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Allergic contact dermatitis in atopic individuals: Results of a 30-year retrospective study

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Abstract

Background: The association between atopic dermatitis (AD) and contact allergy, remains unclear, with studies to date showing conflicting results.

Objectives: To investigate the prevalence of contact allergy in AD individuals compared to those without AD.

Methods: Results of 46 250 patients patch tested in a single centre over a span of 30 years were reviewed, comparing those with AD with those without AD. Collected data were analysed with corrections for multiple confounding variables, including date of patch testing to account for changes in allergens tested over the period.

Results: Nine allergens showed a statistically significant difference between the two groups. Contact allergy to nickel, cobalt and primin was less likely to arise in those with AD, whilst substances found in topical dermatological products were more likely to be associated with AD.

Conclusions: This is the largest single centre study of contact sensitization in atopy reported to date. The previously reported association between contact allergy to sesquiterpene lactone and AD is reinforced. The decreased incidence of metal allergy suggests distinct immunological effector mechanisms in sensitization to these allergens. In keeping with previous publications, exposure to topical treatments for AD can result in sensitisation and contact allergy and clinicians should consider patch testing in AD individuals who report worsening of their skin despite continued treatment with topical medicaments.

KEYWORDS

allergic contact dermatitis, atopic dermatitis, contact allergy, contact dermatitis

1 | INTRODUCTION

Atopic dermatitis (AD) is a relapsing, inflammatory condition influenced by both genetic and environmental factors. Contact allergy has a reported prevalence of up to 20%.¹ There is discordance in the literature, with some studies suggesting an increased

prevalence of contact allergy in individuals with AD and other studies either failing to confirm this or showing the reverse.²⁻⁴ Previous studies have suggested a higher threshold for induction of contact allergy in atopic individuals²; however, patients with AD may have increased exposure to topical medicaments with consequent increase in risk of developing contact allergy.⁵ To probe this complex relationship between contact allergy and AD, we analysed data in a large series of patients undergoing patch testing in our centre

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and compared sensitisation in patients with AD compared to those without AD.

2 | METHODS

We performed a retrospective study of patients referred for patch testing to the Department of Cutaneous Allergy at St John's Institute of Dermatology from 1984 to 2014. Patients with AD were identified during initial clinical assessment prior to patch testing (retrospectively and prospectively conforming with the UK Working Party's diagnostic criteria)⁶: pruritus, chronic or relapsing dermatitis affecting flexural surfaces in adults and extensor surfaces in children.

Patch testing was performed using Finn Chambers on Scanpor tape and readings performed on days 2/3 and 4/5 compliant with the Menné and White criteria,⁷ with results being considered positive if at least a + reaction was present. Information was extracted from our database on reactions to allergens contained within the extended European baseline series (as used during the pertinent periods). Comparison was made with the group of patients who did not have AD who were patch tested during the same time period. Methylchloroisothiazolinone /methylisothiazolinone (MCI/MI) is considered as a separate category, with methylisothiazolinone alone tested only from 2012. Prevalences and odds ratio (OR) were calculated, with adjusted OR and associated *P*-values calculated by logistic regression for the following variables: age, sex, and year of testing. All *P*-values are presented following correction for multiple testing with the Bonferroni-Holm method with 37 tests used for correction (corresponding to the number of allergens tested in the baseline series).

3 | RESULTS

A total of 46 250 patients (27 061 female patients; 19 189 male patients) were patch tested from 1984 to 2014, of whom 14 732 (31.86%) had AD (Table 1). The median age for those who had one or more positive patch test reactions was 29 (range 0–96 years), with a higher median age of 41 (range 0–94 years) in those who had negative patch tests. At least one positive reaction was seen in 13 592 (73.62%) individuals with AD and 12 657 (70.59%) individuals without AD (Tables 1 and 2).

The 10 allergens with the highest crude prevalence are as follows (Table 3, Figure 1; the prevalences are expressed as percent/100, ie, probability to be sensitised): nickel (0.17), fragrance mix I (0.07), methylisothiazolinone (0.06), cobalt (0.05), colophonium (0.041), neomycin sulfate (0.035), *p*-phenylenediamine (PPD) (0.035), thiuram mix (0.033), *Myroxylon pereirae* resin (0.029), and sodium metabisulfite (0.029). These were largely similar in both subgroups of AD and non-AD patients (Figure 2), aside from neomycin being the sixth (AD prevalence: 0.031; non-AD: 0.037) and potassium dichromate being the ninth most prevalent (prevalence in AD: 0.025; non-AD: 0.027) amongst individuals with AD. Prevalences adjusted for age and sex are also shown for those with and without AD (Table 3, Figure S51).

