

The Journal of Allergy

VOL. 21

MAY, 1950

No. 3

American Academy of Allergy

Sixth Annual Meeting, Los Angeles, Calif., March 6-8, 1950

ATOPIC DERMATITIS

I. AN EXPERIMENTAL CLINICAL STUDY OF THE ROLE OF INHALANT ALLERGENS*†

LOUIS TUFT, M.D., HAROLD S. TUFT, M.D., AND
V. MURIEL HECK, M.T., PHILADELPHIA, PA.

THE TERM "atopic dermatitis," as customarily employed, refers to an acute, subacute, or chronic inflammatory skin disease, especially involving the flexures and characterized by intense itching, papulation, thickening, and lichenification of the involved areas. Its allergic character is generally undisputed. The disease is believed to be induced by sensitization to allergens carried by the circulating blood to the skin of an atopic patient, that is, one predisposed by heredity to develop specific sensitization.

Until recently, allergy to foods has been considered the major etiologic factor of this disease, probably because the sensitization is hematogenous and because it has been shown conclusively that food allergens are absorbed into the blood after ingestion. Furthermore, clinical experience has verified the reports of Hill,¹ Sulzberger and co-workers,^{2, 3} and others which showed that a definite etiologic relationship existed between foods giving positive skin reactions (e.g., egg) and atopic dermatitis. But this was not true of older children and adults, in whom removal of positive skin-reacting foods failed to relieve the skin condition. This naturally resulted in skepticism concerning the value of skin tests in atopic dermatitis and directed attention to other possible etiologies, notably infectious and psychogenic causes.

For some unexplained reason, and despite numerous reports and clinical evidence in recent literature,⁴⁻⁸ it still is not generally appreciated that inhalant allergens may be just as significant etiologically in atopic dermatitis in children or adults as in asthma, which it resembles in many respects. These facts all were emphasized in a recent report by one of us (L. T.).⁹ From a review of

*Read in part at the Sixth Annual Meeting of the American Academy of Allergy, Los Angeles, Calif., March 6-8, 1950.

†From the Clinic of Allergy and Applied Immunology, Temple University Hospital and School of Medicine, Philadelphia, Pa.

more than 50 patients with atopic dermatitis, it was shown, both upon the basis of clinical and skin test evidence, that house dust, pollens (especially ragweed), and wool are outstanding inhalant offenders and that other inhalants like atmospheric molds, animal danders, silk, cooking odors, etc., likewise may be important causes. The evidence upon which these conclusions are based is mostly clinical and, in that regard, conforms to that obtained by previous observers. Although it has been shown previously that such inhalant allergens as silk⁴ and pollen⁵ can be absorbed into the blood stream via the nasal mucosa, the definite relationship of inhalation of allergens, notably house dust, to the induction of atopic dermatitis has not yet been clearly demonstrated. Such an opportunity recently was afforded us in an experimental clinical study of a patient with atopic dermatitis and it is the results of these investigations which form the basis of the present report.

CASE REPORT

The patient, M. B., a 29-year-old man, first seen in our office in September, 1948, presented a long history of "eczema." The lesions first occurred in infancy and were constantly present despite treatment until he was 12 years old when they disappeared spontaneously. This remission in the disease persisted until 1943 when recurrence was noted while the patient was in the army, stationed in Trinidad. He was hospitalized there and in other hospitals without improvement until just before he was discharged from the service. Prior to discharge, he was sent to a hospital in Texas where the lesions disappeared in 3 weeks. This remission lasted until December, 1945, when a severe outbreak occurred in Philadelphia while the patient was living at home.

The systemic review revealed nothing noteworthy. There were no associated nasal or bronchial symptoms. The patient had never had hives or headaches.

The family history showed hay fever in his mother. She also had seasonal asthma.

Physical examination demonstrated a widespread itching, papular, and lichenified eruption, typical of atopic dermatitis. This was most severe in the antecubital fossae, popliteal fossae, wrists, anterior portion of the chest and abdomen, both groin areas, and about the neck. Otherwise, there were no abnormal physical signs.

