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Allergen-Antibody Complexes in the Treatment of Atopic Dermatitis:

Preliminary results of a double-blind placebo-controlled study

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Twenty-three adult patients suffering from chronic atopic dermatitis (AD) have been treated by regular injections of complexes made of *D. pteronyssinus* allergens and specific autologous antibodies. A double-blind placebo-controlled protocol was followed for 4 months, then the patients were treated openly to complete a full year on active therapy. Preliminary results are presented for the first 8 months. Seventy-three percent of patients improved when treated with complexes, showing a mean improvement of more than 70% after 4 months. This study suggests that injections of allergen-antibody complexes is an effective treatment of at least some forms of AD and confirms that airborne allergens are significant exacerbating factors of AD. *Key words: Atopic dermatitis; Immunotherapy; D. pteronyssinus.*

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Clinical evidence has recently emerged showing that at least some forms of atopic dermatitis (AD) can be exacerbated when the patient is exposed to airborne allergens, such as those contained in house dust (1). Long-term avoidance from such exposure can, on the other hand, result in a significant clinical improvement (2). In most AD patients there is serological evidence of immune sensitization to house dust mites, in particular *Dermatophagoides pteronyssinus* (Dpt), whose allergens are ubiquitous in areas of temperate climate and persist at significant levels practically throughout the year (3).

Taken together, these observations suggest that a significant clinical benefit could be obtained for those patients if a therapy were available by which a suppression of the immune response toward Dpt could be achieved in a selective manner. The treatment of allergic patients with allergen-antibody complexes has been shown to achieve this objective (4). Injection of these complexes has resulted in clinical improvement of patients with allergic bronchial asthma and to reduce selectively the level of specific anti-Dpt antibodies. One interpretation of the results obtained in that study was that the administration of allergen-antibody complexes to patients increased the production of anti-idiotypic antibodies to anti-Dpt antibodies; anti-idiotypic antibodies are indeed capable, under defined experimental conditions, of suppressing the production of the antibodies they recognize (5).

Abbreviations:
AD, atopic dermatitis; Dpt, Dermatophagoides pteronyssinus.

Encouraged by the results obtained in allergic bronchial asthma we have conducted an open trial in adult AD, and have shown a rapid and sustained improvement in the clinical condition of the patients (6). A double-blind placebo-controlled study was therefore initiated, whose preliminary results are reported here.

MATERIAL AND METHODS

Patients

Twenty-three adult patients, aged 15 to 64, suffering from severe AD participated in this study. The diagnosis of AD was established according to Hanifin & Rajka's criteria but, in addition, the patients had evidence of sensitization to Dpt (high level of specific IgE to Dpt) and elevated titres of total IgE antibodies (greater than 200 IU/ml). The mean duration of AD was 26 years and an average of 71% of the body surface area was affected by skin lesions. Fifty-six percent of the patients also suffered from allergic bronchial asthma.

Study design

The patient population was randomly allotted to two groups: Group A with 12 patients who were actively treated by injections of allergen-antibody complexes from the start of the study, and Group B, designated as placebo group, with the remaining 11 patients. The study comprised three phases: (1) a 4-week pre-treatment period during which baseline values for disease severity were established and any previous therapy withdrawn; (2) a 4-month period during which the trial was conducted as a double-blind placebo-controlled study; and (3) a final period during which all patients were treated to complete a full year on active therapy.

Preparation of specific antibodies and of allergen-antibody complexes

Specific anti-Dpt antibodies were prepared for each patient by a combination of salt precipitation, gel filtration chromatography and specific immunoadsorption (6). Dpt allergens, obtained from Bencard Ltd (Epsom, Surrey, England) were dialysed and concentrated by ultrafiltration. Allergen-antibody complexes were prepared for each single patient after determination of the ratio at which complexes would be formed in antibody excess (4); this yielded a mean ratio of 1/4 (w/w), which was used for treating all the patients.

Injection schedule

Allergen-antibody complexes were administered to patients in a strictly autologous manner. A total of 250 μg specific antibodies and 62.5 μg allergens were used for the first 4 months, followed by monthly injections of 16 μg of specific antibodies with 4 μg of allergens. Placebo patients received injections of the carrier buffer alone.

Clinical evaluation

Six types of skin lesions were scored by the examining physician on a discontinuous intensity scale, from 0 to 4: erythema, edema, papulation, excoriations, lichenification and desquamation. The extent of skin lesions on the body surface area was evaluated using the 'rule of nines'. A disease intensity score was calculated by multiplying the sum of the symptom scores by the percentage of body surface area af-

fected. In addition, the intensity of pruritus was evaluated by the patient using a 0–4 scale.

RESULTS

The data from 22 out of 23 patients were analysed. Sixteen patients (73%) showed a clinical improvement as a result of injection of allergen-antibody complexes. Fig. 1 shows the evolution of the disease intensity score for these 16 patients over the first 8 months of the study. In order to deal with inter-individual variations, a mean of the three clinical evaluations made during the 4-week pre-treatment period was taken as baseline value, which was then 'normalized' to 1,000. Fig. 1 shows that: (1) group A patients began to improve shortly after the start of the injection schedule; 50% improvement was obtained after 9 weeks of therapy, 72% by the end of the fourth month and 85% after 8 months; (2) group B patients also improved during the first weeks, but then rapidly deteriorated, to resume their initial intensity scores at the end of the fourth month; (3) on active therapy, group B patients showed a rapid and sustained improvement, which reached 71% at the end of the eighth month of the study.

