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CLINICAL REPORT

Contact Allergy and Allergic Contact Dermatitis in Adolescents: Prevalence Measures and Associations.

The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS)

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The aims of this cross-sectional study were to establish the prevalence measures of contact allergy and allergic contact dermatitis in 8th grade schoolchildren (aged 12–16 years) in Odense, Denmark, and to examine the associations with atopic dermatitis, inhalant allergy and hand eczema. Contact allergy to a standard series allergen was found in 15.2% of schoolchildren. The point prevalence of allergic contact dermatitis was 0.7% and the lifetime prevalence 7.2%, predominantly in girls. The most common contact allergens were nickel (8.6%) and fragrance mix (1.8%). Nickel allergy was clinically relevant in 69% and fragrance allergy in 29% of cases. A significant association was found between contact allergy and hand eczema while no association was found between contact allergy and atopic dermatitis or inhalant allergy. In the future this cohort of schoolchildren will be followed with regard to the course and development of atopic diseases, hand eczema and contact dermatitis. ***Key words: schoolchildren; atopic dermatitis; inhalant allergy; hand eczema; multivariate graphical analysis.***

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Information about incidence and prevalence of contact allergy and allergic contact dermatitis in children and adolescents is limited (1). Most studies are cross-sectional, thus giving estimates of the prevalence only, and publications of follow-up studies in this age group are non-existent. Incidence figures are therefore not available. Furthermore, most studies include selected groups of children and adolescents visiting dermatological clinics (2–14), while systematic patch testing of unselected populations has rarely been carried out (15–17). Moreover, all population-based studies consider only the prevalence of positive patch tests, i.e. the prevalence of contact allergy without evaluating the clinical relevance, i.e. the prevalence of allergic contact dermatitis.

The most common contact allergens in children and adolescents are the same as those in adults (1). There is considerable variability from country to country due to variation in exposure to the allergens. Nickel allergy is common (2, 3, 5–12, 14, 16) and has been shown to increase the risk of development of hand eczema in adults (18). It is not known whether other contact allergies also increase the risk and if the relationship between contact allergy and hand eczema already exists in childhood and adolescence. The relationship between atopic dermatitis and contact allergy is frequently discussed (19–26). A reduced (19–21), an equal (22, 23) as well as a higher (24–26) prevalence of contact allergy in atopic dermatitis have been reported. More studies of these relationships in children and adolescents and in follow-up studies have to be carried out before any conclusions can be drawn.

The aim of this study was to estimate prevalence measures of contact allergy and allergic contact dermatitis in an unselected population of adolescents, and to study the relationship to atopic dermatitis, inhalant allergy and hand eczema.

METHODS

Population and study design

The Odense Adolescence Cohort Study (TOACS) is an epidemiological follow-up study. Phase one (1995–1996) was conducted as a cross-sectional study among 1,501 8th grade schoolchildren in 40 schools in the Municipality of Odense. Phase one included questionnaires, interviews and clinical examinations, blood samples for IgE measurement and patch tests. Phase two (1996–1997) was conducted as a case-control study in selected groups of schoolchildren. The population and study design has been described elsewhere (27).

Definitions and description of terms (see also reference 27)

The lifetime prevalence (birth to present age) of *atopic dermatitis* was defined by published questionnaire criteria (28). The one-year period prevalence and the point prevalence of atopic dermatitis were based on the Hanifin & Rajka criteria (29) and the severity of present atopic dermatitis was graduated using the SCORAD index (30, 31).

The lifetime prevalence of *inhalant allergy* (allergic asthma and/or allergic rhinitis) was evaluated from interview.

Asthma was defined as 3 or more episodes of wheezing/whistling in the chest and/or dyspnoea and/or cough. *Allergic*

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asthma was defined as 3 or more episodes of symptoms either at exposure to known allergens or in certain periods.

Rhinitis was defined as one or more of the following symptoms: itching in the nose, watery rhinorrhoea, sneezing and/or nasal congestion. *Allergic rhinitis* was defined as one or more symptoms either at exposure to known allergens or in certain periods or continued for at least 2 weeks without infectious rhinitis or other infections.

The lifetime prevalence of *hand eczema* was evaluated from the questionnaire including part of a Finnish questionnaire (32). Our criteria for a history of hand eczema was eczema (rash) on the fingers, finger webs, palms, or backs of the hands, which had appeared once and continued for at least 2 weeks or had appeared several times or had been persistent.

