

ORIGINAL ARTICLE

Children with atopic dermatitis may have unacknowledged contact allergies contributing to their skin symptoms

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Abstract

Background Whether children with atopic dermatitis have an altered risk of contact allergy than children without atopic dermatitis is frequently debated and studies have been conflicting. Theoretically, the impaired skin barrier in atopic dermatitis (AD) facilitates the penetration of potential allergens and several authors have highlighted the risk of underestimating and overlooking contact allergy in children with atopic dermatitis.

Objective To determine the prevalence of contact allergy in Danish children with atopic dermatitis and explore the problem of unacknowledged allergies maintaining or aggravating the skin symptoms.

Methods In a cross-sectional study, 100 children and adolescents aged 5–17 years with a diagnosis of atopic dermatitis were patch tested with a paediatric series of 31 allergens.

Results Thirty per cent of the children had at least one positive patch test reaction, and 17% had at least one contact allergy that was relevant to the current skin symptoms. The risk of contact allergy was significantly correlated to the severity of atopic dermatitis. Metals and components of topical skincare products were the most frequent sensitizers.

Conclusion Patch testing is relevant as a screening tool in the management of children with atopic dermatitis as they may have unacknowledged contact allergies contributing to or maintaining their skin symptoms. Children with atopic dermatitis seem to be at greater risk of sensitization to certain allergens including metals and components of skincare products.

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Conflicts of interest

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Introduction

Atopic dermatitis (AD) is the most common inflammatory skin disease of childhood. It has a common phenotypic expression, characterized by dry and itchy skin with chronic or recurrent episodes of dermatitis at typical anatomical sites.¹ The prevalence of AD has dramatically increased over the last three decades and now affects between 15% and 30% of children in Western countries.^{2,3}

Allergic contact dermatitis (ACD) is the skin manifestation of a delayed-type hypersensitivity reaction that typically develops after prolonged or repeated skin exposure to chemical allergens.⁴ Although previously considered rare, it is now recognized as a common skin disease in children.^{5,6} Clinically, AD and allergic

contact dermatitis may be difficult to distinguish as they both present as dermatitis and may co-exist.⁷ Whether children with AD have an altered risk of contact allergy as compared to children without AD is frequently discussed and past findings have been conflicting. Authors of early experimental studies found reduced sensitization among patients with AD as compared to controls,^{8–10} but recent research suggests that contact allergy and allergic contact dermatitis may be a significant problem in AD patients.^{11,12} The impaired skin barrier in AD facilitates the penetration of potential allergens¹³ and as children with AD are exposed to emollients and topical agents from an early age and for prolonged periods of time,¹⁴ this could theoretically increase the risk of contact sensitization to both ingredients and

vehicles.⁴ Although several authors have emphasized the possibility of unacknowledged contact allergies maintaining or worsening the skin symptoms,^{7,15–17} children with AD are not routinely patch tested.¹⁷ The existing knowledge on contact allergy in children with atopic dermatitis is primarily based on retrospective analyses of children with and without atopic dermatitis that have been referred for patch testing because of suspected allergic contact dermatitis. Since 1977, only seven studies have been published in which authors have patch tested children with atopic dermatitis without suspecting allergic contact dermatitis and only two address the possible relationship between disease severity and risk of contact sensitization. The weighted average prevalence of contact allergy in the existing studies is 26.2%.¹⁸

With this study, we aimed to determine the prevalence of contact allergy in Danish children with AD, to explore the problem of hidden allergies maintaining or aggravating the skin symptoms, and finally to assess the relationship between severity of atopic dermatitis and risk of contact allergy.

Methods

Patients

This was a prospective study performed on children without a clinical suspicion of allergic contact dermatitis, and thus, the patch testing was performed as a screening. During 1 January 2014 – 31 March 2017, 100 children and adolescents aged 5–17 years with a diagnosis of AD were invited to participate. The diagnosis of AD was made by a dermatologist according to the Hanifin and Rajka criteria.¹⁹ All children and adolescents visited one of three dermatology departments in Denmark (Department of Dermatology and Venereology, Aarhus University Hospital, and Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen) as part of their regular follow-up. Parents or holders of custody gave written informed consent for participation. Twenty-nine patients were included from the Department of Dermatology and Allergy, Herlev and Gentofte Hospital, 28 from the Department of Dermatology and Allergy Centre, Odense University Hospital, and 43 from the Department of Dermatology and Venereology, Aarhus University Hospital).

