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CONTACT DERMATITIS

Contact hypersensitivity and allergic contact dermatitis among school children and teenagers with eczema

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Background: Patch testing is an essential procedure in the investigation of eczema in children.

Objectives: To analyse the frequency of contact hypersensitivity and allergic contact dermatitis among Polish children with eczema.

Patients/methods: During an allergy screening programme involving 9320 children aged 7 and 16 years, 12.6% reported symptoms of chronic/recurrent eczema. From this group, a representative sample of 229 eczema children underwent patch testing: 96 children aged 7 years and 133 teenagers aged 16 years. Patch testing was with 10 allergens: methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), nickel sulfate, mercury ammonium chloride, thimerosal, cobalt chloride, potassium dichromate, lanolin, fragrance mix I, *Myroxylon pereirae* (balsam of Peru), and colophonium.

Results: 49.4% tested children were found patch test (PT) positive. 43.8% of 7 year olds with eczema were PT positive, with sensitization to nickel sulfate (30.2%), thimerosal (10.4%), cobalt chloride (8.3%), fragrance mix I (7.3%), MCI/MI (6.3%), potassium dichromate (6.3%), *M. pereirae* (3.1%), mercury ammonium chloride (2.3%), and colophonium (1.0%). 52.6% teenagers were PT positive, with sensitization to nickel sulfate (23.3%), thimerosal (27.8%), cobalt chloride (10.5%), potassium dichromate (6.0%), mercury ammonium chloride (2.3%), *M. pereirae* (1.5%), and MCI/MI (0.8%). The final diagnosis of allergic contact dermatitis was confirmed in 36% of 7 year olds and 26% of 16 year olds.

Conclusions: Every second child with eczema is PT positive, whereas every third child is finally diagnosed with allergic contact dermatitis.

Key words: allergic contact dermatitis; children; contact allergy; contact hypersensitivity; eczema; epidemiology; patch testing. © 2009 John Wiley & Sons A/S.

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Most epidemiological studies of allergy in children are focused on atopic allergy, and in some of these, any form of dermatitis is regarded *a priori* as atopic eczema with apparent neglect of other possible diagnoses (1–5). Other studies, however, indicate that contact hypersensitivity and allergic contact dermatitis are frequent among children (6–9). Special patch test (PT) series for children have been devised (10), while other authors suggest testing children with the same test series as adults (8).

There is only limited information on the frequency of contact hypersensitivity and allergic contact dermatitis in the general population of children and teenagers in Poland. In 1999, Slaweta and Kiec-Swierczynska (11) found positive PT reactions in 21.6% of primary school pupils aged 13–15 years (31.3% girls and 12.2% boys). In 2001–2002, Spiewak examined a random sample of vocational students of 18–19 years of age and found 28.1% of them PT positive (12). The point prevalence of allergic contact dermatitis in this group was 1.6%, whereas lifetime prevalence was 10.9% (13). From a practitioner's point of view, perhaps, more interesting would be to know how frequent is contact hypersensitivity and

allergic contact dermatitis among children and teenagers with eczema. Unfortunately, no such data were available for Poland until recently. The aim of this study was therefore to analyse the rates of contact hypersensitivity and allergic contact dermatitis among Polish school children with symptoms of eczema.

