Acta Derm Venereol 2001; 81: 31–34

CLINICAL REPORT

Allergic Contact Sensitization in an Adult Danish Population: Two Cross-sectional Surveys Eight Years Apart (The Copenhagen Allergy Study)

NIELS HENRIK NIELSEN[1], ALLAN LINNEBERG[2], TORKIL MENNÉ[1], FLEMMING MADSEN[3], LARS FRØLUND[4], ASGER DIRKSEN[5] and TORBEN JØRGENSEN[2]

1Department of Dermatology, Gentofte Hospital, 2Centre of Preventive Medicine, Department of Internal Medicine M, Glostrup Hospital, 3Department of Internal Medicine B, Frederiksberg Hospital, 4Clinical Unit of Preventive Medicine and Health Promotion, Bispebjerg Hospital, and 5Department of Respiratory Medicine, Rigshospitalet, University of Copenhagen, Denmark

In 1990 and 1998 15–41-year-old people were patch-tested in 2 cross-sectional studies of random samples of the population in the western part of Copenhagen County, Denmark. In 1990, 290 subjects and in 1998, 469 subjects were patch-tested. The participation rates were 69% and 51%, respectively. Contact sensitivity to one or more haptens was found in 15.9% and 18.6% in 1990 and 1998, respectively. Nickel sensitivity is still the most common contact sensitivity. The risk of contact sensitivity to the cosmetic-related haptens included in the series (formaldehyde was not included) increased significantly from 2.4% in 1990 to 5.8% in 1998 (odds ratio 2.44, 95% confidence interval 1.04–5.73). The prevalence of contact sensitivity to cosmetic-related allergens has been doubled between 1990 and 1998. ***Key words: hypersensitivity; ubiquitous allergens; prevention.***

(Accepted January 8, 2001.)

Acta Derm Venereol 2001; 81: 31–34

N. H. Nielsen, Department of Dermatology K, Gentofte Hospital, Niels Andersens Vej 65, DK-2900 Hellerup, Denmark.

Allergic contact dermatitis is the consequence of exposure to a hapten exceeding an individual threshold concentration in a contact-sensitized individual. 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. Most information on the prevalence of contact allergies stems from patch testing of patients with severe eczematous skin diseases referred to specialized patch-test clinics. The significance of these data is obvious but referral bias is inevitable and extrapolation to the pattern of contact sensitization in the population in general is not possible.

To obtain insight into the actual population at risk of developing allergic contact dermatitis the prevalence of contact sensitivity in the unselected general population must be determined. Surveillance of the changes in prevalence in the general population over time is an important measure to evaluate focus areas for regulation and to indicate the effects of such regulation of exposure to common haptens such as nickel and fragrance chemicals.

The first patch-test study of an unselected population was performed in 1990 (1). The present study is a recent (1998) cross-sectional study of an unselected Danish 15–41-year-old population using the same sampling method and frame, employing the same patch-test technology (the TRUE test) and with the participation of the same investigative team.

MATERIAL AND METHODS

This study is based on two cross-sectional surveys conducted in 1990 and 1998 at the Centre of Preventive Medicine (former Glostrup Population Studies). Both surveys were preceded by a screening of a random sample of the population in the western part of Copenhagen County performed via a mailed questionnaire of respiratory symptoms. The 1990 sample was a non-stratified sample of 15–41-year-olds, whereas the 1998 sample was stratified on two age groups: 15–22-year-olds and 23–41-year-olds. Citizenship (Danish) and birthplace (Denmark) further restricted the samples. Random samples of the responders to the screening questionnaire were invited to a health examination focusing on allergy. Pregnant women were excluded.

1990 survey

Of a total of 3,603 responders to the screening questionnaire (response rate 86.1%) a random sample of 418 subjects was invited to the health examination. A total of 312 subjects (participation rate 74.6%) was examined between February 1990 and January 1991. These subjects were the 15–41-year-old participants in The Glostrup Allergy Study, Denmark (1).

1998 survey

A total of 592 15–22-year-old subjects and 546 23–41-year-old subjects responded to the screening questionnaire (response rates 72.0% and 78.0%, respectively). A further 102 questionnaires were completed by telephone interviews (overall response rate 81.5% including telephone interviews). Among the 15–22-year-old responders to the mailed screening questionnaire a random sample of 369 subjects was invited to the health examination, and 186 subjects were examined (participation rate 50.4%). Among the 23–41-year-old responders a random sample of 533 subjects was invited to the health examination, and 296 subjects were examined (participation rate 55.5%). The participants were examined between January and November 1998.

