

Pattern of contact sensitization in patients with and without atopic dermatitis in a hospital-based clinical database

Kim Katrine Bjerring Clemmensen¹, Simon Francis Thomsen¹, Gregor Borut Ernst Jemec² and Tove Agner¹

¹Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, 2400 Copenhagen NV, Denmark and ²Department of Dermatology, Roskilde Hospital, University of Copenhagen, 4000 Roskilde, Denmark

doi:10.1111/cod.12229

Summary

Background. Both atopic dermatitis and contact sensitization are common conditions; however, a definite understanding of the relationship between contact sensitization and atopic dermatitis has not been reached.

Objectives. In this descriptive study, we investigated the differences between positive patch test reactions in patients with and without atopic dermatitis in a patch test cohort, and explored the influence of disease severity.

Patients/materials/methods. Patch test results, information on atopic dermatitis and demographic variables were taken from a database, including all patients patch tested at Bispebjerg and Roskilde Hospitals from January 2009 to January 2013. Severe atopic dermatitis was defined as systemic therapy or hospitalization resulting from atopic dermatitis. All other patients with atopic dermatitis were defined as having mild/moderate disease.

Results. The study included 2221 patients: 293 patients with atopic dermatitis and 1928 without. Forty-one per cent of patients with and 46.2% of patients without atopic dermatitis had at least one positive patch test reaction ($p = 0.092$). More patients with severe atopic dermatitis than patients with non-severe atopic dermatitis had multiple positive patch test reactions (19.4% versus 10.0%, $p = 0.046$).

Conclusions. Overall, we found similar frequencies of positive patch test reactions in patients with and without atopic dermatitis. However, a higher frequency of multiple sensitizations was found in patients with severe atopic dermatitis.

Key words: atopic dermatitis; contact sensitization; patch test; severity.

Atopic dermatitis is a common skin disease that mainly affects children (1), with prevalence rates of up to 20% (2). Atopic dermatitis may persist into adulthood, and contact sensitization may, over the years, complicate the disease.

Contact sensitization affects up to 20% of the general population (3); however, the prevalence of contact sensitization in atopic dermatitis has been discussed regularly over the years, and a definite understanding of the relationship has not been reached.

Although studies have shown conflicting results (4, 5), the traditional understanding is that contact sensitization is less frequent in patients with atopic dermatitis, owing to an impaired cellular immune response of the skin leading to a decreased ability to combat skin infections and raise Type IV allergies (6–9).

More recent studies, however, have indicated that contact sensitization may vary with the severity of

Correspondence: Kim Katrine Bjerring Clemmensen, Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Bispebjerg Bakke 23, 2400 Copenhagen NV, Denmark. Tel: +45 29906384; Fax: +45 35316010. E-mail: kimkatrine@gmail.com

Funding: No specific funding.

Conflict of interests: The authors declare no conflict of interests.

Accepted for publication 26 January 2014

atopic dermatitis, suggesting a more complex relationship (10, 11). An experimental study found that only 33% of patients with severe atopic dermatitis could be sensitized with the potent sensitizer dinitrochlorobenzene, as compared with 95% and 100% of patients with moderate and mild atopic eczema, respectively (12). Similarly, an observational study found a decreased prevalence of contact sensitization in patients with severe atopic dermatitis, but not in patients with mild to moderate disease (10). Conflicting results have also been published, reporting a higher frequency of positive patch test reactions in patients with severe atopic dermatitis (61%) than in those with moderate disease (38%) and mild disease (30%) (13).

Since 2006, when loss of function mutations in the filaggrin gene were first associated with atopic dermatitis (14), atopic dermatitis has been considered to be a barrier disease. It has been hypothesized that allergens may penetrate skin in patients with atopic dermatitis more easily than normal skin, and thereby cause contact sensitization.

In the present study, we investigated the differences between contact sensitization (i.e. positive patch test reactions) in patients with atopic dermatitis and in those without atopic dermatitis in a patch test cohort in two outpatient dermatological hospital clinics, and explored the influence of severity of atopic dermatitis on the frequency of contact sensitization.

Materials and Methods

Population

All patients patch tested at the outpatient clinics at the Dermatological Departments of Bispebjerg and Roskilde Hospitals in the period from 1 January 2009 to 1 January 2013 were included in the study.