Table I shows the evolution of pruritus and of individual clinical symptoms during the first 8 months of therapy. The percentages of reduction in severity vis-à-vis the baseline values are also given (italics). This indicates that the clinical evolution was the result of an overall improvement in both acute and chronic signs of AD, together with pruritus. It also shows that most of the placebo effect was attributable to a reduction in pruritus and lichenification, which is the physical consequence of chronic scratching.

DISCUSSION

These preliminary data show that injections of allergen-antibody complexes in adult patients suffering from AD can profoundly improve the clinical condition in a majority of cases. The number of patients treated so far is, however, too small to decide whether a comparable improvement could be obtained in a majority of AD patients, or whether the patients treated here represent a particularly responsive subgroup of patients. However, it should be noted that the criteria used to select the patients, namely, confimed diagnosis of AD coupled with evidence of sensitization to Dpt and high levels of total IgE antibodies, are by no means restrictive, insofar as most AD patients have serological evidence of Dpt sensitivity.

It also remains to determine whether the long-term follow-up of these patients will confirm the benefit of such therapy. The evolution of patients treated by allergen-antibody complexes in the first open trial we conducted (6) already indicates a sustained improvement for at least 2 years in an overwhelming majority of patients *(manuscript submitted)*. Whether or not any significant alteration of the immune response to Dpt accompanies the clinical changes is currently under investigation.

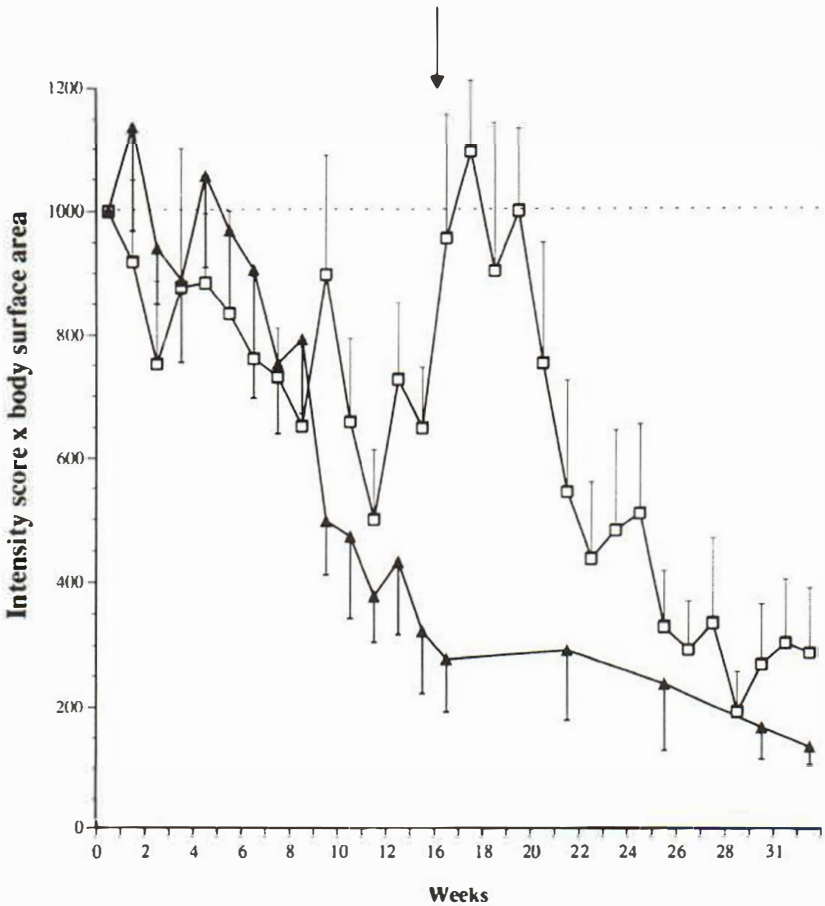

Fig. 1. Evolution of AD intensity score during the first 8 months of allergen-antibody complex therapy: ▲, group A; □, group B; vertical range bars represent SEM.

Table 1. *Clinical symptoms of AD evaluated prior to treatment and after 4 and 8 months of allergen-antibody complex therapy.*

	Mean score (% change from baseline)				
	Week 0	Week 16		Week 32	
	Baseline score	Mean score	% red	Mean score	% red
Group A					
Pruritus	3.25	2.18	*33*	1.39	*57*
Erythema	4.12	2.35	*43*	2.14	*48*
Edema	3.75	1.54	*59*	1.42	*62*
Papulation	2.62	1.2	*54*	0.86	*67*
Excoriations	3	1.77	*41*	1.11	*63*
Lichenification	3.5	1.89	*46*	0.98	*72*
Desquamation	3	1.68	*44*	1.44	*52*
		Active therapy			
Group B					
Pruritus	3.25	2.6	*19*	1.9	*41*
Erythema	4.25	4.16	*2*	3.06	*28*
Edema	4.12	3.83	*7*	2.27	*45*
Papulation	3.87	3.89	*0*	0.81	*79*
Excoriations	3.12	2.87	*8*	1.22	*61*
Lichenification	4.12	2.8	*32*	1.73	*58*
Desquamation	2.25	2.25	*0*	2.18	*3*
		Active therapy			

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