

## Review Article

# Allergic contact dermatitis in children and adolescents

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From a clinical point of view, the prevalence of allergic contact dermatitis (ACD) among children and adolescents seems to be low. However, many children have dermatitis, most often atopic dermatitis. In selected cases, ACD is suspected, and the child is tested. The question remains, whether the prevalence of ACD in children really is low or whether the possibility of ACD is not sufficiently considered. During the last decade, reports have appeared on series of children and adolescents with contact allergy and ACD. Few cases have been reported in infants, but the development of contact allergy and ACD increases with age. Most studies include selected groups of children and adolescents with suspected ACD. Few studies have examined unselected populations, and most consider only the prevalence of contact allergy without evaluating the clinical relevance, e.g., the prevalence of ACD. Furthermore, no follow-up studies exist. Therefore, the incidence and prevalence of contact allergy and ACD in children and adolescents is largely unknown.

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Allergic contact dermatitis (ACD) in children and adolescents is seen occasionally, and several reports on series of children and adolescents with ACD have appeared in the literature (1-7). The frequency of unselected children and adolescents with positive patch tests to standard series allergens is not negligible (8-10). About 8% of unselected adolescents are nickel allergic and about 2% react to fragrance mix (11). When the contact allergy develops, and what the consequences of a positive patch test result are for the individual child, is less clear. This review summarizes the current knowledge from an epidemiological and clinical point of view.

### Epidemiology

#### *Definitions and study designs*

There are many definitions of epidemiology; one of the clearest is the study of occurrence of illness (12). The frequency of ACD can be expressed in terms of its incidence (the number of new cases of ACD during a defined period in a specific popula-

tion) or its prevalence (the number of persons in the population with ACD at a certain point in time or during a certain period of time).

The 3 most important types of observational study in the epidemiology of ACD are follow-up (cohort) studies, case-control studies and cross-sectional studies.

(i) In follow-up studies, selection of subjects is based upon exposure to factors of interest. In the prospective follow-up study, the person is exposed but free of the disease at the beginning of the study and is followed over a certain period of time. When both exposure and disease are historical, the study is described as a retrospective follow-up study. This design is less expensive than the prospective study. The measurement in follow-up studies is incidence.

(ii) In case-control studies, the subjects are selected according to their disease status. Information is collected on the past exposure of diseased persons (cases) and the non-diseased persons (controls). The odds of exposure among cases are compared to the odds of exposure among controls and expressed in form of an odds ratio (OR). A

case-control study includes a defined population in which all diseased persons and only a sample of the non-diseased persons are studied. This design is efficient in studies of rare diseases, where the majority of the population does not have the disease.

(iii) In cross-sectional studies, a study population is selected regardless of exposure or disease status in contrast to case-control and follow-up studies. Cross-sectional studies are suitable to study the prevalence of a disease in a population in relation to characteristics which do not change much over time.

Most studies of the epidemiology of ACD among children and adolescents are cross-sectional, thus giving estimates of the prevalence. Publications of follow-up studies about ACD in children are non-existent, thus incidence figures are hard to obtain. Furthermore, to date most studies of contact allergy and ACD in children and adolescents have been carried out in populations visiting dermatologic clinics, while systematic patch testing of unselected populations has rarely been carried out.

A problem in studying ACD is that the relative importance of contact allergens may be difficult to assess, because there is only a partial concordance between a positive patch test and ACD. This is explained by the fact that sensitization is not necessarily followed by ACD, and a positive patch test does not indicate that the substance in question is the sole or contributing cause of a dermatitis. However, subjects with a positive patch test to environmental chemicals in non-irritant concentration represent a group at risk of developing ACD, if exposed to the chemical in question in a concentration exceeding the individual threshold level.

ACD is also a multifactorial disease and, apart from exposure to an allergen, there are many factors that affect the development of ACD, including age, sex, contact with irritants, and atopic constitution. 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).

#### *Incidence and prevalence of allergic contact dermatitis and contact allergy*

Previously, ACD was considered uncommon in children (13–15). This opinion was based upon 2 concepts: 1) the reduced exposure to contact allergens in childhood and 2) the possibility that the immune system in children may be less susceptible to contact allergens (13, 16). Furthermore, several

authors assumed that the majority of positive reactions in children were irritant (14, 17–20), and that this non-specific irritability of the skin is lost around the age of 8.

