

IMPORTANCE OF INHALANT ALLERGENS IN ATOPIC DERMATITIS*

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Despite the recent advances in allergy, atopic dermatitis (also designated allergic eczema or neurodermatitis) still constitutes a troublesome problem not only for the physician who has to treat this condition but even more so for the patient who suffers on without relief. Before its true etiology was recognized, this disorder was included in the general category of dermatologic scrap-heap or eczemas and treated as such. Because of the associated nervousness and excessive itching and since its etiology often is undetermined, the designation neurodermatitis, originally given to it by Brocq still is used, especially by those who feel that psychogenic factors serving especially to aggravate the desire to scratch, are of paramount importance. However, in more recent years and particularly through the efforts of Sulzberger and Hill and their co-workers (1A, 1B, 2, 3, 4) the relationship of allergic factors to this condition has been definitely established. The basis for this was the frequent association of this dermatosis with allergic asthma or hay fever, either concomitantly or one before the others; also the high incidence of positive family histories of certain other allergic diseases; the common finding of eosinophilia; and finally, the conclusive demonstration of the high incidence of positive skin tests to specific food and inhalant, so-called "protein," allergens and the occasional demonstration of clinical exacerbations of exposure to these allergens either by ingestion, inhalation, external contact or in other ways. These evidences of a special form of allergy prompted Sulzberger and Coca (5) to designate this condition *atopic dermatitis*, the word "dermatitis" indicating its inflammatory nature and the term 'atopic' signifying that it was associated with the specified forms of human allergy in which hereditary predisposition was especially prominent. This distinction as well as its clinical characteristics, which have been so clearly defined in infancy, childhood and adult life by Sulzberger and Hill and other co-workers, serve to differentiate atopic dermatitis distinctly from contact-type allergic eczematous dermatitis. According to these criteria, atopic dermatitis may be described as an acute, subacute or more often chronic inflammatory disease of the skin involving especially the flexures, and characterized by intense itching, papulation, thickening and lichenification of the involved areas. It is associated with skin-sensitizations to "protein" allergens in an atopic patient, that is, it occurs in an individual who has been predisposed by virtue of heredity to the development of certain characteristic forms of clinical disease based on specific sensitizations.

It is unquestionably true that the lesions when seen by the practitioner often are not truly primary but represent secondary traumatic effects of the patient's constant scratching. This accounts for the marked excoriations and also for

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the subsequent thickening of the skin. The most prominent initial symptom undoubtedly is intense itching. This causes the patient to scratch and rub and explains the secondary changes. But if the patient had no basic reason for the primary itching, there would be no incentive to scratch and no secondary changes. Allergic sensitization, in the opinion of allergists and of many dermatologists supplies the basic reason for the primary itching. Once the lesion has developed, other factors including psychogenic ones, then may aggravate the condition.

Allergy to food has long been considered the major etiologic factor in atopic dermatitis, probably because the sensitization is hematogenous and food allergens are known to be absorbed into the blood after being ingested by the patient. Thus as early as 1915 Schloss (6) stated that infantile eczema often was due to allergy to such foods as eggs, milk and cereals. This observation subsequently was corroborated repeatedly by many others both by clinical and skin test evidence. Hill (7), for example, has shown that removal of the positive reacting foods from the diet of infants or young children with atopic dermatitis is followed by marked improvement or even cure, whereas their reintroduction into the diet brings about a recurrence. But this is not always true of older children or adults afflicted with this disease. Despite positive skin tests to many foods, removal of these foods from the diet fails to relieve the skin condition as it does in infants or younger children. This naturally has resulted in considerable skepticism concerning the value of skin tests in atopic dermatitis. In fact, as a consequence, some authorities have recommended dispensing altogether with the skin testing; more attention has been focused upon other possible etiologies, including particularly infectious and psychogenic factors.

For some unexplained reason and despite adequate clinical evidence in many offices and clinics, little or no attention has been paid to inhalant allergens as possible causes of atopic dermatitis. This is not due to lack of publications calling attention to this possibility. In 1918, Walker (8) reported two patients with "eczema" provoked by exposure to horse dander. Since, then, many others have reported instances in which various inhalants were prominent factors, as emphasized by Sulzberger, Spain and co-workers (3) Feinberg (9) and others. Furthermore, clinical proof also has been furnished showing that inhalation of such allergens as house dust, silk, flour, horse dander, or pollen is followed in susceptible patients by exacerbation of the dermatitis. Thus for example, Figley and Parkhurst (10) reported 5 patients with atopic dermatitis apparently secondary to the inhalation of silk and Sulzberger and Vaughan (11) conducted experiments showing that silk allergens can reach the skin after inhalation.