Allergic contact dermatitis (present or past) was defined as contact allergy by patch testing in combination with exposure history, dermatitis history and present dermatitis pattern.

Contact allergy/Type IV sensitization was defined as at least one positive reaction to allergens in the TRUE Test® including a nickel dilution series.

Patch tests

The TRUE Test® panels 1 and 2 (Pharmacia & Upjohn, Hillerød, Denmark) was used together with a TRUE Test patch dilution series consisting of nickel sulphate ($NiSO_4$, $6H_2O$) in 3 concentrations (200, 10, 1 $\mu g/cm^2$) and one placebo (33, 34). The patch tests were applied to the upper back for 2 days (35) and removed by the investigators in order to control the quality of patch adhesion. The tests were read and scored after 3 days, according to standard procedure (35). The relevance of a positive patch test result was evaluated in relation to the history of exposure, and dermatitis pattern. The relevance was recorded as present, past or unknown. Present relevance was accepted if the positive patch test explained the person's present dermatitis in relation to the allergen exposure, site, course and relapses of dermatitis. When the positive patch test explained a previous episode of contact dermatitis, the term "past relevance" was used.

Ethics

The ethics committee for Vejle and Funen County (proj. no. 95/22) approved the study. Informed consent was obtained from both the schoolchildren and their parents.

Data handling and statistics

All data were entered twice in the databases; when differences were found, a comparison with raw input forms was made and corrections made accordingly. Statistical analyses were performed with Stata 5.0 (Stata corporation, TX, USA), except for graphical models.

The prevalence proportion was defined by the number of positive answers divided by the total number of schoolchildren questioned. The 95% confidence intervals are shown in parentheses (95% CI). The prevalence proportions for boys and girls are given, and if a significant sex difference was found, the *p*-value is given or significance is indicated. Comparisons were made by χ^2-based table analysis.

Odds ratio (OR) is given as Mantel Haenzel odds ratios stratified by sex, with associated confidence intervals in parentheses (95% CI). Differences by sex are noted, when the stratum specific estimates indicate significant "effect modification". Statistical significance was defined as $p < 0.05$.

Because of the close association between the investigated diseases, a multivariate analysis was performed which at the same time could account for the interdependence and possible association with external factors (control for all associations at the same time). The analysis was performed using specialized software, Digram®, as used in the Framingham Heart Study (36). The results are expressed in the form of a graph on which non-random associations between variables are represented by a line. The direction of association (arrow) is chosen by the researcher based on contents, and does not constitute a result of the analysis. The final graph is settled by a procedure in which the user works towards the simplest overall representation of the associations controlled for (conditional on) all other variables. Because the variables are binary or ordinal, the strength and degree of statistical significance of an association can be measured by Kruskal and Goodman's gamma coefficient in the form of a conditional or partial gamma (37). By partial is meant that the coefficient is a weighted average across the variable (-s), which are used in the particular conditioning. Because of the many statistical tests in these analyse, a significance level of 0.01 was used to compensate for false associations (Type I error). Gamma coefficients numerically less than 0.15 indicate weak associations, between 0.15 and 0.30 moderate associations, and more than 0.30 strong associations.

RESULTS

Patch test characteristics

Patch testing was performed in 76.3% (1,146/1,501) of the schoolchildren. The patch tests had a good attachment to the skin in 93.5%. Reactions to the test tape were seen in only 2.0%. Mild reactions (faint erythema only) to one or more allergens were seen in 14.2%. In 3 cases, the patch test reactions were judged to be irritant, 2 for thimerosal and one for nickel.

In 40 schoolchildren, readings were performed after 2 days (n = 17), 4 days (n = 22) or 7 days (n = 1) due to absence on day 3, and in 6 schoolchildren informed parents performed the readings.

Prevalence of contact allergy and allergic contact dermatitis

One or more positive patch test reactions were seen in 15.2% (174/1146) of the schoolchildren. Significantly more girls than boys had positive reactions (Table I). Present or past relevance for one or more reactions was found in 47.7% (83/174) of schoolchildren who tested positive in the patch test (Table I), suggesting present or past allergic contact dermatitis in 7.2% (83/1,146). Significantly more girls than boys had clinically relevant positive patch tests (Table I) and present or past allergic contact dermatitis was more frequent in girls than in boys (girls 11.3% vs. boys 2.5%, $p < 0.001$). Present allergic contact dermatitis was found in 0.7% (8 girls, 2 boys).

