

THE INCIDENCE OF SUBSEQUENT RAGWEED POLLINOSIS IN SYMPTOM-FREE PERSONS HAVING POSITIVE REACTIONS TO RAGWEED POLLEN EXTRACT

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INTRODUCTION

IN THE course of complete skin testing of allergic patients of all ages, it has been our custom for many years to include ragweed pollen regardless of the allergic condition and age of the patient. It was felt that eventually the information so obtained might shed some light upon the natural history of the development of ragweed pollinosis. The purpose of this article is to report on patients so tested with respect to those who gave positive cutaneous reactions to ragweed pollen but who did not suffer from pollinosis of any kind (tree, grass, or weed) at the time of the tests. The particular problem was whether or not a positive reaction in such cases had any prognostic value. This would test the truth of the general assumption by most allergists that such a finding indicates that in all probability the patient will eventually develop ragweed pollinosis. This study shows the results obtained after such patients were actually followed for a number of years. The implication of this is that if a significant number of these patients were later to develop pollinosis the practice of giving injections of ragweed or other pollen as a prophylactic measure when the patient receives other injections, such as house dust, would be justified.

METHOD

Since 1931 every patient who had been skin-tested because of a known or suspected allergy and who had given a positive skin test reaction to ragweed pollen, but who did not have clinical ragweed pollinosis, was recorded. In May, 1957, a follow-up study of those patients was started. Fifty-six patients were contacted by telephone. In some cases, the patient's wife or mother (if the patient were still a child) was interviewed instead of the patient, but in all such cases only those wives or mothers living in the same house as the patient were consulted. Twelve of the total of sixty-eight patients were questioned by mail. Each patient was asked if he had developed rose fever (grass pollinosis) or hay fever (ragweed pollinosis), and the symptoms were described to the

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patient. These symptoms are, in lay terms, itching, red, swollen eyes; running, obstructed, itching nose; sneezing; or wheezing. Any or all of these symptoms were accepted as diagnostic if they occurred seasonally and only during the time of ragweed pollination (August 15 to October 1).

Other information was obtained from the original charts. Skin test reactions were considered only if they were 2 plus by scratch test or 3 plus by intradermal test. Age was recorded as of the date of the skin test, and sex was also noted. The original diagnosis has not been considered for correlation, since all the patients had some allergic disease (many patients had more than one) but none had ragweed pollinosis. Furthermore, these diseases were not regarded as essential for the purpose of the current study. In short, the valid information being reported is the age, the sex, the cutaneous reaction to ragweed pollen, and the ultimate development or nondevelopment of ragweed pollinosis.

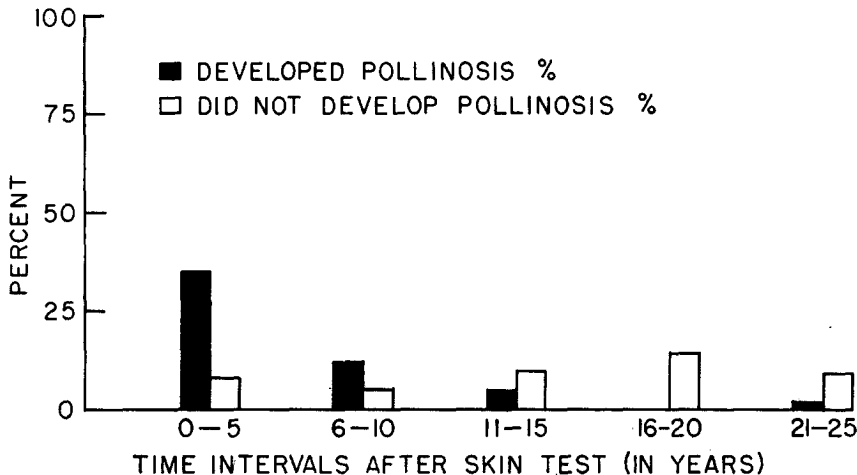


Fig. 1.—This graph shows the ultimate outcome for all age groups totaled. The vertical height of each column represents per cent of all the sixty-eight patients studied, and the columns are grouped at various time intervals after skin testing. See text for discussion.