TABLE 1 Demographics

	n = 46 250
Sex	
Male	19 189
Female	27 061
Male patients with and without AD	
With AD	4579
Without AD	12 305
Female patients with and without AD	
With AD	9006
Without AD	18 055
Age in relation to test results (median, range in years)	
≥1 positive	29 (0–96)
Negative	41 (0–94)
Diagnosis of AD (n, %)	
With AD	14 732 (31.86)
Without AD	31 518 (68.14)
Patients with ≥1 positive test result (n, %)	
With AD	13 592 (73.62)
Without AD	12 657 (70.59)

Abbreviation: AD, atopic dermatitis.

To correct for age, sex, and date of testing, we calculated adjusted OR and associated *P*-values by logistic regression. Significant differences between AD and non-AD patients were found in nine allergens: cobalt, imidazolidinyl urea, sesquiterpene lactone (SL) mix, neomycin, nickel, fragrance mix I, primin, tixocortol pivalate, and lanolin (wool alcohol) (Figure 3). Sensitisation to cobalt, nickel, and primin (adjusted OR of 0.80, 0.65, and 0.49 respectively) were less likely in AD patients, with nickel being highly significant (*P* < .0001). Conversely, sensitisation to imidazolidinyl urea (adjusted OR: 1.53), SL mix (1.44), neomycin (1.27), fragrance mix I (1.19), tixocortol pivalate (1.88), and lanolin (1.56) were more likely in individuals with AD.

4 | DISCUSSION

Individuals with AD may be at higher risk of contact sensitisation than those without AD, due to defective skin barrier and frequent usage of topical products.⁴ In keeping with this hypothesis, filaggrin gene mutation, which is associated with contact allergy, may cause skin barrier dysfunction in atopy.⁸ Interestingly, interleukins associated with Th2-driven immune responses may lead to reduced filaggrin levels,⁹ further increasing the risk of contact sensitisation in individuals with AD.^{10–12}

Despite interest in this area, epidemiological studies have been conflicting.^{4,13} A recent meta-analysis by Hamann et al showed no significant difference in the overall prevalence of contact sensitisation to common allergens in those with AD versus those without AD,³ although there was an increase amongst atopic individuals compared to the general population. Comparison of children with and without

TABLE 2 Results by allergen in those with AD and without AD

Allergen	AD positive (n)	AD negative (n)	Non-AD positive (n)	Non-AD negative (n)	Total tested (n)
<i>Myroxylon pereirae</i> resin	289	12 040	891	26 232	39 816
2-Bromo-2-nitropropane-1,3-diol	114	11 791	185	25 104	37 194
Caine mix	117	11 705	294	25 167	37 283
Carba mix	45	7983	172	17 098	25 298
Cetostearyl alcohol (cetearyl alcohol)	30	10 860	77	22 402	33 369
Chlorocresol	12	9353	37	21 229	30 631
Cobalt chloride ^a	730	12 435	1837	28 098	43 100
Colophonium	489	12 902	1297	28 720	56 799
Potassium dichromate	342	12 970	818	29 208	43 338
Quaternium-15	221	13 017	610	29 282	43 130
Epoxy resin	106	13 173	352	29 692	43 323
Ethylenediamine	145	13 131	393	29 658	43 327
Methyldibromo glutaronitrile	109	9179	256	17 659	27 203
Fragrance mix II	43	1818	68	2589	4518
Formaldehyde	270	13 122	767	29 257	43 416
Imidazolidinyl urea ^a	83	11 910	208	25 601	37 802
Diazolidinyl urea	78	9747	182	19 264	29 271
Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI)	202	12 342	416	27 249	40 209
Sesquiterpene lactone mix ^a	107	10 440	330	21 475	32 352
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	24	2690	45	4066	6825
Mercaptobenzothiazole	130	13 149	321	29 713	43 313
Mercapto mix	118	13 282	294	29 756	43 450
Methylisothiazolinone	63	958	93	1438	2552
Neomycin sulfate ^a	416	12 994	1141	28 892	43 443
Nickel sulfate ^a	2078	11 170	5268	24 549	43 065
Paraben mix	54	13 345	189	29 849	43 437
Fragrance mix I ^a	863	12 493	2171	27 762	43 289
<i>p</i> -Phenylenediamine (PPD)	293	9789	792	19 514	30 388
<i>N</i> -Isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine (IPPD)	45	13 230	164	29 876	43 315
Primin ^a	26	13 186	212	29 610	43 034
PTBP resin	94	13 176	328	29 708	43 306
Quinoline mix	55	12 006	196	25 572	37 829
Sodium metabisulfite	14	844	50	1283	2191
Thiuram mix	373	13 022	1092	28 932	43 419
Tixocortol pivalate ^a	134	9053	196	17 089	26 472
Lanolin ^a (wool alcohols)	222	13 192	466	29 571	43 451
Disperse Yellow 3	53	8761	107	16 389	25 310