The diagnosis of atopic dermatitis was based on the registered MOAHLFA index in the database, including all patients who underwent patch testing during this period. Atopic dermatitis was indicated in this index if the patient had had atopic dermatitis (based on the question 'have you ever had childhood eczema/atopic eczema?'), or if current atopic dermatitis was present [based on UK criteria (15)]. Information on patch test results and demographic variables were obtained from the database. Age was defined as the age of the patient at patch testing.

Information on treatment was obtained from the patient files. The routine in the two departments was that patients were referred to the clinic, patch tested in relation to their first visit, and then, if necessary, prescribed systemic therapy. Only data on the treatment

that the patients received in the hospital clinics were used in this study. Information on treatment prior to referral to one of the two clinics was not used, because it was too uncertain. Patients were coded as having severe atopic dermatitis if they had received systemic therapy for atopic dermatitis (i.e. systemic corticosteroids, azathioprine, mycophenolate mofetil, methotrexate, ciclosporin, biological treatment, acitretin, or alitretinoin) in the hospital clinic, or had been hospitalized because of atopic dermatitis (hospitalization because of eczema during childhood was not registered). Patients who had received systemic therapy for hand eczema on an atopic basis as the only indication were not considered to have severe atopic dermatitis. All other patients with atopic dermatitis were defined as having mild/moderate disease. For 2 patients with atopic dermatitis, the patient files could not be traced; these 2 patients were not included in the analysis of differences between patients with severe and non-severe disease.

The diagnosis of atopic dermatitis in the database was, from January 2011 onwards, always registered by a physician according to the criteria described above. Before 2011, registration was performed partly by technicians, and, to assess the validity of the registered diagnosis of atopic dermatitis before 2011, the information in the database was compared with the information in the patient files. If there were discrepancies, the information from the patient files was used.

Patch testing

All patients were patch tested with the European baseline series (16) supplemented with a number of allergens included as standard in the test series for the two dermatological departments (Table 1). Finn Chambers® (8 mm) were used for patch testing, patches were left on the back for 2 days, and readings were performed on D3 and D7.

In the analysis, the frequency of contact sensitization was investigated as at least one positive test result, including allergens not tested because of an earlier positive test result (NTP), as compared with patients with no positive test results or NTPs. NTPs only comprise test results for allergens where the patients had a recent positive test result with a reaction so strong that the patient would not accept further tests with the allergen. Multiple contact sensitizations were defined as positive patch test reactions to three or more allergens (17).

Patch test results were reported for the individual allergens and for the groups of fragrances, formaldehyde releasers, topical steroids, and isothiazolinones. The fragrance group consisted of *Myroxylon pereirae* (balsam

Table 1. Distribution of contact allergies stratified by atopic dermatitis (AD)

