

## CLINICAL REPORT

# Children with Atopic Dermatitis Should Always be Patch-tested if They Have Hand or Foot Dermatitis

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**Atopic dermatitis is the most common chronic inflammatory disease among children in industrialised countries. Many factors influence this disease in a negative way and contact allergy is one such factor. The aim of the study was to examine the frequency of contact allergy among children with the diagnosis atopic dermatitis. Contact allergy was found in 22/82 children (26.8%), the most common from Amerchol L101 (11.0%), potassium dichromate (7.3%), and nickel sulfate (4.9%). A statistically significant difference in contact allergy frequency was demonstrated for those with hand and/or foot eczema compared to those without. Children with atopic dermatitis who suffer from hand and/or foot dermatitis should always be patch-tested to evaluate whether they have a relevant contact allergy and thus allergic contact dermatitis. Key words: baseline series; contact allergy; Amerchol L101; lanoline; eczema; corticosteroids; wool alcohol; allergic contact dermatitis.**

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Atopic dermatitis (AD) is seen in 15–20% of all Swedish children. Twenty percent of all 7-year-old youngsters have or have had AD (1). In industrialised countries AD is the most common chronic inflammatory disease among children. The prevalence of AD has increased 2–3 fold since the 1960s (2–4).

Approximately 50% of those with AD in childhood are afflicted with eczema as adults. Early onset and severe eczema during childhood and adolescence are considered to be negative prognostic factors (5).

The risk of hand eczema in adult life is increased 3-fold compared to those without AD in childhood, independent of occupation (1). Hand eczema is also the most common manifestation of AD in adults, especially irritant contact dermatitis. Therefore it is of great importance that young people with AD receive detailed information about limitations concerning their future occupation (1).

It has previously been stated that individuals with AD do not develop contact allergy to the same extent as

those without atopy (6), but in reality the risk seems to be the same. One study even showed that after a diagnosis of contact allergy was demonstrated, a reduction of dermatitis in adults was seen, possibly because the allergen could be avoided (7).

The aim of the present study was to determine the frequency of contact allergy among children with AD in the city Malmö and to evaluate if a significant degree of contact allergies in these children is missed when not patch-testing them. We also aimed to compare the outcome of patch test reading on day (D)3 with the outcome of D7.

## MATERIAL AND METHODS

### Patients

Eighty-two children with AD were included between 2004 and 2007. They were mainly collected by going through case records from the Department of Paediatrics and the Department of Dermatology, Skåne University Hospital, Malmö, Sweden and picking out the ones with the diagnosis ‘atopic eczema’. Some children were randomly included after referral from the eczema school at the Department of Dermatology in Malmö and from the primary care centres in Malmö. Inclusion criteria were children from age 5 years up till 14 years who had used topical corticosteroids during at least 2 months altogether, but the treatment did not need to have been given continuously. None of the children had been treated with oral corticosteroids 14 days prior to patch testing, and the test area of patients had not been treated with topical corticosteroids 3 weeks prior to patch testing or been given UV treatment.

### Patch testing

Patch testing was performed on the upper part of the back with small (Ø 8 mm) Finn Chambers® (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgeplaster A/S, Vennessla, Norway) with the children’s baseline series and a corticosteroid series used in Malmö (Tables I and S1<sup>1</sup>). In each test chamber 20 mg of each petrolatum preparation was preloaded. For the liquids 15 µl of each solution was micropipetted on to the paper discs in the test chambers just prior to testing. Supplier of allergens in the baseline series was Chemotechnique Diagnostics (Vellinge, Sweden). The corticosteroid series was prepared at our laboratory from substances bought from various companies (Table S1<sup>1</sup>). The tests were removed after 48 h and readings were performed on D3 and D7. The patch testing was performed by the same technician with more than 10 years of testing experience.

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Table I. The childrens' baseline series in Malmö

Patch test substances	Conc (% w/w <sup>a</sup> )
Potassium dichromate	0.5
p-Phenylenediamine	0.94
Thiuram mix	1.0
Neomycin sulfate	20.0
Cobalt chloride	0.5
Quaternium 15	1.0
Nickel sulfate	5.0
Quinoline mix	6.0
Colophony	20.0
Paraben mix	16.0
Black rubber mix	0.6
Sesquiterpene lactone mix	0.1
Mercapto mix	2.0
Epoxy resin	1.0
<i>Myroxylon pereirae</i>	25.0
p-tert-Butylphenol formaldehyde resin	1.0
Primin	0.01
Formaldehyde	1.0*
Fragrance mix	8.0
Ethylenediamine dihydrochloride	1.0
Diazolidinyl urea	2.0*
Methylchloroisothiazolinone/methylisothiazolinone	0.02*
Amerchol L101	100.0
Caine mix II	10.0
Lichen acid mix	0.3
Tixocortol-21-pivalate	0.1
Toluenesulphonamide formaldehyde resin	10.0
Budesonide	0.01
Methyldibromo glutaronitrile	0.5
Textile colour mix**	3.2

