

OPHTHALMIC AND NASAL MUCOSAL TESTS AS AN AID IN THE DETERMINATION OF HOUSE DUST ALLERGY

A Comparative Study

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ALLERGY to house dust undoubtedly is one of the most important causes of seasonal and perennial allergic rhinitis and/or asthma. Diagnosis of dust allergy depends usually upon a history of the induction of symptoms after exposure to dust contact and upon a positive skin test reaction in that patient to house dust extract. But in the absence of a clear-cut positive clinical history of aggravation of symptoms from dust exposure, it is difficult to determine whether a positive skin test reaction to house dust is of clinical significance (a "*clinical positive*"), or has no clinical relationship to the patient's symptoms (a "*non-clinical positive*"). Thus a positive clinical history confirming the positive skin test reaction is easier to obtain in housewives who are constantly being exposed to dust inhalation than in those patients (such as older children or adult males) whose most likely exposure to house dust occurs at night in their bedrooms or in their home on weekends, and in young children who crawl around on floors and rugs. Under those circumstances, when it is not easy to ascertain from the history that contact with house dust actually provokes symptoms, the diagnosis and subsequent treatment of allergy to house dust in such patients often is based chiefly upon the positive skin test reaction to house dust extract, especially if the reaction is of moderate or marked degree. Treatment for dust allergy usually involves many changes in the household furnishings (rugs, carpets, bedding, pictures, etc.) and injections of house dust extracts for purposes of hyposensitization. Since, in the absence of a definitely positive clinical history, such therapy might be based solely upon the finding of a positive skin test reaction to house dust, it actually would be superfluous were it possible to prove that the positive skin test reaction is a nonclinical positive. This is true also in patients with hay fever in whom, for some unexplained reason, positive skin test reactions may be obtained to house dust extract in moderate to marked degree, sometimes without confirmatory histories of clinical sensitivity.

Because of these considerations, the senior author long has felt that a more accurate determination of clinical allergy to house dust was needed so as to

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Received for publication May 16, 1962.

spare patients the bother and expense of unnecessary therapeutic procedures which depended solely upon a positive skin test. It was thought that the additional use of mucosal tests might provide the needed assistance in determining the clinical importance of positive skin test reactions to house dust. At first we thought this aid might be provided by the ophthalmic or eye test and used the latter for the initial study. Later, we found that additional help could be provided by the use of nasal tests carried out in a somewhat modified form. The results of these studies form the basis of the present report.

The value of eye tests in patients with house dust allergy was first reported by Abram¹ in 1949. He found that eye tests done with dried house dust powder were specific. Their use confirmed existing clinical sensitivity to house dust in the majority of patients (444 out of 490) tested. However, in 23 patients with negative skin tests to house dust, positive eye tests helped to reveal the presence of clinical allergy to house dust. Abram considered, therefore, that eye tests with house dust were helpful adjuncts in diagnosis.

Our own experience with eye tests with house dust dates back to 1954 when we began to do eye tests with numerous inhalant allergens, including house dust, in patients with various allergic conditions, mostly respiratory. The results of our studies with these eye tests were reported in 1959.² We learned from that experience that dry micronized house dust powder, such as that used for scratch test, could be put into the conjunctival sac of allergic individuals without inducing nonspecific or irritative reactions; hence, a positive ophthalmic reaction to house dust was immunologically specific and not the result of irritation. Included in that report were eye tests done with house dust powder on 209 patients; 46.9 per cent of the 209 had negative eye tests even though many had definite and, often, marked positive skin test reactions to house dust extract. Since we were not concerned at that time with the relationship of the eye test to the clinical history, no attempt was made to correlate the latter with the eye test results. But since then, and as part of our present study, we wanted to ascertain whether mucosal tests would aid in determining the clinical significance of a positive skin test to house dust, especially in patients with doubtful or negative clinical histories. As previously mentioned, in our first group of patients the eye test findings alone were compared with the results of the skin tests in relation to the clinical history of dust sensitivity. But, in the second part of our studies, we utilized both the eye and nasal mucosal tests for a similar comparison.

