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Hyposensitization with Dermatophagoides pteronyssinus Antigen: Trial in Asthma Induced by House Dust

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Summary

A double-blind clinical trial of hyposensitization with aqueous extracts of *Dermatophagoides pteronyssinus* (the house-dust mite) and human skin scales showed a substantial improvement in symptoms in 11 asthmatics allergic to house dust treated with the *D. pteronyssinus* extract and a reduction in their need for other therapy. Five patients were well for a year but six relapsed. These results contrasted with the generally unfavourable course of the patients treated with the extract of human skin scales. Asthma due to house-dust allergy may be substantially improved by hyposensitization with *D. pteronyssinus* extract.

Introduction

The role of the house-dust mite (*Dermatophagoides pteronyssinus*) as the major allergen in house dust has been well established (Voorhorst *et al.*, 1967; Maunsell *et al.*, 1968; Morrow Brown and Filer, 1968; Pepys *et al.*, 1968). Patients known to be allergic to house dust also show marked skin, nasal, and bronchial allergy to the house-dust mite. The treatment of house-dust allergy by hyposensitizing injections has been disappointing (McAllen, 1961; British Tuberculosis Association, 1968), presumably because of the low concentration of mite antigen in the extracts used. We therefore carried out a double-blind trial to determine the hyposensitizing effects of injections of aqueous extract of *D. pteronyssinus* in a small group of patients with asthma induced by house dust.

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Patients and Methods

Twenty-two patients were selected who had perennial asthma, with or without rhinitis; attacks of asthma on contact with house dust (as in sweeping or making beds) and frequent nocturnal and early morning attacks of asthma; an immediately positive result to a prick test with 1:10,000 extract of *D. pteronyssinus;* no history of other allergies; and negative skin tests to *Aspergillus fumigatus*, other moulds, pollens, and animal fur. Further information about them is presented in Table I. All had suffered from asthma for many years.

TABLE I—*Distribution of the Patient's Characteristics between the Two Treatment Groups*

	Mite-treated Group	Control-treated Group
Total No.	11	11
Age range (years)	11-47	13-48
Males/females	5/6	9/2
Smokers	4	1
Atopic family history	10	9
Allergic rhinitis	10	8
Severity of asthma: (Grade)		
Mild	0	0
Moderate	5	3
Severe	4	7
Very severe	2	1
No. on steroid	3	4
No. on disodium cromoglycate	1	1

The grading of asthma before entering the trial was based on the number of days off work in the previous six months, the severity of breathlessness, the frequency of nocturnal attacks, the frequency with which an aerosol bronchodilator was used during the month before treatment, and the type of therapy previously received by the patient.

One group of 11 patients received house-dust mite extract and the other 11 patients an extract of human skin scales. The mite extracts were prepared by Dr. Kate Maunsell in the way she has described (McAllen *et al.*, 1970), and the control extracts were prepared in the same fashion. There was no loss of skin-reacting property in the mite extract after heating, and the strength was unimpaired after storage at room temperature for 12 months.

The trial was divided into a run-in period of one month, an injection period, and a follow-up period of six weeks. The patients were seen weekly and assessed in the same manner each time. After the follow-up period they continued to attend but at longer intervals. Active or control treatment was dispensed to each patient at the start of the injection period in a random, double-blind fashion, and the extracts were given weekly by subcutaneous injection in doses of 0·1, 0·2, 0·4, 0·6, and 0·8 ml of 1 : 100,000 extract and then 0·1, 0·2, 0·4, 0·6, 0·8, 1·0, 1·5, and 1·5 ml of 1 : 10,000 extract. If an immediate localized skin reaction occurred the same dose was repeated the next week.

Patients were instructed to vacuum their mattresses twice weekly and to pay particular attention to domestic hygiene. Each patient kept a daily record of symptoms, allocating scores for each symptom. The number of attacks of wheezing (day asthma score), the degree of breathlessness (points allocated on a 1-6 scale according to exercise limitation), and the number of times an aerosol inhaler was used were recorded each night. Each morning the patient recorded the night asthma score (points allocated according to the frequency of nocturnal attacks of wheeze sufficient to waken him) and the number of times the inhaler had been used during the night. At each visit to the clinic the daily scores for each symptom were summed to provide a single weekly figure for statistical purposes. The best of three consecutive peak flow rate readings and any changes of treatment were also recorded.