Patients and Methods

As a part of an allergy screening programme commissioned by the Municipal Council of Krakow, a questionnaire survey of the presence of allergic symptoms was conducted in all the city's public schools in 2007 involving 3846 children of 7 years and 5474 teenagers (16 years old), altogether 9320 school children. The Polish version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used (2, 14), supplemented with questions concerning the risk factors and appearance of symptoms suggestive of contact allergy (Table 1). The questionnaire for 7 year olds was answered by their parents, whereas the 16 year olds filled in the questionnaire by themselves. Of 1175 children reporting symptoms of eczema, a group of 229 children representative for each age group and sex were invited for patch testing. The test series consisted of 10 contact sensitizers, regarded most common in children according to the analysis of 23 European epidemiological studies from the years 1980–2001 (15). The series thus included nickel sulfate 5% petrolatum (pet.), mercury ammonium chloride 1% pet., thimerosal 1% pet., cobalt chloride 0.5% pet., potassium dichromate 0.25% pet., methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) 0.01% aqueous (aq.), lanolin (wool alcohols) 30% pet., fragrance mix I 8% pet. (contents: cinnamyl alcohol, cinnamal, eugenol, isoeugenol, hydroxycitronellal, *Evernia prunastri* absolute, geraniol, and alpha amyl cinnamal), *Myroxylon pereirae* (balsam of Peru) 25% pet., and colophonium 20% pet. (Chemotechnique Diagnostics, Vellinge, Sweden). These substances were applied in Chemotechnique's IQ Ultra Chambers for 2 days. Readings of the test results

Table 1. Additional questions towards contact allergy and symptoms of allergic contact dermatitis [adapted from Spiewak (13)] with a summary of answers regarding the patch-tested eczema children[a]

Question	Answers	7 years old	16 years old	*P* value
1. Have you ever worn costume jewellery (earrings, ear clips, chains, bracelets made of metals other than gold, silver, platinum)?	Yes	10.5% (4.0–16.9%)	50.0% (40.7–59.3%)	<0.001
	Since…	5 (3–6) y.o.	10 (1–16) y.o.	
2. How frequently do you wear costume jewellery?	(Almost) everyday	1.4% (0.0–4.1%)	21.3% (13.0–29.5%)	<0.001
	From time to time	11.1% (3.8–18.4%)	33.0% (23.5–42.5%)	<0.01
	(Almost) never	87.5% (79.9–95.1%)	45.7% (35.7–55.8%)	<0.001
3. Have you ever pierced your earlobes or any other part of your body?	Yes	26.7% (17.4–36.1%)	53.1% (43.0–62.4%)	<0.001
	When…	3 (0.5–7) y.o.	7 (1–16) y.o.	
4. Do you have a permanent tattoo (i.e. made with a needle)?	Yes	0%	0%	—
5. Have you ever had a temporary tattoo (i.e. painted on the skin)?	Yes	12.6% (21.4–30.2%)	14.4% (7.9–20.9%)	NS
6. Have you ever worn orthodontic appliances?	Yes	3.5% (0–7.4%)	46.0% (36.8–55.2%)	<0.001
	Since…	7 (6–7) y.o.	10 (5–16) y.o.	
7. How frequently are you using cosmetics (skincare creams, perfumes, make-up)?	(Almost) everyday	28.2% (18.2–38.2%)	63.2% (54.0–72.4%)	<0.001
	From time to time	19.2% (10.5–28.0%)	25.5% (17.2–33.8%)	NS
	(Almost) never	52.6% (41.5–63.6%)	11.3% (5.3–17.3%)	<0.001
8. Have you ever used a hair dye?	Yes	0%	29.2% (20.8–37.6%)	<0.001
	Since…	—	14 (9–16) y.o.	
9. Have you ever noticed that contact with particular substances or objects causes eczema (itchy rash) of your skin? If yes, please specify	Yes	27.9% (18.4–37.4%)	38.9% (29.9–47.9%)	NS
	Cosmetics	12.8% (5.7–19.8%)	9.7% (4.3–15.2%)	NS
	Drugs	8.1% (2.4–13.9%)	5.3% (1.2–9.4%)	NS
	Metal	3.5% (0.0–7.4%)	15.9% (9.2–22.7%)	<0.01
	Rubber	0%	0%	—
	Other	10.5% (4.0–16.9%)	14.2% (7.7–20.6%)	NS
10. Do you have such an itchy rash now?	Yes	17.4% (9.4–25.5%)	9.7% (4.3–15.2%)	NS
11. Have you had such an itchy rash within the last 12 months?	Yes	46.5% (36.0–57.0%)	45.1% (36.0–54.3%)	NS
12. Have you had such an itchy rash earlier than 1 year ago?	Yes	68.6% (58.8–78.4%)	54.0% (44.8–63.2%)	<0.05

NS, not significant; y.o., years old.

