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STUDIES IN ATOPIC DERMATITIS

V. Problems in Inhalant Hyposensitization and Results of Treatment

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IN PREVIOUS studies my associates and I conclusively demonstrated that such inhalant allergens as house dust, pollens, and/or molds were important causes of atopic dermatitis.¹⁻⁴ We were able to induce the dermatitis in susceptible subjects both by the inhalation of powdered house dust, alternaria, and ragweed pollen and by the injection of extracts of these allergens.

The demonstration of the etiological importance of inhalant allergens focused attention upon the question of hyposensitization with extracts of these allergens. Contact with inhalant allergens is neither easily nor completely avoided, even though the amount of exposure to them may be somewhat reduced; hence, proper treatment in these patients, as in asthmatic patients allergic to similar inhalants, must include attempts at hyposensitization with extracts of the offending inhalants. This method had been employed to some extent by both allergists and dermatologists but, judging from sporadic reports in the literature, not with any consistent degree of success.

The literature pertaining to the effect of hyposensitizing treatment in atopic dermatitis is scant. Prior to our own publications relating to the management of this condition, only occasional mention was made of the use of extracts of house dust or pollen in treatment. For example, in 1946 Rowe⁵ reported instances of atopic dermatitis of the hands due to plant pollen and discussed in a general way the use of hyposensitizing injections with pollen extracts. None of the previous articles, however, included details of the methods used or of the end results of treatment. Since the publication of our own studies, Diamond⁶ also reported on the value of hyposensitization with inhalant allergens.

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Undoubtedly, those physicians who first see these patients (for example, allergists, dermatologists, and pediatricians) have attempted to employ hyposensitization, especially with house dust extract, in selected cases but apparently without consistent success. Thus, Nexmand,⁷ in a monograph on this subject published in 1948, finally concludes both from his own experience and from a review of an extensive amount of literature on atopic dermatitis that "this method of treatment (hyposensitization) is not generally recommended for Besnier's prurigo" (atopic dermatitis). That Nexmand should have come to such a conclusion is not surprising since, up until the time of his publication in 1948, the significance of inhalants as a cause of atopic dermatitis remained, at best, a clinical suspicion. Now that our studies have directed attention to the inhalant allergens as important causes, however, more opportunities have arisen to utilize hyposensitization with extracts of house dust, pollens, or molds in the treatment of these patients. This has been true in our experience especially in the past ten years, during which time we have had an opportunity to treat a larger number of patients with extracts of inhalant allergens. During this period, as the result of the institution of treatment with these extracts, we encountered some unexpected problems and experiences which perhaps serve to explain some of the previous treatment failures, both our own and those of others. We also learned many lessons, sometimes at the expense of the patient's comfort, which were helpful in our treatment of subsequent patients. These experiences form the basis of the present report, and it is my hope that they might assist others in the treatment of patients with atopic dermatitis.

TABLE I. SUMMARY OF 183 PATIENTS WITH ATOPIC DERMATITIS*

Atopic dermatitis as chief complaint	137	
Allergic manifestations		
Atopic dermatitis only	34	
And hay fever	29	
And asthma	43	
Asthma and hay fever	60	
Other allergies	17	
Number of patients treated by diet only		18
Number of patients treated by hyposensitization		125
Number of patients who did not return		40

*All but fifteen patients were from the author's private practice.

The series of patients reviewed for this report comprise a total of 183 patients, most of whom were from my private practice (Table I). Of these, 137 were seen primarily because of atopic dermatitis and forty-six primarily for other allergic complaints (hay fever and asthma, among others). Most of the patients had more than one allergic condition at the time they were first seen; thus, only thirty-four had atopic dermatitis alone. Of the 183 patients, forty either did not return or went back to the referring physician for follow-up treatment and eighteen were treated solely by dietary exclusion. This leaves 125 patients, eighty-two of whom were treated since 1949, the date of my first publication concerning the role of inhalant allergens. The general

