and no longer felt miserable. Improvement was maintained at five months' follow-up. The third patient had seven sessions of implosion (two in fantasy and five in practice). The main changes occurred after the fifth session (third in practice), during which she was able to pick up a spider and have it crawling on her hand. She married and looked forward to having children. At eight months' follow-up she remained able to pick up a live spider without fear. The fourth patient had 18 sessions of implosion (16 in fantasy and two in practice). Minor transient changes occurred which did not last. This patient had shown more free-floating anxiety at the start of treatment than the other three patients (a mean of 2·8 against 1·7 on a 1–5 self-rating scale). At six months' follow-up she showed the same picture she had presented before treatment began.

Physiological changes paralleled clinical ones, and are seen in detail for Case 2 in Fig. 2. Fig. 2 A shows the galvanic skin resistance and heart rate during visualization of a phobic fantasy. The periods during which the fantasy was held are indicated by the solid black lines. Heart rate increased during this period, as did spontaneous fluctuations in skin resistance. In contrast there were no changes during visualization of a neutral fantasy (Fig. 2 B). After six sessions of implosion the same phobic fantasy as in Fig. 2 A no longer produced any tachycardia or increase in fluctuations of galvanic skin resistance (Fig. 2 C), while the neutral fantasy again produced no changes (Fig. 2 D). To minimize the influence of habituation the examples on each of the two occasions are chosen from similar points on the patient's polygraph record.

Discussion

The main point of this preliminary report is that three out of four patients who were treated by implosion showed pronounced improvement, and this was greater than that usually obtained with the most effective treatment of phobias to date—namely, desensitization. These results warrant a proper controlled trial of implosion, but are only suggestive of its value, since the effects of enthusiasm and unwitting modelling by the therapist may also have played a part. It is not clear how much improvement was due to implosion in imagination and how much to implosion in the real life situation, and whether there is not an optimum balance in the way implosion should be given. The most interesting question of all is whether implosion is a special form of abreaction or whether it constitutes a specific learning experience. All these problems require to be worked out in future controlled trials.

The two agoraphobic patients had received much treatment elsewhere to no avail and were not considered particularly easy candidates for desensitization. The spider-phobic patient would probably have responded anyway to desensitization. The only patient with free-floating anxiety did badly. This would be expected with desensitization as well, and suggests that though implosion might eventually be a faster treatment for some patients who would in any case respond to desensitization it may not be applicable to patients who are unsuitable for desensitization—that is, those with free-floating anxiety.

This work was partly supported by a grant from the Medical Research Council. Thanks are due to Dr. J. H. J. Bancroft, Dr. S. Rachman, and Mr. A. Mathews for helpful comments on the manuscript.

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Clinical Significance of Skin Reactions to Mite Extracts in Children with Asthma

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British Medical Journal, 1969, **2**, 723–726

Summary: The mite Dermatophagoides pteronyssinus has been identified in dust from the houses of children in Birmingham suffering from asthma. Skin tests were carried out on 150 asthmatic children with extracts of D. pteronyssinus, of the related species D. farinae, of other mites found in house dust, and of crude house dust. Though positive reactions to D. pteronyssinus were obtained more frequently and were of greater size than those to the other extracts, it was considered that D. farinae is a suitable substitute for D. pteronyssinus for skin testing.

In further tests on 302 asthmatic children with mite extracts and with extracts of allergens obtained commercially reactions to the former extracts were much more common than reactions to the latter.

Major skin reactions (weals with diameter of 5 mm. or more) were present in 77% of children with a history of perennial asthma and house-dust sensitivity. Hence allergy to house-dust mites, particularly D. pteronyssinus, is of considerable importance in childhood asthma, and further study of the ecology and control of the mites in dust is desirable.

Introduction

House dust has long been known to cause sneezing and wheezing in sensitive subjects (Storm van Leeuwen, 1922; Maunsell, 1960). In Birmingham, house dust appears to be the most common allergen precipitating asthma in children as judged by the clinical pattern and skin tests with crude dust extracts (Smith, 1960).