Allergen	With AD (n = 293), no. (%)	Without AD (n = 1928), no. (%)	p-value
Potassium dichromate	39 (13.3)	154 (8.0)	0.003
Neomycin sulfate	4 (1.4)	35 (1.8)	0.585
Thiuram mix	3 (1.0)	45 (2.3)	0.151
p-Phenylenediamine	6 (2.0)	56 (2.9)	0.407
Cobalt chloride	20 (6.8)	137 (7.1)	0.862
Benzocaine	1 (0.3)	9 (0.5)	1.000*
Colophonium	10 (3.4)	69 (3.6)	0.886
Clioquinol	1 (0.3)	14 (0.7)	0.709*
<i>Myroxylon perei</i>	12 (4.1)	80 (4.1)	0.966
N-isopropyl-N-phenyl-p-phenylenediamine	0 (0.0)	12 (0.6)	0.386*
Lanolin alcohol	1 (0.3)	10 (0.5)	1.000*
Mercapto mix	1 (0.3)	12 (0.6)	1.000*
Epoxy resin	1 (0.3)	17 (0.9)	0.497*
Paraben mix	2 (0.7)	8 (0.4)	0.630*
Butyl phenolformaldehyde resin	2 (0.7)	17 (0.9)	1.000*
Fragrance mix I	11 (3.8)	112 (5.8)	0.152
Quaternium 15	4 (1.4)	15 (0.8)	0.302*
Nickel sulfate	39 (13.3)	353 (18.3)	0.037
Mercaptobenzothiazole	1 (0.3)	23 (1.2)	0.356*
Sesquiterpene lactone mix	5 (1.7)	31 (1.6)	0.806*
Primin	1 (0.3)	4 (0.2)	0.507*
Budesonide	4 (1.4)	13 (0.7)	0.266*
Tixocortol pivalate	3 (1.0)	27 (1.4)	0.789*
Methyldibromo glutaronitrile	6 (2.0)	55 (2.9)	0.432
α -Hexyl cinnamal	7 (2.4)	55 (2.9)	0.654
Fragrance mix II	10 (3.4)	137 (7.1)	0.018
2-Bromo-2-nitropropane-1,3-diol	2 (0.7)	10 (0.5)	0.666*
Sorbic acid	2 (0.7)	4 (0.2)	0.182*
Sorbitan sesquileate	3 (1.0)	24 (1.2)	1.000*
Diazolidinyl urea	2 (0.7)	11 (0.6)	0.686*
Imidazolidinyl urea	1 (0.3)	9 (0.5)	1.000*
<i>Evernia furfuracea</i>	12 (4.1)	78 (4.0)	0.968
Iodopropynyl butylcarbamate	1 (0.3)	15 (0.8)	0.711*
Ethylenediamine dihydrochloride	7 (2.4)	26 (1.3)	0.190*
Disperse Blue mix 106/124	5 (1.7)	22 (1.1)	0.390*
Phenoxyethanol	0 (0.0)	2 (0.1)	1.000*
Formaldehyde	7 (2.4)	25 (1.3)	0.181*
Methylchloroisothiazolinone/methylisothiazolinone	4 (1.4)	47 (2.4)	0.253
Chlorhexidine digluconate	4 (1.4)	22 (1.1)	0.768*
Hydrocortisone-17-butyrate	3 (1.0)	14 (0.7)	0.483*
DMDM hydantoin	5 (1.7)	9 (0.5)	0.028*
Methylisothiazolinone	1 (0.3)	16 (0.8)	0.716*
Benzisothiazolinone	0 (0.0)	1 (0.1)	1.000*
At least one contact allergy	120 (41.0)	891 (46.2)	0.092
Three or more contact allergies	36 (12.3)	221 (11.5)	0.681
Fragrance group	31 (10.6)	290 (15.0)	0.043 [†]
Formaldehyde releaser	11 (3.8)	50 (2.6)	0.257
Topical corticosteroids	6 (2.0)	41 (2.1)	0.930
Isothiazolinones	5 (1.7)	50 (2.6)	0.363

*Fisher's exact test.

[†]Significant.

of Peru), fragrance mix I, fragrance mix II, α -hexyl cinnamal, and *Evernia furfuracea*. The formaldehyde releaser group consisted of the allergens quaternium 15, 2-bromo-2-nitropropane-1,3-diol, diazolidinyl urea, imidazolidinyl

urea, formaldehyde, and DMDM hydantoin. The topical corticosteroid group consisted of budesonide, tixocortol-21-pivalate, and hydrocortisone-17-butyrate. The isothiazolinone group consisted of methylchloro

isothiazolinone/methylisothiazolinone (3:1 mixture), methylisothiazolinone, and benzisothiazolinone.

Statistical analysis

The characteristics of the patients were compared by use of the chi-square or Fisher's exact test. The Mann–Whitney *U*-test was applied to test for differences in continuous variables between groups. Data analysis was performed with SPSS™ 20.0 (SPSS Inc., Chicago, IL, USA). Logistic regression analysis was used to adjust for age differences between patients with and without atopic dermatitis for the tests shown in Table 1 that had a *p*-value of < 0.100. The allergens in Table 1 that reached a significance level of 0.05 were analysed for differences between atopic dermatitis patients with severe and those with non-severe disease.

The study was approved by the Danish Data Protection Agency.

Results

The study included 2221 patients: 293 patients with atopic dermatitis and 1928 without atopic dermatitis. In total, 788 (35.5%) males and 1433 (64.5%) females were registered in the database. Among the patients, 11.3% had occupational disease, 29.6% had hand eczema, 7.5% had leg eczema, 11.1% had face eczema, and 42.5% were > 40 years of age.

MOAHLFA

Table 2 shows the MOAHLFA index stratified by atopic dermatitis. The two groups did not differ with respect to sex, occupational eczema, hand eczema, leg eczema, or face eczema, but fewer patients were > 40 years of age in the group of patients with atopic dermatitis than in the group of patients without atopic dermatitis (24.6% versus 45.2%, *p* < 0.0001). The median/mean age for patients with atopic dermatitis was 32.4/34.5 years, as compared with 48.0/48.1 years for patients without atopic dermatitis.

