

POLLEN TOLERANCE NASAL TESTS IN HAY FEVER. EXPERIMENTAL AND CLINICAL OBSERVATIONS*†

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INTRODUCTION

ACCURATE analysis of the degree of subjective relief afforded by specific pollen therapy has always presented a problem to the practicing allergist. Up to now the information depended either upon the judgment of the symptomatic relief reported by the patient or by personal observations made during the pollinating period. Both methods represent crude, uncertain measurements which will not withstand close scientific scrutiny. Personal unpublished observations have shown that there is considerable variation between the amount of relief reported by the patient at the conclusion of the season and that recorded by means of a daily log. Individuals often claimed good to excellent results from their treatment, while their daily log recorded an appreciable degree of discomfort. Personal observations made by the attending physician during the season also were equivocal, since they depended on one's judgment during short periods that were not representative of the entire season.

Correlation between clinical symptoms and the absolute amounts of atmospheric pollen frequently has been lacking. This has created much confusion and skepticism regarding the significance of the daily pollen counts as recorded in many metropolitan newspapers along the Eastern seaboard. This discrepancy has been attributed variously to low barometric pressures, to dampness, to sudden changes in temperature, to changes of season, etc. Actually we know very little about its exact mechanism. It is possible that the presence of other nonpollen factors might accentuate the oculonasal symptoms of an already-established hay fever although the same factors in themselves might be incapable of producing threshold symptoms.

Regardless of the nature of these factors and the manner by which they affected individual patients, it seemed desirable to replace our crude yardstick for measuring the degree of clinical relief with a more accurate and objective method. Since pollen was the chief excitant in hay fever, and a constant factor, it occurred to us that by bringing it into direct contact with the principal shock organ, it should be possible to determine more definitely the results of specific desensitization. For this purpose the direct nasal or inhalation test employing pollen in varying concentrations might offer the best approach. Accordingly, in 1944, such an investigation was begun and the results obtained form the basis of the present report.

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PROCEDURE

The nasal or inhalation test used was similar to that previously reported,¹ except that one had to be more certain that the amount of inhaled pollen was as nearly constant as possible. This was accomplished by blowing the pollen from the blunt end of a toothpick on to a petrolatum-covered slide and then counting all the granules thus deposited. The applications were made by one individual while the counting was done by several technicians. The percentage deviation was then determined. The next problem was to find a diluent that permitted good admixture and distribution of pollen, that was nonirritating to normal nasal mucosa on multiple instillations, and that was sufficiently light and fluffy to permit easy inhalation. The following mixtures of pollen and diluent were first prepared.

1:1000	1:75	1:8
1:500	1:50	1:6
1:250	1:40	1:4
1:200	1:30	1:2
1:150	1:20	Concentrated
1:100	1:10	

The pollen mixture was then delivered to the nasal mucosa by means of a powder blower. This provided for delivery of a measured amount of pollen under what was considered standard conditions. Early experiences uncovered two drawbacks to this method; the first being the irritating nature of the forced draft used to deliver the pollen mixture, while the second revolved around the loss of pollen mixture due to its adherence to the rough surface of the nozzle of the blower. When this was found wanting, it was deemed advisable to permit the patient to insufflate the mixture by forced inspiration through one nostril. Although the depth and force of inspiration varied with each patient, it had many advantages over the blower method of application. The patient's tolerance to pollen was determined by single applications of the mixture beginning with the 1:1000 dilution and increasing the strength of the mixture upon each subsequent visit until a positive reaction occurred. Rhinorrhea and blockage were not sufficiently definite and objective criteria to be used to determine a positive reaction. Sneezing, together with rhinorrhea and blockage, was considered a positive test. Because of length of time required after instillation to determine the pollen tolerance in a single patient, a modification in procedure was made. This consisted of successive applications of pollen mixture on the same visit until a positive reaction was obtained. The number of dilutions originally used was too cumbersome and was correspondingly reduced to the following:

1:1000	1:10
1:250	1:2
1:50	Concentrated

Each patient was tested first with the diluent. If no reaction followed, the 1:1000 dilution was instilled. Five minutes were permitted to elapse before a second or subsequent application was made. If no reaction occurred, the next higher concentration was instilled. This was continued until a positive reac-

tion resulted. In order to insure adequate distribution of pollen in the diluent it was found necessary to agitate the mixture each day before using it.