plan of treatment followed closely that usually used in cases of asthma. All patients had complete allergy studies, which included intracutaneous skin tests with extracts of food allergens and with seasonal and nonseasonal inhalant allergens. The patient then was given a list of the positive-reacting allergens with instructions as to their avoidance or, in the case of house dust, the methods by which exposure to it could be minimized. In patients in whom sensitivity to pollens or molds could be established as etiological factors (either by clinical history or by testing), or in dust-sensitive patients for whom complete avoidance was difficult, hyposensitization treatment with the extracts of these allergens was instituted. Of the 125 patients (Table II), 107 were treated with house dust extract, seventy-eight with ragweed pollen extract, forty-three with the extract of a spring pollen mixture containing timothy and plantain—and five with alternaria (either alone or mixed with hormodendrum). In thirty-five patients who were sensitive both to ragweed and to the latter molds, the mold extracts usually were combined with the ragweed extract in a single vial and used in treatment. Patients sensitive to more than one allergen were treated whenever necessary with more than one extract, for example, house dust and ragweed or house dust and ragweed mold. This was true in all but fourteen of the 125 patients.

TABLE II. SUMMARY OF EXTRACTS USED

House dust	107
Ragweed pollen	78
Mixture of timothy, plantain, and sweet vernal	43
Mixture of alternaria and hormodendrum molds	5
Mixture of ragweed (giant and dwarf) and alternaria	35

Among the first of the patients treated with dust extract was a 62-year-old man who was first seen by me in 1939 because of fall hay fever of many years' duration and severe generalized atopic dermatitis which had begun in November, 1938. This cleared after hospitalization but recurred upon his return home. The clinical suspicion that he was sensitive to his own environmental house dust was substantiated by specific positive skin reactions and specific reagins to an autogenous house dust extract. Treatment with the latter and with ragweed pollen extract was instituted on a perennial basis. The hyposensitization treatment, which was given in the same manner as to an asthmatic patient, began with a small dose of the extract which was increased gradually until the maximum tolerated dose was being given. No difficulties were encountered in the administration of these extracts; in fact, the patient was able to tolerate the concentrated autogenous dust extract and a large dose of ragweed pollen extract (see Patient M. in Table IV) without reaction. Excellent clinical results were obtained, and after three years treatment was discontinued. We last heard from this patient in 1949, when he stated that up to that time he had not had any recurrence of the dermatitis and his hay fever was considerably improved.

Following this experience, I treated other atopic dermatitis patients in similar fashion, but not always with the same success. For example, in several

patients receiving hyposensitizing injections of allergenic extracts temporary improvement of the dermatitis would follow institution of this treatment, but after a while unexplained relapses would occur and not infrequently the treatment would be discontinued by the patient. We puzzled at length about this situation until the reason became evident following our experimental clinical studies first reported in 1950.² In the patient used for most of these studies (Patient M. B. in Table V), after our attempted hyposensitization was begun, we encountered an exquisite degree of sensitiveness to an extent not previously anticipated. Reactions could be induced from almost infinitesimal amounts of extract. Furthermore, in contrast to the immediate form of reaction sometimes observed in hay fever patients receiving pollen hyposensitization, the reaction in the atopic dermatitis patient was so delayed that it could be easily overlooked. The patient utilized for these studies was a 29-year-old male veteran first seen in 1948 because of an extensive generalized atopic dermatitis for which he had been hospitalized on several occasions. Clinical observation, as well as direct and indirect skin testing, revealed specific reaginic sensitivity especially to house dust, both autogenous and stock. Subsequently, we were able to demonstrate that the atopic dermatitis could be induced repeatedly in him both by the inhalation of micronized particles of house dust and/or of alternaria and also, on five separate occasions, by intracutaneous injection of the concentrated autogenous dust extract. By contrast, as a control, inhalation of tale or of timothy pollen (to which he was not allergic) and intracutaneous injection of timothy pollen extract in high concentration failed to induce the lesions of his atopic dermatitis. As part of his treatment, we began a program of hyposensitization with extracts of autogenous house dust and with a mixture of ragweed and alternaria extracts, but we soon encountered unexpected difficulties. Injection of unbelievably minute doses of the pollen-mold extract was followed by an exacerbation of the dermatitis, similar to that originally induced by injection of larger amounts. In order to exclude any extraneous factors as possible causes of the exacerbation, we repeatedly, and without the patient's knowledge, substituted either buffered saline, the diluent employed for the preparation of these extracts, or at times timothy pollen extract (0.1 N strength) to which he was not sensitive. When the latter solutions were used, no increase in symptoms followed, whereas the reintroduction of the specific extract produced a definite reaction. The extracts then were diluted progressively to reach a dilution and a dose which no longer induced a reaction. The safe dosage finally was ascertained to be ragweed and alternaria 0.000003 N. This experience was duplicated in the patient frequently enough to warrant the conclusion that the reaction must have been the result of the injection of the minute amount of the allergenic extract. In all instances, the reactions did not take place immediately but after a lapse of twelve to twenty hours or longer.