Abbreviations: AD, atopic dermatitis; PTBP, *p*-tert-butylphenol formaldehyde resin.

^aStatistically significant difference.

AD suggested a similar risk of developing contact allergy but with differences in the spectrum of sensitisation.¹⁴

Due to their increased usage of topical products, atopic individuals may be more likely to become sensitised to fragrances, topical antibiotics, and preservatives.^{5,8,12,15,16} This was reflected in our data, with fragrance mix I, tixocortol pivalate, neomycin, imidazolidinyl urea, and lanolin allergy

more likely in AD patients, although formaldehyde itself did not reach the threshold of significance. Overall prevalence of sensitisation to neomycin has decreased in several countries in recent years, possibly due to availability being more restricted.¹⁷ Although other formaldehyde-releasers aside from imidazolidinyl urea showed adjusted ORs of >1 (2-bromo-2-nitropropane-1, 3-diol: 1.41; diazolidinyl urea: 1.38), this was not

TABLE 3 Prevalence (expressed as probability to be sensitised) and odds ratio of contact allergy in extended baseline series in those with and without AD

Allergen	Overall prevalence	PR in AD (95% CI)	Age-adjusted PR in AD	Sex-adjusted PR in AD	PR in non-AD (95% CI)	Age-adjusted PR in non-AD	Sex-adjusted PR in non-AD	Adjusted OR	Adjusted P-value
Myroxylon pereiirae resin	0.029	0.023 (0.008–0.026)	0.027	0.021	0.032 (0.030–0.350)	0.026	0.0291	0.70	1.04 >.99
2-Bromo-2-nitropropane-1,3-diol	0.008	0.009 (0.007–0.011)	0.009	0.008	0.007 (0.006–0.008)	0.005	0.006	1.31	1.41 .15
Caine mix	0.011	0.009 (0.008–0.011)	0.013	0.008	0.011 (0.10–0.012)	0.008	0.009	0.85	1.40 .08
Carba mix	0.008	0.005 (0.004–0.007)	0.004	0.003	0.009 (0.085–0.011)	0.005	0.005	0.56	1.10 >.99
Cetearyl alcohol	0.003	0.002 (0.001–0.003)	0.002	0.002	0.003 (0.002–0.004)	0.002	0.002	0.80	1.31 >.99
Chlorocresol	0.001	0.001 (6.0×10^{-4} –0.002)	0.001	9.60×10^{-3}	0.001 (0.001–0.002)	0.001	0.001	0.73	1.43 >.99
Cobalt chloride ^a	0.059	0.055 (0.051–0.059)	0.055	0.052	0.061 (0.058–0.064)	0.062	0.061	0.89	0.80 .0001
Colophonium	0.041	0.036 (0.033–0.039)	0.042	0.035	0.043 (0.040–0.045)	0.041	0.042	0.83	1.03 >.99
Potassium dichromate	0.026	0.025 (0.023–0.028)	0.0295	0.025	0.027 (0.025–0.029)	0.025	0.026	0.94	1.20 .15
Quaternium-15	0.019	0.016 (0.014–0.019)	0.018	0.015	0.020 (0.018–0.022)	0.019	0.020	0.81	0.93 >.99
Epoxy resin	0.010	0.007 (0.006–0.009)	0.009	0.008	0.011 (0.010–0.013)	0.010	0.011	0.67	0.92 >.99
Ethylenediamine	0.012	0.010 (0.009–0.012)	0.012	0.010	0.013 (0.011–0.014)	0.012	0.012	0.83	1.17 >.99
Methyl(dibromo glutaronitrile	0.013	0.011 (0.009–0.014)	0.010	0.007	0.014 (0.012–0.016)	0.007	0.008	0.81	0.96 >.99
Fragrance mix II	0.024	0.023 (0.016–0.031)	0.003	0.003	0.025 (0.020–0.032)	0.002	0.002	0.90	1.13 >.99