At the time of inclusion, the patient's exposure history was noted in order to ensure a targeted patch test, and the severity of AD was assessed according to the SCORAD index.²⁰ SCORAD is a clinical tool used to assess the extent and severity of atopic dermatitis. It is made up of three items. The first item is 'area', that is the extent of the dermatitis. This is measured using the rule of 9 to calculate the affected area as a percentage of the whole body. The second item is 'intensity': a representative area of eczema is selected, and the intensity of six different symptoms (redness, swelling, oozing/crusting, scratch marks, skin thickening and dryness of the skin without inflammation) is assessed as none

(0), mild (1), moderate (2) or severe (3). The third item is the patient's subjective symptoms in terms of sleep loss and itch. This is scored by the patient using a visual analogue scale with 0 being 'no itch' (or 'no sleep loss') and 10 being 'worst imaginable itch' (or 'worst imaginable sleep loss').

Patients receiving systemic immunosuppressive treatment were excluded from the study as were patients with severe generalized dermatitis, including dermatitis on the back, in which cases we were unable to apply the patch test.

The study was approved by the National Committee on Health Research Ethics (1-10-72-267-13) and the Danish Data Protection Agency (1-16-02-396-13).

Patch testing

All patients were patch tested with a paediatric series of 31 allergens (Table S1) supplemented by additional allergens as indicated by the child's history as well as the child's own emollients, skincare products and prescribed topical treatment. At the Department of Dermatology and Venereology, Aarhus University Hospital, patients were patch tested with allergens retrieved from AllergEAZE/SmartPractice Denmark (Hilleroed, Denmark). At the Department of Dermatology and Allergy Centre, Odense University Hospital, patients were patch tested with allergens retrieved from Chemotechnique Diagnostics (Malmö, Sweden), Almirall Hermal GmbH (Reinbek, Germany) and allergens from TRUE test[®] retrieved from SmartPractice Denmark (Hilleroed, Denmark). Patch tests were applied in Finn Chambers on Scanpor tape (Norgesplaster[®], Vennesla, Norway). At the Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, patients were patch tested with allergens retrieved from Chemotechnique Diagnostics (Malmö, Sweden) and AllergEAZE/SmartPractice Denmark (Hilleroed, Denmark).

After patch test application at day 0 (D0) and allergen exposure for 2 days, readings were performed D3–4 and D7. In one department, patch tests were also evaluated on the day of removal (D2). Patch test reactions were classified as '+1', '+2', '+3', '+?', 'IR' or 'negative' according to the International Contact Dermatitis Research Group criteria.^{21,22} For a patch test reaction to be considered positive, homogeneous infiltration and erythema of the entire test area were required for a weak positive reaction (+1), with additional vesicles defining a strong positive (+2) and coalescing vesicles an extreme positive (+3) reaction. An irritant reaction, doubtful reaction or negative reading was interpreted as a negative (non-allergic) response.

Relevance of the positive reactions was evaluated according to national guidelines²³ based on patient history, product labels, spot tests or product analyses.

Statistics

A SCORAD <25 was designated as 'mild AD' (grade 1), ≥25–50 as 'moderate AD' (grade 2) and ≥50 as 'severe AD' (grade 3).²⁴

Crude odds ratios were calculated using Fisher's exact test. To adjust for possible confounding factors, a binary logistic regression analysis was performed with 'at least one positive patch test' as the dependent variable, and gender, age group (5–10 years, 11–17 years) and SCORAD severity (grade 1–3) as independent, explanatory variables. To evaluate the risk of contact allergy by localization of eczema, another binary logistic regression analysis was performed with 'at least one positive patch test' as the dependent variable and localization (face and neck, hands, arms, trunk, thighs, lower legs and knees, feet) as independent, explanatory variables.