The distribution of positive reactions to the different allergens is presented in Table II. Positive reactions were seen to 20 out of 24 allergens. Sensitivity was most common to nickel (8.6%), fragrance mix (1.8%), colophony (1.0%), cobalt (1.0%), and thimerosal (1.0%). Significantly more girls than boys were sensitized to nickel, whereas no significant differences between girls

Table I. *Point prevalence of contact allergy and associated relevance*

	Total population (% and 95% CI)	Girls	Boys
Point prevalence of contact allergy (one or more positive patch test reactions)	15.2% (13.2–17.4%)	19.4% (16.3–22.7%)*	10.3% (7.8–13.2%)
Relevance (patch test positive with one or more relevant reactions)	47.7% (40.1–55.4%)	58.3% (49.0–67.3%)*	24.1% (13.5–37.6%)

Results are from patch testing with TRUE Test® and TRUE Test patch dilution series with nickel sulphate. In the TRUE Test®, 170 schoolchildren had one or more positive patch test reactions. In the TRUE Test patch dilution series with nickel sulphate, 76 had positive reactions. Of these 4 had no reactions in the TRUE Test®.
*$p < 0.001$ for sex difference.

Table II. *Distribution of contact allergy to the individual allergens in the TRUE Test® including TRUE Test patch dilution series with nickel sulphate and associated relevance*

	Contact allergy (%)			Relevance (%)
	Girls ($n = 620$)	Boys ($n = 526$)	Total population ($n = 1,146$)	(Number positive with relevance/ number positive)
Nickel sulphate[d]	13.7*	2.5	8.6	69.4 (68/98)
Lanolin[a]	0.5	0.0	0.3	33.3 (1/3)
Neomycin sulphate	0.2	0.2	0.2	0.0 (0/2)
Potassium dichromate	0.2	1.0	0.5	16.7 (1/6)
Caine mix	0.2	0.2	0.2	0.0 (0/2)
Fragrance mix	1.6	2.1	1.8	28.6 (6/21)
Colophony	1.3	0.8	1.0	33.3 (4/12)
Epoxy resin	0.3	0.0	0.2	0.0 (0/2)
Quinoline mix	0.0	0.0	0.0	–
Balsam of Peru	0.3	1.0	0.6	14.3 (1/7)
Ethylenediamine	0.2	0.2	0.2	0.0 (0/2)
Cobalt chloride	1.5	0.6	1.0	58.3 (7/12)[e]
PTBP resin[b]	0.6	1.1	0.9	20.0 (2/10)
Paraben mix	0.2	0.0	0.1	0.0 (0/1)
Carba mix	0.2	0.8	0.4	20.0 (1/5)
Black rubber mix	0.3	0.4	0.3	0.0 (0/4)
Kathon CG[c]	0.0	0.0	0.0	–
Quaternium 15	0.2	0.2	0.2	50.0 (1/2)
Mercaptobenzothiazole	0.0	0.2	0.1	0.0 (0/1)
p-Phenylenediamine	0.2	0.2	0.2	0.0 (0/2)
Formaldehyde	0.0	0.0	0.0	–
Mercapto mix	0.0	0.0	0.0	–
Thimerosal	1.0	1.1	1.0	0.0(0/12)
Thiuram mix	0.0	0.2	0.1	0.0(0/1)

[a]Wool alcohols.
[b]PTBP resin (p-t-butylphenol-formaldehyde resin).
[c]Isothiazoliones (5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one).
[d]Including only TRUE Test® panels 1 and 2, nickel allergy was found among 8.0% (girls 13.2% vs. boys 1.9%, $p < 0.001$). Including only nickel dilution series 6.6%, (girls 11.3%, vs. boys 1.1%, $p < 0.001$) had nickel allergy.
[e]Relevance for cobalt was evaluated in relation to concomitant reaction to nickel.
*$p < 0.001$ for sex difference.
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and boys were found for the other allergens (Table II). Clinical relevance was found for 69.4% of the reactions to nickel. Cobalt was evaluated in relation to concomitant reaction to nickel and was found to be relevant in 58% of the schoolchildren. Clinical relevance was found for 29% of the reactions for fragrance mix, and 33% of the reactions for colophony. None of the schoolchildren reported clinical symptoms of thimerosal allergy.

