

Contact Dermatitis in Children: Do We Need Regular Patch Testing?

Iris Ale, Uruguay

The prevalence of allergic contact dermatitis (ACD) in children may be underestimated. In the first years of life ACD it is often confused with other types of dermatitis, such as irritant dermatitis or atopic eczema (AE).

In fact, contact sensitization may be found in 13.3 to 24.5% of randomly selected children; moreover, 56.5% - 94.4% of the positive test results are clinically relevant. ACD acquired in childhood has important repercussions for patients, and may affect decisions regarding occupation in adulthood.

ACD was once viewed as a disorder of the adult population. Children were thought to be spared due to a lack of exposure to potential allergens and a deficient reactivity of the immune system. Patch testing has also been limited in this population because of technical difficulty owing to small physical size.

Results of a first study on the frequency of contact allergy in children were published in 1961 by Brigitte Langer: Among 25 children with dermatitis she found 15 with positive patch tests. Shortly afterwards, in a study of 583 children without skin diseases, Kreissl and Wiedermann found that lowest rate of positive patch tests was among the youngest. At that time, a paper was also published by Marcussen, who regarded all positive patch tests in young children as an unspecific irritation. Other authors shared the belief about rarity of contact allergy and the impression that irritant reactions dominate in children (Hjorth, Röckl and Rudzki)

Langer B.: Testungen bei Säuglings- und Kleinkindereczem einschließlich Milchschorf. Dtsch.Gesundheitsw. 16, 140 (1961)

Kreissl H., G. Wiedermann: Epikutane Testungen bei hautgesunden Kindern und Jugendlichen. Derm. Wochenschr. 46, 536-541 (1963).

Marcussen P V. Primary irritant patch-test reactions in children. Arch Dermatol 1963; 87: 146–150.

Hjorth N.: Contact dermatitis in children. Acta Derm. Venereol. Suppl. 95, 36-39 (1981)

Röckl H., E. Müller, W. Hiltermann: Zum Aussagewert positiver Epikutantests bei Säuglingen und Kindern. Arch. Klin. Exp. Dermatol. 226, 407-419 (1966)

Rudzki E., Z. Grzywa, P. Rebandel, D. Litewska, K. Parapura: Alergia kontaktowa u dzieci. Przegl. Dermatol. 74, 322-326 (1987).

Sensitization and ACD in children

However, in the last twenty years most studies demonstrated a high prevalence of contact sensitization in children, with figures similar to those seen in adult populations. Also, most studies shown an increase in the positive reaction rates for most allergens over time.

This rise in contact sensitization is partly due to a greater awareness in allergologists, pediatricians and dermatologists leading to an increase in patch testing in the pediatric

population. However, there is also a real increase due to more chemical exposures than in the past.

Modern life has introduced a variety of allergens into children's lives, including fragrances, cosmetics, preservatives, vaccines, dental braces, and tattoos.

It is commonly accepted that ACD increases with age as a result of the opportunity for more exposures. However, some studies found the highest prevalence of sensitization in children or even in infants.

In an large study in Austria, patch testing was performed on 2776 consecutive patients (76.5% female) with a locally revised standard series of 34 contact allergens and the results analyzed for age- and gender-specific differences. At least one positive epicutaneous test reaction occurred in 48.9% of patients. Nickel (20.9%), ethylmercuric chloride (13.2%), thimerosal (11.8%), fragrance mix (9.3%), metallic mercury (8.9%), palladium (5.8%), balsam of Peru (3.8%), copper (3.7%), cobalt (3.3%), and chromium (2.3%) were the 10 most important sensitizers.

The overall sensitization rate was higher in children less than 10 years old (62%).

On the other hand, the lowest rates were observed in patients older than 70 y.o. (34.9%) The rate of positive reactions to Ni, Co, Pa, Cu and Thiomersal decreased with age, whilst the rate of positive reactions to fragrances and balsam of Peru stayed at the same level through all age groups

Wöhrl S, Hemmer W, Focke M, Götz M, Jarisch R. Patch testing in children, adults, and the elderly: influence of age and sex on sensitization patterns. *Pediatr Dermatol.* 2003;20(2):119-23.)

Other study from the Information Network of Departments of Dermatology and the German Contact Dermatitis Research Group included 285 children (6-12 y), and 2175 adolescents (13-18 y) and a control group composed of 7904 adults (60 - 66 y).

Patients were tested with a locally adjusted standard series including 30 allergens.

The percentage of sensitization was:

52.6% children

49.7% adolescents

52.2% adults

The most frequent allergens in children were: thimerosal, benzoyl peroxide, mercurials, gentamicin sulphate, nickel, cobalt, fragrance, Compositae mix, propylene glycol and turpentine.

Heine G, Schnuch A, Uter W, Worm M. Frequency of contact allergy in German children and adolescents patch tested between 1995 and 2002: Contact Dermatitis. *2004;51(3):111-7*

Not only the percentage of sensitization was similar or even higher in children than in adults, some studies draw attention to the high frequency of sensitization in infants.