<sup>a</sup>w/w: weight/weight for all allergens in petrolatum; vehicle for all test substances is petrolatum except for substances marked with \*, which are tested in water (weight/volume). \*\*a mixture of 8 disperse dyes, i.e. Disperse Blue 35, Disperse Yellow 3, Disperse Orange 1 and 3, Disperse Red 1 and 17, all at 0.5%, and Disperse Blue 106 and 124, both at 0.1%.

rience in all children and all readings by the same dermatologist experienced in reading tests for the past 15 years. The reactions were scored according to the International Contact Dermatitis Research Group (ICDRG) criteria (8).

#### Statistical analysis

Fisher's exact two-sided test was used. A  $p < 0.05$  was considered statistically significant.

#### Ethics

The study was approved by the Lund University Ethics committee (LU 764-02) and parents signed an informed consent prior to inclusion.

## RESULTS

Positive reactions were seen in 22/82 children (26.8%) (Table S1<sup>1</sup>). Fourteen had one contact allergy, 5 had 2 contact allergies, 1 had 3 contact allergies, and 2 had 4 contact allergies. The most common contact allergies were to Amerchol L101 (11.0%), potassium dichromate (7.3%), nickel sulfate (4.9%), fragrance mix 1, cobalt chloride, lichen acid mix, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) (2.4% each), *p*-tert-

butylphenol formaldehyde resin, *p*-phenylenediamine, formaldehyde, 2,5-diazolidinylurea, quinoline mix, *Myroxylon pereirae*, and sesquiterpenelactone mix (1.2% each). There were no positive reactions to any corticosteroids.

Among the 22 children Amerchol L101 and potassium dichromate were the most common allergens with allergic patch test reactions in 40.9 and 27.3%, respectively. Thirty-two of the tested children had or had had hand and/or foot dermatitis. Among these children 14/32 (43.8%) had positive patch test results. Of the remaining 50 children 8/50 (16%) had positive reactions. The difference was statistically significant ( $p = 0.009$ ).

No positive reactions were seen only on D7.

## DISCUSSION

Our cross-sectional survey differs from most other patch test studies performed in atopic children in that our patients were not patch-tested because of present eczema as in most other studies.

In the past 10 years, there have been less than 20 studies in which children with AD have been patch-tested to common allergens. Furthermore, to our knowledge there are no studies with corticosteroids from all 4 groups of these substances in terms of allergenicity and cross-reactivity.

The prevalence of contact allergy in children with AD has been estimated at 14.9–64.2% (9–16). Some authors claim that atopy may be regarded as a predisposing factor for the development of type IV hypersensitivity reactions (10–12), while others argue that there is no association between AD (or other atopic diseases) and an increased risk of contact sensitisation (13–16).

Many cases of contact allergy can be linked to the basic treatment of AD, namely corticosteroids and emollients (12, 17). Mostly, it is a component in the emollients that has been the culprit (1).

Children with AD are seldom patch-tested to evaluate whether they are suffering from contact allergy and allergic contact dermatitis or whether a contact allergy may be an aggravating factor to their skin disease. This may depend on the belief that children with AD rarely develop contact allergy. In our study only 1 of the 82 children with AD had ever been patch-tested in the past (pat. No. 19).

Our study shows a frequency of contact allergy of 26.8% in children with AD. This is in accordance with some previous studies (12, 18, 19). Our study also shows that contact allergy is frequently missed in children with AD. This is very unfortunate because having a contact allergy and being exposed to the allergen carries a great risk of developing therapy resistant dermatitis.

In the present study, Amerchol L101 was the most common allergen with a contact allergy frequency of 11.0%. This figure is high compared to other studies, where the frequency has been reported to be 2.8–4.5% (12, 20, 21). In one American study in which children were tested, 15.8% showed contact allergy to wool alcohols. The relevant contacts were emollients and ointments, notably in AD patients (22). Amerchol L101 is a lanoline derivative used in furniture polish, waxes, cutting oils, textiles, furs, leather, inks and paper, as an emollient and emulsifier in ointments and in cosmetic products such as soaps, shampoos and hair conditioners, aftershave, baby and bath oil, hand sanitisers, lipstick, and creams (23). Currently, none of the recommended emollients prescribed by physicians in Sweden contain lanoline. As Amerchol L101 has a mineral oil component that constitutes 5% of the total test substance, this could give irritant reactions, interpreted as false positive reactions (Magnus Bruze, personal communication). Perhaps atopic skin has a tendency to give more irritant reactions when patch-tested to Amerchol L101. However, the morphology of the test reactions was in line with allergic reactions, i.e. erythema and infiltration covering the whole patch test area and additionally some or many papules were noted. We also considered the lanoline allergy to be relevant.