Reactions to two or more contact allergens were seen in 14.9% (26/174) of those whose patch tests were positive. Of the 26 with 2 or more reactions, 25 had concomitant reactions to 2 different allergens and only

one child showed 7 concomitant reactions. The most frequent concomitant reactions were to nickel and cobalt (7/26). Only one child had concomitant reactions to nickel and chromate, and none had concomitant reactions to chromate and cobalt.

Contact allergy in relation to atopic dermatitis, inhalant allergy and hand eczema

Contact allergy was significantly correlated to adolescents with present or past hand eczema (Table III). No significant association was found between contact allergy and a history of atopic dermatitis or inhalant allergy (Table III). Furthermore, no significant association was found by separating atopic dermatitis into present atopic dermatitis versus past atopic dermatitis (without present symptoms) and analyses of the relation to contact allergy (OR 1.52, 95% CI 0.69–3.35, $p = 0.292$, stratified by sex). No significant association was found between moderate versus mild atopic dermatitis and contact allergy (OR 0.98, 95% CI 0.22–4.40, $p = 0.974$, stratified by sex). Contact allergy and present atopic dermatitis were found in 10 schoolchildren. Contact allergy was found in 21.7% (5/23) of those with mild atopic dermatitis and in 20.8% (5/24) of those with moderate atopic dermatitis. The one with severe atopic dermatitis had no contact allergy.

A multivariate analysis with contact allergy (Type IV sensitization) as outcome is illustrated in Fig. 1 and Table IV. The 3 different boxes in Fig. 1 indicate outcome variable (Type IV sensitization), investigated diseases and background variables. The figure should be read from right to left. Arrows indicate associations between different levels (boxes) and lines associations within the same level (box). The analysis shows a very strong association between atopic dermatitis and inhalant allergy and between atopic dermatitis and hand eczema. Strong associations were found between Type IV sensitization and hand eczema and between Type IV sensitization and sex. The analysis is unstable for the association between sex, atopic dermatitis and hand eczema, respectively. This analysis does not show any association between Type IV sensitization and atopic dermatitis or inhalant allergy. A self-reported wet work (present or past) was not associated with contact allergy or hand eczema in this age group.

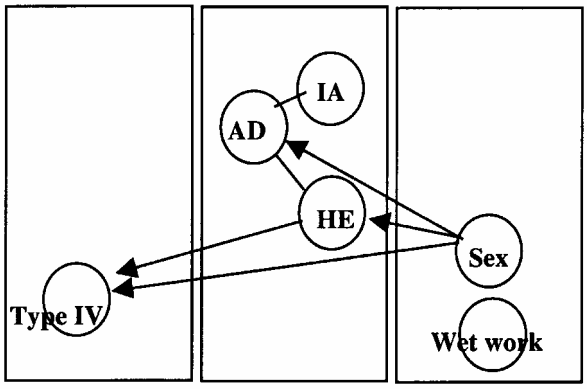

Fig. 1. Results from a multivariate graphical analysis with Type IV sensitization as outcome are summarized in the graph ($n = 1146$). See also Table IV. Type IV: Type IV sensitization – positive patch test; AD: present or past atopic dermatitis; IA: present or past inhalation allergy (allergic asthma and/or allergic rhinitis); HE: present or past hand eczema; Wet work: present or past wet work.

DISCUSSION

The development of the ready-to-use patch test system, TRUE Test®, made it possible to conduct standardized patch tests in a large population. Contact allergy was common among adolescents (15.2%), which is concordant with the findings of other population-based studies in this age group (13.3%–23.3%) (15–17). In our study, we read the reaction on day 3. Nielsen & Menne (38) found a similar prevalence of contact allergy in 567 unselected Danish adults patch-tested with TRUE Test®, and reading on day 2. However, results between studies are difficult to compare owing to variations in demographic, clinical and technical factors such as age and

Table III. *Associations between contact allergy and, respectively, atopic dermatitis, inhalant allergy and hand eczema. Odds ratio (OR) is given as Mantel Haenzel odds ratio stratified by sex*