Results

Twenty patients completed the course of injections, and two left the trial during the injection period. They were classed as failures of treatment and were subsequently found to belong to the control group. The average course of injections lasted 16 weeks.

Ten of the 11 patients treated with mite extract completed the follow-up period without needing any further therapy, compared with 5 of the 11 patients in the control group. The difference between the number of patients in each group reaching the end of the follow-up period without additional treatment is significant (0·05>P>0·01).

At the end of the injection period the patients were asked for a subjective opinion of their treatment and the investigator recorded his own impression. Significantly more patients felt better in the mite-treated group than in the control group (Table II). The scores of the patients' symptoms were assessed at the end of the six-week follow-up period, but if additional therapy was needed before then the scores were assessed for the six-week period immediately preceding the start of further treatment. The mean weekly score for the run-in period was compared with the weekly score in the six-week period being assessed. Wilcoxon's ranking method was used and the scores were tested to determine the significance of the changes in the weekly scores in the follow-up period compared with those in the run-in period. If a patient was found to be significantly improved he was classified as better in respect of that symptom. Deterioration was detected in the same manner. The results are recorded in Table III.

Of the patients in the two groups significantly more in the mite-treated group were less breathless during the daytime (P<0·005), had fewer attacks of nocturnal breathlessness (P<0·005), and used their inhalers less at night (P<0·01). More patients in the mite-treated group were classified as better in respect of the number of attacks of wheezing and the daytime inhaler score, but not enough to exclude the possibility of the findings being due to chance (P>0·10 and P>0·05 respectively).

The peak flow rate results showed pronounced improvement in only four mite-treated patients—a result that cannot be accorded significance (P>0·10). Rhinitis improved in four of the mite-treated patients but in none of the control group. No serious side effects were seen. Eight patients in the mite-treated group had recurrent episodes of localized wealing and erythema at the injection site. There were no intermediate or late reactions, and precipitins against *D. pteronyssinus* were not detected in the serum of the eight patients tested. Of 10 mite-treated patients followed up for over a year five remained well and needed no further treatment: the remainder relapsed at 2, 4, 6, and 10 months respectively after the injections had ceased. It was possible to withdraw treatment from the three mite-treated patients on corticosteroid therapy but not from the four patients in the control group. The dose of disodium cromoglycate was reduced in one patient in the mite-treated group.

TABLE II—*Subjective Assessment at Cessation of Injections, before Calculation of Scores and Breaking the Key of the Trial*

	Patient's Assessment		Doctor's Assessment	
	Mite Treated	Control Treated	Mite Treated	Control Treated
Much better	7	0	7	0
Better	3	3	3	1
Same	1	8	1	10
Worse	0	0	0	0
Much worse	0	0	0	0
P	<0·005		<0·001	

Probability of the observed changes being due to chance calculated by the fourfold table test.

Discussion

Specific symptoms improved in more patients in the mite-treated group than in the control group. The improvement was associated with a favourable subjective response and reduction in other forms of treatment but was not detected by weekly measurements of air flow obstruction. It was in anticipation of the last observation that as much information as possible was sought from the patients, and clearly this decision was borne out by the results. The statistical method of evaluating the results was purposely rather insensitive, and only pronounced, persistent improvement over the whole six-week follow-up period was enough to be classified as "better." Therefore, the tendency of the measurements of airflow obstruction to vary produced occasional results during the assessment period which were low enough to exclude them from that category. Daily measurements of peak flow rate would probably have given a more reliable indication of

TABLE III—*Number of Patients Achieving Significant Changes in Scores in the Two Groups Treated at Six Weeks after Cessation of Treatment or, if Opting Out of the Trial, in the Last Six Weeks of Assessment*