Patch-test method

The patch test used was the ready-to-apply TRUE test (ALK-Abelló) (2–4). Patch testing was not performed during the 3 weeks of the summer vacation. The haptens and mixtures of haptens in this test series comprise widely used environmental chemicals such as metals, preservatives, substances in cosmetics, glues, rubber and medicaments. In 1990 formaldehyde was not included. The haptens further differed from the European Standard Series (Hermal-Chemi, Germany) by including thiomersal and excluding primine. Directions 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 30 min to 1 h 30 min after removal. Reactions were classified according to the International Contact Dermatitis Research Group (5). A positive

 ISSN 0001-5555

reaction (+) was defined as at least homogeneous redness and palpable infiltration in the test area. Reactions not fulfilling these criteria, whether these were follicular reactions, faint erythema or typical irritant reactions, were classified as non-allergic reactions. If the tests were not applied 2 days before attending, or if the contact with the skin was poor, a new appointment was made when possible. In 1998 the second author (AL) read all reactions. The authors TM and NHN revised photos of the test sites, and in case of disagreement consensus was reached by discussion. In 1998 two attendants removed the nickel patch from the test series. Consequently, reactivity to nickel is missing for the 2 participants.

Statistical analysis

The changes in the prevalence of allergic contact sensitivity to the haptens, mixtures of haptens and groups of haptens were expressed by odds ratios comparing 1998 to 1990. Because formaldehyde was not included in 1990 this hapten has been excluded when reporting the prevalence of more than one sensitivity. The odds ratios were adjusted for differences in sex and age distribution (age groups 15–21 years and 23–41 years) in a logistic regression model. All data were analysed with the Statistical Products and Service Solutions package (SPSS) for Windows (Release 8.5) and 95% confidence intervals were used.

RESULTS

The participation pattern and the sex and age distribution of the participants in 1990 and in 1998 are shown in Table I. Table I shows the prevalence of allergic contact sensitivity to the individual haptens and mixtures of haptens in the test series in 1990 and 1998 among men and women in the 2 age groups (15–22 and 23–41-year-olds). Table II shows the prevalence of allergic contact sensitivity to one or more hapten, to one or more hapten other than nickel, and to one or more of the cosmetic-related haptens included in the test series in 1990 and in 1998. Table II also shows the odds ratios for allergic contact sensitivity separately for males and females adjusted for age, and the total odds ratio adjusted for sex and age group. Allergic contact sensitivity to nickel was by far the most common, and its prevalence was unchanged from 1990 to 1998. The only prevalence that seemed to increase from 1990 to 1998 was allergic contact sensitivity to cosmetic-related haptens, which increased significantly from 2.4% to 5.8%.

DISCUSSION

The prevalence of allergic contact sensitization to cosmetic haptens among younger adults in the general population has increased significantly from 2.4% in 1990 to 5.8% in 1998. The increase is caused mainly by an increasing number of fragrance mix-sensitive females. Questionnaire surveys in Denmark also including an unselected sample of the general population have produced similar results (6). Studies including patch-tested patients in the UK and Denmark have similarly shown a significant increase in positive reactions to the fragrance mix during the past 10–15 years (7, 8). The relevance of a positive patch test in relation to allergic contact dermatitis has been firmly established in the scientific literature. The documentation includes studies on the history of the individuals with positive tests compared with controls, extensive exposure assessment including chemical analysis and experimental double-blind exposure studies with fragrance chemicals in specific sensitized individuals (9–14). Because patch-test reactions were read on day 2 only, the frequencies of sensitization in this study were probably underestimated.