METHODS AND TECHNIQUES

Clinical History of Dust Sensitivity.—All patients included in this study were questioned as to the effects of exposure to house dust contact, both at the initial visit and, later, after the results of the skin tests to house dust were known. If the patients stated that dust contact induced sneezing, coughing and/or wheezing, the clinical history was recorded as positive. As already mentioned, a clinical history of the effect of dust contact was easy to obtain in those patients with known frequent exposure to house dust contact, as in housewives. Even if the patient stated that symptoms were induced only by exposure to large

amounts of dust and not by ordinary exposure, the clinical history was considered positive. But in many patients, as for example in most males and in many children, it was not easy to obtain a definite history as to the effect of the dust contact. Whenever there seemed reasonable doubt as to the effect of dust contact we recorded the clinical history as negative, so that histories used in our evaluation, and recorded as negative, included some histories which were doubtful.

The patients utilized for the first part of our study (eye tests only) were all private patients from the office of the senior author. The clinical effect of dust exposure was noted both at the time of the initial history and after the results of the skin tests were reviewed with the patient. On the other hand, most of the patients in the second group (who had both eye and nasal tests) were from Temple University Medical Center Outpatient Allergy Clinic; although the histories all were taken by one person (P. T.), it was more difficult to get as accurate a history in many patients because of language and/or of intelligence differences.

Eye Test.—The technique for performing this test was described in our first report.² The test is done by instilling a small amount of dry micronized dust powder* into the conjunctival sac from the blunt end of a toothpick. If no reaction appeared within 10 minutes, the dust powder was removed with a cotton-tipped applicator. If a positive reaction was observed within a few minutes, the powder was removed and eye drops (epinephrine in rose water) were instilled to prevent discomforting reactions. While positive eye reactions were reported in accordance with their intensity as slight (+), moderate (++), or marked (+++), a report as to the degree of reaction has little value since in many patients the powder was removed before the reaction could reach its maximum in order to prevent discomforting symptoms. The occurrence of numerous negative reactions corroborated our previous experience with eye tests with house dust in proving that the instillation of the powder into the conjunctival sac will not induce a nonspecific or irritative reaction. Since most of our patients were having eye tests done with other inhalant or pollen powders to which they gave negative reactions, we did not use a control in these instances. But where dust was the only allergen being tested, a small amount of powdered talc was instilled into the opposite eye as a control. We have never observed any reaction to the talc in any of the patients tested with it.

The *nasal* or "*sniff test*" was performed in the same manner as it has been for many years but with certain modifications made to improve the end results. Before the test is done, the nasal cavities of both sides of the nose are inspected with a rhinoscope. The latter, like the otoscope, has a small magnifying lens attachment which permits an excellent and detailed view of the character and color of the cell tissues within the nasal cavities and especially of any changes which take place after the test material is instilled. The patient then is asked to sniff a small amount of the dry talc from the blunt end of a toothpick into one nostril. If no reaction occurs within a few minutes, an equal amount of dust powder then is sniffed into the opposite nostril. If the patient begins to

*Obtained from C. G. Blatt & Co., Independence, Mo.

have symptoms (sneezing, nasal obstruction, or rhinorrhea), the nasal cavity is again inspected with the rhinoscope and the degree of reaction noted. If no symptoms are noted at the end of a 10 minute period, inspection of both nasal cavities likewise is made. If no change was noted on the test side compared to the other or control side (into which talc was sniffed), the reaction was recorded as negative. If there was definite pallor of the mucosa, very little swelling of the turbinates, and no symptoms, the reaction was recorded as one plus or slight; if there was definite pallor and moderate swelling of the turbinates with minimal symptoms (such as itchy sensation, nasal blockage, or rhinorrhea), the reaction was recorded as two plus or moderate; and finally, if there was definite pallor, moderate to marked swelling of the turbinates, and moderate symptoms, including sneezing, the reaction was recorded as three plus or marked. Little difficulty was experienced in reading the moderate or marked positive reactions. But determination of the slight positives was somewhat more difficult, although the reading of such reactions as distinct entities became easier with increased experience. Whenever doubt existed as to the reaction, it was recorded as a negative rather than as a doubtful positive reaction, a procedure which we adopted also in recording the eye test results.