The results of testing cases of hay fever treated by preseasonal and perennial methods are presented and the clinical implications and usefulness of this method of testing are discussed as follows: (a) the variability of reaction of the nasal mucosa to absolute amounts of pollen; the nature of some of these factors and the role they play in clinical hay fever; (b) the results of pollen tolerance tests before and after treatment by the preseasonal method; attempts to correlate the subjective improvement with objective observations and with the total and maximum dosages of pollen extracts; (c) the changing state of pollen tolerance before and after numerous years of consecutive perennial treatment; and (d) the usefulness of this method in determining the existence of spontaneous remissions or clinical cures.

RESULTS

The amount of pollen that was contained on the blunt end of a toothpick was fairly constant for pollen of the same size. Ragweed counts were 18,445, 18,746, and 18,248, a deviation of only 2.6 per cent.

Timothy counts were 9,882 and 10,176, a deviation of 3.5 per cent.

Many different types of diluents were considered before a selection was made. Pollen not indigenous to the locality seemed to offer many advantages over the artificial media, such as good admixture and distribution because of size and physical qualities. In our early trials, however, tale seemed to compare favorably in all respects with all other types of diluents. It was found that after long use the tale showed a slight tendency to cake. When this occurred, the mixtures were renewed.

The reactivity of the nasal mucosa to measured amounts of pollen was fairly constant. This was demonstrated by repeatedly precipitating clinical symptoms with a given dilution of the pollen-tale mixture. Most reactions were mild and required no therapy to counteract them. The occasional severe reaction could be controlled adequately by the topical application of vasoconstrictors and the oral administration of antihistaminic agents.

The threshold of nasal sensitivity to absolute amounts of pollen varied with individual patients. Thus, some reacted to dilutions of 1:1000 and others required a 1:2 dilution to precipitate a reaction. There was no absolute correlation between their initial threshold reaction and the severity of clinical hay fever, although more individuals with relatively low tolerances had more discomfort during the season. Fig. 1 displays this variability as determined with single applications of pollen before any specific treatment had been rendered. Fig. 2 depicts this same variability as determined by the multiple and successive method in patients receiving the preseasonal form of therapy. The tests were performed at least 5 months after the completion of specific therapy.

A total of 44 patients manifesting clinical hay fever were tested by this method before preseasonal treatment had been started and again after the termination of the pollinating season; 25 showed increased tolerance, 14 showed no change in tolerance, and 5 showed decreased tolerance.

Of the 25 showing increased tolerance, 19 reported good results from specific therapy, 6 reported fair results from specific therapy, and there were no poor results.

Of the 14 showing no change in tolerance, 9 reported good results, 2 reported fair results, and 3 reported poor results.

Of the 5 showing decreased tolerance all reported good results.



Fig. 1.—Nasal threshold reactions as demonstrated by pollen tolerance tests with single applications.

It had been hoped originally that this test would provide the medical attendant with an objective method by which he could gauge more accurately the degree of symptomatic relief obtained by the patient at the completion of specific pollen therapy. The lack of correlation between the change in nasal pollen tolerance before and after the season, and the degree of symptomatic relief reported by the patient renders this an uncertain means of estimating the actual response to specific pollen therapy. Furthermore, the changes in pollen tolerance noted above could not be correlated either with the total amount of pollen extract received by the patient, or with high dosage. Thus, some reported excellent results and objectively showed increased pollen tolerance from a low total and maximal pollen dose, whereas others reported poor results from higher total and maximal doses.