Formaldehyde	0.023	0.020 (0.017–0.022)	0.022	0.019	0.025 (0.023–0.027)	0.0252	0.025	0.78	0.86 >.99
Imidazolidinyl urea ^a	0.007	0.006 (0.005–0.008)	0.008	0.006	0.008 (0.007–0.009)	6.18×10^{-3}	0.006	0.85	1.53 .04
Diazolidinyl urea	0.008	0.007 (0.006–0.009)	0.007	0.005	0.009 (0.008–0.010)	0.005	0.006	0.84	1.38 .49
Methylchloroisothiazolinone/ methylisothiazolinone (MCI / MI)	0.015	0.016 (0.014–0.018)	0.017	0.014	0.015 (0.013–0.016)	0.013	0.013	1.07	1.03 >.99
Sesquiterpene lactone mix ^a	0.010	0.010 (0.008–0.012)	0.011	0.008	0.015 (0.013–0.016)	0.009	0.010	0.66	1.44 .04
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	0.010	0.008 (0.005–0.013)	0.002	0.001	0.010 (0.008–0.014)	0.001	0.001	0.80	0.94 >.99
Mercaptobenzothiazole	0.010	0.009 (0.008–0.011)	0.009	0.009	0.010 (0.008–0.014)	0.010	0.010	0.91	1.13 >.99
Mercapto mix	0.009	0.008 (0.007–0.010)	0.009	0.008	0.009 (0.008–0.010)	0.009	0.009	0.89	1.18 >.99
Methylisothiazolinone	0.061	0.061 (0.004–0.078)	0.005	0.004	0.060 (0.049–0.074)	0.002	0.003	1.01	1.18 >.99
Neomycin ^a	0.035	0.031 (0.028–0.034)	0.038	0.030	0.037 (0.035–0.040)	0.034	0.037	0.81	1.27 .002
Nickel sulfate ^a	0.170	0.156 (0.150–0.163)	0.149	0.145	0.176 (0.172–0.181)	0.182	0.178	0.86	0.65 <.0001
Paraben mix	0.005	0.004 (0.003–0.005)	0.004	0.003	0.006 (0.005–0.007)	0.005	0.006	0.63	1.02 >.99
Fragrance mix I ^a	0.070	0.064 (0.060–0.068)	0.076	0.062	0.072 (0.069–0.075)	0.067	0.071	0.88	1.19 .001
p-Phenylenediamine (PPD)	0.035	0.029 (0.025–0.032)	0.025	0.020	0.039 (0.036–0.041)	0.024	0.026	0.73	0.83 .36
N-Isopropyl-N'-phenyl-p- phenylenediamine (IPPD)	0.004	0.003 (0.002–0.004)	0.003	0.003	0.005 (0.004–0.0006)	0.005	0.005	0.61	0.77 >.99
Primin ^a	0.005	0.001 (0.009–0.027)	0.003	0.001	0.007 (0.006–0.008)	0.006	0.007	0.27	0.49 .0003

(Continues)

TABLE 3 (Continued)

Allergen	Overall prevalence	PR in AD (95% CI)	Age-adjusted PR in AD	Sex-adjusted PR in AD	PR in non-AD (95% CI)	Age-adjusted PR in non-AD	Sex-adjusted PR in non-AD	Adjusted OR	Adjusted P-value
PTBP resin	0.009	0.007 (0.005–0.008)	0.007	0.006	0.010 (0.009–0.012)	0.010	0.010	0.64 0.69	.08
Quinoline mix	0.006	0.004 (0.003–0.005)	0.005	0.004	0.007 (0.006–0.008)	0.005	0.006	0.59 1.12	>.99
Sodium metabisulfite	0.029	0.016 (0.009–0.027)	0.001	9.88×10^{-3}	0.037 (0.028–0.049)	0.001	0.001	0.42 0.52	>.99
Thiuram mix	0.033	0.027 (0.025–0.030)	0.034	0.027	0.036 (0.028–0.049)	0.033	0.036	0.75 1.09	>.99
Tixocortol pivalate ^a	0.012	0.014 (0.012–0.017)	0.010	0.009	0.011 (0.009–0.013)	0.005	0.006	1.29 1.88	<.0001
Lanolin ^a	0.015	0.016 (0.014–0.018)	0.020	0.016	0.015 (0.014–0.016)	0.014	0.015	1.06 1.56	<.0001
Disperse yellow 3	0.006	0.006 (0.004–0.007)	0.004	0.003	0.006 (0.005–0.007)	0.003	0.003	0.92 0.93	>.99