The results of laboratory examinations were negative except for eosinophilia which ranged from 3000-4000 per cu. mm.

Intracutaneous tests revealed significant positive reactions to the following:

Inhalants: House dust, feathers, orris root.

Foods: Barley, corn meal, oats, rye, pork, cheese, chocolate, asparagus, celery, sweet corn, lima bean, olive, string bean, tomato, banana, strawberry, Brussels sprouts, eggplant, kidney bean, mushroom, pumpkin, rhubarb, sweet potato, turnip, nutmeg, paprika.

Pollens: None.

Molds: *Alternaria*, *Hormodendrum*.

Passive transfer tests to those substances italicized above were positive only to the following:

Inhalants: House dust.

Foods: Chocolate.

Pollens and molds: *Alternaria*, *Hormodendrum*.

Patch tests with the concentrated solutions of those allergens giving intracutaneous positive skin reactions were negative.

Treatment while in army hospitals had included all of the usual dermatologic therapy plus x-ray and fever therapy. The latter resulted in temporary clearing of the lesions, but x-ray had little or no effect on the condition.

Trial diet under outpatient regimen with subsequent addition of foods at 3-day intervals produced no response. The patient's skin condition grew so much worse that he was hospitalized for further treatment at Temple University Hospital on Nov. 26, 1948. Shortly after admission, and without any local or general treatment other than inhalant avoidance and trial diet, the condition spontaneously improved. Within 5 days, the acute lesions had almost completely regressed, and the lichenified and thickened skin became noticeably softer. Since subsequent addition of all foods (even those with positive skin reactions and circulating reagins) failed to influence the patient's condition, it became apparent that the improvement was the result of environmental change and that inhalant allergens, especially house dust, must be etiologically important. This led to an attempt on our part to prove that house dust or some other inhalant allergen present in the patient's environment was responsible for his symptoms.

EXPERIMENTAL STUDIES

The first experimental study was made using the dust of the patient's house. Vacuum sweepings were obtained from the mattress, pillow, living room furniture, and rugs of his home environment. The dust was coarsely filtered and the fine dust filtrate further powdered in a mortar. Nasal instillation of amounts sufficient to cover the end of a toothpick produced marked nasal blockage and visible edema of the turbinates, but no skin reaction. The patient was discharged, improved, for the holiday season on Dec. 23, 1948.

On December 27, he was skin tested with an extract of the dust collected above and showed a marked positive reaction. The next day, he telephoned to say that there was a severe flare-up in the skin lesions and that he felt the test had caused it. However, he admitted that he was practically confined to the house because of the weather and that he had taken no precautions to avoid inhalant factors.

Regardless of whether this increase in symptoms could be attributed to the autogenous dust test done immediately prior to the flare-up or possibly to the exposure to the house dust allergen in his living room or to both, the condition became so marked that he was readmitted on Jan. 17, 1949. The lesions did not clear up so readily this time, and it was discovered that dusting in the ward was carried out in a dry manner and seemed to delay improvement. When the patient was moved to another ward and the hazards of dry dusting explained, the condition regressed more quickly.

When his skin cleared up sufficiently, further experiments were performed in order to explain the reaction.

Samples of dust from the various pieces of furniture in the living room and bedroom were obtained. These were powdered in a mortar. Extracts for scratch testing were made by addition of enough 14 per cent ethyl alcohol to moisten thoroughly approximately 4 Gm. of dust. This was allowed to stand for 24 hours and the supernatant fluid squeezed out and used for the scratch test. Scratch tests done with the various dust samples showed the dust collected from the living room sofa to give the largest positive reaction.