Following the completion of the nasal test, the patient was instructed to blow his nose into a handkerchief or tissue to remove any remaining dust powder from his nasal cavities. None of the patients who had nasal tests with dust powder had any discomforting symptoms from the test. Administration of antihistaminics or instillation of vasoconstrictors into the nasal cavities was not required in those patients.

The nasal test, while simple to do and to read, was found to possess two major disadvantages which greatly hindered its frequent clinical application. The major one was the inability to perform the test whenever one wanted to, in contrast to the eye test. Obstruction of one or both nostrils either from large spurs, or a marked septal deviation, or from swelling of the turbinates due to inflammation or to allergy made it impossible to perform a satisfactory "sniff" test and necessitated postponing the test until the swelling subsided. In patients with organic obstructions, although the dust powder was sniffed into the freer side, one could not be certain that the powder reached the sensitized areas of the nasal cavities. A less frequent drawback was the possibility that inhalation of the dust powder might in occasional patients induce an acute and discomforting attack of rhinitis and/or asthma. As already mentioned, this did not prove to be a major obstacle in any of our patients who were instructed to blow out the dust powder at the completion of the test.

A rather curious but interesting finding reported by one of us (P. T.) who did all the nasal tests was the observation that patients with positive nasal tests to house dust nearly always volunteered the information that they could smell the dust powder which was instilled. It seemed to them to have a distinctive, though peculiar, odor. This was not true in patients with negative reactions either to house dust or to talc or even in patients with positive nasal tests to pollen powder, none of whom noted any abnormal odor even after being questioned about it. The reason for this curious phenomenon is not clear.

RESULTS

One hundred and twenty-three patients are included in the first part of the study, in which the eye test was the only mucosal test performed. Of this group, 49 had perennial asthma, 26 had allergic rhinitis, 15 had seasonal hay fever, and the remaining 33 had a combination of all three conditions. All but 3 had positive skin test reactions to house dust extract*; in the remaining 120, 43 reactions were slight positive, 37 were moderate, and 40 were marked in intensity.

The 3 patients with negative skin tests had perennial asthma. All had non-reactive skins with completely negative skin tests to all allergens tested. Of the 3, 2 were females (72 and 56 years of age) who thought that dust affected them but were not certain. The third patient, a 44-year-old male, was affected by occupational dust (tobacco dust and barn dust). The eye tests in all 3 patients were negative.

Of the 120 patients with positive skin tests, 31 had a negative clinical history and also had negative eye tests; 61 with positive clinical histories had positive eye tests. Thus there was good correlation between the three factors (history, eye test, and skin test) in 92, or approximately three fourths of the patients (74.8 per cent). This leaves for consideration 28 patients with positive skin tests in whom there was no correlation between the eye test and/or clinical history. Seven of the 28 had positive eye tests and negative (or doubtful) clinical histories. None of the 7, including 1 female adult, 3 adult males, and 3 older children were certain as to the effect which dust contact had on their symptoms. The remaining 21 patients with positive skin tests had negative eye tests. Six of the 21 were housewives who had frequent exposure to house dust contact and who stated that such exposure induced symptoms; 3 other adult females had much less contact with house dust and thought that dust caused some irritation (one from old books only). There were 9 adult males in this group—2 thought they were affected by dust in excess, one had little actual dust contact but stated it affected him during the grass pollen season only. One patient was not certain of the effect of house dust but thought that at one time, when he had worked in a foundry, the dust there had induced coughing. Similarly another patient was worse after exposure to feather dust in a hen house but he also was sensitive to feathers. The remaining 4 adult male patients all thought that dust exposure induced symptoms but were not too sure about its effect when questioned. The remaining 3 patients were older children who were uncertain both as to the extent and the effect of dust exposure—one 14-year-old girl thought it would induce sneezing; a second girl, 16 years of age, sneezed only when in contact with old books or old papers; and the third patient, an 11-year-old boy, had symptoms only when exposed to the dust of an old quarry where he sometimes played.