Table I. *Allergic contact sensitization in unselected 15–41-year-old Danes in 1990 and 1998: participation in the patch test and prevalence of positive reactions to haptens included in the TRUE test*

	Males				Females			
	1990		1998		1990		1998	
Age (years)	15–22	23–41	15–22	23–41	15–22	23–41	15–22	23–41
No. of participants	*n*=28	*n*=108	*n*=76	*n*=117	*n*=48	*n*=106	*n*=102	*n*=174
Participant rate (%)	56.0	66.7	41.1	49.8	75.0	72.1	55.4	56.1
Nickel sulphate	0	2.8	2.6	1.7	16.7	17.0	11.8	20.3
Wool alcohols	0	0	0	0.9	0	0.9	0	0
Potassium dichromate	0	0	0	0.9	0	0.9	0	1.1
Caine mix	0	0	0	0	0	0	0	0.6
Fragrance mix	0	0	2.6	0	2.6	0	2.9	3.4
Colophony	0	0	0	0	0	0	0	2.3
Epoxy resin	0	0	0	0	0	0	0	0.6
Balsam of Peru	0	0	0	0	0	0	2.0	2.3
Ethylenediamine dihydrochloride	0	0	0	0.9	0	0.9	0	2.3
Cobalt chloride	0	1.9	0	0.9	0	0.9	0	1.7
p-tert-Butylphenol formaldehyde resin	0	0	0	0	0	0	0	1.1
CI+Me-isothiazoline (MCI/MI)	0	0	0	0	0	0	0	0.6
Quarternium 15	0	0.9	0	0	0	0	0	0.6
p-Phenylene diamine	0	0	1.3	0	0	0	0	0
Formaldehyde	nt	nt	0	0	nt	nt	0	1.7
Mercapto mix	0	0.9	0	0.9	0	0.9	0	0
Thiomersal	0	4.6	2.1	2.8	1.3	1.7	1.0	2.3
Thiuram	0	0	0	0	0	0	1.7	0

Positive reactions to paraben mix, carba mix, black rubber mix, mercaptobenzotiazole, quinoline mix and neomycin sulphate were not observed. nt: not tested.

Table II. *Prevalence (%) of allergic contact sensitization in 15–41-year-old Danes in 1990 and 1998 to nickel and groups of haptens included in the TRUE test*

	Men			Women			Total		
	1990	1998	OR (CI)[a]	1990	1998	OR (CI)[a]	1990	1998	OR (CI)[a]
Nickel	2.2	2.1	0.96 (0.21–4.50)	16.9	17.2	1.05 (0.62–1.77)	–[d]	–	–
One or more sensitivities[b]	8.8	7.3	0.87 (0.38–1.98)	22.1	26.4	1.31 (0.82–2.10)	–	–	–
One or more sensitivities other than nickel[b]	6.6	5.2	0.84 (0.33–2.17)	9.1	13.8	1.70 (0.88–3.26)	–	–	–
Cosmetic-related haptens[c]	0.7	2.1	2.29 (0.24–21.6)	3.9	8.3	2.38 (0.94–5.99)	2.4	5.8	2.44 (1.04–5.73)

Figures are given for males (n=136, 1990; n=193, 1998), females (n=154, 1990; n=276, 1998) and the total study population (n=290, 1990; n=469, 1998).

[a]The odds ratio value (OR) and the 95% confidence interval (CI) are calculated with the hapten or the groups of haptens as the dependent variable with adjustment for age group and sex when relevant.

[b]As in 1990, formaldehyde was not included in the 1990 TRUE test, nor is it here.

[c]*p*-Phenylene diamine, fragrance mix, colophony, balsam of Peru, parabens, 5-chloro-2-methyl-4-isothiazolin-3-one, 2-methyl-4-isothiazolin-3-one (MCI/MI), quarternium 15 and wool mix.

[d]The cells are empty because of the diversity between the odds ratio estimates among men and women.

The main causes of primary sensitization to fragrance chemicals are cosmetic products, particularly deodorants and fine perfumes. The prevalence of fragrance allergy is 3 times higher among patch-tested Danish female patients than in the background population (11% vs 3%) (8). This marked difference may indicate that those allergic to fragrances often need referral to a patch-test centre because of a troublesome allergic contact eczema.

The high prevalence of fragrance allergy and the identified significant increase are unacceptable and not in accordance with EU directive 96/335/EF. Action has been taken by the EU Commission to handle this problem, either by restricting the use of the most frequently encountered allergens, by demanding labelling similar to other cosmetic ingredients, or by a combined action.

The risk of nickel allergy was equally frequent in both surveys, and also the most common contact sensitivity in both surveys. Danish nickel regulation came into force in 1991 and regulates nickel release from metal objects in close contact with the skin (15). The effect of this regulation may explain why there was no increased prevalence, indicating that nickel allergy has reached a plateau among the youngest females. A similar effect was observed in a study comparing patch-tested Danish patients (8).

