

Allergic contact dermatitis in Danish children referred for patch testing – a nationwide multicentre study

Anne Birgitte Simonsen¹, Mette Deleuran¹, Charlotte Gotthard Mortz², Jeanne Duus Johansen³ and Mette Sommerlund¹

¹Department of Dermatology and Venereology, Aarhus University Hospital, 8000, Aarhus C, Denmark, ²Department of Dermatology and Allergy Centre, Odense University Hospital, 5000, Odense C, Denmark, and ³Department of Dermato-Allergology, National Allergy Research Centre, Copenhagen University Hospital, 2900, Hellerup, Denmark

doi:10.1111/cod.12129

Summary

Background. Although contact allergy among children was previously considered to be rare, data from the past decade have shown that it is common among children and that the prevalence may be increasing.

Objectives. To describe the demographics of all children referred for patch testing in Denmark during 2003–2011, to examine the frequency and relevance of positive patch test reactions, and to assess the most common allergens.

Methods. A retrospective analysis of the patch test data from the Danish National Database of Contact Allergy was performed.

Results. Of 2594 children and adolescents aged 1–17 years, 25.1% had one or more positive patch test reactions. The associated relevance was 66.4%. The most common sensitizers were metals, fragrances, and hair dyes. The frequency of positive patch test reactions and allergic contact dermatitis was significantly higher among girls.

Conclusions. Allergic contact dermatitis in children is a significant clinical problem. Contact allergy should always be considered when children with recalcitrant eczema are encountered, and special attention should be paid to girls. Patch testing is important, and children may be tested with the same patch test concentrations as adults.

Key words: allergic contact dermatitis; children; contact allergy; patch testing

Allergic contact dermatitis acquired in childhood has important consequences for the individual, as it may affect the quality of life (1, 2). It may interfere with play, sports activities, and school (2), and affect decisions regarding future occupation. The morbidity from allergic contact dermatitis depends on the ability to avoid exposure to the contact allergen, and the patient may experience chronic or recurrent episodes of dermatitis if the source is not identified as early as possible by patch testing (3).

Traditionally, allergic contact dermatitis was considered to be uncommon in the paediatric population (4, 5). Children were thought to be less exposed to allergens, and the immune system of children was considered to be less susceptible to contact allergens (5, 6). Data from the past decade have shown that contact allergy is common among children, and suggest that the prevalence may be increasing (7, 8). Several patch test studies from different parts of the world on symptomatic children have been published. We previously reviewed the existing literature on the prevalence of contact allergy and allergic contact dermatitis, and found reported sensitization rates of 26.6–95.6% in selected groups of children who were referred for patch testing. The associated relevance was 51.7–100% (8).

Correspondence: Anne Birgitte Simonsen, Department of Dermatology and Venereology, Aarhus University Hospital, P.P. Orumsgade 11, 8000 Aarhus C, Denmark. Tel: +45 78461861; Fax: +45 78461860. E-mail: anbsim@rm.dk

Conflicts of interest: The authors have declared no conflicts.

Accepted for publication 30 June 2013

The apparent increase in allergic contact dermatitis among children is thought to be the result of increased exposure to allergens at a younger age, new trends in body piercing, the use of cosmetic products, and participation in sports and hobbies, in addition to improved recognition of allergic contact dermatitis and more frequent patch testing of children (9).

Allergen exposure varies throughout the world, and is determined by different factors, such as climate, cultural habits, and legislation (10). Furthermore, the frequency of positive patch test results may vary with referral patterns, criteria for patch testing, selection of patch test series, and patch test methodology (8, 11).

The aim of this study was to describe the demographics of a sample of children referred for patch testing in Denmark during 2003–2011, to examine the frequency and relevance of positive patch test reactions, and to assess the most common allergens. This is the first study on the prevalence of contact allergy and allergic contact dermatitis in Danish children referred for patch testing since 1982, when Veien et al. (5) found a sensitization rate of 45.8% and a prevalence of allergic contact dermatitis of 36.9% among 168 children.

Materials and Methods

Our retrospective analysis was based on data from the Danish National Database for Contact Allergy. From 1 January 2003 to 31 December 2011, a total of 2594 patients aged 1–17 years were patch tested in 12 dermatology clinics throughout Denmark (Danish Group for Contact Dermatitis), which is estimated to cover approximately one-fifth of patients patch tested in Denmark. Of the 2594 children, 49 were patch tested twice and 2 were patch tested three times during the study period. We included only the primary patch test results in this study.

