

Atopy patch testing with aeroallergens in patients with atopic dermatitis and controls in Singapore

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Summary

The role of allergy in atopic dermatitis is controversial. The atopy patch test (APT) has been used to investigate the association between atopic dermatitis and aeroallergen allergy. To determine the proportion of patients with atopic dermatitis with positive patch tests to common local aeroallergens and to compare this to controls with and without respiratory atopy, we performed APT, skin-prick tests (SPT) and IgE radioallergosorbent tests (RAST) on 73 patients with atopic dermatitis and on 38 nonatopic controls (13 with and 25 without respiratory atopy). The allergens used were house dust mite, cat dander, Bermuda grass and German cockroach. Only the APT for house dust mite showed a significant difference between the two groups. APT for house dust mite correlated with the RAST test, while APT for cat fur correlated with the SPT. The APT may be useful to evaluate aeroallergens in atopic dermatitis, but further work is needed to make it more reliable.

Introduction

The role of allergy in atopic dermatitis (AD) is controversial. In some patients with this condition, exacerbation of pruritus and eczematous skin lesions have been described after contact with certain allergens, with aeroallergens being most commonly implicated.

The atopy patch test (APT) has been used to investigate the association between AD and aeroallergen allergy. The commonest aeroallergens used in the APT are house dust mite (*Dermatophagoides pteronyssinus*), animal (especially cat) dander, and grass. Other aeroallergens used are tree (especially birch) and weed pollen, moulds and cockroach.¹ Recently, *Malassezia* has also been implicated as a triggering factor for AD.²

The purpose of this study was to determine the proportion of patients with AD who had positive patch tests to common commercially available aeroallergens relevant to the local population and to compare this with the proportion in controls with and without

respiratory atopy. Where there was a statistically significant difference, patients with positive patch tests to specific allergens could be advised on allergen avoidance, which may lead to a decrease in the frequency and severity of exacerbations of their AD.

We also performed skin-prick tests (SPT) and radioallergosorbent tests (RAST) for specific IgE to the same allergens to investigate any possible correlation between these tests of type I immediate-type hypersensitivity and the APT.

Patients and methods

The study was approved by the ethics committee of the National Skin Centre. Informed consent was obtained, and the tests were performed at the centre's contact dermatitis clinic. Hanifin and Rajka's criteria³ were used as the basis for diagnosis of AD.

We performed the APT on 73 patients with AD and on 38 nonatopic controls (13 with and 25 without respiratory atopy) who had been patch tested for the evaluation of suspected contact dermatitis at the National Skin Centre. The study subjects were patch tested to house dust mite (*Dermatophagoides pteronissinus*), cat dander, Bermuda grass and German cockroach

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allergens (obtained commercially from Stallergenes, Antony, France). We also performed SPT and IgE RAST to the same allergens (for SPT, we used the DermaPIK allergens from Greer Laboratories, Lenoir, NC, USA, and RAST was performed with the UniCAP system from Pharmacia Diagnostics, Uppsala, Sweden).

The study subjects had not been on systemic corticosteroids and systemic antihistamines for at least 2 weeks prior to testing. All test areas had been untreated with topical corticosteroids for at least 2 weeks prior to patch testing.

APTs were applied to non-pretreated skin on the subjects' backs or deltoid regions and removed 48 h later. The allergens were applied onto 7-mm Finn chambers fastened with Scanpor tape. The readings were performed at 72 h. The scoring system was in accordance with the International Contact Dermatitis Research Group recommendations⁴ (+/- = doubtful reaction, faint erythema only; + = weak positive reaction: erythema, infiltration, possibly papules; ++ = strong positive reaction: erythema, infiltration, papules, vesicles; +++ = extremely positive reaction: intense erythema and infiltration and coalescing vesicles; - = negative reaction; IR, irritant reaction of different types; NT, not tested).

SPT with the allergens and with positive (histamine) and negative (normal saline) controls was performed on the flexor aspects of the subjects' forearms either on the day of application of the patches or on the day of reading. Prick tests were read at 20 min, and scored according to the Greer DermaPIK scoring system (1+ = weal, if present = negative control reaction, erythema

> negative control, but < 10 mm diameter; 2+ = weal up to 7 mm in diameter, erythema up to 20 mm in diameter; 3+ = weal up to 10 mm in diameter, erythema > 20 mm in diameter; and 4+ = weal > 10 mm diameter, erythema > 20 mm diameter).

Statistics

Statistical analyses were performed using SPSS (version 11.5; SPSS Inc., Chicago, IL, USA). Differences in quantitative variables were determined using ANOVA when normality assumptions were satisfied (checked using the Komolgorov-Smirnov one-sample test). Otherwise, the equivalent nonparametric Kruskal-Wallis test was applied. Associations of categorical variables with the atopic/control groups were assessed using χ^2 or Fisher's exact test. Correlations between the APT, SPT and RAST for each of the four allergens were determined using Spearman's correlation coefficient. Statistical significance was set at $P < 0.05$.