In summary, therefore, in this group of 21 patients with positive skin tests but negative eye tests, the clinical history was definitely positive in 6, uncertain

*All skin tests were done by injecting intracutaneously 0.02 ml. of the concentrated stock dust extract prepared in our own laboratory.

in 9, and limited to the hay fever season in one. The remaining 5 patients had symptoms apparently only from contact with miscellaneous environmental dusts (paper dust, quarry dust, etc.) other than ordinary house dust. Whether this means they were sensitive to the latter dust as well is not certain; if not, perhaps one explanation for the negative eye tests with the regular dust powder is that we were not using the dust powder actually responsible for their symptoms (e.g. paper dust, etc.). From the results obtained, it was evident that the eye test provided a better index of clinical sensitivity to house dust than did the skin test.

As previously indicated, in order to provide an additional means of determining clinical sensitivity, a second group of patients was studied in similar fashion but with the added use of the nasal test. This group totalled 122 patients; 31 of them had uncomplicated seasonal hay fever, 24 had perennial rhinitis, 44 had asthma, and the remaining 23 had combinations of all three conditions.

Of the 122 patients, all with positive skin test reactions to house dust, 56 had a negative clinical history. Of the 56, 42 had negative nasal tests. The remaining 66 patients had a positive clinical history; 55 of these had a positive nasal test. Thus there was good correlation between the clinical history, the skin test, and the nasal test in 97, or 79.5 per cent, of patients, which likewise was true of the eye test (74.8 per cent).

Of the 66 patients with positive skin tests and positive clinical histories, 50 had positive nasal and positive eye tests, 4 had positive nasal and negative eye tests, 5 had negative nasal and positive eye tests, and 7 had negative nasal and negative eye tests. The 4 patients with positive nasal and negative eye tests included a 59-year-old male with perennial asthma, a 47-year-old female with perennial asthma, a 66-year-old female with perennial rhinitis, and a 40-year-old female with perennial rhinitis, all of whom, according to their histories, were affected by dust contact. Three of the 4 had a slightly positive skin test, the fourth had a markedly positive skin test. The 5 patients with negative nasal tests and positive eye tests included a 22-year-old female with seasonal pollinosis, an 11-year-old female with allergic rhinitis and recurrent otitis media, a 28-year-old female with perennial asthma, a 20-year-old female with perennial rhinitis, and a 14-year-old female with perennial rhinitis and asthma. Three of the 5 had a markedly positive skin test reaction, and the remaining 2 had a moderately positive skin test. Of the 7 patients with negative nasal and negative eye tests, 3 had seasonal pollinosis and 4 had perennial asthma. The results of the studies in those patients with a positive clinical history of aggravation of symptoms after dust contact showed, therefore, that either one or both mucosal tests were positive in 59 of 66, or 89.3 per cent, of patients.

Of the 56 patients with negative clinical histories and positive skin tests, only 26, or 46.4 per cent, had negative nasal and negative eye tests. Thirteen patients had positive eye and positive nasal tests. Sixteen patients had a negative nasal and a positive eye test. Only one patient had a positive nasal and a negative eye test. This patient was a 29-year-old female of extremely low intellect

who had perennial rhinitis but who was uncertain of the effect of dust contact. The 16 patients with negative clinical histories, negative nasal tests, and positive eye tests included 5 patients with perennial asthma, 4 with perennial rhinitis, 5 with seasonal pollinosis, and 2 with a combination of these. It is apparent from these results that greater discrepancy existed between the history and the mucosal tests in those patients with a negative history than in those with a positive history.