Symptom Score Results	Day Asthma Score		Day Breathlessness Score		Day Inhaler Score		Night Asthma Score		Night Inhaler Score		Peak Flow	
	Mite Treated	Control Treated	Mite Treated	Control Treated	Mite Treated	Control Treated	Mite Treated	Control Treated	Mite Treated	Control Treated	Mite Treated	Control Treated
Better	5	2	8	1	6	2	10	3	8	2	4	1
Same	6	9	3	10	2	7	1	7	1	5	7	9
Worse	0	0	0	0	1	0	0	1	0	2	0	1
P	>0·10		<0·005		<0·10>0·05		<0·005		<0·01		>0·10	

If the number of patients in either group which shows improvement is significant, P<0·05.

significant changes. We therefore agree with Chai *et al.* (1968) that as many criteria as possible need to be studied in a long-term assessment of asthmatic patients and that single, infrequent observations are of limited value.

The symptoms of house-dust allergy tend to fluctuate over the course of a year (Voorhorst *et al.*, 1967), and the possibility that the improvement in our mite-treated group could be due to this was considered. But since no similar improvement occurred in the patients in the control group over the same period it was concluded that seasonal variation was not a significant factor. Furthermore, patients who had other seasonal allergies which could confuse the results were carefully excluded from the trial. We had no information about the mite content of the house dust in the patients' homes, but no patients moved house, installed central heating, or noticeably altered their environment in any other way during the trial.

Commercial extracts of *D. pteronyssinus* for hyposentitizing treatment are unavailable. However, the more easily cultured *D. culinae* seems to have antigenic properties similar to those of *D. pteronyssinus* and it is probable that similar results would be obtained with it. Indeed, Munro-Ashman *et al.* (1970) reported successful treatment in an uncontrolled series of patients with *D. culinae* extract.

We have concluded from this trial that hyposensitizing treatment with *D. pteronyssinus* extract in patients with house-dust allergy is worth while and can offer considerable relief from their perennial asthma.

I am indebted to Dr. Kate Maunsell, who made the extracts. I thank Dr. R. S. Bruce Pearson and Dr. P. Hugh-Jones for permission to study patients under their care and for their helpful criticism. I am grateful to Miss Irene Renton for secretarial assistance and to Mr. M. Curwen, of Guy's Hospital, for help with the statistical aspects of this study.

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Metabolic Responses to Oral Glucose in the Kalahari Bushmen

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Summary

The plasma glucose, immunoreactive insulin, and growth hormone levels after a 50-g oral glucose load have been measured in 15 adult Bushmen subjects living in the Kalahari region of Southern Africa. Compared with 10 non-obese white controls, they showed relative glucose intolerance and significantly impaired insulin secretion. Growth hormone responses showed no significant differences between the two groups. Factors such as inadequate or unusual nutrition and stress do not appear to account completely for the abnormalities in carbohydrate metabolism observed in the Bushmen. Of interest are the clinical and hormonal similarities that seem to exist between the Bushmen and the Central African Pygmies.

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Introduction

The Bushmen are believed to constitute a distinct ethnic group, nowadays virtually confined to the Kalahari wastelands of Southern Africa. Physical differences from the neighbouring Negroid peoples are well described, with characteristic facial features and body build (see Fig.). They live by hunting game and collecting wild vegetation ("veldkos"), certain species of which seem to have high nutritive value (Wehmeyer *et al.*, 1969), though their dietary habits are such that periods of semi-starvation give way to episodes of overindulgence (Bronte-Stewart *et al.*, 1960).

Isolated biochemical studies in the Bushmen have shown distinctive patterns of serum proteins (Bronte-Stewart *et al.*, 1960) and lipids (Miller *et al.*, 1968), attributed to environmental rather than genetic influences, but little data exist on, potentially, one of the most intriguing metabolic aspects of all—namely, their capacity to dispose of and their hormonal response to an oral carbohydrate load. The following study was primarily undertaken in an attempt to answer this question.

Subjects and Methods

In October 1970 an expedition was made to the Dobe area in the north-western region of Botswana, where a group of !Kung Bushmen had congregated. They were all participating in the Harvard University Bushmen Project and consequently were *not* unaccustomed to contact with white research workers or venepuncture procedures. Fifteen apparently healthy adult members of the group were chosen for the study and a simple explanation of the intended investigation was given (by a member of the university team assisting our party). Various pertinent physical characteristics of the selected subjects are