Patch test results

Table 1 shows the distribution of positive patch test results for the 43 allergens tested. Overall, 41.0% and 46.2% of patients with and without atopic dermatitis, respectively, had at least one positive patch test reaction (*p* = 0.092). A higher proportion of patients with atopic dermatitis than of patients without atopic dermatitis had positive patch test reactions to potassium dichromate (*p* = 0.003) and

Table 2. MOAHLFA index stratified by atopic dermatitis (AD) status

	With AD (n = 293), no. (%)	Without AD (n = 1928), no. (%)	<i>p</i> -value
Male	95 (32.4)	693 (35.9)	0.241
Occupational	30 (10.2)	220 (11.4)	0.554
Hand eczema	96 (32.8)	561 (29.1)	0.200
Leg eczema	18 (6.1)	148 (7.7)	0.353
Face eczema	39 (13.3)	207 (10.7)	0.191
Age > 40 years	72 (24.6)	872 (45.2)	< 0.0001*

*Significant.

to DMDM hydantoin (*p* = 0.028). A lower proportion of patients with atopic dermatitis than of patients without atopic dermatitis had positive patch test reactions to nickel sulfate (*p* = 0.037), and there was also a lower proportion of patients with atopic dermatitis than of patients without atopic dermatitis with positive patch test reactions to fragrance mix II (*p* = 0.018). When these contact allergy frequencies were age-adjusted, reactions to potassium dichromate (*p* < 0.0001), nickel sulfate (*p* = 0.024) and DMDM hydantoin (*p* = 0.034) differed significantly between patients with and without atopic dermatitis (Table 3).

When fragrance allergens were combined, a significantly lower proportion (10.6%) of patients with atopic dermatitis than of patients without atopic dermatitis (15.0%) had at least one positive patch test reaction or NTP (*p* = 0.043), but this difference was not significant after age adjustment (*p* = 0.283) (Table 3). There were no significant differences between patients with and without atopic dermatitis for the allergen groups formaldehyde releasers (*p* = 0.257), topical corticosteroids (*p* = 0.930), and isothiazolinones (*p* = 0.363).

With respect to multiple allergies, no difference between patients with and without atopic dermatitis was found (*p* = 0.681).

Effect of severity of atopic dermatitis on contact sensitivity

Among patients with atopic dermatitis, we found a non-significantly higher proportion of patients with at least one positive patch test reaction among patients who had undergone systemic therapy or been hospitalized because of their eczema than among patients with less severe disease (50.0% and 38.4%, respectively, *p* = 0.100) (Table 4). Patients with severe atopic dermatitis had a higher frequency of allergy to nickel sulfate than patients with non-severe atopic dermatitis (21.0% versus 11.4%, *p* = 0.049). This was also seen for potassium dichromate (21.0% versus 11.4%, *p* = 0.049) (Table 4). There was

Table 3. Distribution of contact allergies stratified by atopic dermatitis (AD) adjusted for age

	With AD (n = 293), no. (%)	Without AD (n = 1928), no. (%)	OR (95% CI)	p-value (chi-square)	Adjusted OR [†] (95% CI)	p-value
Potassium dichromate	39 (13.3)	154 (8.0)	1.77 (1.22–2.57)	0.003	2.37 (1.59–3.55)	< 0.0001*
Nickel sulfate	39 (13.3)	353 (18.3)	0.69 (0.48–0.98)	0.037	0.66 (0.45–0.95)	0.024*
Fragrance mix II	10 (3.4)	137 (7.1)	0.46 (0.24–0.89)	0.018	0.55 (0.28–1.08)	0.080
DMDM hydantoin	5 (1.7)	9 (0.5)	3.70 (1.23–11.12)	0.028	3.59 (1.10–11.70)	0.034*
At least one contact allergy	120 (41.0)	891 (46.2)	0.81 (0.63–1.04)	0.092	0.88 (0.68–1.14)	0.337
Fragrance group	31 (10.6)	290 (15.0)	0.67 (0.45–0.99)	0.043	0.80 (0.53–1.20)	0.283

CI, confidence interval; OR, odds ratio.

Fragrance group: *Myroxylon pereirae* (balsam of Peru), fragrance mix I, fragrance mix II, α -hexyl cinnamal, and *Evernia furfuracea*.

Three patients with no age data were excluded from the adjusted analysis.

*Significant.