RESULTS AND DISCUSSION

A total of 167 patients have been studied since 1931. During this time approximately 10,000 allergic persons have been seen in this office. Thus, about 1.7 per cent of all our allergic patients had positive skin test reactions to ragweed pollen but did not suffer from ragweed pollinosis. Of the 167 patients recorded, ninety-nine were unacceptable for this series (1) because they had less than the specified value for skin tests (2+ scratch or 3+ intradermal); (2) because they had received prophylactic pollen injections in the interim (no patients in this series received any pollen injections prior to the development of ragweed pollinosis); or (3) because of error in the original diagnosis of absence of pollinosis, discovered when the patients were queried later. Thirty-one patients had moved out of town and were requested by letter to answer

the same questions that the others were asked on the telephone. Nine letters were returned as undeliverable, thus, only about one-third of the mail contacts failed to respond. The sixty-eight patients reported here include twelve who answered by letter and fifty-six who answered directly by telephone.

The general trend of outcome for these patients can be seen in Table I. Of the group as a whole, 53 per cent of the patients developed ragweed pollinosis and 47 per cent did not.

TABLE I

AGE WHEN SKIN-TESTED (YEARS)	TIME INTERVAL (YEARS) PATIENTS FOLLOWED AFTER SKIN TESTS										TOTAL PATIENTS IN AGE GROUP
	0-5		6-10		11-15		16-20		21-25		
	A	B	A	B	A	B	A	B	A	B	
0-5	14	2	4	1	1	2	0	1	0	1	26
6-10	3	2	2	1	0	1	0	1	1	2	13
11-15	3	1	2	0	2	0	0	3	0	1	12
16-20	1	0	0	0	0	1	0	2	0	2	6
21-40	2	0	1	1	0	2	0	0	0	2	8
41-57	0	0	0	0	0	1	0	2	0	0	3
Totals	23	5	9	3	3	7	0	9	1	8	68

A = Number of patients in any age group who developed pollinosis at a given time interval after the skin test was done.

B = Number of patients in the same age group who did not develop pollinosis in that same interval. For example, of twenty-six patients tested between the ages of 0 and 5 years, there were sixteen who were followed up to a 5-year period; of these, fourteen developed pollinosis and two did not; of five patients followed for six to ten years, inclusive, four developed pollinosis and one did not, etc.

This table is illustrated graphically in the figures that follow.

Of the thirty-six patients who developed symptoms, 88 per cent did so within ten years after testing and 64 per cent did so five years after testing. In other words, regardless of the age at the time of skin testing, if pollinosis does not develop within ten years it probably will not develop at all.

Another fact of interest is revealed in Figs. 2 to 7 and summarized in Fig. 8, A and B.

It can be seen that as the age at which the skin tests were first performed advances, fewer patients will ultimately develop pollinosis. That is, of the seventeen patients aged 16 years and over, only four (25 per cent of all patients over 16 years of age) developed pollinosis at any time interval after testing, as compared to a total of thirty-two patients less than 16 years of age (63 per cent of all patients under 16 years of age) who developed pollinosis. Of those four patients over 16 years of age who did develop pollinosis, the majority developed it in the first ten years, just as patients in the other age groups did.

Finally, another fact of importance is that most of the patients who do not develop pollinosis are concentrated in the older age groups. This is a corollary of the facts noted previously. A total of thirteen patients 16 years of age and over (70 per cent of all patients over 16) did not develop pollinosis, as compared to a total of nineteen patients (35 per cent of all patients under 16 years) who did not develop pollinosis.

In summary, it would appear that those patients under 16 years of age at the time of skin testing will develop most of the pollinosis that is developed (63 per cent), whereas most of those over 16 years at the time of skin testing will escape pollinosis (70 per cent).

