

The natural history of ragweed hay fever

A twenty-year study of 120 patients

*Francis M. Rackemann, M.D., and TTyne Lamsa, R.N.,
Boston, Mass.*

A group of 120 patients with ragweed hay fever, of various ages and both sexes, has been followed for over twenty years. A study of their progress shows the natural course of the disease and throws a little light on its mechanism.

In the spring of each year each patient has reported for advice and treatment, and, for the first few years at least, he or she has been given a course of injections with aqueous ragweed extract beginning two or three months before the pollen season.

The technique of treatment is familiar: The ragweed extract is made fresh each year by extracting 1.0 Gm. of clean, dry, defatted pollen with 100 ml. of Coca's buffered phosphate solution.* After standing for 24 hours at room temperature, with occasional shaking, it is filtered through a Seitz filter and if sterile is labeled 1 to 100 and is used as such.

At the start of treatment each year, new scratch skin tests with serial dilutions of the ragweed extract, controlled by similar tests with extracts of pollen from one or two grasses and trees, will show whether on the one hand the degree of sensitiveness has changed from previous years and whether, on the other hand, the strength of pollen extract is different than before as suggested by the reactions to tests on a group of patients. Ordinarily the skin test reactions—recorded always by drawings with measurements of the wheal and erythema in millimeters—will be about the same size as the reactions of the previous year. It is, however, the record of previous treatment rather than the skin tests which will tell most about the patient's tolerance and what his reactions, both local and general, are likely to be. If these reactions to early doses have been small, the new doses can begin at a high level. For example, if in the last year or two the patient could take as much as 0.40 c.c. of the

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*Coca's buffered phosphate extracting fluid contains 3.63 Gm. KH_2PO_4 , 14.31 Gm. $\text{Na}_2\text{HPO}_4 \cdot 12 \text{H}_2\text{O}$, 5.0 Gm. Na Cl. and 4.0 ml. carbolic acid in water to 100 ml.

strong 1 to 100 extract without any great reaction, the new course of pre-seasonal treatment has begun at once with this same strong extract and a first dose of, say, 0.15 c.c. or even 0.20 c.c. In this way most of the small doses, given in the early stages of previous treatment courses, have been omitted, and the new treatment is simplified. The first injection is given six to eight weeks before the hay fever season. The size of further doses and the intervals between them will depend partly on the size of the reaction from the last dose and partly on the record of the year before. If a course of treatment was successful before, it will usually be so again. In general, doses are adjusted to produce a local redness and swelling about 3 or 4 cm. in diameter. If doses of "fair size" can be taken without much local reaction, larger quantities can be injected and the intervals can be lengthened. In many older patients four or five, or perhaps only two, "booster" doses will be enough for the entire season, especially if they can be regulated close to the tolerance level but not over it.

If a general systemic reaction has been produced in any year, the dose which caused it defines the tolerance level which I described in 1947,¹ and that dose must not be given again. The level varies in different patients from 1.00 ml. of the strong 1 to 100 extract to 0.10 ml. of the 1 to 5,000 dilution.

Two factors in this technique are essential. First, it is the record of treatment in previous years which makes the plan possible; the record becomes an item of primary importance, and the keeping of accurate notes which are neat and readable has been well worth the small effort. Second, the ragweed extract used in the new year must have approximately the same strength as that used before.

In our hands this method of treating hay fever has worked well. Results have been good, the number of treatments has been held to a minimum, and general systemic reactions have been infrequent. More important, our patients have been satisfied.

Our figures for end results agree with those of other workers. Back in 1926 I² reported that 75 per cent, of the total 808 patients treated in six years for ragweed hay fever were improved. Feinberg's³ book of 1944 quotes Dundy and co-workers⁴ who obtained "satisfactory results" in 84 per cent of 314 patients, and it quotes Spain and Fuchs⁵ who brought relief to 73.4 per cent of the group treated with a few doses given before the season—preseasonal treatment—and 94.2 per cent of the other group treated with doses given at intervals throughout the year—perennial treatment—in a total of 950 hay fever patients treated.

Vander Veer, writing a chapter in Dr. Cooke's⁶ book, says: "With proper care and experience 80 per cent of the treated patients should have at least 80 per cent relief . . . These figures are gathered from the reports of many physicians over the country . . . If the results fall below this, the physician is not up to standard. . . ." In the last thirteen years the literature says little about end results in hay fever, and none of the papers deal with more than the one year of treatment. In this present paper the point is not that good results have been produced, but that only a small number of doses has been needed to produce them.

