensitization was not higher in the psoriasis group (41.9% *vs* 40.0%), whereas subjects with atopic eczema showed a tendency toward a higher frequency of contact sensitization (48.0% *vs* 39.9%; OR = 1.39, CI 0.59–3.28).

According to the study design, half of the subjects

Table 1. Frequency of positive patch tests in 1141 adults by allergen and sex

Allergen (concentration %*)	Overall	Women	Men
1 Wool wax alcohols (0.5)	1.4	1.9	1.0
2 *p*-Phenylenediamine (1)	1.5	2.0	1.0
3 Thiuram mix (1)	0.7	0.9	0.5
4 Neomycin (sulfate) (20)	1.4	1.2	1.5
5 Cobalt chloride (1)	2.4	3.4[a]	1.4
6 Nickel sulfate	13.1	20.4[b]	5.8
7 Benzocaine (5)	1.0	1.0	1.0
8 Colophony (20)	1.6	2.2	1.0
9 IPPD (0.1)	0.6	0.9	0.3
10 Potassium dichromate (0.5)	1.1	1.5	0.7
11 Mercapto mix (1)	0.3	0.2	0.3
12 Epoxy resin (1)	0.6	0.2	1.0
13 Balsam of Peru (25)	3.8	4.8	2.7
14 Butylphen. formaldehyde resin (1)	0.4	0.5	0.3
15 Paraben mix (16)	0.6	0.5	0.7
16 Fragrance mix (8)	15.9	20.2 [c]	11.7
17 Mercaptobenzothiazol (2)	0.3	0	0.5
18 Ammoniated mercury (1)	1.0	1.0	1.0
19 Cetylstearyl alcohol (20)	0.8	1.0	0.7
20 Zinc-diethyldithiocarbamate (1)	0.3	0	0.5
21 Methyldibromoglutaronitrile (1)	1.7	1.2	2.2
22 Thimerosal (0.1)	4.7	6.0 [d]	3.4
23 Formaldehyde (1 in water)	0.6	0.3	0.8
24 Isothiazolinone (0.01 in water)	1.8	2.2	1.4
25 Turpentine (10)	2.5	4.3 [e]	0.7
Any	40.0	50.2[f]	29.9

OR (CI) (women *vs* men):
[a] 2.57 (1.06–6.40)
[b] 4.15 (2.74–6.33)
[c] 1.92 (1.37–2.70)
[d] 1.81 (1.00–3.29)
[e] 6.56 (2.24–26.08)
[f] 2.36 (1.84–3.03).
* In petrolatum if not stated otherwise.

(50.1%) exhibited allergen-specific IgE antibodies to aeroallergens. This group, however, did not show a strikingly higher frequency of contact sensitization than those without type I sensitization (41.8% *vs* 38.1%, OR 1.16, CI 0.91–1.49).

When extrapolating these results to the representative study base by taking our selection criteria into account, we estimate that 28.0% of the general adult population exhibit at least one positive patch-test reaction with fragrance mix (11.4%), nickel (9.9%), and thimerosal (3.2%) accounting for the majority of positive findings. These estimates, together with the results of the tested study population and findings from a large patient database are displayed in detail in Table 2. The relative frequency of contact sensitization to the tested allergens was highly comparable between the three study groups. In general, the patient-based tests revealed the highest results, followed by this study and the estimates for the general adult population.

Discussion

We here report results on contact allergy and sensitization from a population-based, nested case-control study

Table 2. Frequency of positive patch tests in 1141 adults (own results), 40 000 patients (Information Network of Departments of Dermatology, IVDK [7]), and estimates for general population derived from results of this study

Allergen (concentration %*)	Population-based estimates	Own results	IVDK
1 Wool wax alcohols (0.5)	1.0	1.4	2.5
2 *p*-Phenylenediamine (1)	1.2	1.5	5.0
3 Thiuram mix (1)	0.5	0.7	2.8
4 Neomycin (sulfate) (20)	1.3	1.4	2.6
5 Cobalt chloride (1)	1.5	2.4	4.7
6 Nickel sulfate	9.9	13.1	15.7
7 Benzocaine (5)	1.0	1.0	1.7
8 Colophony (20)	1.0	1.6	3.4
9 IPPD (0.1)	0.4	0.6	1.1
10 Potassium dichromate (0.5)	0.8	1.1	4.6
11 Mercapto mix (1)	0.2	0.3	0.9
12 Epoxy resin (1)	0.5	0.6	1.1
13 Balsam of Peru (25)	2.4	3.8	6.5
14 Butylphen. formaldehyde resin (1)	0.2	0.4	0.9
15 Paraben mix (16)	0.5	0.6	1.3
16 Fragrance mix (8)	11.4	15.9	10.2
17 Mercaptobenzothiazol (2)	0.2	0.3	2.5
18 Ammoniated mercury (1)	0.7	1.0	2.5
19 Cetylstearyl alcohol (20)	0.5	0.8	1.4
20 Zinc-diethyldithiocarbamate (1)	0.3	0.3	0.7
21 Methyldibromoglutaronitrile (1)	1.1	1.7	1.7
22 Thimerosal (0.1)	3.2	4.7	5.7
23 Formaldehyde (1 in water)	0.3	0.6	2.1
24 Isothiazolinone (0.01 in water)	1.1	1.8	2.5
25 Turpentine (10)	1.2	2.5	0.4