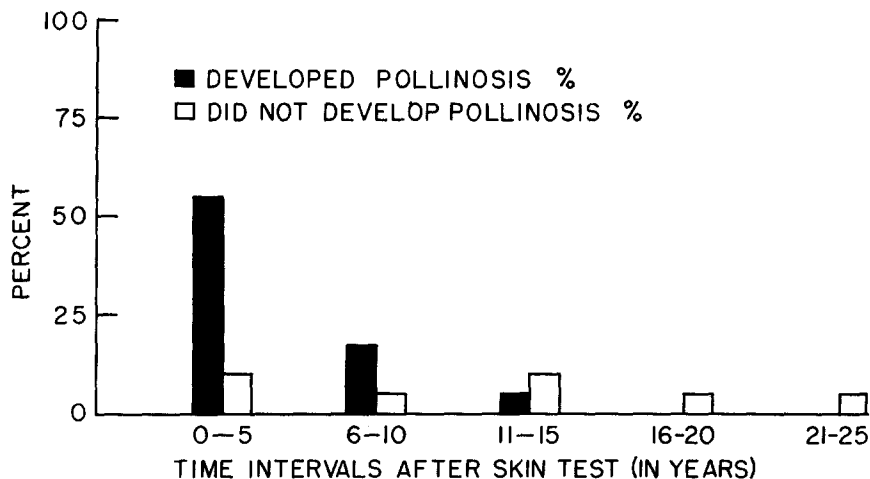


Fig. 2.—Age group 0 to 5 years.

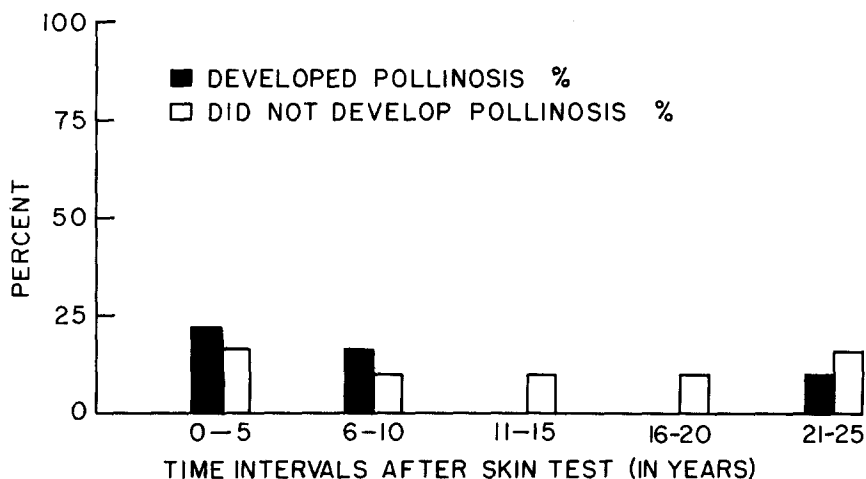


Fig. 3.—Age group 6 to 10 years.

Figs. 2 to 7.—Each drawing shows the ultimate outcome for the particular age group noted, and shows it in per cent of the total number of patients in that age group. The age is taken at the time of skin testing. Each figure shows the outcome for its age group at various time intervals after skin testing. See text for discussion.

Actually, it is not possible to be so positive about the outcome for those patients who failed to develop ragweed pollinosis. Although all patients recorded have been followed up to May, 1957, the length of follow-up varied from less than two years (but more than one year) up to twenty-four years. Thus, these figures are partly influenced by a factor of time—whether the

patients were seen two years ago, ten years ago, or twenty years ago. More useful figures can be obtained from Figs. 2 to 7, which show the ultimate outcome for any age group of patients. These graphs give the whole spread of time, and a better, although incomplete, idea can be gained from them. For