Results were expressed as odds ratios (OR) with 95% confidence intervals (CI) and employing a 5% significance level. Statistical significance was predefined as a *P*-value of <0.05.

The data analysis was performed using statistical software (STATA statistical software, College Station, TX, USA: StataCorp LP, Release 12).

Results

Sixty-one girls and 39 boys aged 5–17 years (mean age 9.8 years) were included in the study. The severity of AD as assessed by the SCORAD index ranged from 0 to 64.3 (mean SCORAD 29.6). According to the SCORAD index, 44% of the patients had mild AD (SCORAD <25), 45% had moderate AD (SCORAD ≤25–50), and 11% suffered from severe AD (SCORAD ≥50).

Thirty per cent (*n* = 30) of the children had at least one positive patch test reaction (Table 1). Eleven children were sensitized to more than one allergen and 17 children had at least one positive patch test reaction that was relevant to the current skin symptoms. The number of irritant reactions was 15, and 140 reactions were designated as doubtful. The rate of doubtful reactions was the same in children with mild, moderate or severe AD. No irritant reactions were observed among children with severe disease, and the rate of irritant reactions did not differ between children with mild or moderate AD.

Positive patch test reactions

Table 2 shows the allergens listed by frequency of positive reactions. Fifty per cent (*n* = 24) of the positive reactions were to metals (nickel sulphate, cobalt chloride and/or potassium dichromate) with cobalt chloride being the allergen that most often gave a positive reaction as well as the highest number of doubtful and irritant reactions. Cosensitization to more than one metal allergen was seen in three children, and one-third of the positive reactions were considered relevant to the current skin symptoms.

Allergens found in skincare products (formaldehyde, fragrance mix I, diazolidinyl urea, imidazolidinyl urea, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), methylisothiazolinone (MI) and Quaternium 15) constituted 22.9% (*n* = 11) of the positive reactions and 54.5% (*n* = 6) of these reactions were considered relevant to the current

dermatitis. Formaldehyde was the allergen that most often gave relevant reactions (75%). Three children had relevant reactions to sesquiterpene lactone mix, and all had widespread dermatitis including facial dermatitis. One child reacted to one of the corticosteroid markers (hydrocortisone 17 butyrate). This reaction was of current relevance and was only positive on day 7.

Table 3 shows the results of the statistical analysis. The risk of having contact allergy was significantly higher among girls but was not associated with age.

Severity of atopic dermatitis and risk of contact allergy

Having at least one contact allergy was significantly correlated to the severity of AD. Among children with severe AD, 54.5% had at least one positive patch test reaction as compared to 35.6% and 18.2% among children with moderate and mild AD, respectively. We further found a significant association between having hand eczema and contact allergy (Table 4).

Discussion

Our findings confirm that contact allergy is a significant problem in children with AD. In the present study, 30% had one or more unacknowledged contact allergies and in 17% of the children, the allergy was considered relevant to the current skin symptoms, which corresponds well to the latest research.^{17,18,25,26}

As in other similar material on children with AD, metals were the most common allergens. Previous studies have reported the same pattern of sensitization in adult patients^{27–29}, and an increased risk of metal contact allergy in patients with AD has been suggested.^{30,31} In a recent study by Malajian and Belsito,³¹ positive patch test reactions to nickel sulphate, cobalt chloride and potassium dichromate were significantly more frequent among patients with AD as compared to controls. The association between AD and filaggrin is well established.³² Based on a recent study on nickel, which was shown to bind strongly to filaggrin,³³ it has been hypothesized that filaggrin deficiency might facilitate percutaneous penetration of metal allergens.¹³

Worldwide, nickel is the most common allergen in children as well as in adults.^{34,35} However, in the present study cobalt chloride gave the highest rate of positive patch test reactions. This was somewhat surprising but very interesting, as cobalt was named allergen of the year in 2016, the reason being that new information regarding potential sources of exposure to cobalt has come into light.³⁶ Historically, cobalt allergy was linked to concomitant exposure to nickel. However, it is increasingly recognized as an independent sensitizer.³⁷ Eight of the 11 positive reactions to cobalt were solitary, and similar high rates of isolated positive reactions to cobalt have been reported by others.^{37–39} In a previous Danish study, the prevalence of isolated reactions to cobalt chloride was associated with AD.⁴⁰

