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Allergic Contact Dermatitis in Atopic Dermatitis

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Of 73 adult patients attending a clinic specially provided to treat patients with atopic dermatitis, 31 (42%) showed one or more positive patch reaction on contact testing. There was a striking female preponderance in the patch test positive group (26F:5M) in contrast to those with negative test results (9F:17M). The commonest allergens identified were fragrances in 13 patients, nickel (7), rubber (5), lanolin (4) and formaldehyde (3). In 21 patients, topical preparations, cosmetic or medically prescribed, could be implicated. Contact sensitivity seems to be relatively common in adult patients who have a continuing problem with their atopic dermatitis. Recognizing this sensitization may be important in their management.

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INTRODUCTION

The relative frequency and importance of contact allergy in patients with atopic dermatitis (AD) is debated. Some authors report a reduced (1, 2) incidence while others report similar (3) or increased (4, 5) figures, when compared with a non-atopic population. This variation may to some extent reflect the population studied. Selective referral could falsely associate the two conditions: some studies are based on disease groups, while others are concerned with patients attending for patch testing.

Whatever the explanation, patients with severe AD pose a difficult management problem which may necessitate second-line treatment. Phototherapy, immunosuppressants, interferon and cyclosporin have all been tried (6). Recognition of an associated contact sensitivity, coupled with the appropriate avoidance advice, may alleviate disease activity and avoid the need for these potentially toxic agents.

METHODS

Clinical details

Our study is based on 73 patients (32 male : 41 female) with AD, attending a specially designated clinic for adult atopic patients between January 1989 and December 1990. The patients were in the age range 12–68 years (mean 25.6). All had the typical clinical features of AD. Age at onset was early in 63 (84%) (Table I, column 1). Fifty-four patients had developed the disease while under the age of 2 years, 9 between 2 and 5 years; 10 patients had a later disease onset. 68 (93%) had current or past flexural involvement. 55 (75%) patients also had allergic respiratory disease (Table I, column 1), while 22 patients (30%) had two conditions, usually asthma and hay fever. 18 patients (25%) had no associated allergic respiratory disease. The family history was positive for atopy in 38 (52%) and was present in a first-degree relative in 32 (44%). A family history was not available for the 3 patients who were adopted.

Specific IgE (RAST) testing was carried out on 57 patients. Allergens tested included house-dust mite, grass, food mix (egg, milk,

Table I. *Clinical details of patients*

N = ...	All patients 73	Group A 31	Group B 26	Group C 10	Group D 6
Male:Female	32:41	6:25	17:9	8:2	2:4
Mean age	25.6	26.7	28.5	18.6	22.7
Age at onset					
<2 years	54	19	22	8	5
2–5 years	9	7	1	1	
>5 years	10	5	3	1	1
Associated ARD					
Asthma	39	16	16	5	2
Hay fever	32	16	11	4	1
Other	6	4	2	–	–
>2 diseases	22	12	9	1	–
None	18	7	6	2	3
Family history					
Positive	38	18	14	4	2
1st degree	32	16	10	4	2
Negative	32	12	11	5	4
Adopted	3	1	1	1	1

The clinical details of the whole group are shown in col. 1.
Group A had one or more positive patch test reactions.
Group B were negative on patch testing.
Group C were defaulters and Group D await testing.

Table II. *Results of RAST-specific IgE testing*

	All patients	Group A	Group B	Group C	Group D
House dust mite					
>7.5 U/ml	42	19	15	3	5
<7.5 U/ml	7	2	5	–	–
Negative	4	1	2	1	–
Grass					
>7.5 U/ml	36	12	18	3	3
<7.5 U/ml	12	8	1	1	2
Negative	5	2	3	–	–
Dog/cat	21	9	8	2	2
Food mix[a]					
>7.5 U/ml	12(16)	4(5)	6(8)	1(2)	1(1)
>3.5 U/ml	5(8)	2(3)	2(3)	1	0(2)
<3.5 U/ml	17(13)	6(4)	10(9)	–	1
Negative	20	13	3	2	2
All negative	4	3	1		
Not Tested	16	6	3	6	1

[a]Results in parentheses represent patients with reactions to individual food allergens.

wheat, peanut, soya) and cod fish, using the Pharmacia RAST system. The relevant food allergens were tested separately whenever the food mix proved positive. Tests for dog and cat dander were also included if clinically indicated or where therewas a household pet.