However, during the last 10–20 years, several reports have described a considerable number of children with contact allergy and ACD (1–10, 21–32), confirming that contact allergy and ACD is not infrequent in children and may cause a significant clinical problem. Weston et al. (33) estimated that ACD accounts for up to 20% of all dermatitis in childhood. ACD seems to be rare in the first few months of life. A few cases resulting from exposure to epoxy resin, neomycin, balsam of Peru, ethylenediamine and nickel have been reported (34–36). Motolese et al. (28) studied 53 infants (3 months to 2 years) with dermatitis and patch tested with their standard series using the same concentrations as in adults. Positive patch tests were seen in 32 (60%), and at least 20 out of the 32 sensitized infants had clinically relevant contact allergies. Novak et al. (37) patch tested 62 infants and small children (3–45 months) without dermatitis. Positive reactions to 0.02% thimerosal were seen in 4.9%. Experimental contact allergy to plants of the *Rhus* genus (including poison ivy) has also been induced in infants, showing that sensitization is possible. However, infants were less susceptible to sensitization (16). Thus, the general impression is that contact allergy and ACD is rare in young children compared to older children, and that contact allergy and ACD becomes more frequent with increasing age, especially after the 1st decade, as exposure to environmental allergens increases (2, 6, 14, 26, 29, 31, 38).

Table 1 shows results from a number of patch test studies from different centers (1–7, 22–25, 28–32, 38). These selected patient materials vary in size from 53 to 1023 patients. The authors reported positive patch tests results in 14.5% to 70.7% of the cases, and an associated relevance in 56.4% to 93.3% of those with positive reactions. Among the children with a positive patch test 3.2% to 54.4% had multiple contact allergies. As in adults, the most common allergens were nickel sulfate, cobalt chloride, potassium dichromate, neomycin sulfate, thimerosal, fragrance mix, balsam of Peru and rubber allergens. Most of these studies show a female dominance (2, 23, 29–31, 38) although some studies show an equal sensitization rate among girls and boys (4, 24). It is especially nickel allergy that has been found to be more common among girls (2, 6, 23, 24, 29, 31). However, it is difficult to compare the results between studies, because they vary with regard to patient-related and technical factors, such as age and sex distribution, criteria for atopy, criteria for patch testing,

Table 1. Results of diagnostic patch tests in selected groups of children and adolescents with suspected allergic contact dermatitis

| Ref. | No. children | Age (years) | Children with positive reactions $\geq 1$ (%) | Polysensitization (%)   | Relevance <sup>a)</sup> (%) | 3 most common allergens                                            |
|------|--------------|-------------|-----------------------------------------------|-------------------------|-----------------------------|--------------------------------------------------------------------|
| (1)  | 323          | $\leq 14$   | 35.3                                          | 8.7                     | 77.2<br>61.7 <sup>b)</sup>  | 1 nickel<br>2 neomycin<br>3 thimerosal                             |
| (30) | 585          | $\leq 14$   | 14.5                                          | 3.2                     | not given                   | 1 nickel<br>2 cobalt<br>3 ethylenediamine                          |
| (24) | 416          | 6–15        | 40.9                                          | not given               | not given                   | 1 nickel<br>2 thimerosal<br>3 fragrance mix                        |
| (2)  | 329          | $\leq 14$   | 51.7                                          | 23.1                    | 65.3                        | 1 nickel<br>2 thimerosal<br>3 cobalt                               |
| (29) | 232          | $< 16$      | 43.5                                          | not given               | not given                   | 1 nickel<br>2 cobalt<br>3 fragrance mix                            |
| (38) | 67           | $< 16$      | 28.4                                          | not given               | 84.2                        | 1 nickel<br>2 balsam of Peru/carba mix/<br>colophony/fragrance mix |
| (22) | 670          | $\leq 12$   | 42.1                                          | 17.8                    | not given                   | 1 thimerosal<br>2 nickel<br>3 Kathon CG                            |
| (28) | 53           | $\leq 2$    | 60.4                                          | 30.2                    | 62.5                        | 1 thimerosal<br>2 nickel<br>3 ammoniated mercury                   |
| (25) | 366          | $\leq 14$   | 22.1                                          | not given <sup>b)</sup> | 21.4 <sup>b)</sup>          | 1 nickel<br>2 chloramphenicol<br>3 parabens                        |
| (3)  | 147          | 3–16        | 70.7                                          | 54.4                    | 93.3                        | 1 nickel<br>2 cobalt<br>3 PADP                                     |
| (4)  | 125          | $< 12$      | 48.0                                          | not given               | 91.7                        | 1 nickel<br>2 cobalt<br>3 chrome                                   |
| (5)  | 1023         | $< 14$      | 31.1                                          | not given               | 69.5                        | 1 nickel<br>2 thimerosal<br>3 mercapto mix                         |
| (31) | 626          | 3–16        | 42.7                                          | not given               | not given                   | 1 nickel<br>2 chrome<br>3 cobalt                                   |
| (6)  | 272          | 2–14        | 37.1                                          | 15.8                    | 56.4                        | 1 nickel<br>2 mercuric chloride<br>3 cobalt                        |
| (32) | 92           | 3–14        | 32.6                                          | 13.0                    | 87                          | 1 nickel<br>2 fragrance mix<br>3 thimerosal/ neomycin              |
| (7)  | 168          | $\leq 14$   | 45.8                                          | not given               | 80                          | 1 nickel<br>2 chromate<br>3 rubber                                 |
| (23) | 234          | $\leq 14$   | 49.1                                          | not given               | not given                   | 1 thimerosal<br>2 nickel<br>3 ethylmercuric chloride               |