All patients either suffered from recalcitrant eczema or had a suspected diagnosis of allergic contact dermatitis. Characteristics according to the MOAHLFA index (Male, Occupational dermatitis, Atopic dermatitis, Hand dermatitis, Leg dermatitis, Face dermatitis, Age >40 years) were registered. Atopic dermatitis was evaluated according to the Hanifin and Rajka criteria (12). The children were tested with either the European baseline series (allergens obtained from either Chemotechnique Diagnostics, Vellinge, Sweden, or from Almirall Hermal, Reinbek, Germany) or with TRUE Test™ (SmartPractice Denmark, Hilleroed, Denmark) supplemented with the allergens from the European baseline series that are not included in the TRUE Test™. In a few cases, the patient had an already known contact allergy and was therefore not tested with the specific allergen.

Patch tests were removed on D2. Readings were performed according to the International Contact Dermatitis Research Group guideline on D3 or D4, and often also on D2 and D7. Reactions designated as either 1+, 2+ or 3+ were regarded as positive. Skin reactions characterized by dry skin, scaling, pustules, shiny skin and a silk or cigarette paper-like surface were regarded as irritant reactions. The relevance of the positive reactions was evaluated according to national guidelines (13), on the basis of patient history, product labels, spot tests, etc. For the purpose of this study, reactions of past or current relevance were combined, and all reactions were designated as either relevant or not.

Data analysis was performed with the statistical software program STATA™ 12.0. Comparison of sensitization rates was performed with the χ^2 -test, employing a 5% significance level. Linear regression analysis was used to compare sensitization rates in multiple age groups. An *F*-test was used to test whether age coefficients from the regression were jointly equal.

Results

A total of 2495 children and adolescents aged 1–17 years were patch tested. The characteristics summarized by the MOAHLFA index were as follows: 34.1% were male, 2.7% had an allergy that was related to occupation, 44.8% had atopic dermatitis, 28.0% had hand dermatitis, 1.5% had leg dermatitis, and 19.2% had facial dermatitis.

A positive reaction to at least one allergen was seen in 25.1% of the children, and 66.4% of these were considered to be of current or past relevance. The number of children annually referred for patch testing increased steadily during the study period (Fig. 1). The pronounced increase from 2008 was attributable to the addition of more clinics reporting to the database. There could be a trend for an increase in sensitization rates, which calls for further investigation (Fig. 2).

We divided the patients into four different age groups. Table 1 shows the positive and relevant reactions by age group and sex. Overall, more girls than boys were patch tested. The female dominance was evident from the age of 5 years, and the sex difference with regard to frequency of patch testing increased with age. Overall, girls were significantly more likely to have a positive patch test reaction (26.7% versus 22.1%, $p < 0.05$). This sex difference became apparent after the age of 13 years.

There were no significant differences in sensitization rates or relevance between age groups (Table 1).

Metals were the most frequent sensitizers (12.2%), followed by fragrances (4.7%) and hair dyes/*p*-phenylenediamine (PPD) (3.5%). Table 2 shows all

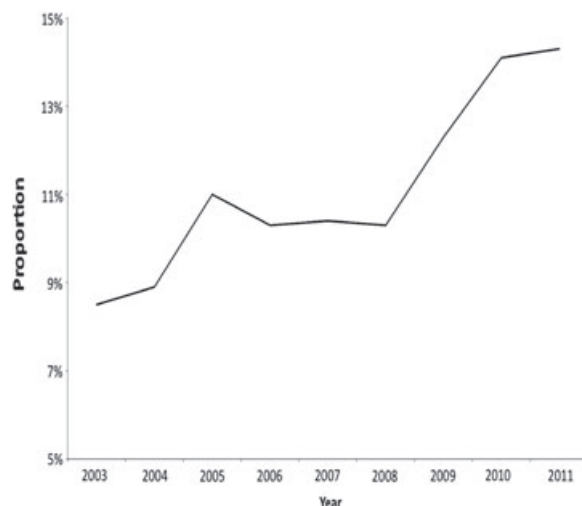


Fig. 1. The proportion of children referred annually out of all children in the cohort (n = 2594).

allergens listed by frequency of positive reactions, and the rate of sensitization listed by groups of allergens. Table 3 shows the most common sources of exposure.

Nickel was by far the most common allergen. Of the 2587 children tested with nickel, 9.7% were sensitized, and the associated relevance was 69.0%. The next most common sensitizers from the European baseline series were cobalt chloride (4.4%), PPD (3.5%), and fragrance mix I (2.5%). This pattern appeared from the age of 5 years. As patients sensitized to caine mix or benzocaine may show cross-reactivity to PPD, we also examined concomitant reactions to PPD and caine mix; 3.7% of the 434 children tested with both PPD and caine mix reacted to both substances. Among the 2079 children tested with both PPD and benzocaine, 0.6% reacted to both substances. Table 4 shows the most common allergens in the different age groups. Of all of the children who were sensitized, 40.1% were sensitized to more than one allergen.