The reason for this discrepancy can be explained theoretically, at least as follows: thus, it is possible that in doing the nasal test the dust powder may not come into direct contact with the sensitized cells actually responsible for the symptoms, as in patients with nasal obstructions of various types; or that, as in asthmatics, the most sensitive cells are in the bronchial mucosa rather than in the nasal mucosa; or, perhaps, the ophthalmic mucosa, although less sensitive than the skin, may be more sensitive than the nasal mucosa and thus may indicate the early presence of allergic sensitization, perhaps in a preclinical phase, before the nasal mucosa is involved. And finally, as already mentioned, a possible reason for the discrepancy was the uncertainty in some patients about the actual amount of exposure they had to the house dust allergen and as to its effect upon their clinical symptoms. The latter possibility is strengthened by our observation that in only 46.4 per cent of the patients was there correlation between the mucosal tests and the negative clinical history, whereas in patients with positive clinical histories, the percentage of correlation was almost double (89.3 per cent).

It seemed to us, therefore, that a better history of the effect of house dust could be obtained in patients with hay fever whose symptoms were seasonal and who perhaps were more aware of the provocative effect of house dust contact, both during the season and at other times. The frequency with which hay fever patients have had positive skin test reactions, often in marked degree, long has been observed. But the clinical significance of such skin test reactions has not been easy to ascertain. Not infrequently such patients have been given injections of house dust extract along with that of the pollen extract solely upon the basis of a marked positive skin test reaction. It seemed worth while, therefore, to see what the results of the comparative studies with the eye and nasal tests were in our seasonal hay fever patients.

In the first group of 123 private patients, eye tests with house dust powder were done only in those hay fever patients who were uncertain as to the effect upon them of dust contact. This was true of only 6 patients in that group. All 6 patients had positive eye tests. Two of the 6 had marked positive skin tests, and the remaining 4 had moderate positive reactions. Seven additional patients had hay fever complicated by asthma; all 7 had positive clinical histories, but only 6 of the 7 had positive eye tests. The one negative reaction was a young boy with a marked positive skin test reaction who thought his symptoms were aggravated by dust contact during the season. Of the 6 with positive eye tests, 2 had slight positive skin tests, and the other 4 had marked positive reactions. On the whole, in this small series of patients with positive clinical histories, the eye tests were confirmatory in nearly all instances.

Because of the relatively small size of this series, we attempted to get a clearer idea of the value of both mucosal tests in an unselected group of hay fever patients from our Outpatient Allergy Clinic studied out of season. This series comprised 31 patients, 27 with purely seasonal hay fever and 4 with asthma as a seasonal complication. All had positive skin tests to house dust; 2 were slight, 7 moderate, and 22 marked in degree. Of the 31 patients, 19 had a positive clinical history of aggravation of symptoms from dust contact, but in only 2 was it limited to the pollen season. Three of the 19 had negative eye and nasal tests, although the skin tests in 2 were markedly positive and, in the third, moderately positive. Two of the 3, a male, 18 years of age and a 20-year-old girl thought they were affected at all times by dust contact; the third, a male 23 years of age, was only affected by excessive dust contact. One patient, a 20-year-old female with a marked positive skin test, had a positive eye and a negative nasal test. She thought dust bothered her but was not certain. Fifteen of the 19 with positive histories had positive eye and nasal tests; of the 15, the skin tests were slight in one, moderate in 3, and marked in 11.

Twelve patients had a negative clinical history of aggravation by exposure to house dust; 5 had negative eye and nasal tests. Of the 5, the skin test reaction was marked in 4 and slight in one. An additional 5 patients had positive eye tests and negative nasal tests; 2 of the 5 had marked positive skin test reactions, in 2 it was moderate and in one was slight. The remaining 2 patients in this group with negative clinical histories had both positive eye and nasal tests and had markedly positive skin tests.