Table I. *Ragweed hay fever, 120 cases followed for twenty years*

Year	Total cases	Cases treated and results						Not treated				
		No.	Doses per patient	Systemic reactions	No. cleared	No. relieved	% cleared plus relieved	No.	No. cleared	No. relieved	% cleared plus relieved	Result unknown
1942	86	74	11.1	12	2	24	35.0	12	0	2	16.6	4
1943	97	82	10.4	5	1	29	35.5	15	0	2	15.4	3
1944	100	86	10.8	9	2	25	31.5	14	1	2	21.5	3
1945	124	111	10.2	9	6	51	51.5	13	0	1	7.7	2
1946	123	111	8.8	8	20	51	64.5	12	1	3	33.3	1
1947	123	108	8.2	6	23	58	75.0	15	3	6	60.0	2
1948	121	97	8.1	4	18	60	81.0	24	5	5	41.7	3
1949	121	97	7.5	5	15	68	86.0	24	4	12	66.5	2
1950	121	82	8.0	4	19	52	86.5	39	9	16	64.1	3
1951	119	62	7.6	4	17	37	87.0	57	12	25	64.5	3
1952	118	56	7.9	4	9	38	84.0	62	17	24	66.0	2
1953	118	53	8.8	3	11	35	86.5	65	20	28	73.8	4
1954	115	44	7.4	3	15	24	88.6	71	24	28	73.2	4
1955	114	38	7.5	3	10	19	76.3	76	29	26	72.5	6
1956	114	36	8.3	5	8	22	83.0	78	31	28	75.6	9
1957	112	33	7.3	2	9	20	87.7	79	32	30	78.4	7
1958	111	30	6.7	3	6	18	80.0	81	31	30	75.3	9
1959	111	29	6.8	1	9	14	79.5	82	33	29	74.0	7
1960	111	28	6.3	0	6	16	78.0	83	34	34	81.9	8
1961	111	23	6.8	0	11	11	95.0	88	38	32	79.5	10
1962	110	24	5.1	0	8	12	83.3	86	38	26	74.4	14
1963	111	24	4.9	0	9	14	95.8	87	38	23	70.1	16

Table I shows the general picture. In 1945, 124 patients with ragweed hay fever were treated with a series of injections given during the two or three months before the season of pollination. Before 1945, and since then, the total number of patients in the study has varied a little from year to year. If the number of patients treated added to those not treated does not always make 124, it is because before 1945 some patients had not joined the group, and after 1945 some had left the group, either because they had moved away or died or because their hay fever had improved so that specific injection treatment was no longer necessary.

Table I shows that back in 1942 each patient received an average of 11.1 doses of ragweed extract. Systemic reactions were frequent, even if not severe, and the result was poor. Ten years later, in 1952, the number of doses was down to an average of 7.9, systemic reactions occurred four times instead of twelve times, and results which were "good"—patients cleared of symptoms plus others "relieved"—made 84 per cent of the total. Finally, in 1962 and 1963 the average number of doses was reduced to 5.1 and 4.9, respectively, and good results—"cleared" plus "relieved"—were again over 80 per cent. As time passes, the number of treated cases falls off at a steady rate and the number not treated goes up. In 46 of the total 122 cases the hay fever has cleared entirely—the number increasing each year up to that figure. In 1950 the percentage of cleared cases was 23, in 1955 it was up to 33, and in 1960 it was 36. In 1963 the hay fever had cleared away in 42 per cent of the patients.

Does this improvement depend merely upon the advancing age of the patient or does it reflect improvement in the technique of treatment? To throw