<sup>a)</sup> Relevance: no. children with relevant positive patch test reaction(s)/number of children with positive(s) patch test reactions.

<sup>b)</sup> No. relevant positive patch test reactions/ number of positive patch test reactions.

Table 2. Results from patch testing in children in defined subgroups of the population

| Ref. | Type of subgroup                                   | No. children | Age (years) | Tested allergens | Children with positive reactions $\geq 1$ (%) | Relevance |
|------|----------------------------------------------------|--------------|-------------|------------------|-----------------------------------------------|-----------|
| (27) | dermatologic and pediatric outpatients             | 100          | $\leq 11$   | metals           | 20.0                                          | not given |
| (37) | pediatric patients with non-dermatological disease | 62           | $< 4$       | thimerosal       | 4.9                                           | not given |

Table 3. Results from patch testing in children and adolescents in population based studies

| Ref. | No. children | Age (years) | Children with positive reactions $\geq 1$ (%) | Polysensitization (%) | Relevance | 3 most common allergens                     |
|------|--------------|-------------|-----------------------------------------------|-----------------------|-----------|---------------------------------------------|
| (8)  | 562          | 5–14        | 13.3                                          | 2                     | not given | 1 neomycin<br>2 thimerosal<br>3 PTBPF resin |
| (9)  | 424          | 7–12        | 23.3                                          | 8.5                   | not given | 1 nickel<br>2 cobalt<br>3 Kathon CG         |
| (10) | 314          | $< 18$      | 20.3                                          | not given             | not given | 1 neomycin<br>2 nickel/chromate             |

selection of patch test series and patch test methodology. Social and regional differences in exposure may also modify the pattern of contact allergies.

Few studies have patch tested defined subgroups of children in the population to evaluate the sensitization rate (Table 2). Camarasa et al. (27) patch tested 100 consecutive children from 8 months to 11 years randomly selected from a dermatologic and paediatric outpatient clinic. Of these, 20% were sensitive to metals (nickel, chromate, cobalt and mercury). The relevance was not given. However, the majority of the nickel-sensitized children were 8 years or older, and 8 out of 9 were girls with their ears pierced in early childhood.

Novak et al. (37) patch tested 62 infants and small children aged 3–45 months admitted to a paediatric department with non-dermatological disease. A positive reaction to thimerosal was seen in 4.9%, possibly related to the use of the triple vaccine containing thimerosal as preservative. Boss et al. (39) tested female hairdresser apprentices aged between 16 and 22 years. Nickel was positive in 11 of 43, and 1 reacted to cobalt. The positive reactions were found among those with previous earlobe dermatitis. Due to selection bias, data from these studies may not give a true picture of the occurrence of contact allergy and ACD in children and adolescents.