Potassium dichromate yielded positive patch tests in 6/82 (7.3%) of the children. Patients with this contact allergy can react after contact with chromate-tanned leather in shoes and gloves. The parents of one girl (Table SII<sup>1</sup>, No. 4) had experienced deterioration of their child's dermatitis after she had sat in the family's leather sofa. Two of the children (Nos. 5 and 2) had eczema on the dorsal aspects of their feet. They had both been using leather shoes and the dermatitis waned when changing to another shoe material not containing leather. In another 3 children (Nos. 6, 13, 18) with chromate allergy no previous or present clinical relevance could be found. They did not have any problems with hand or foot dermatitis, which is common when allergic to chromate (24).

Nickel sulfate has previously been used in silvery metal alloys in non-precious jewellery. Four children (4.9%) were allergic to nickel. One of them (No. 18) had had eczema on her ears lobes after wearing cheap earrings. Another child (No. 19) experienced discomfort from his metal jean studs. In the remaining 2 children (Nos. 14, 22) no clinical relevance was found for this sensitiser.

Irritant patch test reactions to metals, e.g. nickel and cobalt, were not seen in any of the children.

The children in our study had a low frequency of contact allergy to nickel compared to children in other countries (24). The EU Nickel Directive, aimed at the prevention of nickel allergy, came fully into force by July 2001. It regulates the permitted release of nickel from metal alloys intended for close skin contact, such

as jewellery, jeans studs, buttons, and spectacle frames. In Sweden as early as in 1989 a limitation of the amount of nickel present in material intended for piercing was made (0.05%). This and the EU Nickel Directive might be one contributing factor to the low frequency of nickel allergy in our study. Of the 10–14-year-old youngsters, 3 were females and one male. Not one child younger than 10 years was allergic to nickel and these had grown up during the nickel regulation. The same has been seen in Denmark where the directive has been in force since 1991 (24). There could also be a cultural aspect. Nickel allergy is more common in girls than boys due to girls having pierced ears to a higher degree. In countries where piercing is more common in young girls compared to Sweden, nickel allergy is also more common. A recent German study linked AD (and loss-of-function filaggrin mutations) to both immediate-type and delayed-type hypersensitivity reactions. The study found a strong association between having AD, a loss-of-function filaggrin mutation, and nickel sensitisation (25). The low frequency of nickel allergy in our AD children then speaks in favour of nickel release having been restricted while these youngsters grew up.

Two children (2.4%) had contact allergy to p-tert-butylphenol formaldehyde resin. This resin is commonly used in glues for shoes and leather wrist straps for watches. One child (No. 16) reported eczema on the skin in contact with her wrist strap made from leather. The other child (No. 1) did not have any skin problems related to this substance. This allergen is also used as glue in neoprene articles and is sometimes the culprit in shin guards and wetsuits (22).

We found one child (No. 22) with contact allergy to sesquiterpene lactone mix and lichen acid mix. This child suffered from severe dermatitis on her hands, feet and face from May until October. In her case notes it was stated that 'her dermatitis comes when she begins to run outside without stockings and when in contact with grass'. Her dermatitis improved significantly once she knew to avoid sesquiterpene lactone-containing weeds and flowers such as dandelions (26).

Concerning the other contact allergies we could not find any clinical relevance related to the children's dermatitis. However, all the diagnosed contact allergies may have future relevance, as the patients will be able to avoid contact with the sensitiser and thus prevent a possible dermatitis or aggravation of the atopic eczema (7).

We found a higher frequency of contact allergy among the children with hand and/or foot dermatitis (43.8%) compared to those without eczema on hands or feet (16.0%) ( $p=0.009$ ). Furthermore, of the 14 patients with hand and/or foot eczema, 10/14 (71.4%) had a relevant contact allergy compared to the 8 patients without hand and/or foot eczema, in which 4/8 (50%) had a relevant contact allergy. The difference is however not statistically significant,  $p>0.3$ .

We did not detect any contact allergy to corticosteroids. If the inclusion criteria instead had required a longer exposure time to topical corticosteroids it is possible that we would have detected it. On the other hand, then we would have had fewer children in the study.

In general, one will miss 15% of all contact allergies in a baseline series if you do not perform a D7 reading, i.e. a late reading (Iskasson M, et al. unpublished observations, 2014). However, in this study, all 35 positive reactions were seen at day 3 and 18 of them also at day 7.

### Conclusion

We suggest that children with AD should be tested for contact allergy more often, especially when hand and/or foot dermatitis is present or the patient has therapy resistant and severe AD.

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