[a]This is the wording of the questionnaire version for the 16 y.o. In the version for the 7 y.o. (to be filled by parents), the words 'your child' and 'your child's' were used instead of 'you' and 'your', respectively. *P* value was calculated using chi-squared test. For percentages, 95% confidence intervals are given in brackets; for age (y.o.), medians are given with ranges in brackets.

were carried out on D2 and D3, according to International Contact Dermatitis Research Group guidelines (16).

Statistical analysis

The frequency rates with 95% confidence interval (95% CI) were calculated for children reporting any symptoms of eczema and separately for a positive answer to the question suggestive of allergic contact dermatitis (no. 9 in Table 1) and of atopic eczema (positive answer to the ISAAC question 'Has your/your child's eczema affected at any time any of the following places: folds of the elbows, behind the knees, fronts of the ankles, under the buttocks, or around the neck, ears, or eyes?'). For patch-tested children, positivity rates of PTs (overall and for each allergen) and of the final diagnosis of allergic contact dermatitis were calculated. Comparisons were made between age groups (7 year old versus 16 year old) and sex (males versus females) using the chi-squared test with Yates' correction. $P < 0.05$ was considered statistically significant.

Results

Symptoms of an allergic disease (either skin or respiratory) were reported by 42.3% (95% CI: 39.9–44.7) of the 7 year olds and by 31.2% (95% CI: 29.0–33.4) of the 16 year olds. Among 3846 children aged 7 years, 719 (18.7%; 95% CI: 17.5–19.9) reported presence of any eczema symptoms, including 276 (7.2%; 95% CI: 6.4–8.0) with a positive answer to the question suggestive of allergic contact dermatitis and 360 (9.4%; 95% CI: 8.4–10.3) with a positive answer to the question suggestive of atopic eczema. Among 5474 teenagers, 456 (8.3%; 95% CI: 7.6–9.1) reported the past or current presence of any eczema symptoms, including 333 (6.1%; 95% CI: 5.5–6.7) with a positive answer to the allergic contact dermatitis question and 184 (3.4%; 95% CI: 2.9–3.8) with a positive answer to the atopic eczema question.

The results of PTs in 229 children with eczema are shown in Table 2. When comparing age groups (both sexes combined), there were significant differences in the frequency of positive PT to thimerosal ($P = 0.002$), fragrance mix I ($P = 0.006$), and MCI/MI ($P = 0.046$). The frequency of allergy to nickel sulfate did not differ significantly between 7-year-old and 16-year-old schoolgirls. There was, however, significant difference in this respect in boys, with a higher frequency of nickel contact allergy among 7-year-old boys (33.3% versus 6.7%; $P = 0.004$). The analysis of the possible association between wearing earrings and the occurrence of contact hypersensitivity to nickel is presented in Table 3. The frequency of contact hypersensitivity to nickel among 16-year-old girls wearing earrings was almost four times higher compared with their peers who never wore earrings (difference at the border of statistical significance, $P = 0.08$). This analysis was not possible for boys as only one of them was pierced. In the patch-tested group of children with eczema symptoms, allergic contact dermatitis was finally

Table 2. Frequency of positive patch test reactions in children (7 y.o.) and adolescents (16 y.o.) with history of eczema[a]