In a French study in 337 children (1–15 y.o.) patch tested with the European Standard Series and a shortened series for children under 5 years of age, a high percentage of positive patch test reactions was observed (66%). **The highest prevalence of sensitization was observed in infants less than 3 y.o. (88% versus 58.9%)**

Two hundred fifty seven children (76%) had atopic eczema (AE) and the frequency of sensitization was almost the same in atopics than in non atopics (64% vs 70%)

No case of active sensitization was observed among patients who were regularly followed up.

The most frequent allergens were: Nickel, fragrances & rubber

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.

In other study in 53 Italian infants (3 months to 2 years of age) with eczematous dermatitis (39 of them had AE), patch testing was performed with the Italian standard series (same allergens and concentrations as in adults)

Positive PT reactions were seen in 32 (60%), and at least 20 out of the 32 sensitized infants had clinically relevant allergies

No irritant and very few follicular-type reactions were seen.

Sixteen children were polysensitized and 25 of the sensitized children had AE

The haptens responsible for the highest number of positivities were thimerosal, nickel, ammoniated mercury, disperse dyes, fragrances, and preservatives

Motolese A, Manzini BM, Dinini M. Patch testing in infants. *Am J Contact Dermat* 1995; 6: 153–156

A similar study, also from Italy included 321 consecutive children younger than 3 yo with suspected ACD, 42.7% had AE (Padova, 2002 to 2008)

A Standard series of 30 allergens was used.

62.3% had at least one + PT reaction

Ninety-five children (29.6%) were polysensitized, with 69 of 95 having two positive reactions only.

The prevalence of sensitization was similar in children with and without atopic dermatitis

The most frequent patch test reactions were to Ni, Cr, cocamidopropylbetaine, Co, neomycin, Kathon and disperse dyes

Very few irritant reactions were seen and no active sensitization was observed.

Fortina A, Romano I, Peserico A, Eichenfield L. Contact sensitization in very young children. *J Am Acad Dermatol* 2011;65:772-9.

ACD and Atopic Eczema

ACD was previously thought to occur less frequently in patients with atopic eczema because of the existence of a decreased cell-mediated hypersensitivity

Earlier studies reported a diminished prevalence of contact sensitization in patients with AE

On the other hand, skin barrier dysfunction in patients with AE facilitates the penetration of allergens and irritants into the skin. In addition, atopics have greater exposition to allergens from topical medicaments and cosmetics

Several studies from the 1990s supported the need for patch testing in patients with AE, reporting frequencies of 40% of positive patch test reactions in these patients

De Groot A C. The frequency of contact allergy in atopic patients with dermatitis. *Contact Dermatitis* 1990; 22: 273–277.

Cronin E, McFadden J P. Patients with atopic eczema do become sensitized to contact allergens. *Contact Dermatitis* 1993; 28: 225–228

Guillet M H, Guillet G. Enquête allergologique chez 251 patients atteints de dermatite atopique modéré ou sévère. *Ann Dermatol Venereol* 1996; 123: 157–164.

Giordano-Labadie et al, tested 137 children with AE in France. Patch testing was performed with allergens from the European Standard Series. In addition, budesonide, tixocortol, personal emollients and other allergens were included

Positive PT were observed in 43% of the children. The most common allergens were: metals (19.3%, Ni 14.9%) , fragrances and lanolin (4.4% each), B de Perú, neomycin and emollients (2.6% each)

10% of positive reactions were interpreted as irritant

Children older than 5 years had a greater risk of developing contact allergy

Giordano-Labadie F, Rancé F, Pellegrin F, Bazex J, Dutau G, Schwarze H. Frequency of contact allergy in children with atopic dermatitis. *Contact Dermatitis*, 1999, 40, 192-195

In a related study from Poland, 229 school children and teenagers with AE were tested with a 10-allergen panel with the most frequent sensitizers in Europe

49.4% of the children had a positive PT.

The most common allergens were: Ni (30.2%), thimerosal (10.4%), cobalt(8.3%), and fragrances(7.3%)

Czarnobilska E, Obtulowicz K, Dyga W, et al. Contact hypersensitivity and allergic contact dermatitis among school children and teenagers with eczema. *Contact Dermatitis* 2009;60(5):264–9.

Patch testing was carried out in 424 schoolchildren (223M, 201F), aged 7-12 years, in northern Norway.

In 99 (23.3%) of these children, one or more allergic patch test reactions were demonstrated; 30 children reacted to two and 6 to three or more substances.

From a total of 144 positive tests, the most common allergen was nickel (14.9%), followed by cobalt (5.7%), kathon CG (5.2%), lanolin (1.7%) and neomycin (1.4%). Positive patch tests were significantly more frequent in atopic (28.8%) than in non-atopic (17.9%) children, being most pronounced in atopic girls (37.4%)

Dotterud L.K., E.S. Falk: Contact allergy in relation to hand eczema and atopic diseases in north Norwegian schoolchildren. Acta Paediatr. 84, 402-406 (1995).