In this study, the relevance was assessed by reviewing the child's current and past history of exposure. Although many

Table 1 Characteristics of the children with contact allergy

Patient	Age	Gender	Atopic dermatitis severity*	Positive patch test	Maximum strength	Relevance
1	5	F	Mild	PTBP	+2	Glue
2	5	F	Moderate	Potassium dichromate	+1	–
				Black rubber mix	+1	–
				Formaldehyde	+2	Shoes
3	5	M	Moderate	Potassium dichromate	+1	Leather apparel
4	6	F	Moderate	Fragrance mix I	+1	–
5	6	F	Mild	Potassium dichromate	+1	–
				PTPB	+1	–
6	6	F	Moderate	Carba mix	+1	–
7	6	M	Moderate	Nickel sulphate	+1	–
				Cobalt chloride	+1	–
				Potassium dichromate	+1	–
				Sesquiterpene lactone mix	+2	Plants
8	6	M	Moderate	Cobalt chloride	+1	–
				Potassium dichromate	+1	–
9	7	F	Severe	Cobalt chloride	+1	–
10	8	F	Mild	Nickel sulphate	+1	Necklace
11	8	F	Moderate	Formaldehyde	+1	Emollient
12	9	F	Moderate	Nickel sulphate	+1	–
13	9	F	Moderate	Cobalt chloride	+1	–
14	9	F	Mild	Cobalt chloride	+2	–
15	9	F	Severe	Cobalt chloride	+2	Jewellery
16	10	F	Moderate	Fragrance mix I	+2	Emollient
17	10	F	Mild	Cobalt chloride	+1	Earrings
18	11	F	Moderate	Colophonium	+1	–
19	11	F	Severe	Cobalt chloride	+1	–
				Formaldehyde	+1	Emollients
				Sesquiterpene lactone mix	+3	Plants
20	11	F	Severe	Nickel sulphate	+1	Hair clip
				Colophonium	+1	–
21	11	M	Moderate	Potassium Dichromate		–
22	12	F	Severe	Cobalt chloride	+1	Leather shoe
				Potassium dichromate	+1	Leather shoe
23	12	M	Severe	Carba mix	+1	Shin pads
24	13	F	Mild	Nickel sulphate	+1	Relevant, source not given
25	13	F	Moderate	Hydrocortisone-17-butyrate	+1	Topical corticosteroid
26	13	F	Moderate	Cobalt chloride	+1	–
				MCI/MI	+2	Liquid soap
				MI	+3	Shampoo, sunscreen
27	14	F	Moderate	Diazolidinyl urea	+1	–
				Imidazolidinyl urea	+1	–
28	14	M	Moderate	Cobalt chloride	+1	–
				Formaldehyde	+1	–
				Quaternium 15	+1	–
				Sesquiterpene lactone mix	+2	Plants
29	15	F	Mild	Nickel sulphate	+2	–
30	15	M	Mild	Carba mix	+1	–
				Colophonium	+1	–

–, unknown or no relevance to current skin symptoms.

*Severity of atopic dermatitis according to the SCORAD.

Table 2 Allergens listed by frequency of positive patch test reactions

Allergen	Positive	Relevant	Doubtful	Irritant
Cobalt chloride	11	3	19	8
Potassium dichromate	7	2	14	4
Nickel sulphate	6	3	18	1
Formaldehyde	4	3	3	0
Carba mix	3	1	9	0
Sesquiterpene lactone mix	3	3	0	0
Colophonium	3	0	2	0
Fragrance mix I	2	1	15	0
P-tert butylphenol	2	1	2	0
formaldehyde resin				
Black rubber mix	1	0	2	0
Diazolidinyl urea	1	0	3	0
Imidazolidinyl urea	1	0	0	0
Methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI)	1	1	2	0
Methylisothiazolinone	1	1	2	0
Quaternium 15	1	0	0	0
Hydrocortisone 17 butyrate	1	1	1	0
Fragrance mix II	0	0	7	1
Balsam of Peru	0	0	1	0
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	0	0	1	0
Mercaptobenzothiazole	0	0	4	0
Mercapto mix	0	0	1	0
Thiuram mix	0	0	3	0
Paraben mix	0	0	4	1
Lanolin alcohol	0	0	9	0
Tixocortol pivalate	0	0	2	0
Budesonide	0	0	2	0
Ethylene diamine	0	0	4	0
Benzyl alcohol	0	0	0	0
Benzyl benzoate	0	0	3	0
Triethanolamine	0	0	5	0
Phenoxyethanol	0	0	2	0
Total	48	20	140	15