Age	7 y.o.			16 y.o.		
Sex	♀ ($n = 54$)	♂ ($n = 42$)	Total ($n = 96$)	♀ ($n = 88$)	♂ ($n = 45$)	Total ($n = 133$)
At least one test positive (%)	31.5 (19.1–43.9)	59.5 (44.7–74.4)	43.8 (33.8–53.7)	58.0 (47.6–68.2)	42.2 (27.8–56.7)	52.6 (44.1–61.1)
Nickel sulfate 5% pet. (%)	27.8 (15.8–39.7)	33.3 (19.1–47.6)	30.2 (21.0–39.4)	31.8 (22.1–41.5)	6.7 (0–13.9)	23.3 (16.1–0.5)
Thimerosal 1% pet. (%)	11.1 (2.7–19.5)	9.5 (0.6–18.4)	10.4 (4.3–16.5)	27.3 (17.8–36.6)	28.9 (15.6–42.1)	27.8 (20.2–35.4)
Cobalt chloride 0.5% pet. (%)	9.3 (1.5–17.0)	7.1 (0–14.9)	8.3 (2.8–13.9)	13.6 (6.5–20.8)	4.4 (1.6–10.5)	10.5 (5.3–15.7)
Fragrance mix 8% pet. (%)	7.4 (0.4–14.4)	7.1 (0–14.9)	7.3 (2.1–12.5)	0	0	0
Potassium dichromate 0.25% pet. (%)	7.4 (0.4–14.4)	4.8 (0–11.2)	6.3 (1.4–11.1)	8.0 (2.3–13.6)	2.2 (0–6.5)	6.0 (2–10.1)
MCI/MI 0.01% aq. (%)	5.6 (0–11.7)	7.1 (0–14.9)	6.3 (1.4–11.1)	1.1 (0–3.4)	0	0.8 (0–2.2)
Myroxylon pereirae 25% pet. (%)	1.9 (0–5.4)	4.8 (0–11.2)	3.1 (0–6.6)	1.1 (0–3.4)	2.2 (0–6.5)	1.5 (0–3.6)
Mercury ammonium chloride 1% pet. (%)	1.9 (0–5.4)	2.4 (0–7.0)	2.1 (0–4.9)	2.3 (0–5.4)	2.2 (0–6.5)	2.3 (0–4.8)
Colophonium 20% pet. (%)	0	2.4 (0–7.0)	1.0 (0–3.1)	0	0	0
Lanolin 30% pet. (%)	0	0	0	0	0	0

aq. aqueous; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; pet. petrolatum; y.o., years old.
[a]95% confidence intervals are given in brackets.

Table 3. The frequency of positive patch tests to nickel among girls wearing earrings compared with those who had never worn earrings

Group tested	Percentage of Ni(+) among girls with earrings	Percentage of Ni(+) among girls without earrings	Chi-squared test
Girls (7 years old)	23.8 (5/21)	18.2 (6/33)	$P = 0.62$
Girls (16 years old)	23.2 (13/56)	6.3 (2/32)	$P = 0.08$
Chi-squared test	$P = 0.96$	$P = 0.27$	

diagnosed in 35 children who were 7 years old (36.5%; 95% CI: 26.8–46.1) and in 35 teenagers (26.3%; 95% CI: 18.8–33.8).

Discussion

Contact allergy can already develop in the first months of life (17). There are convincing data suggesting that contact hypersensitivity may be more frequent in younger than in older children or adults (8, 10, 18). According to the analysis of 23 European studies, the frequency of contact hypersensitivity in the general children's population can be estimated at 13.3–24.5%, with 56.5–94.4% of positive PTs considered clinically relevant (16). However, not every child with contact allergy will develop allergic contact dermatitis. Mortz et al. diagnosed allergic contact dermatitis in 7.2% of Danish schoolchildren aged 12–16 years (19).

In our study, 7.2% of 7 year olds and 6.1% of 16 year olds reported the presence of eczema symptoms suggestive of contact dermatitis (eczema caused by skin contact with particular substances or objects). The higher rate in younger children could reflect a real increase of eczema frequency in the younger generation; however, it also might be biased by the method of collecting data. The questionnaires for 7 year olds were filled in by their parents, who might be better informed and keep more recent memory of their children's eczema compared with teenagers who were answering the questionnaire on their own. Among children with eczema who underwent subsequent patch testing, the diagnosis of allergic contact dermatitis was finally confirmed in 36.5% of 7 year olds and in 26.3% of 16 year olds Assuming that the above figures are representative for respective age groups, the lifetime prevalence of allergic contact dermatitis in the general population of school children in Krakow would amount to 6.8% among the 7 year olds (36.5% of 18.7% children with eczema were finally diagnosed with allergic contact dermatitis) and 2.2% among the 16 year olds (26.3% of 8.3%). The latter figure seems relatively low, and a possible source of bias (under-reporting) has already been mentioned (self-administration of the questionnaire by the 16 year olds).