The frequency of irritant reactions increased with age; however, the proportions of irritant reactions in the four age groups did not differ significantly. In the youngest age group, of 1–4-year-old children, five irritant reactions were observed in 3 children. These were to cobalt chloride, lanolin (wool alcohols), paraben mix, benzocaine, and mercapto mix, and none were observed in children aged < 4 years. Cobalt chloride was the most frequent irritant, and caused 38.8% of all irritant reactions.

Among the adolescents aged 13–17 years, 3.8% had a positive reaction that was also considered to be work-related. The dermatitis was located on the hands in 81.3% of the cases. The most frequent allergens causing work-related allergy were metals, adhesive chemicals, and PPD.

Discussion

In our retrospective analysis of the results of all patch tests performed on children and adolescents aged 1–17 years in Denmark during 2003–2011, we found a sensitization rate of 25.1% and an associated relevance of 66.4%, which is in agreement with international data. Metals, fragrances and hair dye were the most common sensitizers (Table 2). The frequency of patch testing and the number of both positive and relevant reactions increased with age. However, we found no significant differences with regard to sensitization rates between age groups. This may indicate differences in the threshold for patch testing children, depending on the child's age, and it could also indicate that too few children in the youngest age groups are patch tested.

Almost 45% of the patch tested children had atopic dermatitis. A probable explanation for this high proportion is that many children with treatment-refractory atopic eczema are patch tested to investigate for external aggravating factors such as contact allergy, including contact allergy to medications.

Nickel is by far the most common allergen in Europe, among both children and adults (14). Accordingly, nickel was the most common allergen in all age groups in our

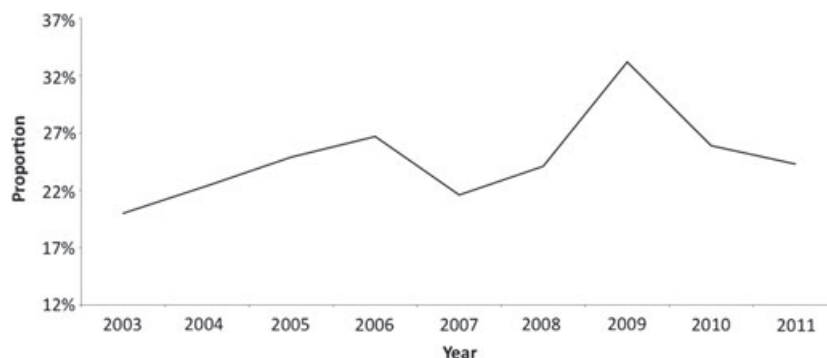


Fig. 2. Sensitization rates during the study period, that is, the proportion of children with at least one positive patch test reaction out of the children patch tested in the specific year.

Table 1. Patch test reactions by age group and sex

Age (years)	Number referred			Positive reactions				Relevance ^a				Irritant reactions ^b			
	Total	Female (%)	Male (%)	Total (%)	Female (%)	Male (%)	p-value	Total (%)	Female (%)	Male (%)	p-value	Total (%)	Female (%)	Male (%)	p-value
1–4	76	31 (40.8)	45 (59.2)	19 (25.0)	9 (29.0)	10 (22.2)	0.5	11 (57.9)	5 (55.6)	6 (60.0)	0.85	3 (3.9)	–	3 (6.7)	0.14
5–8	227	131 (57.7)	96 (42.3)	55 (24.2)	33 (25.2)	22 (22.9)	0.69	37 (67.3)	23 (69.7)	14 (63.6)	0.64	5 (2.2)	5 (3.8)	–	0.05
9–12	579	371 (64.1)	208 (35.9)	152 (26.3)	100 (27.0)	52 (25.0)	0.61	101 (66.4)	68 (68.0)	33 (63.5)	0.57	22 (3.8)	16 (4.3)	6 (2.9)	0.39
13–17	1712	1177 (68.8)	535 (31.3)	425 (24.8)	314 (26.7)	111 (20.7)	< 0.05	283 (66.6)	219 (69.7)	64 (57.7)	< 0.05	75 (4.4)	60 (5.1)	15 (2.8)	< 0.05
Total	2594	1710 (65.9)	884 (34.1)	651 (25.1)	456 (26.7)	195 (22.1)	< 0.05	432 (66.4)	315 (69.1)	117 (60.0)	< 0.05	105 (4.0)	81 (4.7)	24 (2.7)	< 0.05
F-test: equality of age groups:				p = 0.90	p = 0.97	p = 0.76		p = 0.89	p = 0.90	p = 0.97		p = 0.46	p = 0.45	p = 0.32	

^a Relevance: number of relevant reactions/number of positive reactions.^b Irritant reactions: children with at least one irritant patch test reaction out of all children in the specific age group.

study, and the frequency of allergic contact dermatitis caused by nickel increased with age. We found relevant reactions to nickel even in small children aged 1–4 years, and no irritant reactions to nickel sulfate were observed in this age group.