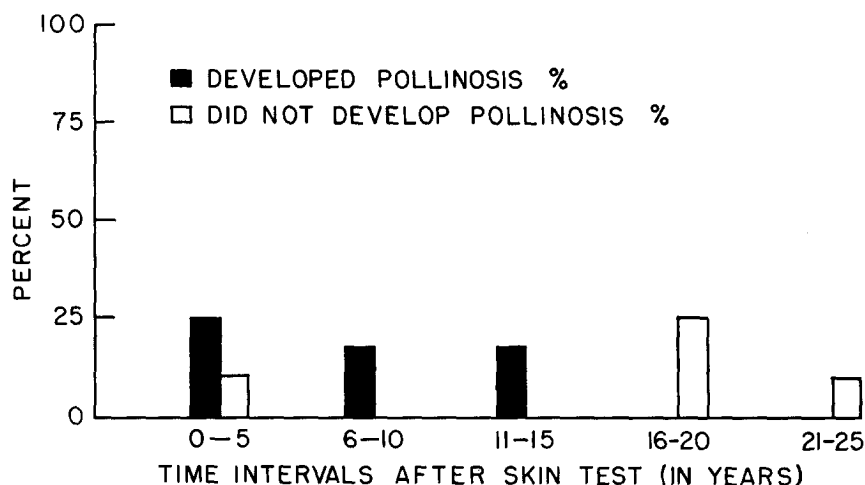


Fig. 4.—Age group 11 to 15 years.

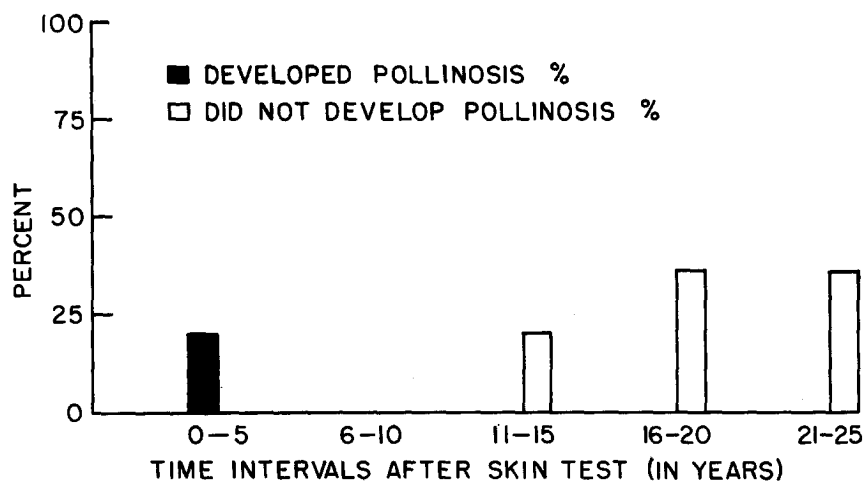


Fig. 5.—Age group 16 to 20 years.

the figures to be entirely adequate, all of these patients would have to be followed for the duration of an average lifetime to determine how long they might go without developing pollinosis. For the present, we can only estimate, on the basis of the facts given, how long the average patient will go without developing symptoms.

Of the thirty-two patients who did not develop pollinosis, eight (25 per cent) were observed for twenty-one to twenty-five years, nine (27 per cent) for

sixteen to twenty years, seven (23 per cent) for eleven to fifteen years, three (10 per cent) for six to ten years, and five (15 per cent) for zero to five years. Again, these figures must be interpreted with caution, since they are dependent

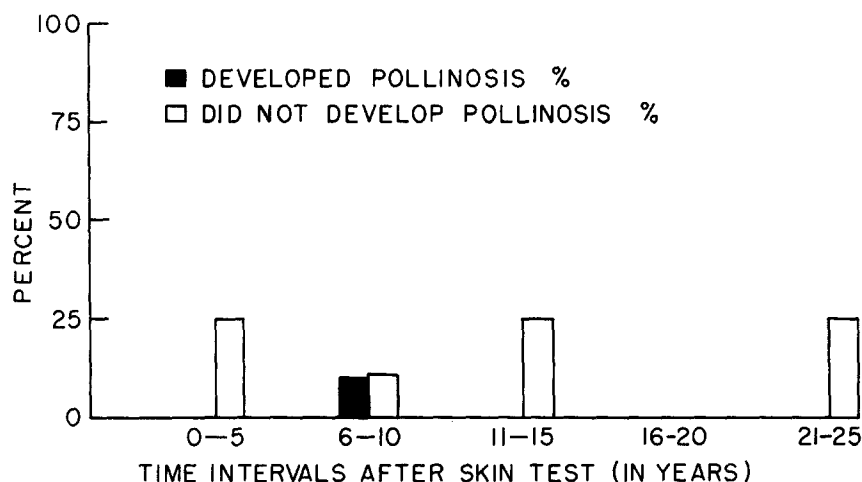


Fig. 6.—Age group 21 to 40 years.