	Contact allergy		
	OR	95% CI	*p*-value
Atopic dermatitis	1.13	0.79–1.63	0.501
Atopic dermatitis excluding inhalant allergy and hand eczema	0.93	0.54–1.60	0.783
Inhalant allergy	1.12	0.75–1.69	0.581
Inhalant allergy excluding atopic dermatitis and hand eczema	0.91	0.47–1.76	0.783
Hand eczema	2.07	1.32–3.25	< 0.002
Hand eczema excluding atopic dermatitis and inhalant allergy	3.53	1.79–6.97	< 0.001

Atopic dermatitis (questionnaire), inhalant allergy (interview) and hand eczema (questionnaire) were evaluated as lifetime prevalence figures. For criteria, see methods. Contact allergy was evaluated from patch testing with TRUE Test® including nickel dilution series.
For each disease, 2 analyses have been performed: one for all children with the disease and another where those with other concomitant disease were excluded.

Table IV. *Results from multivariate graphical analysis with Type IV sensitization as outcome are summarized in the Table (n = 1,146). See also Fig. 1*

Hypothesis	χ^2	df	Exact *p*-value	Gamma	Exact *p*-value (one-sided)
Type IV vs. HE ⊥ Sex	10.7	2	0.002	0.35	0.000
Type IV vs. Sex ⊥ HE	16.3	2	0.000	− 0.32	0.000
AD vs. IA	104.0	1	0.000	0.65	0.000
AD vs. HE ⊥ Sex	78.3	2	0.000	0.67	0.000
AD vs. Sex ⊥ HE	4.7	2	0.094	− 0.17	0.014
HE vs. Sex ⊥ AD	6.2	2	0.048	− 0.28	0.006

The Table contains the statistical- or user-specified non-random associations.
Type IV vs. HE ⊥ sex, e.g. Type IV is associated with hand eczema conditional (⊥) on sex. Conditional in this context means the "sex", plus all other information in the analysis.
Type IV: Type IV sensitization – positive patch test; AD: present or past atopic dermatitis; IA: present or past inhalation allergy (allergic asthma and/or allergic rhinitis); HE: present or past hand eczema; Wet work: present or past wet work.

sex distribution, selection of patch test series and patch test methodology. In this study there were more schoolchildren with a history of atopic dermatitis and hand eczema participating in the patch testing than schoolchildren without a history (27). Because of the association between hand eczema and contact allergy, overestimation of the point prevalence of contact allergy is possible.

In contrast to other population-based studies, we evaluated the clinical relevance of a positive patch test result. Relevance was found in half of the schoolchildren, significantly more often in girls than in boys. The evaluation of relevance is the most intricate part of the patch test procedure depending on the dermatologist's skill, experience and curiosity. However, for the standard allergens included in the TRUE test, detailed lists are available that provide information about the occurrence of the allergens in the environment.

The point prevalence of allergic contact dermatitis was 0.7%, and present or past allergic contact dermatitis was found in 7.2% of schoolchildren, with a significant sex difference (girls 11.3% vs. boys 2.5%). It would not be appropriate to use the term "lifetime prevalence" here, because an earlier relevant positive patch test result can test negative later in life, and only allergic contact dermatitis to the 24 allergens in the TRUE Test® was included in the figures.

One of the problems in studying allergic contact dermatitis is that the relative importance of contact allergens may be difficult to assess, because there is only partial concordance between a positive patch test (contact allergy) and allergic contact dermatitis. However, subjects with positive patch tests to environmental chemicals in non-irritant concentrations represent a group at risk of developing allergic contact dermatitis, if exposed to the chemical in question in a concentration exceeding the individual threshold level.

Allergic contact dermatitis is a multifactorial disease, and apart from exposure to an allergen, there are many factors that affect the development of allergic contact dermatitis including age, sex and contact with irritants. These factors are confounders in the studies if they are not properly controlled for either in the design of the study (restriction, matching) or in the analysis (stratification, multivariate analysis). In this study all analyses had been stratified for sex, and the age group was restricted to 8th grade schoolchildren. No stratification for exposure to irritants was made in the basic analysis, because of the limited occupational exposure in schoolchildren compared to adults. However, because wet work is a strong risk factor in adults, it was included in the multivariate analysis.

We found that the most common contact allergens are nickel, fragrance mix, colophony, cobalt and thimerosal, which is concordant with the findings of other studies (2–17, 38).

Nickel allergy ranked highest, with a point prevalence of 8.6%. The reported prevalence of nickel allergy among children in other population-based studies varied from 0.9% to 14.9% (15–17). As expected, nickel allergy was the only contact allergy with a significant sex difference (girls 13.7% vs. boys 2.5%) (3, 6, 7, 12, 13).