occupational exposures to cobalt are well known,⁴¹ the knowledge regarding causative consumer exposures to cobalt has been limited³⁷ and this is likely even more pronounced with regard to children. Although recent reports have called attention to new cobalt exposure sources among adult patients such as furniture,⁴² laptop computers⁴³ and cosmetics,⁴⁴ sources of exposure are often difficult to identify, making the clinical relevance of a positive patch test reaction to cobalt chloride difficult to determine.⁴⁰ Thus, it is possible that the rate of relevant reactions to cobalt chloride in the present study could be underestimated. Potential recognized sources of cobalt exposure in children include jewellery, buttons, zippers, snaps, leather shoes and laptop computers.

Table 3 The risk of contact allergy as defined by a positive patch test and explanatory variables

Explanatory variables	PPT* % (n/n _{total})	OR† with 95% CI‡	P-value
Gender			
Male	17.9 (7/39)	1 (ref)	
Female	37.7 (23/61)	3.13 (1.14–8.62)	0.03
Age			
5–10 years	30.3 (17/56)	1 (ref)	
11–17 years	29.6 (13/44)	0.79 (0.31–2.01)	0.62
SCORAD			
<25	18.2 (8/44)	1 (ref)	
25–50	35.6 (16/45)	2.79 (1.01–7.66)	0.05
≥50§	54.5 (6/11)	6.31 (1.42–28.07)	0.02

*PPT, at least one positive patch test reaction.

†OR, odds ratio adjusted for gender, age and severity of atopic dermatitis according to total SCORAD.

‡CI, confidence interval.

§No significant difference between children with SCORAD 25–50 and ≥50, respectively ($P = 0.25$).

Significant p -values are indicated in bold (significance level predefined as 5%).

Table 4 Localization of dermatitis and risk of contact allergy

Localization of dermatitis	Number of children	Children with PPT* n (%)†	OR (95% CI)	P-value
Face and neck	51	19 (37.3)	2.32 (0.87–6.17)	0.09
Hands	46	19 (41.3)	2.83 (1.04–7.66)	0.04
Arms	65	21 (32.3)	1.17 (0.04–3.40)	0.78
Trunk	30	10 (33.3)	0.82 (0.27–2.51)	0.73
Thighs	21	9 (42.9)	2.30 (0.70–7.56)	0.18
Knees and lower legs	44	17 (38.6)	1.75 (0.67–4.58)	0.25
Feet	15	7 (46.7)	1.59 (0.42–5.99)	0.44

OR, odds ratio; CI, confidence interval.

*PPT, at least one positive patch test.

†Share of children with at least one positive patch test out of all children with dermatitis at the specific localization.

Cobalt chloride is a strong sensitizer and is considered a difficult substance to use for testing, as it may result in irritant or doubtful reactions,^{41,45} which was also the case in our study. Furthermore, Rystedt⁴⁵ has highlighted the difficulties of reproducing weak (+1) patch test reactions to cobalt chloride, and thus, it could be argued that the high number of positive reactions does not necessarily reflect true cobalt allergy.