Patch test reactivity to cobalt is often associated with sensitization to nickel (14), as was also shown in our study; 58.8% (n = 67) were co-sensitized with nickel.

Fragrance contact allergy is increasingly common among children, and even small children are exposed (15, 16). It is caused mainly by exposure to cosmetic products, but exposures to household and industrial products may contribute (17). In our study, 2594 children were tested with one or all of the four fragrance markers: fragrance mix I, fragrance mix II, hydroxyisohexyl 3-cyclohexene carboxaldehyde, and *Myroxylon pereirae*. Of these children, 4.7% were sensitized to at least one of the markers. The likelihood of having a positive patch test reaction to one of the fragrant markers did not differ significantly between sexes. This is in contrast to previous studies on adults, which found a significant preponderance of women with contact allergy to fragrance (18, 19). This discrepancy could possibly be explained by the pattern of exposure to fragrance, which is likely to increase with age, especially for women. In order to identify sources of fragrance exposure, we plan to investigate the exposure pattern among Danish children further.

PPD is known as a strong sensitizer (20). Testing with the standard 1% concentration may cause severe allergic reactions, and it has been argued that the patch test concentration should be lowered (21, 22). Furthermore, several authors have stressed the risk of active sensitization from patch testing with PPD (22–24). In our study, 3.5% of the children who were patch tested with PPD had a positive reaction, the youngest being 4 years old. This pattern of sensitization in children is probably attributable to new trends involving products

containing PPD, especially temporary black henna tattoos and the use of hair dye at a young age (23, 25), although patch test reactivity may also occur as a result of cross-sensitization with other allergens (20, 23, 26). Unfortunately, we have limited information on what exposures caused the sensitization in our cohort. Patients sensitized to caine mix or benzocaine may show cross-reactivity to PPD. We did not observe enough cross-reactions to explain the high number of positive reactions to PPD. In a similar adult population, Thyssen et al. (27) found sensitization rates of 2.2% among women and 1.7% among men. In contrast to this, we did not find any sex difference with regard to PPD allergy in any age group. Most cases of contact allergy to PPD are caused by contact with hair dyes in either consumer or hairdresser products (14), so it seems likely that a sex difference in exposure to PPD develops with age.

Girls were, overall, significantly more likely to have a positive patch test reaction. This sex difference was mainly driven by nickel. Among girls, nickel accounted for 29.6% of all positive patch test reactions. This figure was 13.5% for boys, and the sex difference in terms of nickel sensitization was significant. Sex differences with regard to sensitization rates reflect the pattern of exposure, and the difference in nickel sensitization could be explained by the fact that girls are more likely to have their ears pierced and wear jewellery at an earlier age (28). It has also previously been suggested that hormonal factors play a role (14, 15, 29, 30).

The rates of sensitization to rubber chemicals and topical steroids were significantly higher among boys. Again, this probably indicates sex differences in exposure patterns. It seems probable that boys, as a result of leisure activities and hobbies, are more exposed to rubber. The sex difference in sensitization to topical steroids calls for further elucidation. It may reflect the group of children with atopic dermatitis, and we plan to investigate this in future work.