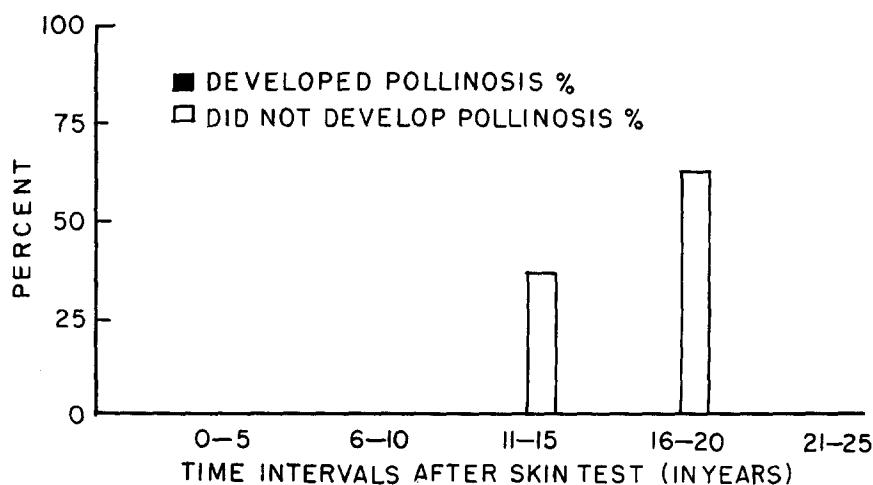


Fig. 7.—Age group 41 to 56 years.

on the patient's age at the time of skin testing and on the length of follow-up. The figures indicate that if pollinosis has not developed up to ten years after testing it is extremely unlikely that it will develop at all.

It was found that correlation of these figures with the duration of allergic symptoms, although obviously desirable, was not feasible, since the original histories were unavoidably not accurate enough for the purpose. The nature of the allergic disease often could not be determined from the one or two visits which the patient made to the office. The duration of the allergic disease was often noted in general terms, such as "all his life," "many years," or "since

childhood." This information would be retrospective, since it was not specifically sought for this purpose at the original visit. Because such figures would only be misleading, they were not included.

Of further interest is the fact that, of the sixty-eight patients, thirty-two were males and thirty-six were females. Sex distribution varied somewhat by age group, but the numbers in various age groups were insufficient to make a valid statistical correlation. From these figures, it is our feeling that there is no particular relationship between sex and the problem being reported.

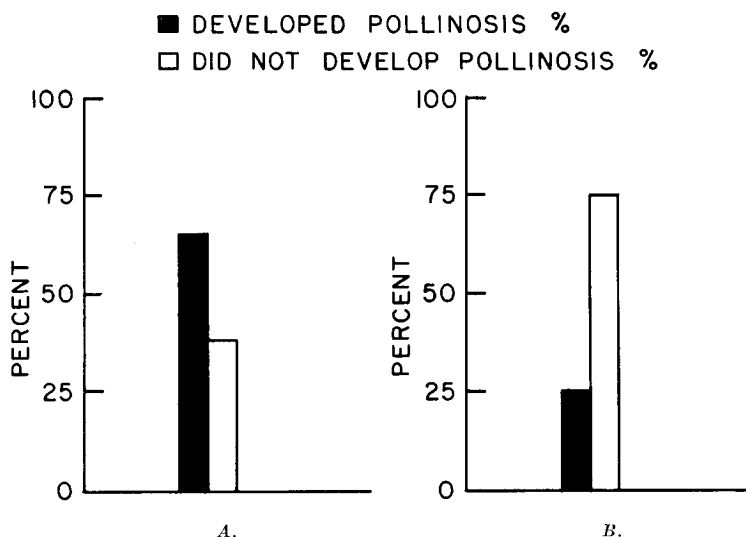


Fig. 8.—A, The outcome for all patients 16 years of age or under (at the time of skin testing).
 B, The outcome for all patients 16 years of age or over (at the time of skin testing).