[†]Adjusted for age.

no difference in the frequency of positive patch test reactions to fragrances and DMDM hydantoin between patients with severe and non-severe atopic dermatitis. More patients with severe atopic dermatitis had multiple positive patch test reactions, with 19.4% having more than three contact allergies as compared with 10.0% of the non-severe atopic dermatitis group ($p = 0.046$). Demographic differences were seen between severe and mild/moderate atopic dermatitis; almost half (43.5%) of the patients with severe atopic dermatitis were males, as compared with 29.7% of those with non-severe disease ($p = 0.039$). The group with severe disease was older (mean age of 38.4 versus 33.5 years, $p = 0.031$) (Table 4).

Discussion

Overall, we found no differences in the proportion of patients with positive patch test reactions between patients with and without atopic dermatitis. When all fragrance allergens were combined, fewer patients with atopic dermatitis than patients without atopic dermatitis had fragrance allergy, but this difference was not significant after adjustment for age. After age adjustment, patients with atopic dermatitis had a higher frequency of potassium dichromate and DMDM hydantoin allergy and a lower frequency of nickel sulfate allergy than patients without atopic dermatitis. Assessment of relevance was not attempted.

Many factors should be considered when discussing the association between contact sensitization and atopic dermatitis. Traditionally, patients with atopic dermatitis have been considered to have a decreased risk of contact sensitization, owing to suppression of cell-mediated immunity (18). However, as atopic dermatitis is now considered to be primarily a skin barrier disease, atopic dermatitis patients could be at higher risk of contact

Table 4. Distribution of contact allergy allergen groups stratified by severity of atopic dermatitis (AD)

	Severe AD (n = 62), no. (%)	Mild/moderate AD (n = 229), no. (%)	p-value
Male	27 (43.5)	68 (29.7)	0.039*
Mean age (years)	38.4	33.5	0.031*
Contact allergies			
At least one contact allergy	31 (50.0)	88 (38.4)	0.100
Three or more contact allergies	12 (19.4)	23 (10.0)	0.046*
Potassium dichromate	13 (21.0)	26 (11.4)	0.049*
Nickel sulfate	13 (21.0)	26 (11.4)	0.049*
Fragrance mix II	3 (4.8)	7 (3.1)	0.449 [†]
DMDM hydantoin	0 (0.0)	5 (2.2)	0.588 [†]
Fragrance group	8 (12.9)	23 (10.0)	0.517

Severe AD: systemic therapy including oral corticosteroids or hospitalization because of AD. Not severe AD: no systemic therapy or hospitalization because of AD.

Fragrance group: *Myroxylon pereirae* (balsam of Peru), fragrance mix I, fragrance mix II, α -hexyl cinnamal, and *Evernia furfuracea*.

Note: Allergens included in the table were those with differences in frequency among patients with and without AD.

*Significant.

[†]Fisher's exact test.

sensitization, because of a dysfunctional skin barrier facilitating the penetration of potential allergens (18, 19). However, different patterns of exposure should also be considered. Increased exposure to topical treatment may lead to a higher prevalence of contact sensitization, but, on the other hand, patients with childhood atopic dermatitis may be more aware of allergen exposure throughout their lives, and may have done more to limit their exposure, for example choosing non-fragranced cosmetics.

In the present study, we found no overall significant differences in the frequency of contact sensitization

between patients with and without atopic dermatitis. Previously, some studies have reported a lower frequency of contact sensitization in patients with atopic dermatitis (6–9); however, a recent general population study found a higher rate of contact sensitization (19), whereas a study from the same group using data from a tertiary hospital registry found a lower prevalence of contact sensitization in patients with atopic dermatitis (10). These discrepancies suggest that additional observational and experimental data are urgently needed.

When comparing the results of this study with the results of other studies, it is important to keep in mind differences in study design. In particular, differences in study population, in patch test readings and in the diagnostic criteria used for atopic dermatitis may influence the results.

In this study, increased contact sensitivity to potassium dichromate in patients with atopic dermatitis was found, as was also the case in previous studies (10, 20). It is well known that patch testing with metals may cause irritant reactions in atopic skin; however, in the present study, the reading of patch tests was performed according to International Contact Dermatitis Research Group recommendations (21), and the fact that chromium allergy was increased but nickel allergy was decreased in atopics is in support of irritant reactions not being mistaken as allergic. Previously, a positive association between nickel sensitization and flaggrin loss of function mutations has been suggested (22), but we found decreased nickel contact allergy in the patients with atopic dermatitis, in disagreement with this hypothesis. However, as we have no data on flaggrin mutation in our study, no definite conclusion can be drawn. The relevance of the increased contact sensitivity to DMDM hydantoin in atopic dermatitis patients has not been assessed, but could be related to the use of cosmetics, soaps and lotions containing this preservative. An increased use of topical treatment could also hypothetically lead to an increased frequency of allergy to other biocides or corticosteroid allergy, but this was not found.