Abbreviations: AD, atopic dermatitis; CI, confidence interval; OR, odds ratio; PTBP, *p*-tert-butylphenol formaldehyde resin^aStatistically significant.

statistically significant. Imidazolidinyl urea was previously shown to have been present in many cosmetic products in both Europe and the USA,¹⁸ with a reported rise in prevalence of contact allergy to it in the United Kingdom between 2000 and 2004–2005,¹⁹ from 0.5% to 0.9%. Our overall prevalence for this is slightly lower, at 0.7%. Sensitisation to lanolin alcohol (wool alcohol; found in cosmetic products and topical medications) is associated with AD, leg ulceration, and stasis dermatitis, conditions that typically result in prolonged application of topical products.^{14,20,21} Weak allergens, such as lanolin alcohol, can result in sensitisation following exposure over many years.²⁰ Increasingly, SL mix sensitivity has been associated with AD, and may be mediated via inhalation of airborne pollen or usage of topical products with compositae allergens.^{3,22}

Age is an important determinant of the risk of sensitisation, and allergens exhibit differential changes in incidence of sensitisation in association with chronological aging. A previous publication from our centre has shown increasing prevalence of contact allergy with age in our population of patients referred for patch testing,²³ including allergy to fragrance mix I, formaldehyde, and methylisothiazolinone. However, peak prevalence to nickel and cobalt sensitisation occurs earlier in life, with prevalence gradually decreasing with age.²³ Differences in the age composition of the population are therefore adjusted for when comparing patients with and without AD. In our cohort, the median age of those with at least one positive result on patch testing was young (29 years) compared to those who were completely negative on testing (41 years). It is therefore important to correct for differences in the age composition of the tested population in patients with and without AD.

We observed a highly significant decrease in the risk of sensitisation to nickel and cobalt in individuals with AD. The overall prevalence of sensitisation to nickel, cobalt, and chromium in our population is similar to those reported by the European Surveillance System on Contact Allergies (ESSCA)²⁴ and, consistent with previous reports,^{25–27} nickel was the most common allergen to which sensitisation occurred (crude prevalence 0.17). Of note, metal contact allergens, in contrast to other contact allergens, can directly stimulate TLR-4, promoting sensitisation. Interestingly, cytokines associated with atopic dermatitis (IL-4 and IL-13) have been shown to “downregulate” TLR-4 expression.^{28,29}

Filaggrin deficiency has been identified as a risk factor for development of nickel sensitisation.³⁰ It has been proposed that a reduction in nickel chelation due to reduced filaggrin levels may increase the risk of sensitisation to nickel in individuals with AD^{31–33}; however, our data do not support this hypothesis. We do not have information on ear piercing in our patient population, which could be pertinent since sensitisation following ear piercings is thought to occur via an alternative route. For example, Thyssen et al found a positive association between nickel allergy and AD only in non-pierced individuals.³⁴

We also observed a reduced risk of sensitisation to primin in individuals with AD. Primin is an extremely potent allergen; however, it is rarely clinically relevant now due to the availability of primin-free *Primula obconica*,³⁵ and consequently it has been omitted from the European baseline series.³⁶ It was difficult to determine the mechanism by which primin allergy was reduced in our cohort of AD patients. One could postulate that general avoidance of plants in AD

