

Report

Contact sensitization pattern in 172 atopic subjects

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Abstract

Background Some authors have claimed a decreased cell-mediated immunity among atopic individuals, which would lead to observations of decreased rates of allergic contact dermatitis (ACD).

Objectives The purpose of our study was to investigate contact sensitization patterns in atopic subjects compared with non-atopic subjects.

Methods Patch test data for 1247 patients undergoing patch testing at Massachusetts General Hospital between 1990 and 2006 were reviewed. Using accepted criteria, 172 subjects were classified as atopic individuals (AIs), and 1075 were classified as non-atopic individuals (NAIs). Sensitization rates were compared between these two groups.

Results Sensitization rates (65.0% and 57.4% in the AI and NAI groups, respectively) and average numbers of positive responses (1.5 and 1.2 in the AI and NAI groups, respectively) were higher in AIs. Leading allergens observed were similar for both groups. Sensitization to potassium dichromate and phenylmercuric acetate was significantly greater in the AI group. The most frequent diagnosis in both groups was ACD (41.9% and 45.5% in the AI and NAI groups, respectively). In addition, more NAIs who were employed in occupations with exposure to wet and/or irritant conditions had hand eczema ($P < 0.005$).

Conclusions Atopic individuals were shown to be at least as likely to have ACD as NAIs. The most common sensitizers were similar in both groups, suggesting common sources of sensitization.

Introduction

The term “atopy” describes a polygenic inherited disposition to develop one or more of the following disorders: atopic dermatitis (AD), allergic rhinoconjunctivitis (AR), and allergic asthma (AA). Although consensus exists that atopic individuals have a heightened tendency to develop immunoglobulin E (IgE) type I antibodies to environmental factors, some authors have claimed a decreased cell-mediated immunity,¹ which would lead to the observation of decreased rates of allergic contact dermatitis (ACD). The purpose of our study was to investigate contact sensitization patterns in atopic patients compared with those without atopy.

Materials and methods

Study approval was obtained from the Institutional Review Board of Massachusetts General Hospital (MGH). Data were then collected from chart review for 1247 patients who underwent patch testing to the standard and, depending on the individual's history and clinical picture, to the supplemental series (e.g. preservatives, cosmetic tray, etc.) available at the Contact

Dermatitis Clinic, MGH, between 1990 and 2006. Test procedures and readings were conducted using a standardized technique in accordance with international recommendations by applying Finn chambers (Epitest Oy, Tuusula, Finland) affixed with Scanpor tape (Norgesplaster A/S, Vennesla, Norway) to the upper back.² Allergens were purchased from Almirall-Hermal (Reinbek, Germany). Tests remained in place for two days, and sites were initially evaluated at 48 hours and again at 72 hours. In selected rare cases, a 120-hour and/or 168-hour reading was performed. In this analysis only 48- and 72-hour readings were incorporated. All interviews and interpretations of patch test reactions over the 17-year study period were performed by a single observer (EG). Patch test readings were classified according to the International Contact Dermatitis Research Group (ICDRG) recommendations as allergic (+, ++, +++), questionable, irritant, or negative.²

To reduce the potential for false positive reactions, positive allergic results were rated based on a minimum of erythematous infiltration, vesiculation or both. Questionable, irritant and negative reactions were considered negative.

Using accepted criteria, 172 patients were classified as atopic individuals (AIs) according to a current history of at least one of AD, AR, or AA.³ The remaining 1075 subjects were categorized

Table 1 General epidemiologic data on tested atopic and non-atopic individuals following the MO(A)HLFA^a index

	Als (n = 172)	NAIs (n = 1075)	P-value, Als vs. NAIs
Male, n (%)	51 (29.7%)	322 (30%)	0.936
Occupational, n (%)	5 (3%)	109 (10%)	0.020
Hand, n (%)	42 (24.4%)	371 (34.5%)	0.009
Leg, n (%)	21 (12.2%)	168 (15.6%)	0.246
Face, n (%)	48 (27.9%)	261 (24.3%)	0.306
Age, years, mean $\pm$ SD	46.7 $\pm$ 15.21	46.2 $\pm$ 15.19	0.702

^aAtopy was deleted and is not tabulated.

MOAHLFA index: *male*, *occupational*, *atopic*, *hand*, *leg* or *face* dermatitis, *age* > 40 years.

Als, atopic individuals; NAIs, non-atopic individuals; SD, standard deviation.

as non-atopic individuals (NAIs). In cases of AD, patients were only tested during periods of quiescent inflammatory disease. For a descriptive characterization of the patient population, the MOAHLFA index (*male*, *occupational*, *atopic*, *hand*, *leg*, or *face* dermatitis, *age* > 40 years) was used as shown in Table 1.⁴ The relevance of positive results was determined by assessing the subject's past history of contact with the allergen and whether the symptoms expressed were consistent with the clinical picture and history. Probable and definite relevance were pooled under "relevant", whereas possible, past and unknown relevance were designated "non-relevant".