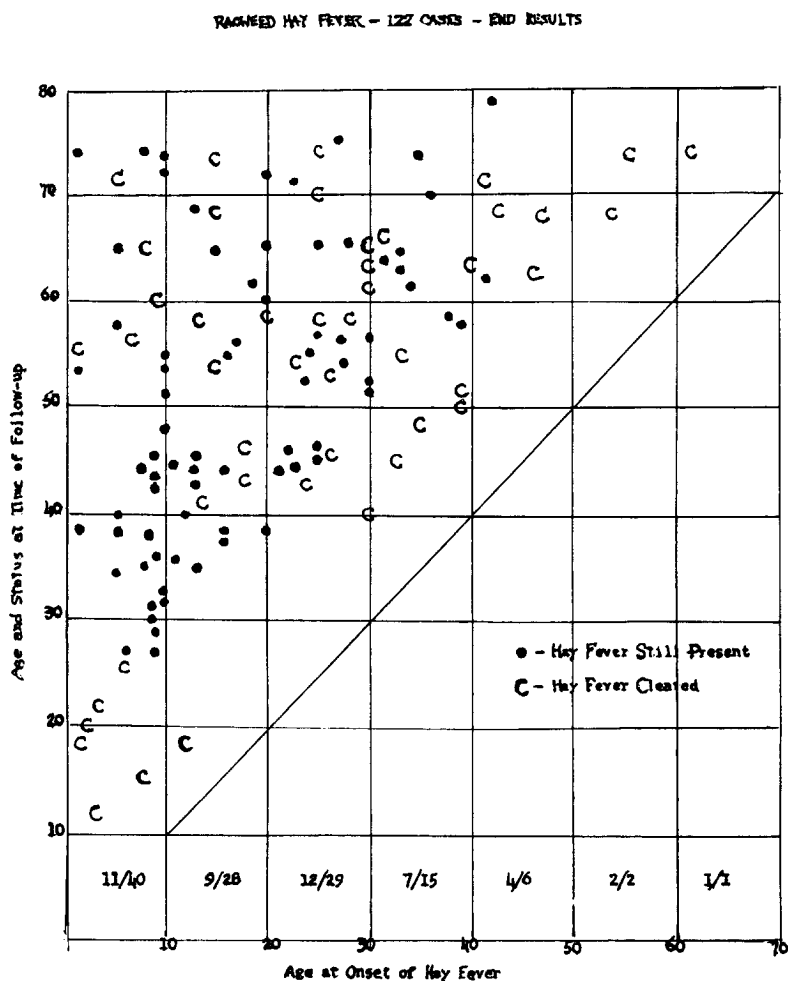
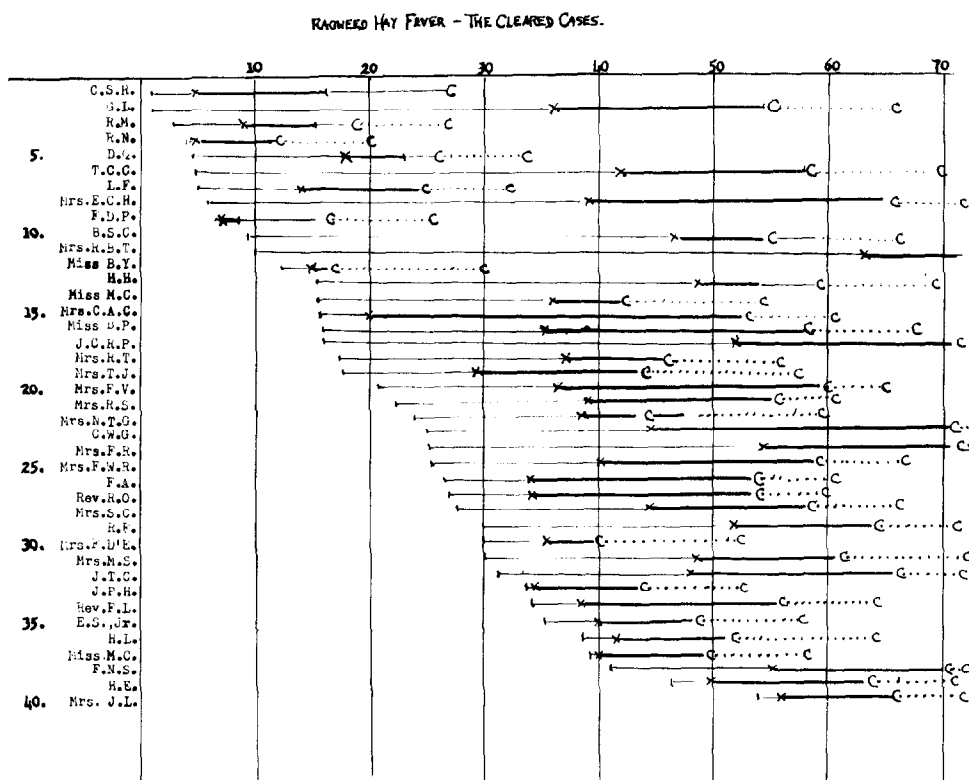


Fig. 1

Ragweed hay fever, 122 cases. End results of a follow-up study. Age at onset is plotted horizontally on the abscissa. Age at follow-up is followed vertically on the ordinates. Black dots mean hay fever still present. C means hay fever cleared (see text). Figures at the bottom show the number of cases in each decade cleared compared with the total number in that decade of onset.

light on this the cases have been plotted by symbols on a chart. Fig. 1 shows the outcome in all 121 cases up to the time of study. The age at onset is plotted horizontally on the abscissa; the age at follow-up is shown vertically on the ordinates. Solid circles mean that hay fever still continues; the C means clearance, which is more accurate than cured. It is true that in most of the cases marked C the patient has been free of hay fever with no need for treatment of any kind for about ten years, but there are a few cases (9 out of 122) in which the hay fever recurred after several (2 to 4) years of freedom and was troublesome enough to make the patient ask for an extra "shot" or two of ragweed—and that booster has been enough to clear the condition once more. Another reason to be skeptical of cure is the persistence of positive skin tests. At