According to a recent estimation, nickel allergy may affect as many as 65 million citizens of the EU, including 54 million women and 11 million men (20). The higher frequency among women may be explained with early piercing and wearing of earrings by girls (21–24). In our study, the frequency of contact allergy to nickel among 16-year-old girls wearing earrings was nearly four times higher than that among girls of the same age who have never had these. A surprising finding of our study was the significantly higher positivity to nickel among boys aged 7 years (none was pierced) compared with 16 year olds (Fig. 1). Interestingly, similar results were presented recently by Vigan (25), who placed this on account of a higher frequency of irritant reactions among younger boys. However, in the study of Norwegian children aged 7–12 years, none of the positive PT reactions to nickel sulfate 5% pet. seen in 44 girls and 19 boys appeared irritant (26). In our study, only in 1 of 14 positive PT reactions to nickel seen in 7-year-old boys, the morphology and dynamics might possibly be consistent with an irritant reaction. Moreover, it seems difficult to explain why boys should be more susceptible to irritants than girls in prepubertal age when most physiologic differences between sexes are not yet manifested. This interesting phenomenon would certainly deserve further research.

The frequency of contact allergy to thimerosal was in our study significantly higher among the 16 year olds than in the younger group. Thimerosal is one of the most frequently used vaccine preservatives, and there are suggestions that preventive vaccinations may lead to thimerosal hypersensitivity (21, 27, 28). This seems in line with our observations as the 16 year olds have received six thimerosal-preserved vaccines during their life course, with the last immunization taking place 2–3 years before the PTs. The 7 year olds received only four thimerosal-preserved vaccines, with the last one applied 5 years before the tests. Later immunization at the age of 6 years was performed in this group with new thimerosal-free, diptheria-tetanus-acellular pertussis (DTPa) vaccines Infanrix™ (GlaxoSmithKline Biologicals, Rixensart, Belgium), Tripacel™ or Petaxim™ (both from Sanofi Pasteur S.A., Lyon, France). Most authors consider contact hypersensitivity