Statistical evaluation

Data were recorded, retrieved, and evaluated using a computerized database (Microsoft Access 2000), Microsoft Cooperation, Redmont, WA, USA. Statistical analysis was performed using SPSS Version 15.0 (SPSS Inc., Chicago, IL, USA). Frequencies were compared using the Chi-squared test and Fisher's exact test where appropriate. Statistical analysis was performed on the 23 allergens occurring most frequently among the 172 atopic patients. The multiple level of significance was $\alpha = 0.05$. To adapt for multiple testing, the level of significance for allergens tested was adjusted to $\alpha = 0.002$ (Bonferroni correction of factor 23).

Results

Sensitization rates (65.0% and 57.4% in the AI and NAI groups, respectively) and average numbers of positive responses (1.5 and 1.2 in the AI and NAI groups, respectively) were significantly higher in the AI group ($P < 0.05$). No significant difference between the AI and NAI groups was observed with regard to patient age and gender distribution (Table 1). Leading allergens observed for both groups were nickel and fragrance mix (Table 2).

Although there was a trend among AIs towards higher sensitization to triclosan and wool alcohols, this finding was significant only for potassium dichromate and phenylmercuric acetate.

A subgroup analysis (data not shown) was conducted to investigate possible differences between patients affected by cutaneous (AD) and mucous membrane (AR and AA) involvement. No statistical differences between the groups emerged for any of the allergens listed in Table 2.

Allergic contact dermatitis was the most frequent diagnosis in both the AI and NAI groups (41.9% and 45.5% in the AI and NAI groups, respectively). As demonstrated in Table 3, more NAIs were employed in occupations with exposure to wet and/or irritant conditions ($P < 0.005$), and a final diagnosis of irritant contact dermatitis was seen more commonly in this group (NAI: 3.8%; AI: 2.3%).

Discussion

Early studies suggested that AIs are less prone than NAIs to developing type IV sensitizations. This assumption derived from investigations in which patients with severe AD were not readily sensitized by repeated application of dinitrochlorobenzene (DNCB) in an experimental setting. However, once the AD improved or in periods of remission, the DNCB challenges turned positive.^{1,5} There are several possible reasons why AIs might have an increased incidence of allergic contact sensitization and, more specifically, to allergens from topical medications: AIs are known to use an increased amount of topical medications and moisturizers because of their disease, and the disruption of their skin barrier permits the increased penetration of allergens. Recent findings from patch test studies investigating the sensitization profile of AIs suggest rates and patterns of allergic contact sensitization comparable with those of NAIs.⁶

A comparison of the general epidemiologic data from our study, as presented in Table 1, shows no significant differences between the AI and NAI groups. By contrast, and as an unexpected finding, statistically significantly more NAIs than AIs were evaluated for occupational dermatitis and hand eczema. Furthermore, the NAIs had a higher prevalence of irritant contact dermatitis derived from wet and irritant occupational exposure. Although the low numbers of AIs in these categories are too small for valid comparison, they may reflect avoidance by AIs of occupations with inherently high risk for contact irritation. Conversely, early detection and avoidance may preclude the referral of AIs to specialized clinics for patch testing. Heine *et al.*,⁶ in their comparative patch test study of AIs and NAIs, reported a higher prevalence of face and hand involvement among atopic patients.

Table 2 Most frequent allergens with rate of sensitization and relevancies in atopic individuals (AIs) compared with non-atopic individuals (NAIs)

Allergen	AIs (n = 172)		Relevant reactions, %	NAIs (n = 1075)		P-value, AIs vs. NAIs
	n	%		n	%	
Nickel sulfate	29	16.9	12.1	153	14.2	0.380
Fragrance mix	25	14.5	5.3	170	15.8	0.651
Balsam of Peru	19	11.0	5.8	125	11.6	0.801
N-isopropyl-N-phenyl-p-phenylenediamine (IPPD)	16	9.3	4.7	30	2.8	0.660
Wool alcohols	15	8.7	4.4	43	4.0	0.007
Cobalt chloride	15	8.7	2.0	78	7.3	0.503
Potassium dichromate	14	8.1	1.9	31	2.9	0.001
Thimerosal	14	8.1	3.7	23	2.1	0.685
Phenylmercuric acetate	10	5.8	2.9	20	1.9	0
Quaternium 15	10	5.8	2.9	71	6.6	0.684
Methylchloroisothiazolinone/methylisothiazolinone (3:1 in water)	9	5.2	1.7	12	1.1	0.097
Formaldehyde	8	4.7	4.7	66	6.1	0.436
Neomycin sulfate	7	4.1	1.4	52	4.8	0.605
Thiuram mix	6	3.5	1.2	56	5.2	0.329
Sodium metabisulfite	6	3.5	1.8	8	0.7	0.538
Benzalkonium chloride	5	2.9	0.7	6	0.6	0.907
Colophony	5	2.9	2.3	46	4.3	0.393
Glutaraldehyde	5	2.9	0	5	0.5	0.572
Epoxy resin	4	2.3	1.5	30	2.8	0.722
Triclosan	4	2.3	0	0	0	0.006
Carba mix	4	2.3	0	30	2.8	0.677
Mercapto mix	3	1.7	1.1	14	1.3	0.648
Mercaptobenzothiazole	3	1.7	0	0	0	0.030

