

Persistence of contact allergy among Danish adults: an 8-year follow-up study

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In 1990, a random sample of 567 persons of the 15–69-year-old population living in the Western part of Copenhagen County, Denmark, was patch tested in a cross-sectional study. In 1998, a follow-up study was performed. Out of 540 invited, 365 (68%) were re-patch tested. In the follow-up study, the persistence of allergic contact sensitivity, defined as 1 or more positive patch tests in both surveys, was 71% (37 out of 52 subjects). Nickel allergy persisted in 79% (19 out of 24 subjects), while 60% (21 out of 35 subjects) had a positive patch test reaction to 1 or more allergens, other than nickel, in both surveys. The lowest persistence was 50% (5 out of 10 subjects) and this was found for patch test reactivity to 1 or more of the cosmetic ingredients included in the patch test series. 8 years after the baseline study had demonstrated allergic contact sensitivity, 71% of the subjects still had at least 1 positive patch test. Nickel allergy persisted in 79%. Allergen avoidance should probably be lifelong to prevent elicitation of contact dermatitis.

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Contact sensitivity (contact allergy) is defined as a positive patch test, using one of the standardized technologies, either the chamber test or the TRUE Test. Although still a hypothesis (1), it is assumed that allergic contact sensitivity, once acquired, lasts for many years or throughout life.

A number of follow-up studies of groups of patients some years after baseline patch test have been reported (2–9). These studies show that 40–90% of the positive patch test reactions were positive when repeated. The persistence of nickel allergy was generally between 80 and 100% (4, 5). In some such studies, the patch test reactivity of the patients may have been affected by technical limitations, such as change in patch test technology and change in clinical manifestations (10).

There are no available reports of the natural history of contact sensitivity in the general population. In 1990, a Danish random population sample 15–69 year olds living in the Western part of Copenhagen was patch tested (11). In 1998, the same investigative team conducted a follow-up patch test study of the population, employing the same patch test technology (TRUE Test).

Materials and Methods

Baseline study

The baseline study was a cross-sectional survey conducted in 1990 at the Centre for Preventive Medicine (former Glostrup Population Studies). The non-stratified sample included 15–69 year olds living in the western part of Copenhagen. Citizenship (Danish) and birthplace (Denmark) further restricted the samples. The 1990 survey has previously been described in detail (11). Briefly, a random sample of the responders to a mailed screening questionnaire on symptoms of respiratory allergy was invited to a health examination focussing on allergy. A total of 567 persons were patch tested. The baseline study took place between February 1990 and January 1991.

Follow-up study

At the time of the follow-up study, 18 subjects had died, 5 had emigrated and 4 could not be located. Thus, a total of 540 subjects from the baseline study were invited to a re-examination; 365 sub-

jects were patch tested (participation rate: 68%). To avoid potential seasonal differences, eligible subjects were invited for examination in the month corresponding to the baseline study. The participants were examined between October 1997 and November 1998. The Ethical Committee for Copenhagen County approved the study.

Patch testing

In both studies, the patch tests used were the ready to apply TRUE Test (ALK-Abelló) (12–14). The haptens and mixtures of haptens in these test series comprise widely used environmental chemicals, such as metals, preservatives, cosmetic ingredients, glues, rubber chemicals and medicaments. In 1990 formaldehyde was not included. The haptens further differed from the European standard series (Hermal, Germany) by including thimerosal and excluding primin. Instructions to apply the patch tests to the upper back 2 days before the examination were mailed with the patch test. The patch tests were read $1/2$ – $1 1/2$ h after removal. In both studies, the reactions were classified according to the International Contact Dermatitis Research Group (15). A positive reaction (+) was defined as at least homogenous redness and palpable infiltration in the test area. Reactions not fulfilling these criteria, whether they were follicular reactions, faint erythema, or typical irritant reactions, were classified as non-allergic reactions. If the tests were not ap-

plied 2 days before attending, or if the contact with the skin was poor, a new appointment was made when possible. In 1990 and 1998 Nielsen and Linneberg read all reactions, respectively. In both studies Menné reviewed photographs of the test sites, and in case of disagreement consensus was reached by discussion. The reactions in 1998 were classified without knowledge of patch test reactivity in 1990.

Statistical analysis

χ^2 or the Fisher exact test was used for comparisons. Formaldehyde was not included in 1990 and this hapten has been excluded from calculations. All data were analysed with the Statistical Products and Service Solutions package (SPSS) for Windows (release 8.5).

Results

Participation

The participation pattern and the sex and age distribution in 1990 and in 1998 are shown in Table 1. The age distribution differed significantly because of lower 1998 participation in the oldest age group, of which 18 had died.

Persistence of patch test reactivity

The persistence of patch test reactivity appears in Table 2. Allergic contact sensitivity (1 or more

Table 1. Comparison of baseline characteristics between participants and non-participants in the follow-up study