Despite all this evidence of the importance of inhalant allergens in atopic dermatitis, one still sees many patients in whom attention has been directed entirely to removal of offending foods or to elimination of psychogenic or infectious factors without benefit in either instance to the patient. I have found that in such patients, the investigation and elimination of the offending inhalants often is followed by substantial improvement. This has been so true in my experience that it seemed worth while (even at the risk of repetition) to again emphasize the role of the inhalants with the hope that better therapeutic results might thereby be secured in the treatment of this stubborn condition.

Actually, one should not be surprised that inhalants are important in atopic dermatitis especially in older children. That there is a close resemblance between atopic dermatitis and allergic bronchial asthma has been emphasized repeatedly by many writers (1A, 1B, 2, 3, 4). Those two conditions have so many characteristics in common both in relation to etiology, diagnosis and treatment that atopic dermatitis has properly been designated "asthma of the skin." Thus both conditions frequently co-exist or alternate in the same patient. Atopic dermatitis in infancy often is supplanted by asthma of childhood or later life and vice versa. As in asthma, patients with atopic dermatitis are often worse in the winter and especially at the times of seasonal change from summer to fall and winter to spring. Positive skin reactions occur in both conditions in about the same proportion and have about the same clinical significance. Food allergy is admittedly most important, not only in asthma of infants and young children but also in atopic dermatitis. Likewise inhalant allergens are more prominent than foods in asthma affecting older children and adults; yet strangely enough, the same reasoning has not been applied similarly to its counterpart in the skin.

It has been conclusively demonstrated that inhalant allergens (e.g. pollen) (12) are readily absorbed into the blood from the nasal mucosa; also that in patients with atopic dermatitis, inhalation of silk protein (11), horse dander (8), house dust or even pollen (9) is followed by aggravation of the skin condition. It follows, therefore, as a logical corollary, that inhalants also may be just as important in the etiology of atopic dermatitis as in asthma, especially in older children or adults. Actually this has been the experience of those of us who study these patients from the standpoint of the effect of inhalant allergens.

Not all inhalant allergens are equally significant as etiologic agents. The exact incidence is difficult to estimate in the absence of adequate statistical reports. In order to get some idea of their relative importance, the author reviewed the case histories of a group of patients seen both in hospital and private practice. While all these patients had extensive intracutaneous skin tests, not all were followed long enough to determine the clinical significance of the positive reactions. Nevertheless, there were sufficient clinical data to warrant certain conclusions (table 1). From a review of this data, it is at once obvious that *house dust* is quite prominent as an etiologic agent. Thus of the 54 patients tested, all had positive reactions, 46 or 85% being of moderate to marked degree. Furthermore, at least seven patients noted definite aggravation of symptoms from exposure to dust. This is demonstrated rather strikingly in the following patient:

Male, age 62, admitted to Temple University Hospital, March 11, 1938, was referred for allergic study by Dr. Carroll Wright because of extensive generalized atopic dermatitis, so diagnosed by the dermatologist and present since November 1937. His condition cleared for a while in January while the patient was away from his home in Wilkesbarre, but recurred within ten days after returning home, becoming increasingly severe and extensive. The patient had fall hay fever for ten years, not improved by pollen therapy. Because of the extensive skin involvement, tests were done by passive transfer. Reactions were found in marked degree to house dust, ragweed, timothy and to a lesser extent to some food allergens. His condition cleared up remarkably while in the hospital and subsequently in Atlantic

City so that in almost a month it became normal in texture and appearance. Dust was obtained from the patient's home and an autogenous extract prepared to which he gave both a marked skin reaction and a positive passive transfer reaction. He was instructed to return to Wilkesbarre but not go to his own home for several weeks until the house could be rid of dust-containing articles and until some desensitizing injections of the dust extract had been given. He finally returned to his home without difficulty. The injections were discontinued after about two years and when recently seen, the patient reported that there had been no recurrence for a period of more than 8 years.