Because inhalation of dust by direct nasal instillation resulted only in nasal blockage and rhinorrhea and had no effect upon the dermatitis, perhaps because of poor absorption, a means of by-passing this block was devised. A 15-Gm. sample of the dust from the living room sofa was micronized* and by accurate measurement was found to consist in the main of particles below one micron although some particles of 5 to 10 microns were present. Thus, a majority of the particles could be brought to the finer bronchioles and could be absorbed much in the manner of penicillin dust. Indeed, the bronchial instillation was carried out in this patient by use of the Aerohaler (Abbott), an apparatus which, when used with penicillin as the powder, allows adequate and sustained penicillin blood levels.

Bronchial instillation of that amount which could be carried on the flat end of a toothpick was performed 4 times daily for a period of 2 weeks. Three significant reactions followed this procedure. To begin with, there was a definite and sustained increase in the symptoms and the physical signs of the dermatitis. Second, each inhalation resulted in increased sweating in the areas of the skin previously affected by the lesions of the derma-

*Done by the Micronizer Corporation, Moorestown, N. J.

titis. Itching began at back of neck and sweating occurred there also. Then itching and sweating of antecubital fossae, front of the neck, and chest followed in order. In addition, nasal blockage and postnasal mucus and slight morning sneezing appeared even though the

some of the dust was taken up into the nasal passages during inhalation or perhaps that the allergen was carried to the nasal mucosa by the blood stream.

After the lesions produced by dust inhalation had subsided, the patient was again tested intracutaneously to the aqueous autogenous dust extract as in the first hospitalization. The wheal produced was large and was followed by a mild outbreak in the affected skin areas. Injection of the extract in 0.05 c.c. amounts intracutaneously was carried out at 3-day intervals for 5 injections. Following each injection, increased itching was noted for 24 hours while, after the whole series, definite thickening of the skin in the affected areas was noted. Two weeks after the last injection, the acute dermatitis subsided and the affected areas became softer and less thickened. During the next free period, the patient was injected intracutaneously with 0.1 c.c. of a timothy extract (0.2 mg. total nitrogen) for a total of five injections at 3-day intervals to serve as a control. No unusual reactions were observed.

Because the patient had been seen in September for the first time and because the lesions had been particularly bad through the summer months and, in view of the positive reactions to *Alternaria* and *Hormodendrum*, it was decided to investigate the role of these allergens. Accordingly, nasal inhalation with *Alternaria* powder was performed like an ordinary nasal test. This produced an immediate positive local nasal reaction despite the lack of nasal symptoms in the history. But in addition there occurred a systemic reaction consisting of profuse sweating in the areas where the lesions had been present. This was followed by an outbreak of the dermatitis commencing within 24 hours of the test and lasting the usual 4 to 5 days. This was repeated 6 times and the same results were obtained each time. Control nasal tests performed in the free period with tale, pine pollen, and timothy pollen failed to produce either nasal or skin reaction.

DISCUSSION

As previously mentioned, ample clinical and skin test evidence has already been provided by other investigators to indicate that inhalant allergens are of etiologic significance in atopic dermatitis. Certain clinical features presented by the patient herein reported also emphasize this; thus, significant positive skin tests to extracts of house dust and of *Alternaria* with demonstrable reagins were demonstrated. Furthermore, the beneficial effect of environmental change was indicated by the rapid improvement in the patient's dermatitis which followed each of the 2 hospitalizations, also by the failure of the condition to respond quickly after the second hospitalization until the patient was moved to another ward where his exposure to dust was better controlled. That food allergens were of no causal importance was proved by the failure of the dermatitis to improve while the patient was on diet trial as an outpatient and also because it did not reappear during his hospital stay after the addition of all foods, even those with positive skin reactions and, as in the case of chocolate, with demonstrable reagins. These observations strongly suggest, therefore, that inhalant environmental allergens are important exciting factors in atopic dermatitis and thus confirm previous clinical experience and observations. But because this evidence has been furnished by clinical data only, so far it has been insufficient to be considered as definite and acceptable proof of a specific etiologic relationship. No one previously, at least to our knowledge, has been able to