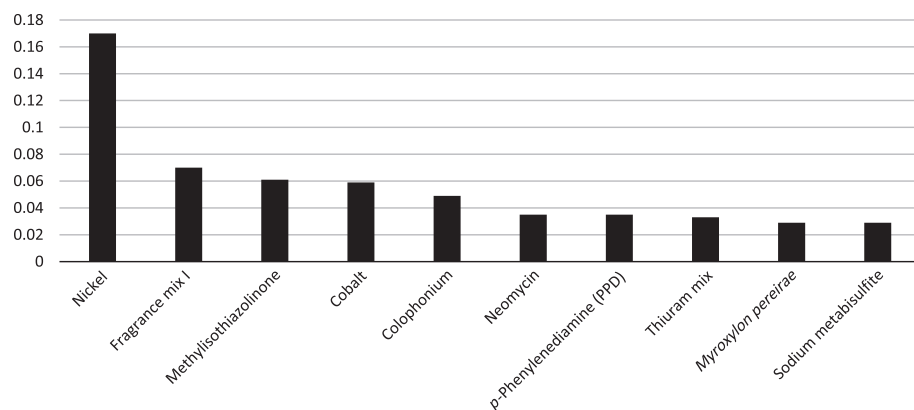


FIGURE 1 Ten most prevalent allergens

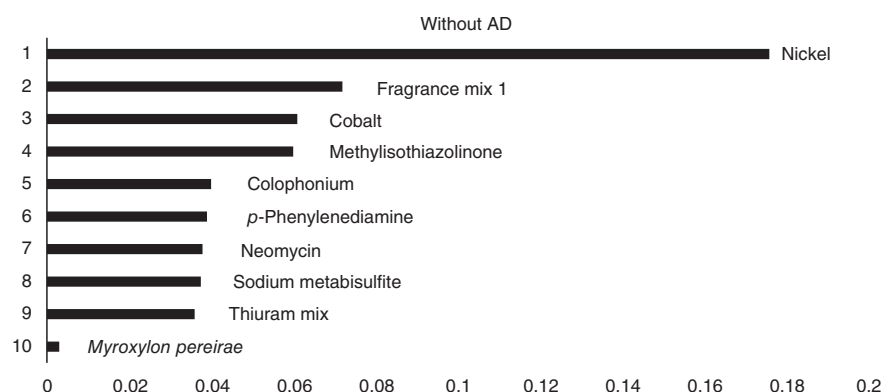
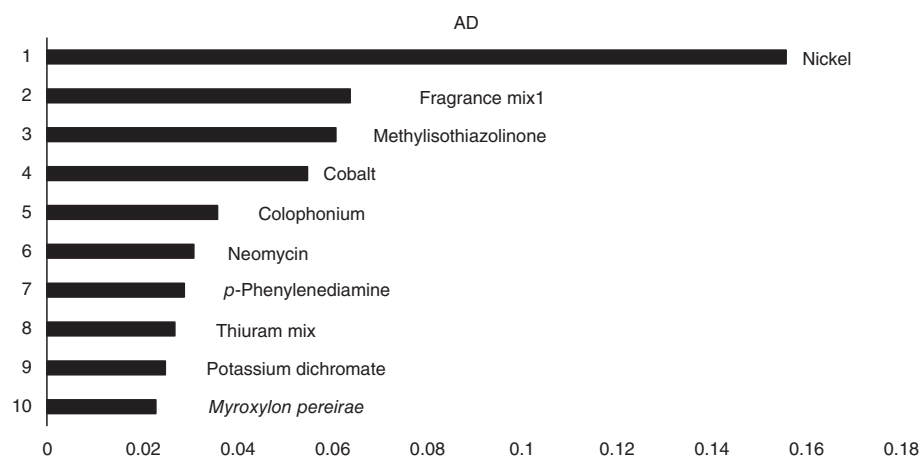


FIGURE 2 Ten most prevalent allergens in those with atopic dermatitis (AD) and without AD

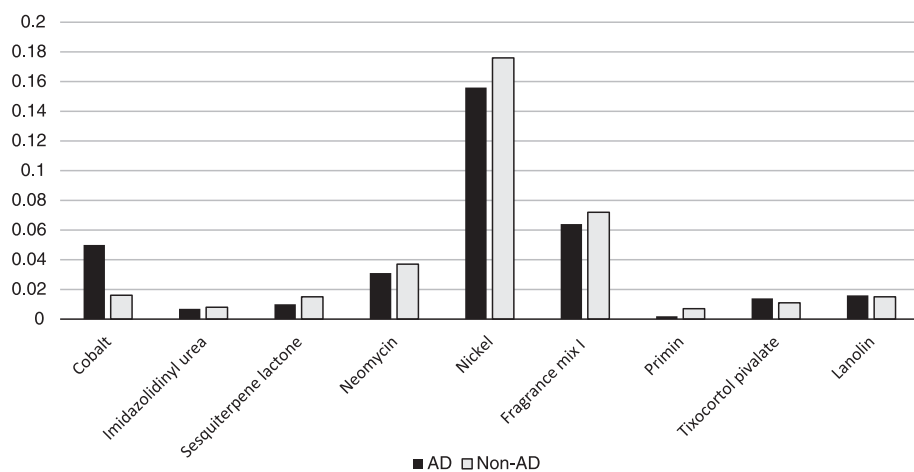


FIGURE 3 Prevalence of allergens with statistically significant difference in those with atopic dermatitis (AD) versus without AD

patients with associated pollen sensitivity could lead to reduced exposure. Alternatively, differences in the immune environment might be contributory. It has been proposed that patients with severe AD are less susceptible to sensitisation to potent allergens, as there is a threshold beyond which exposure through chronically defective skin barrier leads to tolerance.^{2,37,38} Additionally, because AD is considered to be immunologically driven by a Th2 response, it may be anticipated that affected individuals are less susceptible to develop contact allergy, which is primarily Th1-driven.¹⁰⁻¹² Sensitisation to contact allergens via the Th2 rather than the Th1 route has been suggested in individuals with AD,¹⁰ and this could explain differences in sensitisation.