This case report strongly suggests the importance of house dust allergy as an etiological agent in atopic dermatitis. The exact nature of the excitant in

TABLE 1
Incidence of skin test reactions and of clinical sensitivities in atopic dermatitis

ALLERGEN		NUMBER OF CASES STUDIED	NO. AND DEGREE OF REACTIONS TO DIRECT INTRACUTANEOUS SKIN TESTS				NO. OF CLINICAL SENSITIVITIES AS INDICATED BY HISTORY
			Nega- tive	Slight	Moder- ate	Mark- ed	
House dust		54	0	8	31	15	7
Pollens	Ragweed	51	5	14	12	20	22
	Timothy	51	27	15	7	2	4
Molds	Alternaria	50	38	11	1	0	0
	Hormodendrum	50	42	8	0	0	0
Animals danders	Feathers	50	13	13	24	0	1
	Cat	51	33	18	0	0	3
	Dog	51	42	9	0	0	0
	Horse	51	42	9	0	0	1
	Rabbit	51	41	10	0	0	1
Wool		49	15	26	8	0	18
Silk		46	28	14	3	1	0

house dust is as yet unknown, but that it is a prominent environmental allergen appears certain. As with asthma, sensitization to environmental dust may explain the improvement obtained by many patients with dermatitis when they go way from home whether on a pleasure trip or to the hospital, to the seashore, etc. This is shown very nicely in the following patient:

Girl, age, 16, also referred by Dr. Wright, with flexural atopic dermatitis, recurrent since infancy, and only symptomatically relieved by the usual local dermatologic management. Allergic study showed positive reactions to dust, wool, pollens, and some foods. Patient was always improved while at the seashore in the summer. This was attributed to beneficial effect of sun's rays. She was always worse in early fall and winter months. She was asked to go to the seashore in the spring but not return to her own home; instead she remained in the same neighborhood in the house of a relative. The skin condition cleared up at the sesashore and did not recur even in the home of the relative, but it became worse

within a day or two after returning to her own home. Institution of proper dust precautions and desensitization with an autogenous house dust extract in addition to pollen therapy has been followed by marked improvement which has persisted for more than 3 years. It was subsequently determined by clinical trial that none of the positive reacting foods, with the possible exception of chocolate were of etiological significance.

This case likewise indicates the possible importance of environmental dust and the benefit of its avoidance plus dust desensitization.

The question may arise as to whether in these patients the dust excitant acts by inhalation or by direct contact. Since the lesions involve the flexures in most patients and they usually are covered, it appears unlikely that dust will have a chance to act directly, but rather that it operates by inhalation. If a sufficient amount of dust does come into direct contact with the skin, it can cause difficulty, as was clearly demonstrated in one of our clinic patients with hay fever and other allergic manifestations. She observed that when the house dust present on a dust rag was in direct contact with her skin it causes marked itching. When the dust is inhaled, she first would sneeze or wheeze and subsequently if intense enough, some itching of the affected skin would follow. Strict avoidance of contact with dust coupled with injections of the extract has enabled this patient to remain free of dermatitis for more than 6 years.

Pollen allergy may be second only to house dust in provoking exacerbations of atopic dermatitis. This possibility is not generally appreciated despite reports by Cazort (13), Feinberg (9), Rowe (14), and others. So many of my patients have shown positive reactions to pollens, especially ragweed, that it has come to be an expected finding in nearly every patient with atopic dermatitis especially in older children and adults. In fact, of the 51 patients tested only 5 showed completely negative reactions whereas 32 were of moderate to marked degree. In some patients the positive pollen reaction can be explained by concomitant hay fever or by a positive family history of hay fever and has no etiologic relationship to the skin condition. But in others, it is in my opinion definitely causal and may induce marked aggravation, as indicated for example in the following report:

Male, age 35, seen in our allergy clinic March 1945 with marked generalized atopic dermatitis for two years duration and a history of seasonal hay fever and asthma since the age of 9; also occasional migraine and urticaria and a history of hay fever in his father. With the onset of the skin condition in July 1943, he had very little hay fever or asthma—in fact during 1944 he had only one day of hay fever and asthma. But during August and September 1944, his atopic dermatitis was so severe as to require hospitalization for a month with little relief until the hay fever season was over. This experience was so bad that the patient dreaded the approach of another season for fear of recurrence. Intra-cutaneous skin tests showed marked positive reactions to ragweed pollen and house dust and in lesser degree to other inhalants and foods. Ragweed and dust desensitization was instituted with beneficial results until the patient was last seen in the clinic in August 1945.