This experience made us more aware of the possibility that reactions from hyposensitizing injections might be delayed in onset and might follow an

extremely small dosage. We therefore began to be much more careful with the dosage in treating subsequent patients and were alerted for delayed reactions.

Of the 125 patients who were given hyposensitizing injections of various allergenic extracts, thirty-four patients had a total of forty-nine reactions. As shown in Table III, five patients had reactions following testing procedures. In two, there was an exacerbation of the dermatitis after testing with concentrated autogenous house dust extracts; one followed testing with ragweed (0.1 N) and two followed tests (twelve or more) with routine allergens. In four patients, the reactions were deliberately induced for experimental reasons—in one patient by administration of dust extract and in three others by injection of ragweed extract. Twenty-eight patients had a total of thirty-nine reactions which were not intentionally induced but followed hyposensitizing injections of allergenic extracts. Some patients had more than one reaction, either because we did not realize at first that the reaction was induced by the injection or because the injection was repeated to make sure that it was responsible for the reaction. Most of the reactions followed the injection of either house dust extract (seventeen) or of ragweed extract (thirteen), but this was because these extracts were employed in treatment more frequently than other extracts (Table II).

TABLE III. REACTIONS IN ATOPIC DERMATITIS PATIENTS

INDUCED BY	MULTI- PLE TESTS	HOUSE DUST	RAGWEED (GIANT AND DWARF)	RAGWEED AND ALTER- NARIA	ALTER- NARIA	GRASS MIX- TURE*	TOTAL REAC- TIONS	NUMBER OF PA- TIENTS
Tests	2	2	1				5	5
Treatment		17	13	5	2	2	39	28
Experimental induction		1	3		1		5	4

*Grass mixture contains timothy, plantain, and sweet vernal.

The reactions which followed hyposensitizing injections, regardless of dosage, always were delayed in onset from twelve to twenty-four hours or longer. They would consist either of exacerbation of the existing dermatitis or the appearance of new papules, especially in the flexures, which resembled and at times were mistakenly diagnosed as "prickly heat." In most patients, the reaction would occur early in the course of treatment, either after the initial injection or after a few doses had been given. If a reaction did occur, the dose was altered in a manner similar to that employed in the hyposensitization treatment of other allergic diseases such as hay fever. Thus, the dosage would be decreased until no reaction occurred and subsequently increased more slowly until the maximum tolerated dose was reached without induction of reaction. By adopting this procedure, we found that most of our patients, even though they had reactions from one or more doses, were able later to tolerate larger dosages without difficulty. The maximum dosage reached in many patients compared favorably with that given to patients with hay fever or asthma. Some illustrative examples are contained in Table IV.

TABLE IV. ATOPIC DERMATITIS PATIENTS—ABLE TO TOLERATE LARGE DOSAGE

PATIENT	AGE	DIAGNOSIS	MAXIMUM TOLERATED DOSE
M.	62	Atopic dermatitis Hay fever	Ragweed 0.36 N Autogenous dust (c) 0.2 ml.
S. P.	10	Atopic dermatitis	Ragweed 0.18 N Grass mixture* 0.2 N
E. S.	21	Atopic dermatitis	Ragweed 0.36 N Autogenous dust (c) 0.2 ml.
E. M.	46	Atopic dermatitis Hay fever Asthma	Ragweed 0.24 N Grass and tree mixture 0.12 N Autogenous dust (c) 0.33 ml.
C. M.	40	Atopic dermatitis	Ragweed 0.18 N Dust (c) 0.1 ml. Plantain 0.08 N
P. S.	12	Atopic dermatitis Asthma	Ragweed 0.24 N Grass mixture 0.05 N Autogenous dust (c) 0.2 ml.

N = Total nitrogen.

(c) = Concentrate.

*Grass mixture contains timothy, plantain, and sweet vernal.