5 | CONCLUSION

To our knowledge, this is the largest single-centre study over a 30-year period comparing contact sensitisation amongst those with AD to those without AD. As would be expected, sensitisation to allergens found in topical medicaments was more prevalent in those with AD. On the other hand, nickel and cobalt seem to be significantly less likely to occur in this group, although the reason for this remains unclear. Repeated exposure and prolonged usage of topical products in the AD population can result in sensitisation; hence, it is important to consider contact sensitivity and patch testing in those who do not appear to be responding to treatment.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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REFERENCES

- Thyssen JP, Linneberg A, Menné T, Johansen JD. The epidemiology of contact allergy in the general population--prevalence and main findings. *Contact Dermatitis*. 2007;57:287-299.
- Rees J, Friedmann PS, Matthews JN. Contact sensitivity to dinitrochlorobenzene is impaired in atopic subjects. Controversy revisited. *Arch Dermatol*. 1990;126:1173-1175.
- Hamann CR, Hamann D, Egeberg A, Johansen JD, Silverberg J, Thyssen JP. Association between atopic dermatitis and contact sensitization: a systematic review and meta-analysis. *J Am Acad Dermatol*. 2017;77:70-78.
- Milam EC, Jacob SE, Cohen DE. Contact dermatitis in the patient with atopic dermatitis. *J Allergy Clin Immunol Pract*. 2019;7:18-26.
- Halling-Overgaard AS, Kezic S, Jakasa I, Engebretsen KA, Maibach H, Thyssen JP. Skin absorption through atopic dermatitis skin: a systematic review. *Br J Dermatol*. 2017;177:84-106.
- Williams HC, Burney PG, Hay RJ, et al. The U.K. Working Party's diagnostic criteria for atopic dermatitis. I. Derivation of a minimum set of discriminators for atopic dermatitis. *Br J Dermatol*. 1994;131:383-396.
- Menné T, White I. Standardization in contact dermatitis. *Contact Dermatitis*. 2008;58:321.
- Thyssen JP, Linneberg A, Engkilde K, Menné T, Johansen JD. Contact sensitization to common haptens is associated with atopic dermatitis: new insight. *Br J Dermatol*. 2012;166:1255-1261.
- Howell MD, Kim BE, Gao P, et al. Cytokine modulation of atopic dermatitis filaggrin skin expression. *J Allergy Clin Immunol*. 2007;120:150-155.
- Newell L, Polak ME, Perera J, et al. Sensitization via healthy skin programs Th2 responses in individuals with atopic dermatitis. *J Invest Dermatol*. 2013;133:2372-2380.
- Correa da Rosa J, Malajian D, Shemer A, et al. Patients with atopic dermatitis have attenuated and distinct contact hypersensitivity responses to common allergens in skin. *J Allergy Clin Immunol*. 2015;135:712-720.
- Thyssen JP, McFadden JP, Kimber I. The multiple factors affecting the association between atopic dermatitis and contact sensitization. *Allergy*. 2014;69:28-36.
- Uehara M, Sawai T. A longitudinal study of contact sensitivity in patients with atopic dermatitis. *Arch Dermatol*. 1989;125:366-368.
- Lubbes S, Rustemeyer T, Sillevs Smitt JH, Schuttelaar ML, Middelkamp-Hup MA. Contact sensitization in Dutch children and adolescents with and without atopic dermatitis – a retrospective analysis. *Contact Dermatitis*. 2017;76:151-159.
- Shaughnessy CN, Malajian D, Belsito DV. Cutaneous delayed-type hypersensitivity in patients with atopic dermatitis: reactivity to topical preservatives. *J Am Acad Dermatol*. 2014;70:102-107.
- Heine G, Schnuch A, Uter W, Worm M. Type-IV sensitization profile of individuals with atopic eczema: results from the Information Network of Departments of Dermatology (IVDK) and the German Contact Dermatitis Research Group (DKG). *Allergy*. 2006;61:611-616.
- Gilissen L, Goossens A. Frequency and trends of contact allergy to and iatrogenic contact dermatitis caused by topical drugs over a 25-year period. *Contact Dermatitis*. 2016;75:290-302.
- de Groot AC, Veenstra M. Formaldehyde-releasers in cosmetics in the USA and in Europe. *Contact Dermatitis*. 2010;62:221-224.
- Jong CT, Statham BN, Green CM, et al. Contact sensitivity to preservatives in the UK, 2004-2005: results of multicentre study. *Contact Dermatitis*. 2007;57:165-168.
- Fransen M, Overgaard LEK, Johansen JD, Thyssen JP. Contact allergy to lanolin: temporal changes in prevalence and association with atopic dermatitis. *Contact Dermatitis*. 2018;78:70-75.
- Warshaw EM, Nelsen DD, Maibach HI, et al. Positive patch test reactions to lanolin: cross-sectional data from the North American Contact Dermatitis Group, 1994 to 2006. *Dermatitis*. 2009;20:79-88.
- Paulsen E, Andersen KE. Sensitization patterns in compositae-allergic patients with current or past atopic dermatitis. *Contact Dermatitis*. 2013;68:277-285.
- Lynch MD, McFadden JP, White JM, Banerjee P, White IR. Age-specific profiling of cutaneous allergy at high temporal resolution suggests age-related alterations in regulatory immune function. *J Allergy Clin Immunol*. 2017;140:1451-3.e5.
- Uter W, Amario-Hita JC, Balato A, et al. European Surveillance System on Contact Allergies (ESSCA): results with the European baseline series, 2013/14. *J Eur Acad Dermatol Venereol*. 2017;31:1516-1525.
- Mortz CG, Lauritsen JM, Bindslev-Jensen C, Andersen KE. Prevalence of atopic dermatitis, asthma, allergic rhinitis, and hand and contact dermatitis in adolescents. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis. *Br J Dermatol*. 2001;144:523-532.
- Nielsen NH, Linneberg A, Menné T, et al. Allergic contact sensitization in an adult Danish population: two cross-sectional surveys eight years apart (the Copenhagen Allergy Study). *Acta Derm Venereol*. 2001;81:31-34.
- Dotterud LK, Smith-Sivertsen T. Allergic contact sensitization in the general adult population: a population-based study from northern Norway. *Contact Dermatitis*. 2007;56:10-15.