The second case was that of a male, age 31, admitted to hospital in October 1945, with a generalized atopic dermatitis of two years duration affecting especially the flexures. The patient had had hay fever for many years up to two years before. With the onset of the skin condition, there was no further attack of hay fever. Patient's father also had hay fever. Intracutaneous skin tests showed significant positive reactions to ragweed and

timothy pollens; also to house dust, feathers, wool and some animal danders. The patient noted definite aggravation from contact with dust and wool and seemed worse during the pollen seasons. That environmental allergens were operative in his case was suggested by the fact that at the end of his two weeks stay in the hospital and without specific treatment there was marked improvement in his skin condition, improvement which persisted as long as the patient was under observation.

Both case reports, which could be duplicated to a less striking degree by other patients, clearly suggest the possible etiologic relationship of pollen allergy to atopic dermatitis. Thus in the first patient, the hay fever and asthma present for many years was replaced almost completely by the dermatitis which was greatly aggravated by the ragweed sensitivity. When the ragweed season was over, the dermatitis was prolonged and became perennial from the same factors, inhalant or otherwise, which operate in perennial asthma secondary to seasonal hay fever.

While the skin condition did not become aggravated in the second patient as in the first, nevertheless, the hay fever symptoms strikingly disappeared when the atopic dermatitis supervened. This tendency for alternation—that is for one allergic condition to be replaced by another at various times of life—is characteristic of the so-called eczema (atopic dermatitis) hay fever group of patients, and has been noted by Brocq and many early observers.

I am convinced that appreciation of the possible role of pollen sensitivity in atopic dermatitis is quite essential to the proper management of these patients. Where a possible causal relationship can be established by history or skin test findings or both, pollen desensitization, in my experience, has been definitely beneficial. In the absence of a definite history of seasonal aggravation but with positive skin reactions to pollens, it is difficult to decide whether pollen therapy is advisable. If the patient has a positive family history of hay fever or very mild nasal symptoms, I believe that pollen therapy may be valuable from a prophylactic standpoint even if the pollen sensitivity has no bearing on the skin condition. This opinion is not shared by other allergists but I believe that it has proved beneficial to some of my patients.

Allergy to atmospheric *molds* conceivably also may be important etiologic factors in atopic dermatitis. But it is unlikely that it plays much of a role in the eastern area, since the incidence of mold allergy in hay fever or asthma is rather low in this area (about 5%) in comparison with other regions, notably the midwest. A small percentage (possibly 15) of our patients with positive reactions to pollens also reacted in slight degree to such molds as *alternaria* and *hormodendron* but a definite etiologic relationship could not be established in any of those studied. This is in contrast to the experience of Feinberg (15) in Chicago, who finds mold allergy more important in his patients because atmospheric molds are much more prevalent in the midwest area.

Allergy to *animal danders* also may be important in atopic dermatitis but the exact extent is hard to estimate. 37 of the 50 patients tested gave slight or moderately positive skin reactions to feathers but it was not always easy to decide whether they were clinically important, first because feather extracts

often give non-specific positive reactions and also because clinical relationship could not be easily proved. These patients probably do not inhale enough feather allergen to produce atopic skin manifestations; nevertheless, it is possible that feather allergy may be an additional excitant. Elimination of this source of allergenic contact in patients with positive skin tests to feathers, therefore, is advisable. Allergy to horse, rabbit, cat or dog dander are not prominent causes of flare-ups in atopic dermatitis probably because of lessened opportunity for exposure. Only about 10% of the patients studied gave positive skin reactions to extracts of these danders; however, several patients noted definite itching of the affected skin areas or new outbreaks when they were near a cat, dog, rabbit, or horse even though not in direct contact with the animal. In at least three patients, improvement in the skin condition seemed to follow removal of cats to which they gave positive reactions. Skin tests with extracts of cat, dog, horse or rabbit epithelium are quite specific. When present in a patient with atopic dermatitis, one should search diligently for possible sources of contact.

The importance of *wool* as a deleterious factor in many cases of atopic dermatitis is generally unquestioned. But whether wool acts as an inhalant or as a contactant allergen or both, or whether it causes aggravation by nonspecific irritation is not always easy to determine. Of the 49 patients studied, 18 stated that itching followed when wool was brought into contact with their skin lesions or even with the unaffected skin. Undoubtedly, in some of these patients direct contact action is operative and not all of it is due to a specific allergy. Nevertheless, many patients showed definite improvement when the woolen articles of clothing or bedding were removed completely. Since these articles are not always in direct contact with the patient's lesion, one may assume that some of the wool allergen may act because it enters the circulation after being inhaled. As with feather extracts, skin tests with wool extracts may be non-specific in character. Thus, while 34 of the 49 patients tested showed slight to moderate positive reactions, some probably were nonspecific.