Table 3 Occupational backgrounds of tested atopic individuals (AIs) and non-atopic individuals (NAIs)

	AIs (n = 172)		NAIs (n = 1075)		P-value, AI vs. NAI
	n	%	n	%	
Office	51	29.7	274	25.5	0.248
Home/retired	35	20.3	145	13.5	0.017
Medical	25	14.5	147	13.7	0.761
Teaching	12	7.0	91	8.5	0.51
Wet/irritant work	5	2.9	100	9.3	0.005
Sales	5	2.9	24	2.2	0.586
Construction	5	2.9	18	1.7	0.268
Industrial	4	2.3	37	3.4	0.446
Food	4	2.3	26	2.4	0.941
Other and unknown	16	15.5	164	19.8	0.039

The study did not find any statistical differences between the two groups when their occupational backgrounds were assessed.⁶

With regard to whether AIs tend to develop allergic contact sensitization as frequently as NAIs, our study demonstrated that atopic subjects had statistically significantly more positive patch tests than NAIs (1.52 and 1.26 in the AI and NAI groups, respectively; $P = 0.006$).

Other studies have made similar findings, showing that AIs are at least as likely to have ACD as NAIs.^{6–8}

Considerable differences between AIs and NAIs were observed in regard to some of the most frequent sensitizers, such as potassium dichromate, phenylmercuric acetate, triclosan, and wool alcohol. This finding was statistically significant for potassium dichromate and phenylmercuric acetate.

Wool alcohol is a non-drying organic compound produced from lanolin, found in sheep's wool, which has been reacted with acetic acid. For decades, vehicles for prescription creams and skin care products have contained lanolin. Frequent contact sensitization to wool alcohol is associated with stasis dermatitis and leg ulcers.⁹ However, because AIs exhibit dry and inflamed skin, their use of topical agents containing lanolin may be higher than among NAIs. Previous patch test studies have demonstrated similarly increased lanolin sensitization among AIs, with sensitization rates of around 4%.^{6,10} Other reports have shown no significant difference between the groups for atopic eczema status and wool alcohol allergy.⁹

Triclosan, a common antibacterial chemical, is another substance to which AIs show higher sensitization rates. In the USA, triclosan is frequently used as an ingredient in

both medical and consumer products, such as deodorants and toothpastes. Its common presence results in a generally high exposure rate, which may account for increased rates of contact sensitization.¹¹ Our results appear to conflict with European reports showing that triclosan is well tolerated in AIs with low sensitizing potential and citing sensitization rates of <1%, even in high-risk patients affected by eczema.¹²

Phenylmercuric acetate, found in preservatives, is a potent sensitizer described as causing frequent type IV sensitization in AIs.¹³ Dastychová *et al.*¹³ reported a 7.8% prevalence of sensitization in a study population of 194 AIs. Sensitization to phenylmercuric acetate can be linked to the frequent use of moisturizers and topical medications that contain this preservative.

The finding of a higher rate of sensitization to potassium dichromate in the AI group was unexpected, although other studies have also reported this allergen as a frequent sensitizer among AIs, with sensitization rates as high as 7.9%.^{6,12,14,15} Another investigation showed that this antigen sensitized 2.6% of subjects among a pediatric population of 137 atopic children.¹⁰ Because exposure to dichromates, such as are found in cement and leather, is uncommon in childhood, it is conceivable that this study's results¹⁰ may have included subjects with irritant contact dermatitis, rather than a true contact allergy. A German group investigated concurrent patch test reactions to nickel, cobalt, and chromate and found that positive reactions to chromate were consistently associated with atopic eczema.¹⁶ The authors concluded that some false positive reactions may have occurred as a result of the marginally irritating properties of the chromate patch test preparation and the high susceptibility of atopic patients to developing irritant reactions.¹⁶

Conclusions

Atopic individuals were shown to be at least as likely as NAIs to have ACD. The most frequent sensitizers were similar in the two groups, which suggests that the important sources of sensitization do not vary. Nonetheless, a statistically significant higher number of positive results were observed for potassium dichromate and phenylmercuric acetate. Statistically significantly more NAIs were affected by hand eczema and were employed in occupations involving wet or irritant exposure, although the numbers of AIs in our study group were too small to make a statistically valid comparison. The reduced numbers of atopic employees in professions with wet/irritant exposure may reflect the avoidance of these occupations by a population aware of their skin vulnerability. Patch testing is an important tool with which to diagnose eczemas of uncertain

etiologies and is of substantial use in the development of a better therapeutic approach to the management of atopic patients.

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