3 studies patch tested unselected groups of children and adolescents in the general population to get information about the frequency of sensitization to contact allergens (Table 3). Barros et al. (8) patch tested 562 Portuguese school children, 5–14 years old, with 25 allergens. Positive reactions

were seen in 13.3%, most commonly to neomycin sulfate, thimerosal, PTBPF resin (p-tert-butylphenol-formaldehyde resin) and fragrance mix. Multiple sensitivities were seen in 2% of the children. In this study, the 5–6-years-old group gave the highest % of positive reactions, whereas the adolescents (13–14 years old) gave no positive reactions. However, the average age was 8.0 years and the study included only 12 adolescents. Positive reactions were seen in 56% of the boys and 44% of the girls. The most common allergen among boys was PTBPF resin and among girls neomycin ranked highest. In this study, nickel was responsible for only 5 positive reactions (2 boys, 3 girls), all seen in children who had no history of metal allergy. This result differs considerably from results of population studies in other countries (9, 10), although the patch test procedure seems to be the same. Difference in exposure could be the explanation.

Dotterud et al. (9) patch tested 424 Norwegian school children, 7–12 years old, with 20 allergens using a ready-to-use patch test system (Epiguick test®, Hermal, Germany). 1 or more positive reactions were seen in 23.3%, most commonly to nickel sulfate, cobalt chloride, Kathon CG, lanolin and neomycin sulfate. Multiple sensitivities were seen in 8.5% of the children. In this study, there were no differences in the frequency of positive reactions between the age groups. However, there was a sex difference. Positive reactions were found in 17.0% of the boys compared to 30.3% of the girls. Nickel was the most common contact allergen in both sexes. Another publication from this group showed that only 34.2% of the children with a positive

patch test to a metal (nickel, cobalt, chromate) had a history of metal dermatitis (40). Both the studies (8, 9) performed readings only on day 2, which may have given false-positive and/or false-negative results. The clinical relevance of the positive patch test reactions was not given, except for metals.

Weston et al. (10) patch tested with 20 allergens in 314 otherwise healthy American children and adolescents under the age of 18 years and found that 20% had at least 1 positive patch test reaction. The most common allergens were neomycin sulfate, nickel sulfate and potassium dichromate. The relevance of a positive patch test was not given. There was no significant difference in the prevalence of contact allergy in different age groups or between the sexes.

Some population-based studies have evaluated the prevalence of contact allergy only to a few selected allergens. Larsson-Stymne et al. (41) patch tested 960 schoolgirls of ages 8, 11 and 15 years to nickel sulfate 5% pet. and cobalt chloride 1% pet. Positive patch tests to nickel were seen in 9% of the children, 5% reacting to cobalt, but only 0.7% had cobalt allergy alone. A history of nickel allergy was found in only 24% of the girls. Ear piercing seemed to be an important cause of nickel allergy. The prevalence among those with pierced ears was 13% compared to 1% among those without pierced ears.

Peltonen (42) included 158 school children above the age of 10 years in a study of nickel sensitivity among 980 persons from the general population (10 to 74 years old). The children were tested with nickel sulfate 2.5% pet., while the adults were tested with nickel sulfate 5% pet. Only 1.3% of the children had a positive reaction to nickel, compared to 4.5% of the total population.

A Danish population based study in 567 unselected adults reported the prevalence of contact allergy for young adults separately (43). The TRUE Test<sup>TM</sup> panel 1 and 2 were used, and the prevalence of contact allergy in the whole population was 15.2% (11.5% men and 18.8% women), whereas among 197 young adults (15–34 years old) the prevalence of contact allergy was 18.8% (11.8% men and 24.1% women). Nickel allergy was the most common, found in 6.7% of the whole population, and in 12.2% of the young adults. The relevance was not given. However, the same authors confirmed that a positive patch test to nickel was associated with ear piercing (44). As in most population based contact allergy studies, reading was done after 2 days only.

The results from patch testing in children and adolescents in the general population revealed that 13–23% had positive patch tests to standard allergens, suggesting that they theoretically are at risk of developing ACD. The most common allergens

were the same as described in the patient studies. Only few studies have given the relevance of a positive patch test reaction, so it is difficult to estimate the prevalence of ACD. Again demographic, clinical and technical factors varied considerably making comparisons difficult.