Nickel allergy was considered clinically relevant in 69.4% of cases. The relevance of a positive patch test to nickel in this study was higher than in 2 other studies (39, 40), and in accordance with a Danish study among veterinary students (41). Recall bias may explain some of the reactions without a positive history.

Perfume allergy ranked as second highest in our study. Sensitization to fragrance mix was found in 1.8% of the population, and the reactions were judged relevant in 29% of the cases. The prevalence of sensitization to fragrance mix among children in the general population has also been reported to be 1.8% in another study (15), while other population-based studies did not include fragrance mix in their test series (16, 17). Fragrance allergy varies from country to country in relation to the use of cosmetics and toiletries. The use of these products may already start in the preadolescent years. Young children may "play" with cosmetics, and many perfumed products are specially made for children (42).

A positive patch test to cobalt occurs usually in association with a positive test to nickel or chromate. This association is thought to be related to the fact that the metals are usually associated with one another (35). However, enhanced individual susceptibility to sensitization has also been suggested (43). It is difficult to identify the significance of an isolated positive cobalt patch test. However, most of these patients are probably allergic to jewellery. We evaluated cobalt allergy in relation to concomitant reaction to nickel. Cobalt allergy was found in 1% of the schoolchildren and was found to be relevant in 58% of cases. The reported prevalence of cobalt allergy in 2 other studies among schoolchildren varied from 0.5% to 5.7% (15, 16).

Contact allergy to colophony was found in 1% in accordance with other studies among children and adolescents in the general population (15–17). This was clinically relevant in 33% of the cases. Major sources of colophony allergy are adhesives and cosmetics.

The point prevalence of thimerosal allergy was 1%, and none of the reactions was found to be clinically relevant. This supports the view that thimerosal allergy is caused by exposure to vaccines (44).

Of the schoolchildren with contact allergy, 14.9% had 2 or more positive patch test reactions in contrast to 2% and 8.5% in 2 other population-based studies (15, 16). However, 25 of the 26 children with multiple contact allergies had only 2 positive patch test reactions. Furthermore, multiple sensitivities to metals are not uncommon and 8 of the 26 had concomitant reactions to metals (45, 46).

Contact allergy was found with equal prevalence in unselected schoolchildren with and without a history of atopic dermatitis. Furthermore, no relationship between a history of inhalant allergy and contact allergy was found.

The severity of the dermatitis at the time of testing may be important for the patch test result, and it has been hypothesized that reduced Type IV sensitization is secondary to atopic dermatitis and that only active atopic dermatitis with severe symptoms protects against sensitization, and that others with atopic diseases are equally at risk of sensitization as those without atopic diseases (47). We found no difference in the point prevalence of contact allergy in those with present compared to those with past atopic dermatitis. By further dividing present atopic dermatitis into mild, moderate and severe atopic dermatitis, contact allergy was found in equal frequencies in those with mild and moderate atopic dermatitis. The hypothesis that only active atopic dermatitis with severe symptoms protects against sensitization could not be tested in this study because only one child had severe atopic dermatitis.

Although the relationship between atopic dermatitis and contact allergy is still questionable, this study shows that contact allergy is not infrequent in schoolchildren with atopic dermatitis, and if allergic contact dermatitis is suspected, testing should be performed.

Several studies in adults have shown an association between hand eczema and contact allergy (nickel allergy) (18, 45, 48, 49). In children and adolescents the relationship between hand eczema and contact allergy has not been studied before. We found a significant association between contact allergy and hand eczema in the adolescents. However, the risk for development of hand eczema in adolescents with contact allergy cannot be evaluated in a cross-sectional design.

The association between contact allergy and atopic dermatitis, inhalant allergy and hand eczema was evaluated in a simple model using the Mantel Haenzel analysis, stratified for sex. Because of the association between the 3 diseases, the analyses have also been performed for each disease alone excluding schoolchildren with one or both of the other diseases. This is a simplification of real life, and more complicated statistical approaches have been performed for verification of the results. Because of the association between all 3 diseases, a logistical regression model was not considered appropriate and a multivariate graphical analysis was used as an alternative. The multivariate analysis gave results similar to those of the simpler stratified analyses, e.g. verified the association between contact allergy and hand eczema. Furthermore, the multivariate analysis showed that wet work was not associated with contact allergy in this age group.