Contact allergy to components in skincare products was found in 8% of the children, supporting the hypothesis that prolonged use of skincare products increases the risk of contact sensitization to both ingredients and vehicles. Our finding is in accordance with the results of a recent Dutch study,⁴⁶ in which the authors found that children with AD were significantly more likely to have contact allergy to components of skincare products as compared to children without AD. In another frequently cited study

of 641 children with AD, emollients and antiseptics were the most frequent sensitizers.⁴⁷ Similarly, a general population study found that AD patients had a higher prevalence of contact allergy to ingredients in topical products than those without AD.⁴⁸

Fragrance is a common sensitizer in children.⁴⁹ Further, the authors of a large study from the European Surveillance System on Contact Allergies,⁵ found that the prevalence of contact allergy to fragrance mix is increasing in children. Patients with AD may be at greater risk of fragrance allergy. In several studies, authors have found a significantly higher prevalence of fragrance allergy in AD patients compared to patients without AD.^{11,16,27,50,51} We found a low frequency of contact allergy to fragrance, which is in accordance with similar studies in which children with AD were patch tested.^{17,25,26,52–55} This could reflect that children with AD, implying sensitive skin since early childhood, to a large extent are treated with fragrance-free emollients and skincare products carefully selected by the caregiver. Other allergenic ingredients in skincare products may not be as transparent and recognizable to the consumer. In a recent report, Hamann *et al.*⁵⁶ found that 89% of 187 different skincare products marketed as paediatric and labelled as 'hypoallergenic', 'dermatologist recommended/tested', 'fragrance free' or 'paraben free' contained at least one contact allergen.

Although corticosteroids are not potent sensitizers,⁵⁷ contact allergy and allergic contact dermatitis from topical corticosteroids are not infrequent.⁵⁸ Children with AD are likely exposed to topical corticosteroids since early childhood. The combination of a dysfunctional skin barrier and the prolonged exposure to topical product should in theory increase the risk of sensitization, and an association between AD and contact allergy to corticosteroids has been suggested.^{57,59} However, the authors of previous studies on children with AD have found low frequencies of positive patch test reactions to corticosteroid markers^{25,47,54,55} as was the case in our study. Thus, contact allergy to corticosteroids does not seem to constitute a significant problem in children with AD. The possibility of a complicating contact allergy to topical steroids should nonetheless never be ignored in the evaluation of a child with recalcitrant AD.

Compositae contact allergy caused widespread dermatitis in three children. Compositae allergy was previously considered uncommon in children,^{5,60} but it has been suggested that this impression is due to an inadequate screen.^{61,62} We used sesquiterpene lactone mix as a screen for compositae allergy. However, it could be argued that adding compositae mix would have provided a more thorough screen. Patients with AD appear to be in greater risk of sensitization to compositae.⁶³ In previous studies on patch test reactions in children, contact allergy to sesquiterpene lactone mix was significantly associated with AD.¹⁸ The causality of this relationship is unclear. As compositae contact allergy may mimic AD,^{64,65} it is an important allergy to consider, especially in cases with dermatitis located to hands or face, widespread dermatitis, or aggravation of skin symptoms

during spring or summer.^{60,63} Furthermore, children with AD should be warned against topical use of cosmetics and herbal remedies containing compositae extracts.⁶⁶

Girls were significantly more likely to have contact allergy as compared to boys. This gender difference has been demonstrated in several studies in children^{39,67–70} as well as in adults.^{71,72} The gender difference observed in similar material is often driven by nickel, and this was also the case in our study (shown in Table 1).

We found a strong and significant correlation between the severity of AD and the risk of contact allergy. In contrast to this, Forsbeck *et al.*⁸ and Uehara *et al.*⁷³ in early experimental studies found that patients with severe AD were more difficult to sensitize to dinitrochlorobenzene as compared to patients with mild AD. However, recent clinical studies of patients with AD have demonstrated an association between disease severity and risk of contact allergy^{16,25,28,47} in line with the present study. This could reflect that children with severe AD are more exposed to various emollients and topical treatments as compared to children with limited skin involvement. In a Swedish study, children with moderate to severe AD used moisturizers and topical corticosteroids more frequently than children with mild AD.⁷⁴ It has also been suggested that the disturbed skin barrier and inherent immune alterations in AD promote the development of contact sensitization⁷⁵ and this may be more pronounced in patients with severe skin symptoms.