#### *Atopic dermatitis and contact allergy*

The relationship between atopic dermatitis (AD) and contact allergy is frequently discussed (45–52). However, the role of atopy in ACD is still questionable. A reduced prevalence of contact allergy in AD compared to controls has been reported (45–47). This has also been shown experimentally using dinitrochlorobenzene (DNCB) (53, 54), in agreement with the concept that contact allergens preferentially induce a Th1 cell response and that patients with AD have a “down regulation” of their Th1 cells (55). Reduced sensitization to contact allergens in AD may therefore be the clinical reflection of these cellular abnormalities.

However, other studies have shown an equal prevalence of contact allergy in AD compared to controls (48, 49) and further studies have shown an even higher prevalence of contact allergy in AD compared to controls (50–52). A higher prevalence of contact allergy in AD compared to controls could be explained by the fact that a defective epidermal barrier in AD causes an increased accessibility to allergens, and patients with AD are chronically exposed to an array of sensitizers in skin care preparations, suggesting an increased sensitization to these agents. Furthermore, the probability of false-positive reactions in AD is increased, because of the altered skin structure (50).

It is unknown whether the impaired immunoreactivity, the defective epidermal barrier, the chronic exposure to sensitizers or the false-positive reactions in irritable skin are the dominating factor in AD. It is likely that all factors are important and may interact. The severity of the dermatitis at the time of testing is also important for the patch test result. Uehara et al. (56) found that DNCB challenge tests in AD patients were positive in 33% of severe cases, 95% of moderate cases and 100% of mild cases. Moreover, it was demonstrated that decreased sensitization was a reversible phenomenon, because after improvement of the dermatitis in patients with previously severe AD the sensitization rate was not different from the sensitization rate in patients with mild or moderate disease or in non-atopics. This provides evidence for the hypothesis that reduced sensitization is secondary to AD and that only active AD with severe symptoms protects against sensitization, and that other

atopics are at risk for sensitization equally to non-atopics.

The major reason for the variation in results between the different studies is probably the different methodology used: study designs, criteria for AD, the severity of the disease at the time of the study, the nature of the control group, age and sex distribution, allergens included, patch test method and readings. Most studies include selected patient materials with AD patients referred to patch testing because of suspected ACD. They are carried out as case-control studies, and no studies in unselected populations and no follow-up studies exist.

The criteria for the diagnosis of AD differ from study to study (46–48, 52) or are often not given (45, 49–51). A comparison between different studies require the same set of criteria for the diagnosis AD. To date most studies have used the Hanifin & Rajka criteria (57). Now research on improvement of the criteria for the diagnosis of AD is in progress (58–60). Furthermore, it is important to score the severity of disease on the time of testing (56). Until now the most used scoring index has been the SCORAD developed in 1993 (61, 62).

The nature of the control group is also different between the studies. Most often selected patients are included: patients with other types of dermatitis (45, 48), psoriasis (51) or different dermatosis suspected to be contact allergy (49). As with the cases, most of these controls are referred for patch testing because of suspected contact allergy. Controls are only seldom age-matched healthy controls without atopy and dermatitis (46, 50, 52). The best way to select cases and controls is to select persons with AD in an unselected population and graduate the eczema. These persons should then be patch tested and the results compared to tests in healthy persons (without atopy and dermatitis) from the same unselected population. The cases and controls should be matched with regard to factors such as sex, age, occupation and the relevance of the patch test results for both cases and controls should be given. The individual should also be followed in time with respect to later development of contact allergy and ACD.

In the literature, we also found groups (63, 64) who compared atopic patients with dermatitis with non-atopic patients with dermatitis, e.g., they include dermatitis patients with atopy and not only manifest AD. The inclusion criteria in the atopy groups differ. De Groot et al. (63) included dermatitis patients with at least 2 positive skin prick tests/1 positive skin prick test and a (family) history of atopy/classical AD but negative skin prick test. Klas et al. (64) included patients with inhalant allergy/AD referred for contact allergy evaluation. The results from de

Groot et al. (63) showed that atopics with dermatitis are less frequently contact sensitized than are non-atopics with dermatitis, while Klas et al. (64) showed that atopics are at least as likely to have ACD as non-atopics. No conclusion about the role of atopy in contact allergy and ACD can be drawn from these studies.

In summary, contact allergy is not infrequent in patients with AD, and if ACD is suspected, the patient should be tested. However, it seems best to avoid patch testing with suspected allergens during severe AD to minimize the chances of false-negative tests. Then the opposite problem with false positive reactions during active dermatitis is also avoided. However, the relationship between AD and contact allergy/ACD remains questionable.