Patch testing to the European standard series was carried out at the Contact Dermatitis Investigation Unit at Belvidere Hospital using the Trolab series of allergens (Biodiagnostics Ltd., Worcester, England). Other test series were used where indicated. Reactions were read at 48 and 96 h. Patients were tested when their disease was under good control. No patient was taking systemic steroids or anti-histamines when tested and only moderate strength steroids (British National Formulary -3 or less) were allowed topically. Six patients still await testing, 4 of whom are women whose testing was postponed because of pregnancy.

RESULTS

Specific IgE RAST Tests

Fifty-three patients (76%) had one or more positive RAST tests (Table II). Four patients had negative RAST tests and the results are unavailable for 16 patients. Of those with positive tests, 47 patients had a high (>7.5 U/ml) specific IgE to one or more allergens which included one of the aero-allergens (housedust mite or grass) in all except one. One patient had low-level positive RAST tests to both aero-allergens, but had a single high RAST level for eggs. 21 of the 53 patients also had an elevated RAST level to dog or cat dander and 25 patients had an elevated RAST level to an ingested allergen: either the food mix (17 patients >3.5 U/ml, 12 patients >7.5 U/ml) or to a single food allergen (24 patients >3.5 U/ml and 16 patients >7.5 U/ml).

Contact testing

Thirty-one patients (Group A) had one or more positive delayed hypersensitivity reactions, giving a total of 47 positive tests: the detailed results are presented in Table III. No allergens were identified in 27 patients (Group B) and results are unavailable for 16 patients: 10 patients, predominantly young males, defaulted from routine review (Group C) and 6 patients (Group D) still await testing.

The commonest allergens identified were the fragrances (13), which were found as the sole allergen in 5 cases and in association with another allergen in 8. Other allergens found included nickel, which was positive in 7 cases, rubber in 5, lanolin in 4, formaldehyde in 3 and kathon in 2. Ten other allergens were identified, each on a single occasion. Fragrances, lanolin, formaldehyde, preservatives (kathon, sorbic acid, quaternium) and sunscreens are all common ingredients of topical preparations, both cosmetic and medicinal. 21 of the 31 patients (Group A) reacted to an allergen which is contained in a topical preparation.

Table III. *Patch test results*

	Single allergen	Combined	Total
Fragrances	5	8	13
Nickel	4	3	7
Rubber	–	5	5
Formaldehyde	1	2	3
Lanolin	2	2	4
Kathon	–	2	2
Others			
Primin	1		1
Sunscreens	1		1
Sorbic acid	1		1
E45	1		1
Colophony		2	2
Balsam of Peru		2	2
Tinct. benz. co.		1	1
Triethanolamine		1	1
Quaternium		1	1
Neomycin		1	1
Caine		1	1

Column one shows the number of patients having a reaction to a single allergen; column two those reacting to two or more allergens and column three the total number of patients reacting to each allergen.

Of the 13 patients who had a positive reaction to fragrances, 8 also had a positve response to one or more of the individual fragrances in the perfume battery. A further 3 patients reacted to one or more allergens in the perfume breakdown battery although they had a negative reaction to the fragrance-mix in the European Standard battery, possibly due to 'quenching'. Two of these had other markers of fragrance sensitivity: 2 reacted to colophony and one also to Balsam of Peru. Only 2 patients with a positive fragrance-mix were negative to all the constituents of the fragrance-mix.

DISCUSSION

Thirty-one patients (42%) had one or more positive patch test reactions. This was an unexpectedly high figure, to which several factors may have contributed. Firstly, patient selection may have biased the results. All patients with AD who attended the clinic during the study period (1989–90) were included in the study, although some patients had already been patch tested earlier. Patients with severe disease *per se* or those with an associated contact sensitivity may be more likely to be referred to the clinic or, once referred, be more likely to attend regularly.