* In petrolatum if not stated otherwise.

in adults. Contact sensitization was found to be frequent (40.0%) in this sample. We observed a higher risk for women and subjects with lower occupational education. Contact sensitization was significantly associated with a history of adverse skin reactions and a diagnosis of contact allergy based on earlier patch tests. This was true also in detail for intolerance of fragrances and fashion jewelry. Subjects with atopic eczema showed a tendency to a higher prevalence of contact sensitization, whereas individuals with detectable aeroallergen-specific IgE antibodies were not statistically significantly sensitized more frequently to contact allergens. The point prevalence of 2.2% for atopic eczema seems low when compared with studies performed in children, but it is in the range of the limited information which is available for adults (1.0%–4.7%, overview in Ref. 6).

We consider the population-based setting to be a major advantage of this study. Little is known on contact allergy from population-based studies, since most data derive from patient populations (7–10). In some epidemiologic investigations, subjects of a random sample who reported a history of (hand) eczema were patch-tested (11–13). The following studies, although still selective, gave population-based patch-test results. In a Swedish study, 274 patients awaiting hip surgery were tested and 22% exhibited a positive patch test, with 7.3% showing reactions to nickel and 5% to balsam of Peru (14). In Italy, 593 cadets aged 18–28 years received epicutaneous tests, and in 12.5% a positive result was

achieved. The most frequent reaction of the standard series were seen to thimerosal (4.7%), ammoniated mercury (1.2%), and phenol-formaldehyde resin (1.0%) (15). In a study from Finland, the sensitivity to nickel was investigated in a general population setting. A total of 980 subjects comprising schoolchildren, medical students, staff of various workplaces, and inhabitants of a home for the elderly were tested, and 4.5% exhibited a positive reaction (16).

The best population-based estimates, as mentioned in the introduction, were reported from Denmark in 1992 (1). This study of 567 adults (15–69 years) also revealed a predominance of the female sex. However, the prevalence of overall sensitization (15.2%) as well as that for nickel (6.7%) and fragrance mix (1.1%) was much lower than our estimates. Up to 1998, the overall prevalence (18.6%), as well as sensitization to cosmetic-related allergens (5.8%), had obviously increased in Denmark (2).

We compared our findings to data of the Information Network of Departments of Dermatology (IVDK) in Germany from 1997, which comprise about 40 000 tested inpatients (7). We also calculated, from our findings, estimates of the frequency of contact sensitization in the general adult population. It became clear that the relative frequencies of positive patch tests are comparable between these study populations. The absolute frequency is, as expected, lowest for the general population estimates, higher in our study population, and highest in the patient based setting. For allergens, where only a few positive reactions were observed (e.g., benzocaine), the estimates for the general population may not differ from the study results when the sensitized subjects reflect the sampling distribution of our nested study.

The results emphasize that allergic sensitization is frequent in the general population, and that nickel and fragrances are by far the most relevant allergens. In contrast to the other allergens, a higher frequency of positive reactions to fragrance mix and turpentine was found in this study, and for the population-based estimates, as compared to the patient sample. This could mean that the clinical relevance of positive patch-test results for these allergens is lower than for other allergens or that, indeed, the problem of allergy to fragrance contact in the population is greater than estimated from patient-based test results, assuming that affected persons do not necessarily undergo patch testing.

A higher risk of contact allergy in women has been described in numerous investigations and is in accordance with the findings of this study (8, 12, 13, 17). For some allergens, such as nickel and fragrance, it seems plausible that a higher exposure contributes to the higher frequency of allergic reactions. For other allergens such as turpentine and thiuram mix, this explanation might not held true, and it was hypothesized that women are more susceptible to contact sensitization. Although there is some evidence for that hypothesis (18), other studies could not confirm a sex-related difference in susceptibility (19).

Occupation is certainly an important risk factor for allergic contact dermatitis and sensitization, and high frequencies of eczema and sensitization have been reported in specific industries (20, 21). The social gradient of contact sensitization within categories of occupational education, as described here, is likely to be explained by an education-dependent exposure to contact allergens. However, data from population-based studies on that issue are scarce.

Furthermore, we demonstrated a significant association of data on the history of contact allergy and allergen-specific intolerance with the actual patch-test results. This may help to validate the questionnaire and to assess the clinical relevance of population-based patch-test results.

A possible association between atopy and contact allergy is still discussed. Subjects in this study with actual atopic eczema showed a nonsignificant tendency to a higher frequency of positive patch tests. Most studies found either no association or a decreased frequency of contact sensitization in atopic subjects (22–25). In accordance with that, we found no difference in contact sensitization depending on concomitant type I sensitization. This is important from a methodological point of view, because our data are derived from a population-based, case-control study with half of the subjects exhibiting type I sensitization. Because we tested a selected subgroup of a population-based sample, the results are not fully generalizable. However, by taking the selection criteria into account, we were able to calculate estimates for a representative general population group. This allowed us to conclude that contact allergy is a frequent problem in the general population and is associated with sociodemographic parameters.

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