#### *Contact allergy (Type IV allergy) and IgE-mediated hypersensitivity (Type I allergy)*

The relationship between Type I and Type IV allergy has been studied by few groups. Nielsen et al. (65) studied the relationship in an unselected Danish population and found that the probability of contact allergy to 1 or more allergens was independent of serum IgE, and the probability of contact allergy was independent of the number of positive prick test. They concluded that contact sensitization appeared to be independent of enhanced IgE responsiveness. Rysted et al. (66) studied the relationship in adults with AD in childhood, and found no correlation between a high total IgE in serum and contact allergy. On the other hand, Forsbeck et al. (67) found that in patients with AD the frequency of positive reactions to common contact allergens was lower in patients with high IgE values (>1000 U/ml) than in those with IgE<1000 U/ml. More studies about the relationship between contact allergy and IgE responsiveness need to be carried out before any conclusions can be drawn.

#### **Selected Contact Allergens**

The most common allergens in children and adolescents (1–10, 22–25, 28–32, 38) are the same as in adults (43, 68): Nickel sulfate, cobalt chloride, potassium dichromate, fragrance mix, thimerosal, neomycin sulfate and PTBPF resin.

#### *Nickel*

Studies in children visiting dermatological clinics, as well as studies among children in the general population, have shown that nickel allergy is the most common contact allergy in this age group. The prevalence among children in the general

population is 0.9–14.9% (8–10). The most common cause of sensitization appears to be ear piercing (40, 41, 44), and the risk for nickel allergy is increased with the number of piercings (40). Other sources are jewelry, belt buckles, metal fasteners on clothing and eye glass frames. More girls than boys are sensitized, and the most likely explanation is that boys may be ear pierced at a later age, having only piercing in one ear, or that they use jewelry containing less nickel (69). It has also been suggested that women are sensitized by a lower exposure than men (70). A reduction of nickel in jewelry could reduce the number of persons with nickel allergy and a European Union (EU) regulation is in effect (71, 72). However, until now the effect of this regulation have not been evaluated.

#### *Chromate*

The prevalence of chromate allergy in children in the general population has been reported to be 0.2–7.6% (8–10). The most common source in children is chrome-tanned leather, and chromate sensitivity is observed as a major cause of shoe dermatitis (73, 74).

#### *Cobalt*

The prevalence of cobalt allergy among children in the general population is reported to 0.5–5.7% (8, 9). A positive patch test to cobalt usually occurs in association with a positive test to nickel or chromate, more particularly nickel. This association is thought to be related to the metals being commonly associated with one another (69). It is often difficult to identify the significance of an isolated positive cobalt patch test. However, most of these patients are probably allergic to jewelry.

#### *Fragrance mix*

The prevalence of allergy to fragrance mix among children in the general population is reported to be 1.8% in one study (8), while the other population based studies have not included fragrance mix in their test series (9, 10). 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 made especially for children.

#### *Thimerosal*

Thimerosal is used as preservative in vaccines, antitoxins, ophthalmic preparations, contact lens

solutions and eardrops, and diluents for the preparation of antigens for prick or intradermal testing. There has been reported a high prevalence of thimerosal sensitization both in population-based studies 2.3–3.5% (8, 10) and in patient materials (1, 2, 5, 22–24, 28, 32), even in countries where thimerosal is used only in vaccines (37). Most of the sensitized have a negative history of contact dermatitis, and the most likely explanation for the high sensitization rate is exposure to vaccines.

#### *Neomycin*

Neomycin is used in topical preparations, including ear and eye drops, to treat bacterial infections and diaper dermatitis. The prevalence of neomycin sensitization in the general population of children varies from 1.4% in Norway (9), 2.8% in Portugal (8) to 8.1% in USA (10), reflecting different exposure patterns in different geographical locations.

#### *PTBPF resin (p-tert-butylphenol-formaldehyde resin)*

PTBPF resin is used in adhesives in shoe and leather goods. In a recent report from Romaguera et al. (75) it has been described that shoe ACD due to PTBPF resin has increased from 2% in 1979 to 27% in 1985. The prevalence in children in the general population varies from 0.5% in Norway (9), 0.9% in USA (10) to 2.1% in Portugal (8).