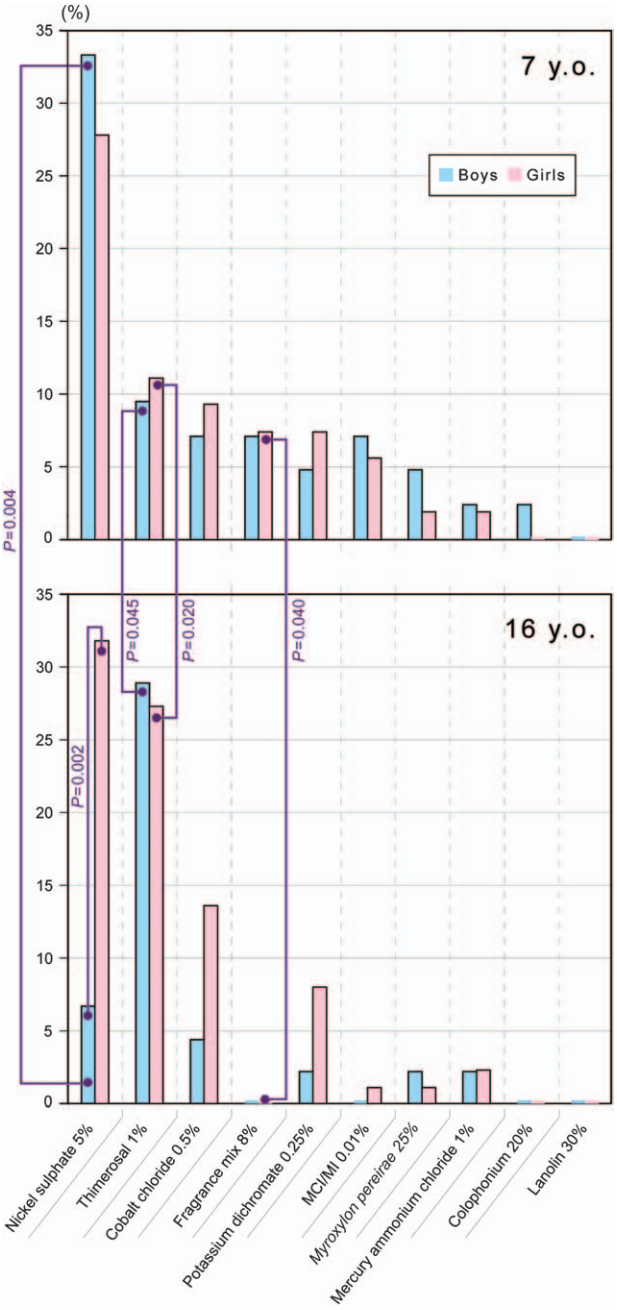

Fig. 1. The frequency of contact hypersensitivity among boys and girls with history of eczema. MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; y.o., years old.

to thimerosal as not clinically relevant, and positive PT to this substance is not regarded as contraindication for the administration of vaccines containing this preservative (29, 30). Reflecting the minimal clinical relevance of contact hypersensitivity to thimerosal, this substance is not included in the current European baseline series (16, 31).

Another preservative, MCI/MI, was in the past decades of the 20th century the most frequent sensitizer of children with eczema, with a PT positivity rate amounting to 21% (Table 4). Because of the decrease in use of this preservative and dropping sensitivity rates, it was not included in more recent studies (22, 27, 32). We have found positive PT reactions to MCI/MI in 6.3% of 7 year olds and 0.8% of 16 year olds with eczema (Fig. 1). As this preservative was prohibited from use in consumer products in Poland preceding the country's accession into the EU (33), we could not identify any exposure that might explain the higher frequency in the younger group. A possible hint with respect to this can be found in the study of Norwegian children aged 7–12 years by Dotterud and Falk (26), who classified 18 of 22 positive PT reactions to MCI/MI 0.01% as irritant. This might suggest that the concentration of 0.01% might be too high for children, leading to a considerable proportion of false-positive results.

A somewhat surprising result of our study is the higher frequency of fragrance allergy among the 7 year olds compared with no positive reactions among the 16 year olds. A possible explanation to this observation might be increasing exposure of young children to perfumed products (toys, books, cosmetics, etc.). Although irritant reactions are possible (34, 35), our data suggest the need for patch testing children with fragrances.

Table 4. The most frequent contact sensitizers among children with eczema – comparison of own results with the analysis of 23 epidemiological studies from 1980 to 2001 (15) and German results from 1995 to 2002 (27)

Allergen	Present 2007 data (7- and 16-year-old groups combined) (%)	23 studies (1980–2001) (%)	German study (1995–2002) (%)[a]
Nickel sulfate	26.2	19.2	16.0
Thimerosal	20.5	14.0	14.8
Cobalt chloride	9.6	13.5	5.0
Potassium dichromate	6.1	12.4	2.1
Fragrance mix I	3.1	11.8	6.0
MCI/MI	3.1	21.0	1.5
Myroxylon pereirae	2.2	10.8	2.6
Mercury ammonium chloride	2.2	14.6	5.6
Colophonium	0.4	9.7	Not given
Lanolin	0.0	12.1	1.9

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.
[a]Cumulative data from German study (children + adolescents) calculated as weighted mean percentages.

Conclusions

Contact allergy is found in every second child with symptoms of chronic or recurrent eczema. In every third child with eczema, the final diagnosis is allergic contact dermatitis. Patch testing is a necessary element of eczema diagnosis in children.

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