A similar situation exists in relation to *silk*. Patients with atopic dermatitis may show positive skin reactions to this allergen. Thus 18 of 49 patients tested showed positive skin reactions, four being of moderate to marked degree. None of these patients apparently noted any evidence of clinical sensitivity although this is not easy for the patient to detect. However, as previously mentioned, evidence that silk can be responsible for aggravation of symptoms in patients with atopic dermatitis has been furnished previously (10). While it had been believed that as with wool, the allergy is provoked by direct contact of the silk with the patient's skin, yet the experiments of Sulzberger and Vaughan (11) conclusively demonstrated that silk protein when inhaled can be absorbed into the circulation and thus could aggravate or induce the lesions of atopic dermatitis. It is not always possible in a silk-sensitive patient to determine which route is operative. Patch tests frequently are negative but this does not exclude a possible contactant action. Regardless of the method of action, it is advisable for patients with positive tests to silk to remove all possible sources of silk contact and silk inhalation.

Other inhalant allergens, like orris root, tobacco, insecticides, goat hair, cereal flours, etc. may be possible but infrequent causes of atopic dermatitis. Thus for example, occasional instances have been reported of atopic dermatitis secondary to inhalation of cereal flours especially in bakers, but these are the exception rather than the rule. Even the inhalation of the odors of cooking (16), especially of fish, or of perfume may cause aggravation in some patients. Interest again has been revived in the possibility that sensitivity to *human dander* maybe a causative factor in atopic dermatitis especially in infancy. Allergy to human dander first was described in 1925 by Van Leeuweun in Holland (17), who considered it important in bronchial asthma. But this was never clearly proved and the subject was dropped. Recently, Frank Simon (18) showed that infants with atopic dermatitis gave positive skin reactions and passive transfer tests to human dander. He believes that in such instances, the human dander present in the scalp of the mother or father may aggravate the lesion either from direct contact with the skin or possibly from inhalation. Simon (19) further demonstrated the allergenic content of the skin, its appendages and derivatives of the epidermis. No conclusive etiologic relationship has been established as yet in these patients. Until it is, one must withhold judgment as to the possibility that human dander is a specific causative factor in atopic dermatitis.

Before concluding, I should like to make it clear that I do not consider inhalant allergy the *sole cause* of atopic dermatitis in older children or adults, even though I believe it to be an important factor often neglected in the management of these patients. Food allergens also may be causes of exacerbations in some patients but less so than has hitherto been regarded. Emotional factors, fatigue, infections, etc. undoubtedly also are significant and should be controlled whenever possible. But as previously stated, if one can remove the allergic basis of reason for the initial scratching, there will be a definite lessening of the irritability and of the scratch habit and as a consequence the emotional condition of the patient will be improved. I also cannot stress too strongly *the necessity for proper local treatment in every patient*, this should be done whenever possible by a competent dermatologist and not by the allergist. As a rule the allergist cannot be a good dermatologist nor the dermatologist be a good allergist. If one attempts to perform the duties of the other, the only one who eventually suffers is the patient. I am certain that my results in patients with dermatitis definitely have been better (even better than my results in asthma) because I have insisted that the local treatment be managed by a competent dermatologist while I tried to discover and eradicate the allergic factors. It is my conviction that it is only through the recognition of the multiplicity of etiologic or aggravating factors and their eradication and through proper team work between both specialities that good therapeutic results can be expected in atopic dermatitis.

SUMMARY

1. Despite numerous clinical reports and the experimental evidence contained in recent literature, it is not generally appreciated that inhalant allergens may

be just as significant in eliciting attacks in atopic dermatitis as they are in asthma, especially in older children and adults. This is corroborated by the author's experience and by a review of treated patients.

2. House dust, pollens, especially ragweed, and wool are outstanding offenders.

3. Other inhalants, including animal dander, silk, cooking odors, possibly human dander and a miscellaneous group are less frequent offenders but nevertheless may be important factors.

4. Best results in treatment can be expected if competent allergists and dermatologists can cooperate closely in the study and the therapy of these cases.

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