The relatively low participation rate in the 1998 survey and the possibility of selection bias may have influenced the results. The screening questionnaire did not include questions on skin symptoms and therefore the possibility of selection bias cannot be specifically evaluated. However, if the observed increase in sensitivity to cosmetic-related haptens were due to selection bias which caused people with contact dermatitis to participate more often than those without contact dermatitis, then increases in sensitivity to other haptens, such as nickel, would also have been expected. This was, however, not the case.

Because the group at risk of developing the skin disease allergic contact dermatitis comprises those with one or more contact sensitivities, preventive strategies should be seriously considered. The group at risk of developing allergic contact dermatitis comprises more than 1 out of 4 young females in the population.

ACKNOWLEDGEMENTS

We thank the staff at the Centre of Preventive Medicine for their valuable assistance. Supported by grants from the Danish Medical Research Council, the Danish Health Insurance Fund, the Danish Ministry of Health (the National Health Fund for Research and Development), the Danish Medical Research Council and the Danish Ministry of Health (Research Centre for Environmental Health: Environmental Health Research Programme 1997), and ALK-Abelló.

REFERENCES

1. Nielsen NH, Menné T. Allergic contact sensitization in an unselected Danish population. Acta Derm Venereol 1992; 72: 456–460.
2. Lachapelle JM, Bruynzeel DP, Ducombs G, Hannuksela M, Ring J, White IR, et al. European multicenter study of the TRUE Test. Contact Dermatitis 1988; 19: 91–97.
3. Kreilgard B, Hansen J, Fischer T. Chemical, pharmaceutical and clinical standardization of the TRUE Test caine mix. Contact Dermatitis 1989; 21: 23–27.
4. Wilkinson JD, Bruynzeel DP, Ducombs G, Frosch PJ, Gunnarsson Y, Hannuksela M, et al. European multicenter study of TRUE Test, Panel 2. Contact Dermatitis 1990; 22: 218–225.
5. Wilkinson DS, Fregert S, Magnusson B, Bandmann HJ, Calnan CD, Cronin E, et al. Terminology of contact dermatitis. Acta Derm Venereol 1970; 50: 287–292.
6. Johansen JD, Andersen TF, Thomsen LK, Kjøller M, Menné T. Rash related to use of scented products. A questionnaire study in the Danish population. Is the problem increasing? Contact Dermatitis 2000; 42: 222–226.
7. Johansen JD, Menné T. The fragrance mix and its constituents: a 14-year material. Contact Dermatitis 1995: 32: 18–23.
8. Johansen JD, Menné T, Christophersen J, Kaaber K, Veien N. Pattern of sensitisation to common contact allergens in Denmark. Changes from 1985–86 and 1997–98 – with special view to the effect of preventive strategies. Br J Dermatol 2000; 142: 490–495.
9. Johansen JD, Rastogi SC, Menné T. Exposure to selected fragrance materials. A case study of fragrance-mix-positive eczema patients. Contact Dermatitis 1996; 34: 106–110.
10. Johansen JD, Andersen KE, Rastogi SC, Menné T. Threshold responses in cinnamic-aldehyde-sensitive subjects: results and methodological aspect. Contact Dermatitis 1996; 34: 165–171.

11. Johansen JD, Andersen KE, Menné T. Quantitative aspects of isoeugenol contact allergy assessed by use and patch tests. Contact Dermatitis 1996; 34: 414–418.
12. Johansen JD, Rastogi SC, Menné T. Contact allergy to popular perfumes; assessed by patch, use tests and chemical analysis. Br J Dermatol 1996; 135: 419–422.
13. Johansen JD, Andersen TF, Veien N, Avnstorp C, Andersen KE, Menné T. Patch testing with markers of fragrance contact allergy. Do clinical tests correspond to patients' self-reported symptoms? Acta Derm Venereol 1997; 77: 149–153.
14. Rastogi SG, Johansen JD, Frosch F, Menné T, Bruze M, Lepoittevin JP, et al. Deodorants on the European market: quantitative chemical analysis of 21 fragrances. Contact Dermatitis 1998: 38: 29–35.
15. Danish Ministry of the Environment. Statutory Order No. 472, 1989, 27 June.