By contrast, however, in five of the 125 patients receiving treatment, reactions followed extremely minute amounts of extracts. Furthermore, even after repeated attempts, these patients could not tolerate any material increase in dosage. The data as to dosage tolerated by this group are summarized in Table V. Reactions in these patients followed extremely minute doses and recurred in most patients when the dosage was repeated. The reactions at times were so severe and incapacitating that further attempts at

TABLE V. ATOPIC DERMATITIS PATIENTS—REACTIONS FROM LOW DOSAGE

PA-TIENT	AGE	DIAGNOSIS	REACTION DOSAGE	SUBSEQUENT TOLERATED DOSE
S. B.	29	Atopic dermatitis	Autogenous dust (1:100,000) 0.05 ml. (i)	Autogenous dust (1:1 million) 0.1 ml. intracutaneous
D. G.	28	Atopic dermatitis Hay fever Asthma	Ragweed 0.0005 N Autogenous dust (1:10,000) 0.15 ml.	Ragweed and alternaria 0.0001 N—0.05 ml. Dust injection temporarily stopped
G. R.	24	Atopic dermatitis	Dust (1:10,000) 0.1 ml.	Dust (1:10,000) 0.05 ml.
M. B.	29	Atopic dermatitis	Ragweed and alternaria 0.000001 N	Ragweed and alternaria 0.000003 N
D. R.	36	Atopic dermatitis	Dust (1:1 million) 0.01 ml. (i)	Dust injection discontinued due to severe reaction

hyposensitizations were discontinued and only symptomatic treatment was instituted. This was true in Patients S.B., M.B., and D.R. Furthermore, because of the reaction induced by treatment and failure to respond, Patient G.R. discontinued further visits. Actually, of the five, we were able to continue treatment only in Patient D.G., in whom good results were obtained

eventually. As an illustration of the possible severity of the induced reactions, the case history of D.R. is worth citing.

D. R., a 36-year-old army veteran, was seen on Oct. 15, 1956, with an eczematous dermatitis of the trunk, hands, and feet which had been present since 1944. He had been treated by numerous dermatologists for "eczematous dermatitis" or "neurodermatitis" and had received various local applications without benefit. Allergy studies showed significant positive skin and eye test reactions to house dust and positive skin test reactions to a few foods of no clinical significance. Diet trial over an extended period failed to bring about improvement, and hyposensitization with stock house dust extract was begun. Severe reactions with eruption of lesions over the arms, face, and abdomen followed small doses of the extract diluted at first 1:100 and later 1:1,000. Because of the reaction, it was decided to give the injections intracutaneously. On two occasions 0.1 c.c. of a 1:1,000 extract was given intracutaneously, but in each instance it was followed within twenty-four hours by a severe reaction. The latter reaction persisted for about ten days and was controlled finally by the administration of sufficient ACTH and corticoids. After the subsidence of the reaction, it was decided to dilute the extract further and to give the patient minute amounts. Accordingly, he was given 0.01 ml. of a 1:1 million dilution intracutaneously weekly for four doses. No apparent reaction followed the first three injections, but after the fourth dose he developed such a severe generalized eruption that he had to be hospitalized for some time before the dermatitis was controlled. The eruption gradually subsided until the skin was almost clear; in fact, according to the patient, following his recovery the skin seemed better than at any previous time since the onset of the eruption. The patient at present is receiving only symptomatic treatment.

This case report illustrates strikingly one of the problems of hyposensitization with the extracts of inhalant allergens, namely, the exquisite degree of sensitization which may be present in a small number of patients, making treatment so difficult that it may have to be discontinued, as was true in three of our five patients. In the patient just cited, it is difficult to explain why no reactions followed the first three injections of 0.01 ml. of the 1:1 million dilution but did occur after the fourth dose. Whether the first three injections had been given to him in a refractory period following his previous reaction and were tolerated for that reason is mere speculation and remains to be proved. This possibility is suggested, however, by the striking improvement which followed his recovery from the reaction. This may have its counterpart in the refractory period of sensitization noted in guinea pigs after recovery from mild anaphylactic shock and similar refractory states (anergy) and also seen in human patients after recovery from constitutional reactions produced at times by injections of pollen extracts.

It is to be noted in the other patients with exquisite reactions to extremely small dosage that such reactions were induced repeatedly by the same dosage. This was true in all cases except the one just cited. Whenever possible, after the subsidence of the reaction, the patient was given a similar dose of either buffered saline or of histamine (1:1 million) by the same route to see if the reaction could be induced nonspecifically, but in no instance did a reaction follow the injection of any agent other than that of the extract to which the patient was specifically allergic.