Table 2. Allergens listed by frequency of positive reactions

Allergen	Sensitization rate, % ($n_{\text{positive}}/n_{\text{tested}}$)	Relevance, % ($n_{\text{relevant}}/n_{\text{positive}}$)	Sensitization rate		<i>p</i> -value
			Girls, % ($n_{\text{positive}}/n_{\text{tested}}$)	Boys, % ($n_{\text{positive}}/n_{\text{tested}}$)	
Nickel sulfate	9.7 (252/2587)	69.0 (174/252)	12.4 (211/1706)	4.7 (41/881)	< 0.05
Black rubber mix ^a	5.5 (26/472)	30.8 (8/26)	3.9 (11/284)	8.0 (15/188)	0.06
Cobalt chloride	4.4 (114/2593)	39.5 (45/114)	5.3 (91/1709)	2.6 (23/884)	< 0.05
Caine mix ^a	3.8 (19/504)	15.8 (3/19)	2.9 (9/311)	5.2 (10/193)	0.19
<i>p</i> -Phenylenediamine	3.5 (88/2513)	85.2 (75/88)	3.4 (56/1669)	3.8 (32/844)	0.57
Fragrance mix I	2.5 (64/2592)	59.4 (38/64)	2.6 (44/1710)	2.3 (20/882)	0.64
Colophonium	2.4 (62/2593)	61.3 (38/62)	2.4 (41/1709)	2.4 (21/884)	0.97
Fragrance mix II	2.4 (43/1823)	74.4 (32/43)	2.4 (29/1187)	2.2 (14/636)	0.75
Potassium dichromate	1.3 (34/2592)	26.5 (9/34)	1.6 (27/1708)	0.8 (7/899)	0.09
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	1.1 (27/2429)	59.3 (16/27)	1.5 (24/1609)	0.4 (3/820)	< 0.05
<i>Myroxylon pereirae</i>	1.0 (27/2591)	48.1 (13/27)	1.1 (19/1708)	0.9 (8/883)	0.62
Mercaptobenzothiazole	1.0 (27/2591)	81.5 (22/27)	0.8 (14/1708)	1.5 (13/883)	0.12
Lanolin alcohol	1.0 (26/2592)	38.5 (10/26)	1.1 (18/1709)	0.9 (8/883)	0.72
Euxyl™ K 400 ^a	1.0 (3/302)	100.0 (3/3)	1.5 (3/202)	0 (0/104)	0.22
Mercapto mix	0.9 (23/2593)	82.6 (19/23)	0.8 (13/1710)	1.1 (10/883)	0.34
MCI/MI	0.8 (21/2593)	42.9 (9/21)	0.8 (14/1709)	0.8 (7/884)	0.94
Thiuram mix	0.8 (21/2594)	52.4 (11/21)	0.6 (11/1710)	1.1 (10/884)	0.19
Sesquiterpene lactone mix	0.8 (20/2542)	65.0 (13/20)	0.6 (10/1678)	1.2 (10/864)	0.13
Formaldehyde	0.7 (18/2593)	50.0 (9/18)	0.7 (12/1710)	0.7 (6/883)	0.95
Benzocaine	0.6 (13/2083)	46.2 (6/13)	0.6 (9/1394)	0.6 (4/691)	0.86
<i>p</i> -tert-Butyl formaldehyde resin	0.6 (16/2590)	43.8 (7/16)	0.4 (7/1707)	1.0 (9/883)	0.06
Budesonide	0.6 (12/1980)	50.0 (6/12)	0.2 (3/1277)	1.3 (9/703)	< 0.05
Carba mix ^a	0.6 (3/507)	33.3 (1/3)	0.6 (2/313)	0.5 (1/194)	0.86
Methyldibromo glutaronitrile	0.6 (14/2451)	35.7 (5/14)	0.7 (12/1605)	0.2 (2/846)	0.11
Paraben mix	0.5 (13/2593)	61.5 (8/13)	0.3 (5/1709)	0.9 (8/899)	< 0.05
Neomycin sulfate	0.5 (12/2592)	16.7 (2/12)	0.4 (7/1705)	0.6 (5/882)	0.58
<i>N</i> -Isopropyl- <i>N</i> -phenyl- <i>p</i> -phenylenediamine	0.3 (7/2131)	57.1 (4/7)	0.3 (4/1430)	0.4 (3/701)	0.57
Epoxy resin	0.3 (8/2523)	38.0 (3/8)	0.2 (3/1678)	0.6 (5/845)	0.08
Imidazolidinyl urea	0.3 (6/2092)	33.3 (2/6)	0.2 (3/1356)	0.4 (3/750)	0.45
Diazolidinyl urea	0.3 (6/2093)	50.0 (3/6)	0.3 (4/1357)	0.3 (2/736)	0.93
2-Bromo-2-nitropropane-2,3-diol	0.2 (3/1475)	66.7 (2/3)	0.2 (2/952)	1.9 (1/523)	0.94
Quaternium-15	0.2 (4/2593)	50.0 (2/4)	0.2 (4/1709)	0 (0/899)	0.15
Tixocortol 21-pivalate	0.1 (3/2009)	66.7 (2/3)	< 0.1 (1/1300)	0.3 (2/709)	0.26
Primin	0.1 (3/2506)	66.7 (2/3)	< 0.1 (1/1649)	0.2 (2/857)	0.32
Clioquinol	0.1 (2/2133)	50.0 (1/2)	< 0.1 (2/1464)	0 (0/712)	0.32
Quinoline mix ^a	0 (0/459)	–	0 (0/282)	0 (0/187)	–
Groups of allergens					
Metals ^b	12.2 (316/2593)	59.8 (189/316)	15.0 (256/1709)	6.8 (60/884)	< 0.05
Fragrances ^c	4.7 (123/2594)	58.5 (72/123)	5.1 (87/1710)	4.1 (36/884)	0.25
Hair dyes ^d	3.5 (88/2513)	85.2 (75/88)	3.4 (56/1669)	3.8 (32/844)	0.57
Adhesive chemicals ^e	3.2 (84/2593)	56.0 (47/84)	3.0 (51/1709)	3.7 (33/884)	0.31
Rubber chemicals ^f	3.0 (79/2594)	58.2 (46/79)	2.3 (39/1710)	4.5 (40/884)	< 0.05
Preservatives ^g	2.9 (75/2594)	46.7 (35/75)	2.7 (47/1710)	3.2 (28/884)	0.55
Topical drugs ^h	1.8 (46/2592)	26.1 (12/46)	1.6 (27/1709)	2.2 (19/883)	0.3
Plants ⁱ	0.9 (23/2544)	65.2 (15/23)	0.7 (11/1679)	1.4 (12/865)	0.06
Topical steroids ^j	0.7 (14/2011)	50.0 (7/14)	0.3 (4/1301)	1.4 (10/710)	< 0.05