In summary, the major sources of contact allergy in childhood are jewelry, perfumes, shoes, preservatives and topical products. There is considerable variability in the prevalence and causes of contact allergy and ACD in childhood from country to country, due to variation in exposure to the allergens.

#### **Patch Testing in Children and Adolescents**

Although the offending allergen may be obvious from the exposure history and clinical picture in some children with ACD, most cases of ACD need patch testing to find the allergen(s) involved in the dermatitis (76). The patch test technique in children is the same as in adults. The same allergens and standard series are used, and to improve comparability of patch test results in different studies the guidelines recommended by International Contact Dermatitis Research Group (ICDRG) should be used (69, 77).

Previously, several authors have suggested that children should be tested with lower concentrations of allergens than adults, because the allergens tend to give irritant reactions and a higher rate of false-positive reactions (14, 19). Hjorth (14)

suggested that patch test concentrations should be adjusted according to the age of the patients, and that all positive reactions to patch tests should be repeated using the substances in 1/2 strength concentration. Fisher (19) recommended using 1/2 the standard concentration when patch testing children.

However, the general opinion today is that children can be patch tested with the same concentrations as adults (1–3, 7, 22, 24, 27, 28, 32, 38, 78). Many studies have been carried out with a high number of negative patch tests suggesting that skin of children can tolerate the same test concentrations as adults. Furthermore, even in a study of infants no irritation and very few follicular-type reactions were reported using the same concentrations as in adults (28). Irritant reactions are only rarely reported in recently published population based studies, which gives further support to this opinion. Weston et al. (10) reported irritant reactions defined as macular erythema, that was not confluent or follicular in pattern, in 6.7% of the population. They used the same concentrations as used in adults except for nickel. Dotterud et al. (9) used the same allergen concentration as in adults, and they found irritant reactions in 7.8% of their children population, defined as weak macular erythema without infiltration or follicular pattern. However, it is difficult to discriminate between weak allergic positive patch tests and nonspecific irritation.

There are two types of test systems: the classical technique, where the allergens, patches and tapes are supplied separately; and the modern ready-to-use system, where all necessary materials are prepared in advance and only a covering material has to be removed before the test is applied (TRUE Test™, Pharmacia & Upjohn, Denmark). The advantage of the ready-to-use system is that it is carefully standardized. It provides an exact dosage, known stability, even distribution and high bioavailability for the allergens (79). Furthermore, TRUE Test™ is easy to use, and this is especially advantageous when performing patch testing in large populations.

### Clinical Relevance in Contact Allergy and ACD

When establishing the diagnosis of ACD at least 2 steps should be considered: 1) demonstrating the existence of contact allergy by patch testing; and 2) demonstrating the clinical relevance of a positive patch test by a careful history in combination with dermatitis pattern and exposure history. Lachapelle (80) suggested a more detailed scoring system for the degree of present and past relevance, in-

cluding relevance not traced, doubtful, possible and likely relevance.

To increase the accuracy of the evaluation of the relevance of a positive patch test, additional procedures should be used, such as serial dilution patch testing, repeated open application test (ROAT) or use test. In the case of a product brought by the patient, chemical analysis and information collected from the manufacturer are also important. Unfortunately, all population based studies lack information about clinical relevance of a positive patch test result (8–10).

### Conclusion

During the last decade a considerable number of children and adolescents with contact allergy and ACD have been described. However, the incidence and prevalence of contact allergy and ACD in children and adolescents is largely unknown, because of a lack of studies in unselected populations with a standardized patch test system and procedure, and with evaluation of the clinical relevance of a positive test result. Test systems like TRUE Test™ have made it possible to patch test large populations. We have initiated a cross-sectional study among all 8<sup>th</sup> grade school children in the city of Odense, Denmark. The school children are offered patch tests with TRUE Test™ performed according to ICDRG guidelines. Adolescents with positive patch test results are identified and the relevance is assessed. Preliminary results show that 15% had at least 1 positive patch test. Sensitization was most common to nickel (8%) and fragrance mix (2%) (11). By questionnaire, interview and clinical examination, adolescents with a history of or present atopic dermatitis, hand eczema and inhalant allergy (allergic asthma, allergic rhinitis) are identified. These groups are going to be followed over time, together with adolescents with a positive patch test result. This design makes it possible to evaluate the relationship between, for example, AD and the later development of contact allergy/ACD, and contact allergy and the later development of hand eczema.

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