Another important consideration in this aspect is that contact allergy to certain allergens may mimic widespread AD.^{64,65,76} It has even been suggested that contact sensitization could result in AD.^{11,77} Thus, patients with widespread AD are likely to have unacknowledged contact allergies maintaining the skin symptoms and the possibility of a contact allergy even causing apparent AD should never be rejected.

The risk of contact allergy was significantly increased in children with hand dermatitis. This is in accordance with a recent study by Isaksson *et al.*¹⁷ who patch tested 82 children with AD and found a significantly higher frequency of contact allergy in children with hand and/or foot dermatitis. AD is a strong predisposing factor for hand eczema at any age^{70,78,79}, and the association between hand eczema and contact allergy is well known.^{79,80} In agreement with a recent report by Heede *et al.*,⁷⁸ our findings indicate that children with AD and hand eczema stand out and seem to be at greater risk of contact sensitization.

A limitation of this study is the relatively small sample size, which may weaken the statistical calculations to some extent. The children were tested for the purpose of this study; that is, they were screened for any unknown contact allergy. However, although all consecutive patients eligible for the study were invited to participate, we cannot reject the possibility that children and parents who suspected ACD were more likely to accept to participate in the study. This would bias our results and cause an overestimation of the frequency of contact allergy.

We patch tested the children with a selected series of allergens, and it could be argued that this selection was too limited, thus implying a risk of missing important contact allergies that would have been detected with a broader series of allergens.

Finally, it is well known that patch testing patients with atopic dermatitis implies a risk of false-positive reactions due to hyper-reactive skin.⁸¹ However, we found a relatively low number of positive reactions as compared to other studies of its kind and we do not believe that false-positive reactions constituted a major source of bias.

Conclusion

Children with AD may have unacknowledged contact allergies contributing to or maintaining their skin symptoms and should be patch tested to exclude any underlying allergy, especially if they have severe AD or hand eczema. Special attention should be paid to metals and ingredients in skincare products, whereas allergy to topical steroids does not seem to constitute a significant problem. Caregivers should be advised to use non-scented products with as few components as possible.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Pediatric series of allergens

Supplementary table 1. Pediatric series of allergens.

Allergen	Test concentration	
Nickel sulfate	5% pet.	200 µg/cm ²
Cobalt chloride	1% pet.	20 µg/cm ²
Potassium dichromate	0.5% pet.	25 µg/cm ²
Fragrance mix I	8% pet.	450 µg/cm ²
Fragrance mix II	14% pet.	14% pet.
Balsam of Peru	25% pet.	800 µg/cm ²
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	5% pet.	5% pet.
Carba mix	3% pet.	250 µg/cm ²
Black rubber mix	0.6% pet.	75 µg/cm ²
Mercaptobenzothiazole	2% pet.	75 µg/cm ²
Mercapto mix	1% pet.	75 µg/cm ²
Thiuram mix	1% pet.	25 µg/cm ²
Paraben mix	16% pet.	1000 µg/cm ²
Formaldehyde	1% aq.	180 µg/cm ²
Diazolidinyl urea	2% pet.	550 µg/cm ²
Imidazolidinyl urea	25 aq.	600 µg/cm ²
Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI)	0.01% aq.	4 µg/cm ²
Methylisothiazolinone	0.2% aq.	0.2% aq.
Quaternium 15	1% pet.	100 µg/cm ²
P-tert butylphenol formaldehyd resin	1% pet.	40 µg/cm ²
Colophonium	20% pet.	1500 µg/cm ²
Lanolin alcohol	30% pet.	1000 µg/cm ²
Sesquiterpene lactone mix	0.1% pet.	0.1% pet.
Tixocortol pivalate	0.1% pet.	3 µg/cm ²
Hydrocortison 17 butyrat	1% eth.	20 µg/cm ²
Budesonid	0.1% pet.	1 µg/cm ²
Ethylene diamine	1% pet.	50 µg/cm ²
Benzyl alcohol	1% pet.	1% pet.
Benzyl benzoate	1% pet.	1% pet.
Triethanolamine	2.5% pet.	2.5% pet.
Phenoxyethanol	1% pet.	1% pet.