Although the pollen tolerance before and after a single year of preseasonal treatment varied considerably, it increased steadily with each successive year of perennial treatment. This observation corroborates the clinical impression held by many regarding the excellence of perennial therapy in the third and successive years of specific pollen treatment. Twenty-one patients

were tested in this manner over periods varying from 3 to 6 years with an average of 3.85 years. There was a significant increase in pollen tolerance in all the subjects tested, although the same variability existed here in the first year of perennial treatment as it had with our preseasonal subjects. Representative graphs of this increased tolerance are shown in Figs. 3 and 4. There was better correlation in this group between their symptomatic relief and the degree of pollen tolerance than in the preseasonal one. No parallelism existed between the total and maximum doses of pollen and either their subjective symptoms or the objective nasal pollen tolerance.

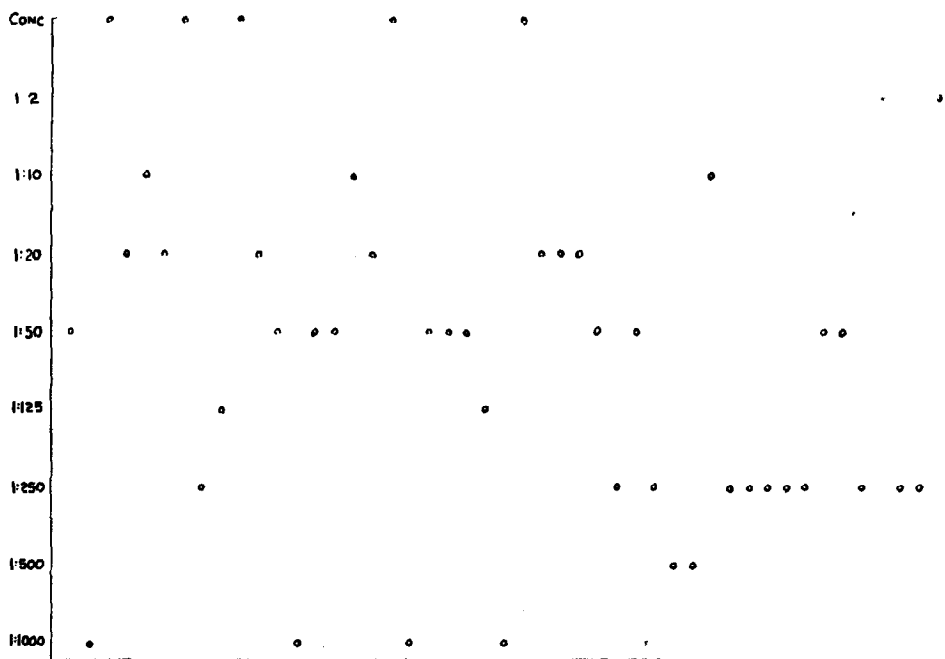


Fig. 2.—Nasal threshold reactions as demonstrated by pollen tolerance tests with successive instillations.

The diagnosis of spontaneous remissions or so-called clinical cures calling for a cessation of treatment has always been a difficult and a highly individualized one. There are those who call for a trial without treatment when the patient has manifested a minimum of symptoms for 3 successive years. Others are loath to stop treatment until every last vestige of hay fever has been eradicated. A small minority favor interrupting treatment when the cure becomes worse than the disease. Many patients take matters in their own hands and stop treatment against their physicians' advice when they think they have attained the desired results. None of the above methods are infallible, nor can any combination give the physician and the patient the assurance they desire against recurrent symptoms. Since each instillation of concentrated, dry pollen corresponded with the average amount of pollen inhaled during a 24-hour period, it seemed likely that any patient capable of withstanding repeated instillations within a relatively short time interval

might not need further treatment. Several modifications were made in the number of instillations and the time interval between applications before the standard procedure of 3 inhalations of the concentrated pollen with a 5-minute interval between each was adopted. Ten patients yielding a negative reaction to this procedure were advised to stop treatment. All 10 have been followed for 2 years without manifesting recurrent hay fever. Before this procedure was established we encountered several patients who had recurrent symptoms within 1 to 3 years after cessation of treatment. When retested by the above method a positive reaction was obtained in each case. The superiority of this method over the less certain and more diverse criteria for clinical cures establishes it as a useful adjunct in the practice of allergy. It should be used in those patients whose response to treatment has been so good as to suspect the existence of a spontaneous remission or clinical cure.