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A few patients appear to be sensitive to the more obvious constituents of house dust—for example, wool, feathers, kapok, moulds, etc.—but in the past the main source of the house-dust allergen has not been detected. A recent suggestion is that many patients are allergic to a mite, *Dermatophagoides pteronyssinus,* which occurs widely in house dust (Solomon, 1961 ; Voorhorst *et al.,* 1967). It is particularly abundant in mattress dust (Maunsell *et al.,* 1968), and extracts of the mite produce skin reactions in some patients with asthma (Voorhorst *et al.,* 1967 ; Maunsell *et al.,* 1968). Similar but smaller reactions are given by extracts of other mites (Brown and Filer, 1968 ; Pepys *et al.,* 1968 ; Williams *et al.,* 1969.

We have studied the skin reactions to extracts of *D. pteronyssinus* and other mites in asthmatic and non-asthmatic children in an attempt to clarify the clinical significance of these reactions.

Methods

The Mites.—Cultures of the mites *D. farinae, Acarus siro,* and *Glycyphagus domesticus* were grown on granular media at 25° C. and 80% humidity, by the methods of Solomon and Cunnington (1964). When cultures were dense enough and the mites exceeded in volume the amount of medium present they were separated from the medium by using dichloromethane (Maunsell, 1967) and picking off individual mites, cold-extracted with 1% phenol-saline and standardized to a protein concentration of 5 mg. of protein nitrogen per 100 ml.

Skin Tests.—Skin tests were done on the ventral surface of the forearms by the single-prick method. Tracings of the weals were made 10 to 15 minutes after pricking and the mean diameters were recorded. Tests were performed with extracts prepared from the four mites and 1% phenol-saline solution as control. In children attending the asthma clinics commercial extracts of common allergens were also used in each case. These extracts were obtained from Bencard Ltd. The strength of these extracts is given as 1–2% weight/volume for house dust, 2·5% for pollens, 5% for moulds, 5% for egg, and 10% for other foods.

The Children.—Three hundred and two unselected children attending the asthma clinics of the Birmingham School Health Service and of Dudley Road Hospital were tested with a wide range of extracts, including the mite extracts. In addition, 60 children who were outpatients or inpatients at Dudley Road Hospital and who had no history of asthma or of allergic disease were tested with the mite extracts. Asthma was diagnosed clinically on the basis of recurrent attacks of wheezing and dyspnoea as defined by Scadding (1966). The clinical diagnosis in children is rarely mistaken (Smith, 1961). A limited quantity of an extract of *D. pteronyssinus* was available by courtesy of Dr. Kate Maunsell. This extract was prepared by extraction of 1 g. of a total culture including both mites and human skin scales used as medium with 0·5% carbol saline. The mites were not separated from the medium manually as was done in the preparation of our own extracts. A separate group of 150 children with perennial asthma were tested with this extract, with our extracts of *D. farinae* and *A. siro,* and with commercial house-dust extract.

Results

Incidence of Positive Reactions to Mite Extracts.—Of the 60 children, outpatients or inpatients, without clinical evidence of allergic disease, only one gave a positive reaction to any of the mite extracts. This child gave a reaction 2 mm. in diameter with all extracts. Of the 302 children attending the asthma clinics, 257 showed a positive skin reaction to prick test to an extract of *D. farinae,* 236 to *G. domesticus,* 232 to *A. siro,* and 165 to house-dust extract (Table I). In only six cases was there a positive skin reaction to crude house dust without a positive reaction to the mite extracts, whereas in 72 cases the opposite was found.

TABLE I.—*Incidence of reactions to Mite Extracts in Allergic and Non-allergic Children*

Group	No. of Children	Extract Used	No. of Positive Reactions
Clinic patients ..	302	*D. farinae*	257 (85%)
		G. domesticus	236 (78%)
		A. siro	232 (78%)
		House dust	165 (55%)
Non-allergic children ..	60	*D. farinae*	1 (1·6%)
		G. domesticus	1 (1·6%)
		A. siro	1 (1·6%)
		House dust	0

Comparison of Weal sizes.—The mean diameters of the weals obtained on prick testing 302 children at the asthma clinics are shown in Table II. The distribution of reactions given by house dust and by *D. farinae* are shown in Fig. 1. The distribution curve of weal sizes for house dust was highest at a negative level in contrast to that for *D. farinae,* which was highest between 5 and 6 mm. This suggests that the house-dust test is of little clinical value, whereas the mite test is positive at an easily read level in a high proportion of the patients tested.