induce the specific lesions of atopic dermatitis repeatedly by deliberate exposure of the patient to the offending inhalant. We believe that the results of the experiments herein reported accomplish this purpose and therefore supply the evidence, previously lacking, of a specific causal relationship between inhalant allergens and atopic dermatitis. For example, deliberate exposure of the patient on numerous occasions to the inhalation of house dust and *Alternaria* spores was followed within a short period of time by reproduction of the specific dermatitis for which he consulted us. These allergens were employed in as nearly a native state as possible; thus, the *Alternaria* powder containing a relatively large percentage of whole spores was produced from properly killed actively growing cultures, whereas the house dust was used after drying and powdering, being micronized only to insure adequate absorption. Although the instillation of the *Alternaria* powder into the nose produced nasal symptoms, it did not induce sufficient nasal blockage to interfere with the absorption of the allergen into the blood as was the case with the unm micronized house dust. Whether the difference in these effects can be explained by a difference in particle size or by a variation in antigenicity or in local effect is problematical and, for our present purposes, unimportant.

Additional proof of the specific etiologic relationship was furnished by the reproduction of the dermatitis repeatedly after intracutaneous injection of house dust extract in doses sufficient to induce reactions. The extract used in this case was obtained from the dust of a sofa in the patient's own home to which he showed specific positive skin reactions and demonstrable reagins. On the other hand, injections of timothy extract to which the patient was not sensitive failed to induce the dermatitis, showing that the reaction was specific.

We believe, therefore, that these experimental clinical studies conclusively prove that inhalant allergens may be as important or even more so than foods in the production of atopic dermatitis. The respiratory mucosa acts as a portal of entry for the absorption of the allergen into the blood. It then is carried to the skin and induces the dermatitis in the predisposed areas. The mechanism involved in the production of these lesions is not known, but from the evidence furnished by additional experiments carried out on this and other patients, we believe that it has something to do with the sweating mechanism. This will be discussed more fully in a subsequent communication.

SUMMARY AND CONCLUSIONS

1. A case of atopic dermatitis in an adult male, in whom clinical evidence pointed to inhalant allergens as etiologic agents, is reported.
2. For the first time, the disease was reproduced repeatedly by controlled exposure to inhalant allergens, namely house dust and *Alternaria*.
3. The results obtained in this clinical experimental study emphasize the validity of impressions gained from clinical experience and earlier reports concerning the importance of inhalant allergens in atopic dermatitis, especially in older children and adults.

REFERENCES

1. Hill, L. W.: Chronic Atopic Eczema (Neurodermatitis) in Childhood, *J. A. M. A* 103: 1430, 1934.
2. Sulzberger, Marion B., Spain, W. C., Sammis, F., and Shanon, H. I.: Studies in Hypersensitiveness in Certain Dermatoses, *J. ALLERGY* 3: 423, 1932.
3. Sulzberger, Marion B., and Goodman, J.: The Relative Importance of specific Skin Hypersensitiveness in Adult Atopic Dermatitis, *J. A. M. A.* 106: 1000, 1936.
4. Walker, I. C.: Causation of Eczema, Urticaria and Angioneurotic Edema by Proteins Other Than Those Derived From Foods XVIII, *J. A. M. A.* 70: 897, 1918.
5. Feinberg, S. M.: Seasonal Atopic Dermatitis. The Role of Inhalant Atopens, *Arch. Dermat. & Syph.* 40: 200, 1939.
6. Figley, K. G., and Parkhurst, H. J.: Silk Sensitivity, With Special Reference to Its Role in Atopic Eczema; *J. ALLERGY* 5: 60, 1933.
7. Sulzberger, Marion B., and Vaughan, W. T.: Experiments in Silk Hypersensitivity and the Inhalation of allergen in Atopic Dermatitis (Neurodermatitis Disseminatus), *J. ALLERGY* 5: 554, 1934.
8. Nexmand, P. H.: Clinical Studies of Besnier's Prurigo, Copenhagen, 1948, Rosenkilde and Bagger.
9. Tuft, L.: Importance of Inhalant Allergens in Atopic Dermatitis, *J. Invest. Dermat.* 12: 4, 1949.