Baseline characteristic (1990)	Participants in follow-up patch testing (<i>n</i> =365) prevalence (%)	Non-participants in follow-up patch testing (<i>n</i> =202) prevalence (%)	<i>p</i> -value ^{a)}
sex			
females	49.0 (<i>n</i> =179/365)	54.0 (<i>n</i> =109/202)	0.23
males	51.0 (<i>n</i> =186/365)	46.0 (<i>n</i> =93/202)	
total	100.0	100.0	
age			
15–34 years	36.4 (<i>n</i> =133/365)	31.7 (<i>n</i> =64/202)	0.03 ^{b)}
35–49 years	36.7 (<i>n</i> =134/365)	30.7 (<i>n</i> =62/202)	
50–69 years	26.8 (<i>n</i> =98/365)	37.6 (<i>n</i> =76/202)	
total	100.0	100.0	
nickel allergy	6.6 (<i>n</i> =24/365)	6.9 (<i>n</i> =14/202)	0.87
1 or more contact allergies	14.2 (<i>n</i> =52/365)	16.8 (<i>n</i> =34/202)	0.41
1 or more contact allergies other than nickel	9.6 (<i>n</i> =35/365)	10.9 (<i>n</i> =22/202)	0.62
1 or more contact allergies to cosmetic ingredients ^{c)}	2.7 (<i>n</i> =10/365)	5.4 (<i>n</i> =11/202)	0.10
1 or more positive skin prick tests to 10 allergens	28.5 (<i>n</i> =104/365)	28.7 (<i>n</i> =58/202)	0.96
pierced ears	58.9 (<i>n</i> =215/365)	62.4 (<i>n</i> =126/202)	0.42
history of flexural eczema	6.8 (<i>n</i> =25/365)	5.4 (<i>n</i> =11/202)	0.51
history of hand eczema	21.9 (<i>n</i> =80/365)	17.8 (<i>n</i> =36/202)	0.25
history of metal contact eczema	22.5 (<i>n</i> =82/364)	21.3 (<i>n</i> =43/202)	0.73

^{a)} Comparison of participants with non-participants (chi-square test).

^{b)} Significant

^{c)} *p*-phenylenediamine, fragrance mix, colophonium, Myroxylon Pereirae resin, parabens, 5-chloro-2-methyl-4-isothiazolin-3-one, 2-methyl-4-isothiazolin-3-one (MCI/MI), quaternium-15 and lanolin alcohol.

Table 2. The persistence of a positive patch test in the 1998 follow-up study of subjects who had a positive patch test in 1990

Positive patch tests in 1990	1998 follow-up study number of positive patch test (reproducibility %)
nickel allergy (<i>n</i> =24)	19 (79%)
1 or more positive patch test (allergic contact sensitivity) (<i>n</i> =52)	37 (71%)
1 or more positive patch test other than nickel (<i>n</i> =35)	21 (60%)
1 or more positive patch test to cosmetic ingredients ^{a)} (<i>n</i> =10)	5 (50%)

^{a)} *p*-phenylenediamine, fragrance mix, colophonium, Myroxylon Pereirae resin, parabens, 5-chloro-2-methyl-4-isothiazolin-3-one, 2-methyl-4-isothiazolin-3-one (MCI/MI), quarternium-15 and lanolin alcohol.

positive patch tests) and nickel allergy are presented separately. Further, 2 groups of patch test persistence are presented: patch test reactivity to 1 or more haptens other than nickel, and reactivity to 1 or more of the cosmetic ingredients included in the test series.

Contact allergy persisted in 71% (37/52) and nickel allergy in 79% (19/24). The persistence of patch reactivity to the 2 other groups of haptens was lower.

Discussion

Over the 8-year follow-up period, contact allergy persisted in 71% of those with allergic contact sensitivity in the baseline study. Reactions to nickel persisted in 79%. Allergic contact sensitivity in the general population lasts for many years. The data indicate that allergen avoidance should be prolonged, and must be emphasised to prevent elicitation of contact dermatitis at the level of the individual patient as well as at the population level.

Population-based studies provide information about the more frequent contact allergies, but have limited value in the study of less common contact allergies. Therefore, only persistence of nickel allergy was presented separately.

In both studies, it was of concern that patch test sensitization might occur. In the 1990 baseline patch testing, 5 subjects returned to the clinic with a newly converted reaction during the subsequent days, whereas no reactions appeared after 7 days (11). In 1998 3 subjects returned during the subsequent days. Because patients did not return later than 7 days, active sensitization from the patch test procedure itself was regarded unlikely.

The choice of patch test technology and the readings of the test also influence the results. The same patch test technology was employed in both surveys. The frequencies to patch test reactions were read at day (D)2 only, and frequencies of sensitization were probably underestimated in both surveys (17). By performing 1 reading at D2 only, probably 10–20% of true positive reactions were lost. We used the TRUE Test that can be mailed

to the participants and applied at home. With 1 reading it was possible to have only 1 visit to the clinic, which could influence participation. At the time of the baseline study, no reports of patch test studies of larger population samples were available.

With the exception of age, the comparison of the baseline characteristics between participants and non-participants did not reveal significant differences. Therefore non-participation seems unlikely to bias the results substantially.

Patch-test reactivity may be influenced by a variety of factors such as hormones, drugs, ultraviolet radiation and the menstrual cycle. Also unknown individual factors may have an influence. The study by Hindsén et al. (18) showed a marked but unexplained intra-individual variation in nickel patch test reactivity among 30 women over a period of 7 months: 2 women were patch test negative on at least 1 occasion.

In this random sample of the general population, most participants had healthy skin and only 1 or 2 contact allergies. The variation in patch test reactivity, related to the exited skin syndrome (16) and clinical manifestation of dermatitis (10), that has been demonstrated among patients was probably of less importance in our study population.

Experimental studies of allergen exposures in subjects with nickel allergy repeated after up to 8 months after the elicitation of a specific allergic inflammation site showed an increasing reactivity to nickel (19, 20). The effect of allergen avoidance on patch test reactivity has not been studied in detail. Follow-up studies are also important for the study of the prognosis of allergic contact dermatitis.

It should be emphasized that, because of variation in patch test reactivity, loss of patch test reactivity does not exclude contact allergy to the allergen in question. Subjects who have had a positive patch test should be regarded as part of the at-risk group for developing contact dermatitis when the exposure exceeds an individual threshold.

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jects still had at least 1 positive patch test. Nickel allergy persisted in 79%. Allergen avoidance should probably continue lifelong to prevent elicitation of contact dermatitis.

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