MCI/MI, methylchloroisothiazolinine/methylisothiazolinone.

Euxyl™ K 400: chemical preservative containing methyldibromo glutaronitrile and phenoxyethanol.

^a From TRUE test™.^b Nickel sulfate, cobalt chloride, and potassium dichromate.^c Fragrance mix I, fragrance mix II, *Myroxylon pereirae*, and hydroxyisohexyl 3-cyclohexene carboxaldehyde.^d *p*-Phenylenediamine.^e Colophonium, *p*-tert-butyl formaldehyde resin, epoxy resin.^f Black rubber mix/*N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine, mercaptobenzothiazole, mercapto mix, thiuram mix, and carba mix.^g Euxyl™ K 400, MCI/MI, formaldehyde, methyldibromo glutaronitrile, paraben mix, diazolidinyl urea, imidazolidinyl urea, and quaternium-15, 2-bromo-2-nitropropane-1,3-diol.^h Caine mix/benzocaine, neomycin sulfate, clioquinol, and quinoline mix.ⁱ Sesquiterpene lactone mix and primin.^j Budesonide and tixocortol pivalate.

Table 3. Most common source of exposure

Allergen group	Source of exposure
Metals	Jewellery, metal buckles, shoes
Fragrances	Deodorant, shampoo, liquid soap
<i>p</i> -Phenylenediamine	Hair dye, henna tattoo, eyebrow dye
Adhesive chemicals	Plasters, medications, cosmetics
Rubber chemicals	Shoes, gloves
Preservatives	Cleansing wipes, cosmetics
Topical drugs	Medications, not specified
Plants	Plants, not specified
Topical steroids	Medications, not specified

It has previously been suggested that children tend to show non-specific irritant reactions, and therefore have a higher rate of false-positive reactions (31). Some authors have highlighted the difficulties in distinguishing an irritant skin reaction from a positive response (32, 33). In our study, we endeavoured to ensure correct interpretation of the patch test reaction by following the International Contact Dermatitis Research Group guidelines. Almost one-third (28.6%) of the children were, in addition to the first patch test reading, evaluated on D7. We did not observe irritant reactions in children aged < 4 years. Our results are in accordance with those of Belloni Fortina et al. (34), who evaluated patch test reactions in 321 children aged < 3 years, and found 'very few irritant reactions'. One possible limitation of our study is the fact that only 8 children were aged < 1 year. It could be argued that this sample is too small to draw any real conclusions on rates of sensitization or irritant reactions that are representative of this age group.

The recommendations for patch testing children have been controversial, and several authors have suggested that children should be tested with lower concentrations of allergens (4, 35, 36). The high rate of negative patch tests and the low number of irritant reactions in our study indicate that even young children tolerate the same test concentrations as adults.

This was a nationwide study and, to our knowledge, it is the largest study of its kind. Although one should exercise some caution when interpreting the results for the young

children in our dataset, because of small sample sizes, our study provides valuable information. The data used in this study were retrieved from 12 different dermatology clinics throughout Denmark. All clinics used standardized preparations of allergens and followed the International Contact Dermatitis Research Group guidelines with regard to application and interpretation of patch test reactions. However, some degree of inconsistency is inevitable, given the large number of clinics reporting to the database. In one area, the patch test methodology differed; two-thirds of patch test reactions were evaluated on D3–D4 only, which implies a risk of missing late reactions (37). Another limitation is the fact that not all children were patch tested with the same allergens, which, to some extent, hinders the drawing of strong conclusions.

Conclusion

This is the first study on the prevalence of allergic contact dermatitis in Danish children referred for patch testing since 1982, and to our knowledge it is the largest study of its kind. Among the 2594 children referred for patch testing during 2003–2011, the sensitization rate was 25.1% and the prevalence of allergic contact dermatitis was 16.7%. The likelihood of having at least one positive patch test reaction and allergic contact dermatitis was associated with being female.

