

SKIN SENSITIZING ANTIBODY

I. Relationship of the Skin Sensitizing Antibody Titer to the Occurrence of Symptoms in Untreated Persons With a Positive Ragweed Skin Test

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DIRECT and indirect evidence supports the hypothesis that the skin sensitizing antibody is the basis of the wheal and flare type of immediate hypersensitivity. This is suggested by the Prausnitz-Küstner phenomenon¹ in which injection of the serum of an allergic individual into the skin of a normal individual passively sensitizes the site so that it reacts with a wheal and erythema when challenged with the specific antigen. Loveless² has shown that transfusions of serum, containing skin sensitizing antibody, from a ragweed-sensitive patient produce a passive general sensitization of the recipient with positive skin, nasal, and eye tests. Heating for 4 hours at 56° C. before transferring destroys the sensitizing capabilities of the serum.³ One of us (W. B. S.⁴) has shown that when prolonged treatment with aqueous ragweed injections results in clinical improvement, the direct skin test and the skin sensitizing antibody titer generally are decreased. Patients who experience constitutional reactions to ragweed injections usually have a much higher titer of skin sensitizing antibody than patients who tolerate equal or greater amounts of antigen without systemic reactions.^{5, 6} Finally, clinical sensitivity to ragweed is rare in patients who have a negative skin test to aqueous ragweed extract.

Since the skin sensitizing antibody is probably the basic cause of the immediate wheal and flare type of hypersensitivity, it is possible that the amount of antibody present in the serum of a patient may be related to the occurrence of symptoms.

The present study is a comparison of the titers of skin sensitizing antibody in the sera of untreated patients with typical ragweed hay fever and in the sera of persons who reacted to intracutaneous tests with ragweed pollen extract but denied symptoms of hay fever during the ragweed pollen season.

MATERIALS AND METHODS

Patients.—The skin sensitizing titers of the sera of 101 untreated persons who showed positive reactions to intracutaneous tests with 0.02 ml. of aqueous

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ragweed extract, 1,000 protein nitrogen units (PNU) per milliliter or less were studied. Sixty-one had typical ragweed hay fever symptoms and were actively seeking treatment. Forty others were seen because of allergies other than ragweed hay fever, or as volunteers for passive transfers, and all denied symptoms of hay fever during the ragweed season. On the basis of observation of sneezing or nasal examination, we suspected that a number of these individuals had allergic reactions of the mucosa so insignificant that subjective symptoms were not noted. One had been exposed to ragweed only one season and the serum drawn 6 months after this season. Unfortunately, this patient was lost to follow-up and her condition during the following season was unknown. One other patient admitted to having had nasal symptoms 20 years previously when uprooting ragweed plants but denied symptoms at any other time. Nasal examination of this patient during the ragweed season led us to believe that he had mild hay fever.

Sera for Skin Sensitizing Antibody Studies.—Sera were collected and handled as in previous studies,⁶ with the usual precautions to avoid transmission of infectious diseases.

Skin Sensitizing Antibody Titers.—Determinations of skin sensitizing antibody were done by passive transfer with progressive dilutions of serum, tested with an excess of antigen.

Subjects used as passive transfer recipients were adult males or females employed for this purpose. They gave negative intradermal skin tests to 0.025 ml. of aqueous ragweed extract 1,000 PNU per milliliter. To obtain a uniform group of recipients, dilutions of a single serum, in which skin sensitizing antibody titer was known, were placed on every back. Thus, a group of recipients was obtained whose responses to sensitization by the known serum were within 25 per cent of each other. This permitted, within this limit of error, a comparison of a large number of sera by titration on different recipients. Relative titers within this series are roughly quantitative based on the reaction produced by the control serum in selected recipients.

Dilutions of serum were made with buffered saline, the total range consisted of 1:1, 1:10, 1:100, 1:200, 1:500, and 1:1,000. The dilutions of each serum for the first test were chosen on the basis of the case history. For instance, in an untreated asymptomatic case, dilutions of 1, 10, 100, and 200 would be used. If this series did not include the end point, additional dilutions were used in subsequent tests.

To perform the test, the recipient's back was sensitized with intradermal injections of 0.1 ml. of each dilution of unknown serum to be tested and of the control serum. After 24 to 48 hours, each site was challenged by intracutaneous injections of 0.025 ml. of aqueous ragweed extract, 1,000 PNU per milliliter. The end point was considered to be the last site which gave a definite visible reaction; titers are expressed as the reciprocal of this dilution. Challenging at either 24 or 48 hours after sensitization did not appear to alter the titer as determined by the end point of the control serum.

Duplicate titrations were not run on the same recipient but were tested on several different occasions on different recipients.

RESULTS

Of the 61 patients who had recognized ragweed hay fever symptoms, all had positive reactions to intracutaneous skin tests with 0.02 ml. of aqueous ragweed extract containing 1 PNU per milliliter or less. Forty (65 per cent) of these had a skin sensitizing titer of 500 or greater, the titers of 15 (25 per cent) were less than 500 but greater than 99, and those of 6 (10 per cent) were less than 99 but greater than 10. None had a sensitizing antibody titer of 10 or less (Table I).

TABLE I. COMPARISON OF THE SKIN SENSITIZING TITER TO THE PRESENCE OF HAY FEVER IN UNTREATED PATIENTS

SKIN SENSITIZING TITER	UNTREATED SYMPTOMATIC	UNTREATED ASYMPTOMATIC
0	0	9
1 to 10	0	16
11 to 99	6	13
100 to 499	15	2
500 to 999	20	0
1,000 or greater	20	0

Forty persons who denied symptoms of ragweed hay fever gave positive reactions to intracutaneous tests of 100 or 1,000 PNU per milliliter. Most of these individuals gave negative reactions to tests with 10 or 1 PNU per milliliter. In this group of untreated "asymptomatic" reactors, the sera of 9 (22 per cent) failed to sensitize the skin of the recipient when passively transferred, sera of 16 (40 per cent) had titers between one and 10, 13 (33 per cent) had titers greater than 10 but less than 99, and 2 (5 per cent) had titers greater than 99 but less than 500. These 2 included the patient who had had symptoms when handling ragweed and the woman who had been exposed to ragweed pollen for only one season.

DISCUSSION

There is a significant difference between untreated ragweed hay fever patients and untreated persons who react to skin tests with ragweed pollen extracts, but do not have hay fever, when their titers of skin sensitizing antibody are compared. In general, the higher the titer, the greater the likelihood that the patient will have hay fever. All patients in this series with titers over 500 had symptoms. Symptoms were present in the great majority of individuals with titers of 100 to 499. With a titer less than 100, symptoms usually were mild and the person frequently was unaware of them. With titers of less than 10, people rarely had significant symptoms. Thus, the titer of skin sensitizing antibody for ragweed pollen is correlated with the occurrence of hay fever.

It is obvious that the degree of exposure to atmospheric pollen would affect the presence or absence of symptoms, as in the case of the patient who stated that he never had hay fever in New York City but did when pulling up rag-

weed plants as a farm laborer. It is also possible that additional antigens, such as dust, molds, or other fall pollens, intensified symptoms in certain symptomatic patients whose sera showed low titers of skin sensitizing antibody for ragweed.

SUMMARY

The titers of skin sensitizing antibody of the sera of untreated hay fever patients differ significantly from those of the sera of persons who react to intracutaneous tests with ragweed pollen extract but who do not have clinical hay fever.

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