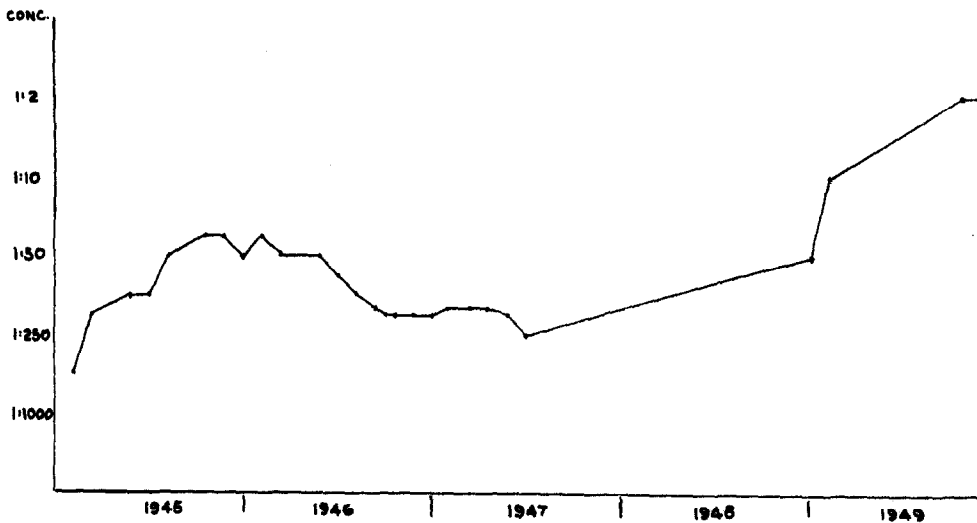


Fig. 3.—Pollen tolerance tests in a patient under continuous perennial pollen therapy.

DISCUSSION

It was evident from these studies that the tolerance of the nasal mucosa is influenced by factors other than the amount of pollen instilled. This alteration was not manifested by all patients but only by those in whom this additional factor was present at the time of testing. Repeated testing on such subjects showed a variable reaction from week to week to fixed amounts of pollen. At such times some of the patients gave positive reactions to our control, tale, whereas under normal conditions this reaction was lacking entirely. Most patients, however, maintained a rather constant reaction to the inhalation of a fixed amount of pollen. A careful review and analysis of these histories showed that those with variable reactions also manifested hay fever-like symptoms out of season, while those with strictly seasonal symptoms were more consistent in their response to pollen. The agents bringing about these alterations included infectious, meteorological, and psychic factors. This is in keeping with the recent experimental work of Wolff, Holmes, Goodell, and

Wolf² which demonstrated the ability of psychic stimuli to enhance the mucosal edema produced by specific pollen. It also corroborates a common clinical impression that the severity of hay fever symptoms is not always directly proportional to the atmospheric pollen concentration. Seasonal hay fever patients, therefore, may be divided into those whose symptoms are strictly seasonal and others who also manifest perennial symptoms. In this latter group one will find a variable reaction to pollen depending upon the presence of other specific sensitivities or nonspecific factors that enhance the allergic response of their shock tissues. The pollen tolerance of patients with strictly seasonal hay fever is much more constant.