A cohort study conducted in adolescents in Denmark including 1501 eighth-grade students found a lifetime prevalence of AE of 21.3%, 6.9% for allergic asthma, 15.7% for allergic rhinitis, and 9.2% for hand eczema.

Twenty of 24 allergens produced positive results, 37% of patients with ACD had a history of AE

Sensitization in children from unselected populations

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

Only few studies have examined unselected populations of children and adolescents, but these studies have revealed a high frequency of sensitization (13 -24.5%)

The commonest allergens were similar to those observed in children with dermatitis.

Sensitization in unselected children

314 asymptomatic children (under 18) from USA (Denver)

20.3% had at least one positive PT reaction

The most frequent allergens were: Neomycin, Ni and Cr.

Sensitization occurred at less than 5 years of age for all but fragrance allergens.

Weston W, et al. Prevalence of positive epicutaneous tests among infants, children, and adolescents. Pediatrics 1986;78: 1070-1074

85 asymptomatic children from USA (Denver) 2000

6 months to 5½ yo

24.5% had at least one positive PT reaction

The most frequent allergens were: Ni, Timerosal , Neomycin, Cobalt and Kathon CG.

Bruckner AL, et al. Does sensitization to contact allergens begin in infancy? Pediatrics 2000;105 (1):1-4

562 schoolchildren from 5 to 14 years in Portugal

Tested with 25 standard allergens

13.3% had at least one positive PT reaction

The most frequent allergens were: Neomycin, thimerosal, PTBFR, Fragrances

Barros M A, et al. Patch testing in children: a study of 562 school children. Contact Dermatitis 1991; 25: 156–159.

How to select allergens for a pediatric standard series?

When studying CD patients we usually employ a screening series, which will pick approximately 80% of allergens

Allergens producing 1% or more positive reactions in tested patients are considered for inclusion in the Standard Series

However, standard series vary from centre to centre, and are often revised or adapted to include allergens of local importance

Ideally, a pediatric series should include allergens with the highest proportion of positive patch test reactions in children and, moreover, those responsible for clinically relevant contact sensitizations

However, consensus is still lacking on which allergens are most commonly implicated in allergic contact dermatitis in pediatric populations

Which allergens are more prevalent in children?

In 2001, Spiewak performed a meta-analysis of 23 epidemiological studies comprising altogether 2794 randomly selected children and 5705 children with suspicion of ACD (Medline and Current Contents up to June 2001)

The results were restricted only to allergens that were tested in at least 3 studies, including at least 2 countries and when the total number of tested children exceeded 1500

Sensitization appeared to be more commonly caused by:

nickel (8.3% random children, 19.2% of children with dermatitis)

thiomersal (2.1% and 14.0% respectively),

cobalt (1.9% and 13.5%),

fragrances (1.7% and 11.8%),

chromate (1.5% and 12.4%),

Kathon CG (1.4% and 21.0%),

lanolin (0.7% and 12.1%)

balsam of Peru (0.5% and 10.8%).

Spiewak R. Allergic contact dermatitis in childhood - a review and meta-analysis. *Allergologie* 2002; 25 (7): 374-381

In another review of 18 studies, the top five global allergens for children were found to be:

Nickel

Cobalt

Antibiotics

Fragrances

Rubber chemicals

Matiz C, et al. Allergic contact dermatitis in children: a review of international studies. *G Ital Dermatol Venereol* 2009; 144: 541-556.

A systematic review and meta-analysis of the medical literature from 1966 to 2010 to investigate which of the allergens tested in at least 100 enrolled children were traced in at least 1% of the paediatric population

Most of the studies that were analyzed were performed in European populations.

A total of 58 allergens had estimates of positive reactions of at least 1%, and 18 of those had been evaluated in at least 10 studies each.

Only nickel sulfate and ammonium persulfate exceeded 10%, and another seven allergens had estimated proportions between 5% and 10% [gold sodium thiosulfate, thimerosal, toluene-2,5-diamine (p-toluenediamine), palladium chloride, cobalt chloride, metallic mercury, and mercuric chloride]

However, it should be pointed out that allergens like ammonium persulfate or p-toluenediamine were tested in only two studies.

Bonitsis, N et al. Allergens responsible for allergic contact dermatitis among children: a systematic review and meta-analysis. *Contact Dermatitis*, 64, 245–257, 2011

However, depending on the availability of data, some countries are over-represented in the analyses, whereas others are not represented at all.

Therefore proper international multicentre studies should be carried out,

Until then, we are left with results of single studies or preferably meta-analyses.

Conclusion

Allergic contact dermatitis (ACD) is an underestimated pathogenetic factor for the development of eczema in children

There are convincing data that sensitization to common contact allergens is frequent and may occur already in the first months of life

ACD acquired in childhood may have lifelong sequelae, so it is very important that any contact allergy in a child is recognized and dealt with in time

Standardized patch testing makes it possible to systematically investigate allergic contact dermatitis and identify relevant allergens in children

Patch testing should be utilized more frequently as a valuable diagnostic tool in the pediatric setting when the clinical presentation is suggestive of allergic contact dermatitis or when studying a persistent recalcitrant refractory dermatitis