We found a significantly lower proportion of patients with atopic dermatitis with positive patch test reactions to fragrances; however, this finding was not significant after age adjustment. In a previous study, increased fragrance allergy in patients with atopic dermatitis was seen; however, this was a general population study, in contrast to our study, which is based on a hospital database and it is therefore not directly comparable (19). In another study, a similar prevalence of allergy to fragrance mix I between all patients and patients with atopic dermatitis was found

(10). When we considered positive reactions to fragrance mix I or II, we found differences between patients with and without atopic dermatitis, but the differences were not significant. For *M. pereirae*, Thyssen et al. found an overall prevalence of 4.5%, as compared with 2.6% among patients with atopic dermatitis, whereas we found the same prevalence in patients with and without atopic dermatitis (10).

Severity and contact sensitization

In this study, a non-significantly higher frequency of positive patch test reactions was found for patients with severe atopic dermatitis, and multiple sensitizations were more frequent in patients with severe atopic dermatitis. This is in agreement with a previous Danish study of polysensitization, which reported that patients with atopic dermatitis were overrepresented among polysensitized patients (23). In a study by Belhadjali et al., where the severity of atopic dermatitis was based on SCORAD, a higher frequency of contact sensitization was found in patients with severe atopic dermatitis than in patients with mild atopic dermatitis (13). An experimental study has indicated a lower rate of development of contact sensitization to dinitrochlorobenzene in patients with severe atopic dermatitis than in patients with moderate and mild atopic dermatitis (12). However, many factors are involved in contact sensitization, and our strongly increased nickel sensitization and the increased frequency of multiple sensitizations should be interpreted in light of the fact that impairment of the skin barrier is generally more pronounced in severe cases. Also, the possibility of irritant reactions being misread as true positive reactions in patients with more severe disease should be kept in mind, as discussed above. When we looked at nickel allergy alone, a significantly higher prevalence of nickel allergy was found in patients with severe atopic dermatitis. Female sex and older age (owing to legislation against nickel that has been in effect in Denmark since 1990) are associated with a higher frequency of nickel allergy (24). However, as a larger proportion of the patients with severe atopic dermatitis were males (43.5% versus 29.7%), and because the difference in mean age was < 5 years, this is not likely to explain the higher nickel allergy prevalence among the patients with severe atopic dermatitis. The fact that chromate contact allergy was found more frequently in patients with severe atopic disease, as well as more frequently in atopics than in non-atopics, may indicate that chromate allergy is of significant clinical importance. However, this assumption needs confirmation from future studies. We found no difference in fragrance and DMDM hydantoin allergy

between patients with severe and moderate/mild atopic dermatitis.

Strengths and limitations

A strength of this study is that it includes all patients patch tested in two hospitals' dermatological departments. Furthermore, the standard panel of allergens in this study included 43 allergens. A limitation of the study is that it was performed on a selected population, so the data cannot be generalized to the general population. Further limitations are that it is not known whether there could be different indications for patch testing for different patient groups, and patients with and without atopic dermatitis differed significantly in age. Also, we were not able to control for the possible use of more extensive testing in patients with severe disease.

Conclusions

Overall, we found a similar frequency of positive patch test reactions in patients with and without atopic dermatitis. With respect to specific allergens, a higher number of positive patch test reactions to chromate and DMDM hydantoin, and fewer positive patch test reactions to nickel, were found in patients with atopic dermatitis than in patients without. When we related contact sensitization to the severity of atopic dermatitis, a higher rate of multiple sensitizations and a higher frequency of positive patch test reactions to nickel and potassium dichromate were found in patients with severe atopic dermatitis than in patients with less severe disease. The importance of patch testing patients with atopic dermatitis is evident, and, in particular, patients with severe atopic dermatitis should be patch tested before the start of systemic therapy.