Fortunately, as already noted, the exquisite type of reaction described above is quite uncommon. It occurred especially in patients with generalized

eruptions, as for example in all five patients included in Table V. However, some of our patients who also had generalized eruptions were able to tolerate high dosage without difficulty. Nevertheless, in treating this type of patient one must be sure to start with extremely dilute extracts to avoid aggravating the already existing dermatitis.

Of interest also in this group of patients was the fact that in those patients who had both atopic dermatitis and hay fever and who developed a reaction after the injection of pollen extract, the ensuing skin reaction always was of the delayed, eczematous, or papular type rather than of the immediate urticarial wheal which at times follows hyposensitizing injections of pollen extracts in patients with hay fever.

The immediate type of reaction was seen in only one patient, a woman who had both atopic dermatitis and asthma, and in this patient the reaction was induced experimentally by the injection of 0.1 ml. ragweed pollen extract (0.01 N) intracutaneously. Marked sneezing followed immediately after the injection and persisted for two days. Upon the third day after injection, the patient developed a moderately severe eruption in the antecubital fossae, wrists, and neck, which cleared within a week after appropriate treatment. Later, when the eruption had practically disappeared, the patient was again injected intracutaneously with 0.1 ml. of a more concentrated ragweed extract (0.4 N). Within a short time she began to sneeze, cough, and wheeze. This was followed later by intense itching in those areas previously affected by the dermatitis, namely, the antecubital fossae, wrists, face, and neck. The respiratory symptoms disappeared within thirty minutes after an injection of epinephrine, but some hours later she had a severe exacerbation of the dermatitis affecting the previously involved skin of the antecubital fossae, wrists, and neck, as well as that of the face which, according to the patient, had been clear previously. The itching was extremely intense, lasted three days, and then gradually lessened until only mild itching remained. Slight wheezing persisted for two days. The patient did well with specific allergy treatment given the following year, after which the skin condition cleared up completely.

This case illustrated strikingly, as did others in whom reactions followed either the usual hyposensitizing injections or the deliberately induced ones, that even if an immediate, urticarial, or atopic type of reaction (such as sneezing or asthma) is first induced, the subsequent reaction affecting the skin in patients with atopic dermatitis is likely to be delayed in onset and to resemble that of the existing dermatitis. It is exceedingly important that the delayed character of these reactions be fully appreciated by the attending physician. If not, the patient will continue to be injected with increasing amounts of the allergenic extract, which in turn will bring about subsequent and continued aggravation of the dermatitis rather than its amelioration. Failure to realize this or to recognize it in treated patients can lead to aggravation of the dermatitis. This, as I learned from early personal experience, may cause patients to become discouraged and to discontinue treatment, as exemplified in the following case report.

V. S., a 2-year-old girl, was first seen in December, 1946, with recurrent atopic dermatitis affecting the cheeks, neck, and flexures. The dermatitis had been present since early infancy (2 to 3 weeks of age). The parents were told that the "patient would grow out of it." The child had been treated by local ointments, which on one occasion caused a marked flare-up on the face. The patient improved at the seashore but the condition returned shortly after her return home. Intracutaneous skin tests were positive to ragweed, house dust, wool,

milk, chocolate, orange, and tomato. The child improved considerably after the elimination of wool, tomato, orange, and milk but had a flare-up in August, 1947, while at the seashore, coincident with the onset of slight ragweed hay fever (for the first time). The condition became worse on her return home. Desensitization with autogenous house dust was begun, with questionable improvement at first. The patient grew increasingly worse, so that her parents decided to discontinue all treatment and move to the seashore, where she improved remarkably. In reviewing her history later, it was noticed (but not recognized at the time) that the patient seemed somewhat worse two to three days after injections and that the dermatitis improved just before she returned for her next treatment. The relationship between her worsening skin condition and the hyposensitizing injection was not recognized, however, because of the delayed onset and an unawareness of the possibility that the treatment was responsible for the aggravation.

It is my belief also that similar failure to recognize the delayed reaction by those who administer hyposensitizing injections (as house dust) to these patients probably explains the reported lack of success with this type of treatment in atopic dermatitis patients.