**Fig. 2**

Ragweed hay fever, the 40 cleared cases. Each patient is represented by a line which begins at the age at onset. x marks the beginning of treatment, and the line is heavy during the years of that treatment. Usually the line ends with clearance, but occasionally treatment is omitted some time before clearance occurs. The dotted line shows the condition still cleared up to the time of follow-up, the final C.

the time of follow-up, skin tests with ragweed and other allergens were repeated in 14 of the 38 not treated and cleared cases and were found positive in 7. Five of these 7 patients were aged 65 and older.

Fig. 1 shows several patients with the onset of hay fever before the age of 15 and clearance before age 25. It shows a slight tendency toward clearing of the symptoms within fifteen years after the onset (the vertical distance of C above the diagonal which gives the age at onset). On the other hand, there is no rule about this, for there are many cases in which the hay fever has persisted through life. In other instances, the symptoms have cleared at odd times and without any obvious time or age pattern. There is a tendency for the C to rise to the top of the chart, which means that hay fever does tend to clear with advancing age.

On the bottom of Fig. 1 the number of cleared cases in each decade of onset has been added and compared with the total cases for that decade. The proportion of C's increases—showing in another way that hay fever tends to subside with age.

Fig. 2 shows the cleared cases in some detail. Here each patient is repre-

sented by a horizontal line which begins at the age at onset of hay fever and continues until the last follow-up report. The figure $\times$ in the line indicates the beginning of specific injection treatment and the line is heavy so long as the yearly treatment continues. The *C* is clearance, and the dotted line with another *C* at the end shows that the patient was still clear at the last follow-up, usually after an interval of about ten years, and without any further treatment.

What relation is there between clearance and treatment? As the length of the heavy line indicates, the patients in this series have been treated each year for an average of about ten years. There are several who have returned for their doses each year for twenty years or more before clearance was finally achieved and recognized (Cases 8, 15, 20, 23, 26). There are 3 who have become cleared after only four years of therapy and have stayed cleared (Cases 12, 14, 30). Again there is evidence of a relation to age. Seven of the 12 patients who developed hay fever in childhood became quite clear before age 27; the other 5 continued to have symptoms until their middle fifties and after. The relation to treatment varies. In most cases clearance has occurred at the end of treatment, but in several of the youthful patients clearance did not come until several years after the annual treatment was omitted (See Cases 1, 3, 5, 9, 13).

Hay fever can begin at any age, but treatment is often deferred. Children are brought to the doctor promptly. Older people tend to tolerate their symptoms for some time before applying for treatment. The chart shows that between 35 to 45 is the common age to see the doctor. As described above, the tendency is for hay fever to improve after age 50. There are, however, older people who have had hay fever all their lives and find that after age 50 the disease is worse instead of better and that asthma has come with it. This last has made them apply for help, and the help has been successful for most of them. Asthma seems to yield to specific pollen therapy better than hay fever.

Long-standing hay fever is not always severe, indeed it is quite true that in many cases there were no real symptoms during the last one or two or three years, and it is quite possible that treatment could have been omitted much earlier without changing the time of clearance. In other words, there are patients cleared of hay fever, but neither they nor the doctor has dared to test that clearance by having the patient go without the usual two or three doses to act as boosters.

Meantime, if further study will show that the total number of doses can be reduced in the majority if not in all of the cases and still produce good results, this method of giving aqueous pollen extract in only one, two, or three doses in amounts close to the tolerance level will compete successfully with the repository method.

SUMMARY

This paper shows what happens to a group of 120 patients with ragweed hay fever during the twenty-odd years after they have applied for treatment. In each year the number of patients under treatment has diminished, partly because some have moved away, but mostly because the symptoms have improved enough to make further treatment unnecessary. The average number

of doses given each year per patient under treatment has been reduced steadily from 10 doses in 1945 to 8 doses in 1950, 7.5 in 1955, 6.3 in 1960, and now to 4.9 doses in 1963. "Clearance" of hay fever has occurred each year in an increasing proportion of the cases.

One cannot say that the so-called specific treatment with pollen extract relieves every patient, nor can one say that this treatment has an effect which is permanent, even if the immediate result of that treatment is to abolish all the symptoms of hay fever for that year. However, the method of treating "old" well-known patients with a small number of doses given close to the tolerance level is useful for hay fever.

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263 BEACON STREET
BOSTON 16, MASS.