Allergic contact dermatitis in children is a significant clinical problem. Contact allergy should always be considered when children with recalcitrant eczema or a history of specific exposure are encountered, and patch testing is important. On the basis of our data, we recommend using the European baseline series supplemented with allergens according to the child's history and with the same allergen concentrations as used in adults. To avoid missing late reactions, we recommend that patch test readings be carried out D3/D4 and D5–D7.

The number of children referred for patch testing increased steadily throughout the study period, but the rates of sensitization or allergic contact dermatitis did not change significantly. A future retrospective study could

Table 4. Most frequent allergens from the European baseline series (%)

All children	1–4 years old	5–8 years old	9–12 years old	13–17 years old
Nickel sulfate (9.7)	Nickel sulfate (14.5)	Nickel sulfate (8.5)	Nickel sulfate (8.3)	Nickel sulfate (10.2)
Cobalt chloride (4.4)	Sesquiterpene lactone mix (4.5)	Cobalt chloride (3.5)	Cobalt chloride (6.2)	Cobalt chloride (4.0)
PPD (3.5)	MCI/MI (4.0)	PPD (3.4)	PPD (4.5)	PPD (3.2)
Fragrance mix I (2.5)	Potassium dichromate (2.6)	Sesquiterpene lactone mix (2.7)	Fragrance mix I (3.6)	Fragrance mix II (3.0)
Colophonium (2.4)	Cobalt chloride (2.6)	Fragrance mix I (2.2)	Colophonium (3.1)	Colophonium (2.3)

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; PPD, *p*-phenylenediamine.

provide us with additional knowledge on the time trends of allergic contact dermatitis in Danish children.

Acknowledgements

Drs Niels Kren Veien, Anne Toftegaard Funding, Hans Lomholt and Henrik Sølvsten (Aalborg), Christian Avnstor, Anne Hjorthor and Bent Staberg (Rødovre), Morten

Østerballe and Aksel Otkjær (Herning), Bo Lasthein (Svendborg), Niels Henrik Nielsen (Bagsværd), Jens and Henrik Thormann (Vejle), Berit and Ove Kristensen (Kalundborg), Anne Grethe Danielsen, Gitte Strauss, Mads Nielsen and Rune Lindskov (Copenhagen) and Susanne Vissing (Hørsholm) are gratefully acknowledged for participating in the data collection.