A follow-up study of this population is planned to determine the course and development of atopic diseases, hand eczema and contact dermatitis in adulthood and after choice of occupation.

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REFERENCES

1. Mortz CG, Andersen KE. Allergic contact dermatitis in children and adolescents. Contact Dermatitis 1999; 41: 121–130.
2. Balato N, Lembo G, Patruno C, Ayala F. Patch testing in children. Contact Dermatitis 1989; 20: 305–307.
3. Brasch J, Geier J. Patch test results in schoolchildren. Contact Dermatitis 1997; 37: 286–293.
4. Manzini BM, Ferdani G, Simonetti V, Donini M, Seidenari S. Contact sensitization in children. Pediatr Dermatol 1998; 15: 12–17.
5. Veien NK, Hattel T, Justesen O, Norholm A. Contact dermatitis in children. Contact Dermatitis 1982; 8: 373–375.
6. Sevila A, Romaguera C, Vilaplana J, Botella R. Contact

dermatitis in children. Contact Dermatitis 1994; 30: 292–294.
7. Rudzki E, Rebandel P. Contact dermatitis in children. Contact Dermatitis 1996; 34: 66–67.
8. Romaguera C, Alomar A, Camarasa JM, Garcia BB, Garcia PA, Grimalt F, et al. Contact dermatitis in children. Contact Dermatitis 1985; 12: 283–284.
9. Pevny I, Brennenstuhl M, Razinskas G. Patch testing in children. (I) Collective test results; skin testability in children. Contact Dermatitis 1984; 11: 201–206.
10. Rademaker M, Forsyth A. Contact dermatitis in children. Contact Dermatitis 1989; 20: 104–107.
11. Pambor M, Kruger G, Winkler S. Results of patch testing in children. Contact Dermatitis 1992; 27: 326–328.
12. Katsarou A, Koufou V, Armenaka M, Kalogeromitros D, Papanayotou G, Vareltzidis A. Patch tests in children: a review of 14 years' experience. Contact Dermatitis 1996; 34: 70–71.
13. Goncalo S, Goncalo M, Azenha A, Barros MA, Bastos AS, Brandao FM, et al. Allergic contact dermatitis in children. A multicenter study of the Portuguese Contact Dermatitis Group (GPEDC). Contact Dermatitis 1992; 26: 112–115.
14. Ayala F, Balato N, Lembo G, Patruno C, Tosti A, Schena D, et al. A multicentre study of contact sensitization in children. Gruppo Italiano Ricerca Dermatiti da Contatto e Ambientali (GIRDCA). Contact Dermatitis 1992; 26: 307–310.
15. Barros MA, Baptista A, Correia TM, Azevedo F. Patch testing in children: a study of 562 schoolchildren. Contact Dermatitis 1991; 25: 156–159.
16. Dotterud LK, Falk ES. Contact allergy in relation to hand eczema and atopic diseases in north Norwegian schoolchildren. Acta Pædiatr 1995; 84: 402–406.
17. Weston WL, Weston JA, Kinoshita J, Kloepfer S, Carreon L, Toth S, et al. Prevalence of positive epicutaneous tests among infants, children, and adolescents. Pediatrics 1986; 78: 1070–1074.
18. Menne T, Borgan O, Green A. Nickel allergy and hand dermatitis in a stratified sample of the Danish female population: an epidemiological study including a statistic appendix. Acta Derm Venereol 1982; 62: 35–41.
19. Angelini G, Meneghini CL. Contact and bacterial allergy in children with atopic dermatitis. Contact Dermatitis 1977; 3: 163–167.
20. Jones HE, Lewis CW, McMarlin SL. Allergic contact sensitivity in atopic dermatitis. Arch Dermatol 1973; 107: 217–222.
21. Rystedt I. Atopic background in patients with occupational hand eczema. Contact Dermatitis 1985; 12: 247–254.
22. Cronin E, Bandmann HJ, Calnan CD, Fregert S, Hjorth N, Magnusson B, et al. Contact dermatitis in the atopic. Acta Derm Venereol 1970; 50: 183–187.
23. Marghescu S. Patch test reactions in atopic patients. Acta Derm Venereol 1985; Suppl 114: 113–116.
24. Lammintausta K, Kalimo K, Fagerlund VL. Patch test reactions in atopic patients. Contact Dermatitis 1992; 26: 234–240.