Sixty-eight scratch tests were done, and twelve intradermal tests were done in those patients whose scratch tests were negative. These tests were distributed randomly, and there was no relationship between development or failure of development of pollinosis and the type of skin test done. Over the twenty-six years of this study, several persons have done the skin testing. The results, however, have been read by a physician in every instance, and most of them have been read by one of us (J. G.). The technique of the tests also has varied somewhat over the years, but at no time was an intradermal test done unless a preceding scratch test was negative. Most of the time the Hill scarifier has been used, and most of the tests have been done by only a few persons during the twenty-six years. The influence of such changes in procedure and personnel cannot be accurately measured or evaluated but, in our opinion, for the purposes of our study, this is not an important objection.

The only work similar to this report, which we have been able to find, was that of Biederman¹ in 1935. He mentioned unpublished data from a review of records of patients at Johns Hopkins Hospital Protein Clinic. He noted that, of 154 patients with pollinosis who had positive skin tests to pollens not

involved in their current seasonal symptoms, 5.5 per cent developed such pollen symptoms the following year. He also found that this could be prevented by the injection of these pollens along with the pollens to which the patients were actually clinically sensitive.

Finally, the problem of controls should be mentioned. Allergic patients who do not have ragweed pollinosis and who have negative skin test reactions to ragweed pollen might be considered as controls. They should be contacted and questioned as to the ultimate development of ragweed pollinosis. This, however, constitutes an entirely separate and different experiment instead of a control. We feel that the present study is controlled in itself, in that we have set out to discover what becomes of allergic patients who have positive ragweed pollen skin reactions but do not have ragweed pollinosis. We believe that we have done this. Conclusions and comparisons other than those noted here cannot be drawn from this study.

SUMMARY

1. Sixty-eight allergic patients were followed for from two to twenty-four years. They had not had ragweed pollinosis initially, but had had positive skin test reactions to ragweed pollen. The purpose of the study was to discover what becomes of such patients with regard to the development of ragweed pollinosis.

2. Of the total number of patients, 53 per cent developed ragweed pollinosis, and 47 per cent did not.

3. Of the persons developing pollinosis, 88 per cent did so within ten years of the skin tests, and 64 per cent did so within five years of the skin tests.

4. The corollary to this is that those who have not developed pollinosis ten years after skin tests are highly unlikely to do so thereafter.

5. Of the thirty-two patients who did not develop pollinosis, approximately 25 per cent were observed for twenty-one to twenty-five years, 27 per cent for sixteen to twenty years, 24 per cent for eleven to fifteen years, 10 per cent for six to ten years, and 15 per cent for zero to five years. These figures are affected by the length of time the patients were followed, and must be interpreted accordingly.

6. There was no evident relationship between sex or type of skin test (scratch or intradermal) and the development of ragweed pollinosis.

7. Of the patients in this study who were 16 years of age or *over* at the time of skin testing 75 per cent did *not* develop ragweed pollinosis and 25 per cent *did* develop ragweed pollinosis.

8. Of the patients in this study who were 16 years of age or *under* at the time of skin testing, 37 per cent did *not* develop ragweed pollinosis and 63 per cent *did* develop ragweed pollinosis.

9. In view of the foregoing findings, the practice of giving injections of ragweed pollen as a prophylactic measure along with periodic injections of other

allergens to patients who have a positive skin test but who do not have ragweed pollinosis appears justified, since there is no evidence to prove that such prophylactic measures are harmful.

REFERENCE

1. Biederman, J. G.: Treatment of Allergic Patients With Added Skin Reactions, *J. ALLERGY* 6: 590-592, 1935.