Secondly, it is possible that patients with severe disease may be more likely to develop a contact allergy than those with milder disease. However, it is generally accepted that patients with AD have impaired cell-mediated immunity as evidenced clinically by their handling of viral and fungal infections and by cutaneous anergy to injected intradermal antigens (7–10). In addition, several studies have shown a reduced incidence of experimentally induced contact allergy in patients with AD, using both poison ivy (1) and DNCB (dinitrochlorobenzene) as the chemical sensitizer (11–13).

However, the experimental and the 'real life' situation are very different. In the experimental situation the chosen sensitizer is applied on a single occasion only. Under these conditions it seems likely that patients with AD have a reduced response on challenge and fewer atopics become sensitized than normal subjects (11–13). However, this single application of a potential sensitizer is in sharp contrast to 'real life' where patients with AD regularly apply large amounts of topical preparations, both proprietary and cosmetic, many of which contain potential sensitizers. In addition, these preparations are often applied to damaged eczematous skin. It is probably significant that the allergen in 21 of our 31 patients with contact sensitivity is present in a topical preparation.

A third consideration is that the skin of patients with AD is more susceptible to irritation than is the normal non-atopic skin (14). The fragrance-mix is associated with irritant reactions. It is possible therefore that some of the reactions in the 13 patients who reacted to fragrances were irritant rather than a true delayed hypersensitivity reaction. However, many also reacted to individual perfumes in the fragrance break-down, and none reacted to the other allergens, such as chrome, which are also commonly associated with irritant reactions. However, in practice, it is probably sensible to give all patients who react to fragrances the same avoidance advice, whether the reaction is irritant or truly allergic.

The clinical features of the four sub-groups are essentially similar (Tables I, II), with one important exception. In the patch test positive group (Group A), females greatly outnumbered males: 25 *v.* 6, in contrast to the negative group (B), where the sex ratio was reversed, with males outnumbering females (17 *v.* 9). The reason for this difference is not clear but could relate to a greater use of cosmetics and other topical preparations by women. In support of this, 11 of the 13 fragrance-sensitive patients were female. However, equally the epidermal barrier could differ in atopic men and women, or they may handle allergens differently. Nevertheless, the higher incidence of contact sensitivity in women may also explain why there is a preponderance of females among adults with AD.

Findings similar to our own have been reported in other studies. Over a 2-year period, de Groot (2) examined 499 patients with dermatitis and routinely prick and patch tested all patients. 271 patients (43%) were atopic. The atopic group had a lower incidence of positive patch test reactions (37%) than the non-atopics (53%). This figure of 37% is not dissimilar from our own and emphasizes the importance of routinely patch testing adolescents and adult patients who have AD.

In 1964, Epstein & Mohajerin (4) also found that 28% of their patients with AD had a contact sensitivity, in contrast to 9% in their control psoriatic group. Interestingly, a high percentage of their reactions were to the topical preparations commonly used at that time, including tar, mercury and neomycin. Our findings also reveal a similar trend of reactions to topical preparations. Recently, Wilkinson et al. (15) have reported the development of contact sensitivity to topical steroid preparations and steroid sensitivity may well become more common in the future.

The recognition of a contact allergy in patients with AD is important in management. Nickel and rubber are common in our environment and patients need to be aware of this. Fragrances are almost ubiquitous in cosmetics and other proprietary preparations. The commonest sources of fragrance include toiletries, particularly shampoos, prescribed bath additives, washing powders and fabric conditioners. Where facial and cape eczema is a particular problem, shampoos can often be a significant factor. Appropriate avoidance advice can significantly alleviate their disease.

Finally it is of interest to consider the role of contact allergy in the pathogenesis of the disease. In general, AD is a self-limiting disease of infancy with spontaneous remission occurring in over 90% of patients (16). Nevertheless in a small proportion it can become a persistent problem. One possible hypothesis is that persistent disease is related to the development of contact allergy: initially to the aero-allergens (17, 18) and later to the environmental allergens discussed here. It is interesting to speculate whether energetic treatment of the disease during infancy could protect the child by providing a more intact epidermal barrier or whether these patients represent a sub-group with a more profound underlying immune abnormality.

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