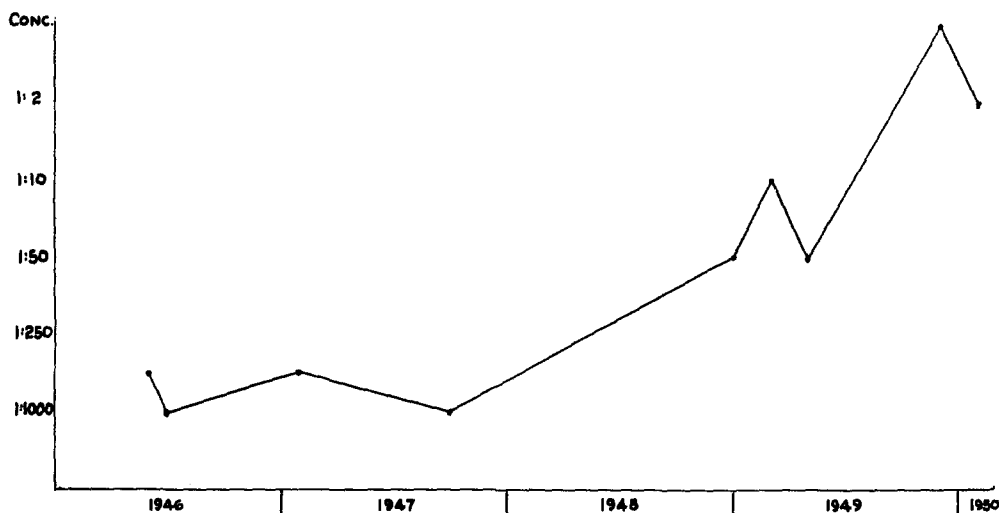


Fig. 4.—Pollen tolerance tests in a patient under continuous perennial pollen therapy.

The pollen tolerance test did not fulfill all the expectations originally held for it. It had been hoped that this method would detect a marked increase in pollen tolerance in those responding well to specific therapy, whereas there would be a negligible change in those with fair to poor therapeutic results. For some unexplainable reason there was no parallelism between the change in pollen tolerance and the degree of clinical relief in the preseasonally treated individuals. By contrast, there was a characteristic increase in tolerance among those treated for many years by the perennial method. It is difficult for one to comprehend why a satisfactory therapeutic response should not be accompanied by increased tolerance to the specific pollen. Yet our observations on a fair proportion of the preseasonally treated group failed to show such correlation. The unexpected results obtained in the latter patients can only be clarified by continued observations on larger groups and perhaps by certain modifications in procedure that would eliminate as many of the variables as possible.

From the results of our studies, it would seem that the pollen tolerance test can be quite useful as a criterion of clinical remission or cure. Since it is an objective method, it obviates the necessity of depending upon historical

data; however, it still may be used in conjunction with the latter in deciding upon the necessity for continued treatment. The mild degree of discomfort occasioned by a positive reaction is easily controlled by the topical application of vasoconstrictors and cannot compare to the prolonged discomfort of recurrent symptoms from an improperly diagnosed spontaneous remission.

SUMMARY

1. The pollen tolerance nasal test is a fairly accurate means of measuring the reaction of the principal shock organ to a given amount of pollen under standard conditions.

2. The reactivity of the shock organ is influenced by other factors, some specific, some nonspecific. Among the specifications are concomitant sensitivities to other foods, pollens, and inhalants. The nonspecific ones include respiratory infections, meteorological factors, and psychic stimuli. These complicating factors are best detected by an accurate and detailed history together with a complete allergic survey.

3. There was a constant and significant increase in pollen tolerance only with prolonged or perennial treatment. The results of pollen tolerance tests with preseasonal treatment for a single year were much more variable. It was impossible to forecast the therapeutic efficacy of specific treatment by this method since there was no parallelism either between the changing tolerance of the patients to pollen and their clinical results, or between the pollen tolerance and the total and maximum pollen dosage.

4. This test offers a satisfactory objective method for the determination of a spontaneous remission or cure. It may be used together with historical data in deciding when specific pollen therapy should be discontinued.

REFERENCES

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2. Wolff, H. G., Holmes, T. H., Goodell, H., and Wolf, S.: Life Situations, Emotions and Nasal Diseases: Changes in Nasal Function Associated With Varying Emotional States and Life Situations, *Tr. A. Am. Physicians* 59: 88, 1946.