In summary, therefore, in this selected group of patients with seasonal hay fever, all with positive skin test reactions mostly in moderate or marked degree, there was agreement between the clinical history and the results of both mucosal tests in 20 of the 31 patients. In 5 of the 31 patients, the clinical history was positive but both mucosal tests were negative. In the remaining 6 patients, there was disagreement between both mucosal tests in relation to the clinical history; but in all of them the eye tests were positive and the nasal tests negative. The possible explanations for this discrepancy have already been discussed and apply equally here. But, since all the patients in this group had nasal symptoms and therefore had sensitized cells in the nasal mucosa which would have reacted with the house dust allergen if specific dust allergy existed, it seems fair to conclude that the nasal test provided a better index of clinical sensitivity than the eye test; thus 10 of the 12 patients with negative clinical history of aggravation by house dust had negative nasal tests, but only 5 of the 12 had coincident negative eye tests.

COMMENT

From a practical standpoint, the results of our studies show that a positive skin test reaction to house dust is clinically significant only in patients with definite histories of aggravation of symptoms after adequate exposure to dust contact. But when such a history is negative or doubtful, before any treatment of the dust allergy is instituted, an attempt should be made to determine the

clinical importance of the positive skin test by the use of mucosal tests. Since the eye test is easier to do and less likely to provoke discomforting symptoms or aggravation of existing allergies, it should be performed first. If negative, it can be assumed that clinical sensitivity is not present and dust treatment is unnecessary. If the eye test is positive, clinical sensitivity probably also is present; however, in cases of doubt and if there is no nasal obstruction or other contraindications, a nasal test with the dust powder should be carried out before treatment is instituted. If the nasal test is positive, treatment is definitely indicated, regardless of the clinical history. But when the nasal test is negative in a patient with a positive skin test and positive eye test, the decision whether or not to include dust hyposensitization in treatment will have to depend upon one's clinical judgement and the nature of the patient's symptoms. If the methods just outlined were followed in all patients, we believe that unnecessary therapeutic measures, based solely upon a positive skin test to house dust, would be avoided.

An additional sidelight revealed by our studies relates to the skin test findings. It long has been felt by some allergists that, if skin tests were positive in moderate to marked degree, clinical sensitization to this allergen was more likely than if the reaction was only slight in degree. Furthermore, it generally has been considered inadvisable to do eye tests with dry pollen in patients showing marked positive skin test reactions. Our studies have shown the fallacy of both these assertions. In the first place, we have been able to do eye tests without difficulty in patients with moderately positive or even markedly positive skin test reactions; yet in many, especially in those with negative clinical histories, there were negative ophthalmic reactions. Thus, in the group of 31 seasonal hay fever patients, most of whom had moderate or marked positive skin test reactions to house dust, of 12 patients with negative clinical histories, both the eye and nasal tests were negative in 5, and, in 5 others, the eye test was positive but the nasal test was negative. Furthermore, in the first group of 123 patients studied with the eye test and in the second one of 122 studied with both mucosal tests, many of the patients with negative clinical histories had moderate or marked positive skin tests to house dust; yet in many of those patients in the first group, the eye tests, and, in the second group, both mucosal tests were negative. This would seem to emphasize, as most of us have learned over the years, that the intensity of the reaction of skin tests is not proportionate to the clinical sensitivity. It also would seem to indicate that a reaction in the ophthalmic mucous membrane does not necessarily parallel that of the skin test and for that reason provides a better index of clinical sensitivity.

SUMMARY

Comparative studies of skin tests, mucosal tests, and clinical histories in 245 patients with various respiratory allergies have shown that eye and nasal mucosal tests may help to determine the presence or absence of clinical allergy to house dust in those patients who have positive skin tests to house dust but who are uncertain as to the effect of dust exposure upon their symptoms. Such

a determination may prevent the unnecessary use in some patients of those therapeutic measures (including hyposensitization) used in dust-sensitive patients. While our studies show that the nasal test is a more sensitive indicator of clinical sensitivity than the eye test, its use often is restricted by the presence of active symptoms, or of nasal obstruction, or of the possibility that the tests might induce active symptoms. Hence, in patients with positive skin test reactions and uncertain clinical histories or in those with negative skin tests and positive clinical histories, it is recommended that an eye test and, when necessary, a nasal test with house dust powder should be done to determine whether clinical allergy to house dust exists.

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