TABLE II.—*Average Sizes of Weals on Prick-testing with Extracts of Three Mites and House Dust*

Antigen	No. of Weals	Average Diameter of Weal
D. farinae	257	6·8 mm.
G. domesticus	236	5·1 mm.
A. siro	232	4·3 mm.
House dust	165	2·6 mm.

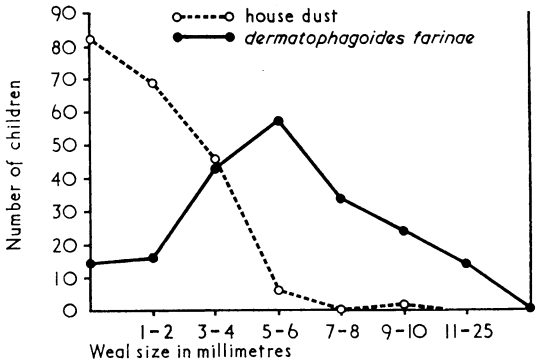

FIG. 1.—Distribution of weal diameters on prick testing 203 clinically dust-sensitive children with extracts of house dust and *D. farinae.*

Comparison of D. pteronyssinus with D. farinae.—One hundred and fifty children, all with perennial asthma, were tested with both species, and *D. pteronyssinus* produced weals in 146 (97%), whereas only 131 (87%) reacted to *D. farinae.* The average weal size obtained from *D. pteronyssinus* was 5·9 mm., slightly larger than with *D. farinae*—4·8 mm. The distribution of weal sizes on testing with the four mite extracts and with house dust in this group of children is shown in Fig. 2.

Frequency of Major Skin Reactions to Mite and Other Extracts.—The assessment of the significance of skin reactions is made difficult by the wide range of severity and type of allergic diseases in the children attending the asthma clinics and by the wide range in size of the reactions obtained. It was therefore decided to calculate the results by using major skin reactions, defined as reactions with weals of a mean diameter of 5 mm. or more. Major wealing reactions were much more common to mite extracts in this group of children than to any other of the 30 or more extracts used in each case. Major skin reactions were given by 202 children to the mite extracts, by 70 to pollen extracts, by 31 to animal danders,

by 21 to foods, and by 16 to various moulds (Fig. 3). The relationship of the clinical condition to the major skin reactions is shown in Table III. Of 74 children with no skin reactions of 5 mm., 27 were considered clinically to have non-allergic asthma. In most cases recurrent attacks of wheezing were associated with infection, and in one or two the association seemed to be with emotional disturbance. In 35 asthma was present alone but was considered to be of allergic origin, and in 11 asthma was present in association with infantile eczema, hay-fever, allergic rhinitis, or food allergy. One patient in this group had eczema without respiratory symptoms. Among the children with major skin reactions only to mite extracts the majority, 96 out of 133, had uncomplicated asthma. When major skin reactions were found to other extracts the majority of the children had asthma together with other allergic conditions, this occurring in 56 out of 95 cases.

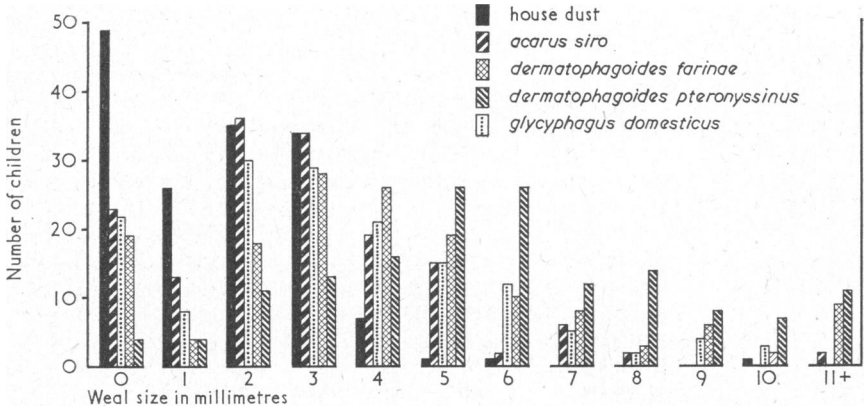

FIG. 2.—Distribution of weal sizes produced by house dust and four mite extracts in 150 clinicaly dust-sensitive children.