A question often raised in relation to hyposensitization treatment in patients with atopic dermatitis concerns the results of this therapy. We tried to obtain an answer to this question by reviewing the case records of the 101 patients whom we had followed for a long enough period to record the results. A summary of these data is contained in Table VI. Inspection of the latter shows that the results of treatment generally were good. Thus, the dermatitis cleared and subsequently did not recur in thirty-two patients. In an additional forty-two the result was considered as "good" when the skin condition improved to the extent that the patient had either only a mild eruption or occasional mild recurrences. In seventeen patients only slight reduction in the dermatitis (recorded as fair) was noted, and in six there either was no change at all or the skin condition became worse.

TABLE VI. RESULTS OF TREATMENT

CONDITION OF SKIN	PERIOD OF OBSERVATION				TOTAL
	0-6 MONTHS	6 MONTHS TO 1 YEAR	1-3 YEARS	OVER 3 YEARS	
Clear	0	5	14	13	32
Good	5	15	15	11	46
Fair	1	7	4	5	17
No change	2	2	2	0	6
Totals	8	29	35	29	101

The management of all our patients with atopic dermatitis, as described in my previous publications, consisted first of attempts at elimination of test-positive foods from the diet and the avoidance as much as possible of contact with the offending inhalant allergens (especially house dust and wool). Additional symptomatic measures were employed in all cases to relieve the itching and to prevent further damage caused by scratching the injured skin areas. Oral administration of drugs, consisting usually of antihistamines and only occasionally of corticoids, was utilized whenever required, along with local applications to the skin of bland, nonirritating medicaments. If these

measures failed to clear the dermatitis, after a lapse of several weeks or longer, in patients allergic to inhalant allergens that could not be avoided (for example, dust, pollens, and molds), hyposensitization treatment with extracts of those allergens was instituted. This was found necessary in ninety-five of the 101 patients treated. Of five patients in whom dermatitis cleared completely in from six months to one year, improvement followed exclusion of test-positive foods from the diet in two patients. Of five patients who improved within six months and whose results were considered good, one improved only after dietary exclusion and one after complete wool elimination. Of the fifteen with a good result within six months to one year, one improved on dietary exclusion alone. This also was true of one patient of the seven considered to have only a fair result.

If we exclude from consideration the six patients treated entirely by elimination and/or avoidance, there remain ninety-five patients in whom hyposensitization with extracts of inhalant allergens was utilized. Good or excellent results were obtained in all but twenty-two, and actual failures were seen in only six. Even of the six who failed to respond, there were possible reasons for failure in three patients; one patient refused to cooperate in carrying out proper dietary and inhalant avoidance, and the other two reported too irregularly for us to determine the effect of the treatment. Actually, therefore, few patients who cooperated in treatment failed to receive some measure of relief, and most patients did rather well.

Therefore, from the results obtained in our series of patients, it is my opinion that the treatment of patients with atopic dermatitis, most of whom received hyposensitizing injections of allergenic extracts, compares very favorably with and, in fact, might even be better than the same treatment of a similar group of asthmatic patients.

SUMMARY

Hyposensitization with extracts of inhalant allergens, including house dust, ragweed, and timothy pollens and such atmospheric molds as alternaria and hormodendrum, is associated at times with certain difficulties which are reviewed in the present report. Of 183 patients with atopic dermatitis, either alone or combined with other allergic manifestations, 125 received hyposensitizing injections of extracts of one or more of the above-mentioned allergens. Thirty-four patients had a total of forty-nine reactions, usually after the injection but also in a few patients after skin testing or deliberate experimental induction. The reaction usually was temporary and could be obviated by reducing the dose and later increasing it more gradually. In five patients, however, reactions consistently followed extremely minute dosage, with subsequent attempted increases resulting in aggravation of the dermatitis rather than its amelioration.

Reactions following injections are delayed in onset from twelve to twenty-four hours or longer. They may go unrecognized, which explains some of the

reported failures in hyposensitization treatment. Awareness of this possibility and exercise of adequate caution to prevent the onset of reactions will bring about better response to treatment.

Results of treatment were evaluated in 101 patients. Six patients were successfully treated by elimination of foods or inhalants alone, and ninety-five also received hyposensitization treatment. Excellent or good results were obtained in seventy-three and actual failures in only six. On the whole, the results obtained compare favorably with those obtained in patients with allergic asthma treated in similar fashion.

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