References

- Williams H C. Atopic dermatitis. *N Engl J Med* 2005; **352**: 2314–2324.
- Beasley R. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; **351**: 1225–1232.
- Thyssen J P, Linneberg A, Menné T, Johansen J D. The epidemiology of contact allergy in the general population: prevalence and main findings. *Contact Dermatitis* 2007; **57**: 287–299.
- Lammintausta K, Kalimo K, Fagerlund V L. Patch test reactions in atopic patients. *Contact Dermatitis* 1992; **26**: 234–240.
- Lugovic L, Lipozencic J. Contact hypersensitivity in atopic dermatitis. *Arh Hig Rada Toksikol* 1997; **48**: 287–296.
- Cronin E, McFadden J P. Patients with atopic eczema do become sensitized to contact allergens. *Contact Dermatitis* 1993; **28**: 225–228.
- de Groot A C. The frequency of contact allergy in atopic patients with dermatitis. *Contact Dermatitis* 1990; **22**: 273–277.
- Jones H E, Lewis C W, McMarlin S L. Allergic contact sensitivity in atopic dermatitis. *Arch Dermatol* 1973; **107**: 217–222.
- Rystedt I. Atopic background in patients with occupational hand eczema. *Contact Dermatitis* 1985; **12**: 247–254.
- Thyssen J P, Johansen J D, Linneberg A, Menné T, Engkilde K. The association between contact sensitization and atopic disease by linkage of a clinical database and a nationwide patient registry. *Allergy* 2012; **67**: 1157–1164.
- Mailhol C, Lauwers-Cances V, Rancé F, Paul C, Giordano-Labadie F. Prevalence and risk factors for allergic contact dermatitis to topical treatment in atopic dermatitis: a study in 641 children. *Allergy* 2009; **64**: 801–806.
- Uehara M, Sawai T. A longitudinal study of contact sensitivity in patients with atopic dermatitis. *Arch Dermatol* 1989; **125**: 366–368.
- Belhadjali H, Mohamed M, Youssef M, Mandhouj S, Chakroun M, Zili J. Contact sensitization in atopic dermatitis: results of a prospective study of 89 cases in Tunisia. *Contact Dermatitis* 2008; **58**: 188–189.
- Palmer C N A, Irvine A D, Terron-Kwiatkowski A et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nat Genet* 2006; **38**: 441–446.
- Williams H C, Burney P G, Pembroke A C, Hay R J. The U.K. Working Party's diagnostic criteria for atopic dermatitis. III. Independent hospital validation. *Br J Dermatol* 1994; **131**: 406–416.
- Bruze M, Andersen K E, Goossens A, on behalf of the ESCD and EECDRG. Recommendation to include fragrance mix 2 and hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyr) in the European baseline patch test series. *Contact Dermatitis* 2008; **58**: 129–133.
- Carlsen B C, Andersen K E, Menné T, Johansen J D. Patients with multiple contact allergies: a review. *Contact Dermatitis* 2008; **58**: 1–8.
- Schnuch A, Uter W, Reich K. Allergic contact dermatitis and atopic eczema. In: *Handbook of Atopic Eczema*, 2nd edition, Ring J, Przybilla B, Ruzicka T (eds): Berlin, Heidelberg, Springer-Verlag, 2006: pp. 178–201.
- Thyssen J P, Linneberg A, Engkilde K, Menné T, Johansen J D. Contact sensitization to common haptens is associated with atopic dermatitis: new insight. *Br J Dermatol* 2012; **166**: 1255–1261.
- Landeck L, Schalock P, Baden L, González E. Contact sensitization pattern in 172 atopic subjects. *Int J Dermatol* 2011; **50**: 806–810.
- Magnusson B, Blohm S G, Fregert S et al. Routine patch testing. II. Proposed basic series of test substances for Scandinavian countries and general remarks on testing technique. *Acta Derm Venereol* 1966; **46**: 153–158.
- Thyssen J P, Johansen J D, Linneberg A et al. The association between null mutations in the filaggrin gene and contact sensitization to nickel and other chemicals in the general population. *Br J Dermatol* 2010; **162**: 1278–1285.
- Carlsen B C, Andersen K E, Menné T, Johansen J D. Characterization of the polysensitized patient: a matched case–control study. *Contact Dermatitis* 2009; **6**: 22–30.
- Thyssen J P, Johansen J D, Menné T, Nielsen N H, Linneberg A. Nickel allergy in Danish women before and after nickel regulation. *N Engl J Med* 2009; **360**: 2259–2260.