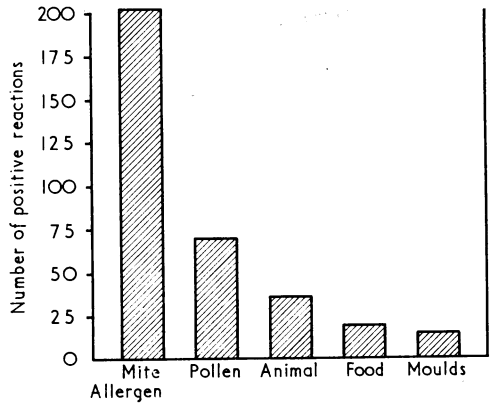

FIG. 3.—Comparison of frequency of positive reactions of 5 mm. or more given by common groups of allergens in 302 children attending asthma clinics.

TABLE III.—*Relationship of Skin Reactions of 5 mm. or more to Clinical Condition in 302 Children Attending Asthma Clinics*

Skin Reactions	No. of Children	Clinical Findings			Other Allergic Conditions Only
		Clinically Non-allergic Asthma	Clinically Allergic Asthma	Asthma + Other Allergic Conditions	
No major reaction to any allergen	74	27 (36%)	35 (40%)	11 (15%)	1 (2%)
Reaction to mite extract	133	2 (1·5%)	96 (73%)	35 (26·5%)	0
Reaction to mite and other extracts ..	69	0	28 (40%)	41 (60%)	0
Reaction to other extracts only ..	26	0	9 (34%)	15 (58%)	2 (8%)

Skin Test Reactions in Children with a Clinical History Suggesting Sensitivity to Common Allergens.—In 12 children there was a clear history of hay-fever and pollen asthma uncomplicated by symptoms outside the pollen season. All showed a positive prick test to pollen extracts, with grass pollen reactions usually the largest. Ten of these 12 (83%) had a reaction of 5 mm. or more, and the mean weal diameter in the whole group was 11 mm. Twenty-six cases of perennial asthma with exacerbation in the pollen season also had positive reactions to pollen, with 18 (69%) reactions of 5 mm. or more and a mean weal diameter of 7·4 mm.

Food Allergy.—Food allergy producing symptoms of vomiting, swelling of the mouth, or urticaria was present in 13 cases. All gave positive skin reactions to the food, 10 (77%) producing major reactions, and the mean weal diameter being 9 mm.

Dust Allergy.—In 203 children there was a history of asthma of perennial type, worse at night or in the early morning, and usually with some indication of dust sensitivity. Of these children 188 gave a positive reaction to mite extract, and 157 of these reactions were of 5 mm. or more, with a mean weal diameter for the whole group of 6·7 mm. Table IV shows that in children considered clinically to be allergic to house dust, grass pollen, or a common food a wealing reaction to the relevant extract of 5 mm. or more was obtained in a similar percentage in each group.

TABLE IV.—*Skin Test Reactions in Children with Clinical Histories Suggesting Sensitivity to Common Allergens*

Clinical Sensitivity	Skin Test	No. of Cases	All Reactions	"Major" Reactions of 5 mm. or More
Pollen ..	Pollen	38	38 (100%)	28 (74%)
Foods ..	Relevant food	13	13 (100%)	10 (77%)
House dust ..	Mite	203	188 (92%)	157 (77%)

Discussion

The results of our investigations show a very high incidence of positive skin reactions to extracts of mites in asthmatic children. Over 50% of schoolchildren in Birmingham suffering from asthma show positive prick test reactions to house dust (Table I), but these reactions are small and relatively less frequent than prick test reactions to grass pollen in children with pollen allergy or to offending foods in children with immediate-type allergy to foods. The reactions to house dust do, however, show a degree of correlation with a history of dust sensitivity and with the commonest form of perennial asthma in children, which is usually worse at night and is often relieved by admission to hospital or to a residential "open-air" school or during a period in a Swiss alpine resort (Smith, 1960).