25. Epstein S, Mohajerin AH. Incidence of contact sensitivity in atopic dermatitis. Arch Dermatol 1964; 90: 284–287.
26. Lugovic L, Lipozencic J. Contact hypersensitivity in atopic dermatitis. Arh Hig Rada Toksikol 1997; 48: 287–296.
27. Mortz CG, Lauritsen JM, Bindslev-Jensen C, Andersen KE. Prevalence of atopic dermatitis, asthma, allergic rhinitis, and hand and contact dermatitis in adolescents. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis. Br J Dermatol 2001; 144: 523–532.
28. Schultz Larsen F, Diepgen T, Svensson Å. The occurrence of atopic dermatitis in north Europe: an international questionnaire study. J Am Acad Dermatol 1996; 34: 760–764.
29. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol 1980; Suppl 92: 44–47.
30. European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology 1993; 186: 23–31.
31. Kunz B, Oranje AP, Labréze JF, Ring J, Taïeb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European task force on atopic dermatitis. Dermatology 1997; 195: 10–19.
32. Susitaival P, Kanerva L, Hannuksela M, Jolanki R, Estlander T. Tuohilampi questionnaire for epidemiological studies of contact dermatitis and atopy. People and Work 1996; 10: 1–26.
33. Fischer T, Maibach HI. The thin layer rapid use epicutaneous test (TRUE-test), a new patch test method with high accuracy. Br J Dermatol 1985; 112: 63–68.
34. Andersen KE, Liden C, Hansen J, Volund A. Dose-response testing with nickel sulphate using the TRUE test in nickel-sensitive individuals. Multiple nickel sulphate patch-test reactions do not cause an "angry back". Br J Dermatol 1993; 129: 50–56.
35. Rycroft RJG, Menne T, Frosch PJ. Textbook of contact dermatitis. 2nd ed. Berlin, Heidelberg: Springer-Verlag, 1995.
36. Klein JP, Keiding N, Kreiner S. Graphical models for panel studies, illustrated on data from the Framingham Heart Study. Stat Med 1995; 14: 1265–1290.
37. Agresti A. Analysis of ordinal categorical data. New York: Wiley and Sons, 1984.
38. Nielsen NH, Menne T. Allergic contact sensitization in an unselected Danish population. The Glostrup Allergy Study, Denmark. Acta Derm Venereol 1992; 72: 456–460.
39. Larsson-Stymne B, Widstrom L. Ear-piercing – a cause of nickel allergy in schoolgirls? Contact Dermatitis 1985; 13:289–293.
40. Dotterud LK, Falk ES. Metal allergy in north Norwegian schoolchildren and its relationship with ear piercing and atopy. Contact Dermatitis 1994; 31: 308–313.
41. Kieffer M. Nickel sensitivity: relationship between history and patch test reaction. Contact Dermatitis 1979; 5: 398–401.
42. Rastogi SC, Johansen JD, Menne T, Frosch P, Bruze M, Andersen KE, et al. Content of fragrance allergens in children's cosmetics and cosmetic-toys. Contact Dermatitis 1999; 41: 84–88.
43. Moss C, Friedmann PS, Shuster S, Simpson JM. Susceptibility and amplification of sensitivity in contact dermatitis. Clin Exp Immunol 1985; 61: 232–241.
44. Novak M, Kvicalova E, Friedlanderova B. Reactions to merthiolate in infants. Contact Dermatitis 1986; 15: 309–310.
45. Gawkrodger DJ, Vestey JP, Wong W-K, Buxton PK. Contact clinic survey of nickel-sensitive subjects. Contact Dermatitis 1986; 14: 165–169.
46. Fregert S, Rorsman H. Allergy to chromium, nickel and cobalt. Acta Derm Venereol 1966; 46: 144–148.
47. Uehara M, Sawai T. A longitudinal study of contact sensitivity in patients with atopic dermatitis. Arch Dermatol 1989; 125: 366–368.
48. Menne T, Holm NV. Hand eczema in nickel-sensitive female twins. Genetic predisposition and environmental factors. Contact Dermatitis 1983; 9: 289–296.
49. Christensen OB, Moller H. Nickel allergy and hand eczema. Contact Dermatitis 1975; 1: 129–135.