Results

Demographic data and history

Demographic data and history of atopy were compared between the AD and control groups (Table 1). There was no significant difference between the two groups in terms of age, gender or ethnic group. Subjects with AD are more likely than controls to have a past history of asthma or allergic rhinitis (71.2% vs. 34.2%). There was no significant difference in family history of atopic

	Atopic dermatitis (n = 73)	Control with respiratory atopy (n = 13)	Control without respiratory atopy (n = 25)	P value
Mean $\pm$ SD age (years)	22.48 $\pm$ 6.17	22.0 $\pm$ 4.22	23.64 $\pm$ 4.88	0.614
Sex				
Male	74.0%	69.2%	88.0%	0.289
Female	26.0%	30.8%	12.0%	
Ethnic group				
Chinese	89.1%	100%	92.0%	0.898
Malay	5.5%	0%	4.0%	
Indian	5.5%	0%	4.0%	
Past history				
Asthma	41.1%	23.1%	0%	< 0.001*
Allergic rhinitis	50.7%	76.9%	0%	< 0.001*
Family history				
Atopic dermatitis	15.1%	23.1%	0%	0.071
Asthma	21.9%	30.8%	24.0%	0.783
Allergic rhinitis	23.3%	23.1%	4.0%	0.096
IgE levels $\pm$ SD (kU/L)	1453.1 $\pm$ 2464.2	491.2 $\pm$ 507.5	335.2 $\pm$ 314.3	0.042*

*Statistically significant.

Table 1 Demographic data and past and family histories of atopic disease in AD and control groups.

Table 2 Atopy patch test results for aeroallergens.

Allergen and group	–	+ / –	+	++	P value
House dust mite					
Atopic (%)	38.4	17.8	42.5	1.4	0.001*
Control with respiratory atopy (%)	46.2	15.4	23.1	15.4	
Control without respiratory atopy (%)	64.0	32.0	4.0	0	
Cat fur					
Atopic (%)	87.5	8.3	4.2	0	0.377
Control with respiratory atopy (%)	92.3	7.7	0	0	
Control without respiratory atopy (%)	80.0	20.0	0	0	
Bermuda grass					
Atopic (%)	89.0	8.2	2.7	0	0.463
Control with respiratory atopy (%)	84.6	15.4	0	0	
Control without respiratory atopy (%)	80.0	20.0	0	0	
German cockroach					
Atopic (%)	74.0	15.1	11.0	0	0.393
Control with respiratory atopy (%)	69.2	15.4	15.4	0	
Control without respiratory atopy (%)	76.0	24.0	0	0	

*Statistically significant.

Table 3 Skin prick test results for aeroallergens.

Allergen and group	0	1	2	3	4	P value
House dust mite						
Atopic (%)	6.8	0	15.1	35.6	42.5	0.007*
Control with respiratory atopy (%)	0	7.7	15.4	46.2	30.8	
Control without respiratory atopy (%)	8.0	24.0	8.0	20.0	40.0	
Cat fur						
Atopic (%)	47.9	31.5	15.1	5.5	0	0.200
Control with respiratory atopy (%)	76.9	23.1	0	0	0	
Control without respiratory atopy (%)	40.0	48.0	12.0	0	0	
Bermuda grass						
Atopic (%)	58.9	32.9	2.7	4.1	1.4	0.266
Control with respiratory atopy (%)	53.8	23.1	23.1	0	0	
Control without respiratory atopy (%)	56.0	36.0	8.0	0	0	
German cockroach						
Atopic (%)	30.1	23.3	21.9	23.3	1.4	0.445
Control with respiratory atopy (%)	46.2	30.8	15.4	7.7	0	
Control without respiratory atopy (%)	29.2	33.3	16.7	12.5	8.3	

*Statistically significant.

disease between the two groups. Total IgE levels were significantly higher in the AD group. Because many subjects in the control group had a history of respiratory atopy, those with and those without respiratory atopy were analysed as separate groups.

Comparison of APT, SPT and RAST results between patients with AD and controls

The APT results for the various allergens are shown in Table 2. The only allergen that showed a significant difference among the three groups was house dust mite. The SPT and RAST results are shown in Tables 3 and 4. Only the house dust mite SPT showed a significant difference among the three groups.

Correlation between APT, SPT and RAST

For house dust mite, a strong correlation was found between the SPT and RAST tests. Spearman's correlation was also significant between house dust mite APT and RAST, cat fur APT and SPT, and cat fur SPT and RAST (Table 5).