There is increasing evidence that the main allergen in house dust is derived from the mite *D. pteronyssinus*. The distribution and ecology of *D. pteronyssinus* has been studied by Spieksma (1967), who found it very commonly in houses in Holland. Maunsell *et al.* (1968) confirmed the widespread presence of this mite in houses in London, and showed that skin reactions to dust extracts in sensitive patients usually depended on the mite content of the extract. We have also recovered mites from bedroom dust in houses in Birmingham. The recovery of mites from the air in bedrooms during bed-making has been reported by Cunnington and Gregory (1968).

The presence of mites in house dust helps to explain not only the variation in antigenicity of house-dust samples but also the frequent occurrence of symptoms of asthma in old

houses, especially in bedrooms, their relief on admission to hospital, and, possibly, even geographical variations such as are found in Switzerland and in South Africa (Ordman, 1964). The evidence in favour of the mites being associated with house-dust asthma has been discussed by the *Lancet* (1968).

D. pteronyssinus feeds on human skin scales and in consequence is found almost everywhere that human beings live, but particularly where they sleep. The cultivation of this mite is, however, a laborious process in the laboratory. Other mites which occur usually much less abundantly in house dust and appear to be of less clinical importance are much easier to cultivate. Other members of the genus *Dermatophagoides* which are not usually found in dust in this country have been used as a substitute. Pepys *et al.* (1968) used extracts of *D. culinae,* which is probably identical to *D. farinae* used by us, and found this gave a significant correlation on skin-testing with clinical evidence of house-dust allergy and with inhalation tests in adult asthmatic patients. We found weal sizes to be slightly smaller and less frequent with extract of *D. farinae* compared with *D. pteronyssinus,* but it is an effective substitute in the majority of cases. It should also be noted that the extract of *D. pteronyssinus* which was kindly supplied by Dr. Maunsell had been prepared by a method slightly different from that used for the other mites.

When studying skin reactions in children the clinical significance of the results is more obvious in the case of the stronger reactions (Smith, 1968). This is most clearly seen in relation to pollen asthma. We found that children clinically allergic to house dust gave major skin reactions to *D. farinae* in 77% of cases. Children with pollen asthma and immediate-type food allergy showed a similar incidence of reactions to pollen and relevant food extracts respectively. This indicates that the mite extracts have the same degree of specificity as these well-established allergens. With regard to the total incidence of positive results, however, sensitivity to mite extracts is by far the commonest finding in asthmatic children (Fig. 3).

When the only positive skin reaction of 5 mm. or more observed was given by the mite extract the majority of patients had an uncomplicated history of perennial asthma, whereas when reactions to other extracts were also obtained the clinical condition was often more complex, including such conditions as infantile eczema, hay-fever, and food allergy. Of equal importance is the finding that in 60 children without clinical evidence of allergic disease positive reactions to mite extract were almost absent, and the same was true of 27 children attending the asthma clinic whose condition was considered to be of infective or emotional origin with no evidence of allergy.

From immunological studies in progress it appears that all the mites we have used for testing have at least one antigen in common. Occasional patients show evidence of a greater degree of sensitivity to one of the other mites than to *D. pteronyssinus*. This may be related to special conditions in their own houses or to differences in individual sensitization. Much further study of the ecology of the house-dust mites is necessary both to clarify the clinical significance and to enable effective methods of control to be developed. Clearly the most satisfactory method of treating this condition would be to eliminate the mites from the domestic environment of the patient.

Desensitization seems likely to suffer from both the limitations and difficulties of pollen desensitization, which in nearly 50 years of use in pollen allergy has made some contribution to the relief of symptoms but virtually none to the cure. However, relief of symptoms by desensitization with mite extracts in dust-sensitive subjects may well be better than that obtainable with crude dust extracts (Research Committee of the British Tuberculosis Association, 1968) and may be worth clinical trial if no other solution is readily available.

One of us (Z. A. G.) is in receipt of a grant from the Asthma Research Council. Equipment was obtained through a grant from the Birmingham Regional Hospital Board Research Committee.

We also wish to express our thanks for the help of Mr. A. M. Cunnington, Dr. M. E. Solomon, and Dr. K. Maunsell. We acknowledge our debt to the nursing staff of the asthma clinics, particularly to Mrs. M. Roper and Mrs. V. Byfield, who carried out most of the skin tests.

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