References

- 1 Beattie P E, Lewis-Jones M S A. comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. *Br J Dermatol* 2006; **155**: 145–151.
- 2 Lewis-Jones M S, Finlay A Y. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol* 1995; **132**: 942–949.
- 3 Clayton T H, Wilkinson S M, Rawcliffe C, Pollock B, Clark S M. Allergic contact dermatitis in children: should pattern of dermatitis determine referral? A retrospective study of 500 children tested between 1995 and 2004 in one UK centre. *Br J Dermatol* 2006; **154**: 114–117.
- 4 Marcussen P V. Primary irritant patch-test reactions in children. *Arch Dermatol* 1963; **87**: 378–382.
- 5 Veien N K, Hattel T, Justesen O, Norholm A. Contact dermatitis in children. *Contact Dermatitis* 1982; **8**: 373–375.
- 6 Weston W L, Weston J A. Allergic contact dermatitis in children. *Am J Dis Child* 1984; **138**: 932–936.
- 7 Militello G, Jacob S E, Crawford G H. Allergic contact dermatitis in children. *Curr Opin Pediatr* 2006; **18**: 385–390.
- 8 Simonsen A B, Deleuran M, Johansen J D, Sommerlund M. Contact allergy and allergic contact dermatitis in children – a review of current data. *Contact Dermatitis* 2011; **65**: 254–265.
- 9 Hogeling M, Pratt M. Allergic contact dermatitis in children: the Ottawa hospital patch-testing clinic experience, 1996 to 2006. *Dermatitis* 2008; **19**: 86–89.
- 10 Thyssen J P, Johansen J D, Linneberg A, Menné T. The epidemiology of hand eczema in the general population – prevalence and main findings. *Contact Dermatitis* 2010; **62**: 75–87.
- 11 Bonitsis N G, Tatsioni A, Bassioulas K, Ioannidis J P. Allergens responsible for allergic contact dermatitis among children: a systematic review and meta-analysis. *Contact Dermatitis* 2011; **64**: 245–257.
- 12 Hanifin J M, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980; **92**: 44–47.
- 13 Menné T, Johansen J D, Sommerlund M, Veien N K. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. *Contact Dermatitis* 2011; **65**: 3–12.
- 14 Johansen J D, Frosch P J, Lepoittevin J-P (Eds). *Contact Dermatitis*, 5th edition: Berlin, Heidelberg, Springer-Verlag, 2011.
- 15 Johnke H, Norberg L A, Vach W, Bindslev-Jensen C, Host A, Andersen K E. Reactivity to patch tests with nickel sulfate and fragrance mix in infants. *Contact Dermatitis* 2004; **51**: 141–147.
- 16 Jacob S E, Castaneda-Tardan M P. Alternatives for fragrance-allergic children. *Pediatr Ann* 2008; **37**: 102–103.
- 17 Rastogi S C, Heydorn S, Johansen J D, Basketter D A. Fragrance chemicals in domestic and occupational products. *Contact Dermatitis* 2001; **45**: 221–225.
- 18 Heisterberg M V, Andersen K E, Avnstor C et al. Fragrance mix II in the baseline series contributes significantly to detection of fragrance allergy. *Contact Dermatitis* 2010; **63**: 270–276.
- 19 Thyssen J P, Carlsen B C, Menné T, Johansen J D. Trends of contact allergy to fragrance mix I and Myroxylon pereirae among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis* 2008; **59**: 238–244.
- 20 Deleo V A. p-Phenylenediamine. *Dermatitis* 2006; **17**: 53–55.
- 21 Ho S G, White I R, Rycroft R J, McFadden J P. A new approach to patch testing patients with para-phenylenediamine allergy secondary to temporary black henna tattoos. *Contact Dermatitis* 2004; **51**: 213–214.
- 22 Becker D, Mahler V, Szliska C et al. The concentration of para-phenylenediamine (PPD) for routine patch testing in a standard series needs to be redefined. *Contact Dermatitis* 2005; **53**: 186–187.
- 23 Schnuch A, Lessmann H, Frosch P J, Uter W. para-Phenylenediamine: the profile of an important allergen. Results of the IVDK. *Br J Dermatol* 2008; **159**: 379–386.
- 24 Devos S A, Van Der Valk P G. The risk of active sensitization to PPD. *Contact Dermatitis* 2001; **44**: 273–275.
- 25 Spornraft-Ragaller P, Schnuch A, Uter W. Extreme patch test reactivity to p-phenylenediamine but not to other allergens in children. *Contact Dermatitis* 2011; **65**: 220–226.
- 26 Malvestio A, Bovenzi M, Hoteit M et al. p-Phenylenediamine sensitization and occupation. *Contact Dermatitis* 2011; **64**: 37–42.
- 27 Thyssen J P, Carlsen B C, Sosted H, Menné T, Johansen J D. Frequency of p-phenylenediamine sensitization among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis* 2008; **59**: 184–185.
- 28 Czarnobilska E, Obtulowicz K, Dyga W, Wsolek-Wnek K, Spiewak R. Contact hypersensitivity and allergic contact dermatitis among school children and teenagers with eczema. *Contact Dermatitis* 2009; **60**: 264–269.
- 29 Veien N K, Hattel T, Justesen O, Norholm A. Why do young girls become nickel sensitive? *Contact Dermatitis* 1986; **15**: 306–307.
- 30 Gonçalo S, Gonçalo M, Azenha A et al. Allergic contact dermatitis in children. A multicenter study of the Portuguese Contact Dermatitis Group (GPEDC). *Contact Dermatitis* 1992; **26**: 112–115.
- 31 Pevny I, Brennenstuhl M, Razinskas G. Patch testing in children. (I) Collective test results; skin testability in children. *Contact Dermatitis* 1984; **11**: 201–206.
- 32 Bruckner A L, Weston W L, Morelli J G. Does sensitization to contact allergens begin in infancy? *Pediatrics* 2000; **105**: e3.
- 33 Matiz C, Russell K, Jacob S E. The importance of checking for delayed reactions in pediatric patch testing. *Pediatr Dermatol* 2011; **28**: 12–14.

- 34 Belloni Fortina A, Romano I, Peserico A, Eichenfield L F. Contact sensitization in very young children. *J Am Acad Dermatol* 2011; **65**: 772–779.
- 35 Roul S, Ducombs G, Taieb A. Usefulness of the European standard series for patch testing in children. A 3-year single-centre study of 337 patients. *Contact Dermatitis* 1999; **40**: 232–235.
- 36 Jacob S E, Steele T, Brod B, Crawford G H. Dispelling the myths behind pediatric patch testing – experience from our tertiary care patch testing centers. *Pediatr Dermatol* 2008; **25**: 296–300.
- 37 Torp Madsen J, Andersen K E. Outcome of a second patch test reading of TRUE Tests(R) on D6/7. *Contact Dermatitis* 2013; **68**: 94–97.