Discussion

The APT with aeroallergens was first performed by Mitchell *et al.* in 1982.⁵ Since then, numerous studies of atopy patch testing to aeroallergens have been performed. However, the outcomes of these studies show large variations, owing to differences in patient selection

Allergen and group	0	1	2	3	4	5	6	<i>P</i> value
House dust mite								
Atopic (%)	11.1	6.9	5.6	4.2	19.4	6.9	45.8	0.059
Control with respiratory atopy (%)	15.4	0	23.1	0	15.4	7.7	38.5	
Control without respiratory atopy (%)	28.0	4.0	16.0	12.0	28.0	4.0	8.0	
Cat epithelium								
Atopic (%)	79.2	5.6	9.7	2.8	1.4	1.4	0	0.807
Control with respiratory atopy (%)	76.9	7.7	15.4	0	0	0	0	
Control without respiratory atopy (%)	9.6	4.0	0	0	0	0	0	
Bermuda grass								
Atopic (%)	66.7	22.2	11.1	0	0	0	0	0.273
Control with respiratory atopy (%)	69.2	15.4	15.4	0	0	0	0	
Control without respiratory atopy (%)	64.0	36.0	0	0	0	0	0	
German cockroach								
Atopic (%)	73.6	4.2	19.4	1.4	1.4	0	0	0.804
Control with respiratory atopy (%)	92.3	0	7.7	0	0	0	0	
Control without respiratory atopy (%)	88.0	4.0	8.0	0	0	0	0	

Table 4 RAST test results for aeroallergens.

Allergen	APT vs. SPT		APT vs. RAST		SPT vs. RAST	
	<i>R</i>	<i>P</i>	<i>R</i>	<i>P</i>	<i>R</i>	<i>P</i>
House dust mite	0.071	0.460	0.242*	0.011	0.509**	<0.001
Cat allergen	0.200*	0.036	0.171	0.075	0.221*	0.020
Bermuda grass	0.088	0.359	-0.007	0.942	0.030	0.754
German cockroach	0.093	0.332	0.086	0.372	0.131	0.174

Table 5 Spearman's correlation between APT, SPT and RAST for the different allergens.

P* < 0.05 level (two-tailed); *P* < 0.01 level (two-tailed). *R*, correlation coefficient; *P*, *P* value.

and methodology. Standardization of the APT procedure has not yet been achieved. Variations in methodology can be due to type of allergen (e.g. whole mite vs. mite extracts), concentration and vehicle, skin condition (whether pretreated or not, e.g. tape stripping), test site and reading time.^{6–8} Furthermore, test agreement between allergens supplied commercially by different companies is poor.⁸

This is the first study of APT to multiple aeroallergens in AD vs. controls in a south-east Asian population. A previous study from Thailand⁹ was published in 1993, in which 30 children with AD were compared with 30 children with respiratory atopy but without AD. In their study, 90% of the children with AD had positive patch-test reactions, compared with 10% of the atopic children without AD. Among the patients with AD, mite, cockroach, house dust, mould mix and grass mix caused reactions in 21 (70%), 21 (70%), 19 (63%), 15 (50%) and 13 (43%) patients, respectively. Our study was performed in an older population, with a mean age of 22.7 years, and we compared patients with AD with controls who had respiratory atopy and with nonatopic controls.

The percentages of patients with AD with APT+ and above for the different allergens were: house dust mite

43.9%, cat fur 4.2%, Bermuda grass 2.7% and German cockroach 11.0%. This is in contrast to those found in studies from Germany: house dust mite 36–80%, grass pollen 17–50% and cat dander 3–30%.^{7,10,11}

In one previous study,⁶ it was suggested that aeroallergen-induced exacerbation of AD occurs in sensitized patients with AD in whom active airway disease is present. The authors of that paper further suggested that active airway disease seemed necessary for distribution of mediators and cytokines from inflammatory cells in airways to the skin.

There has been a recent recommendation to reclassify AD into allergic and nonallergic subsets, with the allergic group being further subdivided into IgE- and non-IgE-associated categories. The IgE-associated allergic group, renamed atopic eczema/dermatitis syndrome¹² is distinguished by elevated allergen-specific IgE antibodies.

In view of this, we had also analysed the APT results of patients with AD and controls, comparing subjects in each group with RAST > 2 and/or SPT > 1 for any of the four allergens (IgE-associated) vs. those with RAST < 3 and SPT < 2 for all of the four main allergens (non-IgE-associated). No significant differences were found.

However, the two subgroups of patients with AD ($n = 2$) and controls ($n = 6$) with RAST < 3 and SPT < 2 for all of the four main allergens were too small to give meaningful results.

The usefulness of the APT to evaluate aeroallergens that may contribute to flares of AD has not yet been determined. In our study, the result of the APT was statistically significant only for house dust mite. We also found that APT results for house dust mite correlated with the RAST test, while APT results for cat fur correlated with the SPT.

It has been suggested that allergy may not be the only mechanism contributing to positive patch tests to house dust mite allergen. Deleuran *et al.*¹³ reported that allergic patch tests towards Der p1 and p2 are rare and that irritant reactions from *D. pteronyssinus* proteolytic activity may be a more common phenomenon when patch testing with house dust mite antigen extract on patients with AD.

Much work remains to make the APT a more reliable tool in identifying relevant aeroallergens that lead to flares of AD. There is a need to standardize the allergens and procedure, improve reproducibility of test results and improve inter-test agreement between allergens from different suppliers. Once this can be achieved, the APT should be a useful tool to identify possible aggravating factors in all patients with AD, especially as certain aeroallergens such as house dust mites are ubiquitous. The demonstration of a positive APT reaction may reinforce patients' and caregivers' resolve to achieve eradication of the offending allergen, leading to significant clinical improvement or even resolution of the AD.

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