28. Schmidt M, Raghavan B, Müller V, et al. Crucial role for human toll-like receptor 4 in the development of contact allergy to nickel. *Nat Immunol*. 2010;11:814-819.
29. Rachmawati D, Bontkes HJ, Verstege MI, et al. Transition metal sensing by Toll-like receptor-4: next to nickel, cobalt and palladium are potent human dendritic cell stimulators. *Contact Dermatitis*. 2013;68:331-338.
30. Thyssen JP, Johansen JD, 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.
31. Hegewald J, Uter W, Pfahlberg A, Geier J, Schnuch A. A multifactorial analysis of concurrent patch-test reactions to nickel, cobalt, and chromate. *Allergy*. 2005;60:372-378.
32. Malajian D, Belsito DV. Cutaneous delayed-type hypersensitivity in patients with atopic dermatitis. *J Am Acad Dermatol*. 2013;69:232-237.
33. Ross-Hansen K, Ostergaard O, Tanassi JT, et al. Filaggrin is a predominant member of the denaturation-resistant nickel-binding proteome of human epidermis. *J Invest Dermatol*. 2014;134:1164-1166.
34. Thyssen JP, Linneberg A, Ross-Hansen K, et al. Filaggrin mutations are strongly associated with contact sensitization in individuals with dermatitis. *Contact Dermatitis*. 2013;68:273-276.
35. Christensen LP, Larsen E. Primin-free *Primula obconica* plants available. *Contact Dermatitis*. 2000;43:45-46.
36. Wilkinson M, Gonçalo M, Aerts O, et al. The European baseline series and recommended additions: 2019. *Contact Dermatitis*. 2019;80:1-4.
37. Kohli N, Nedorost S. Inflamed skin predisposes to sensitization to less potent allergens. *J Am Acad Dermatol*. 2016;75:312-7.e1.
38. Thyssen JP, Johansen JD, 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.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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Supplementary figure 1: Ten most prevalent allergens following age-adjustment in atopic dermatitis (AD) and without AD

