

TREATMENT OF POLLEN HAY FEVER AND ASTHMA WITH AEROSOLS OF POLLEN EXTRACTS

INTRODUCTORY OBSERVATIONS

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ASTHMA has been produced in man and/or guinea pigs with nebulized allergens by Schiller and Lowell¹⁻⁵ and Herxheimer.⁶⁻¹² Herxheimer reported desensitization by aerosols of allergens in guinea pigs and man. Specific local desensitization of passively sensitized guinea pigs by aerosols of antigens and haptens has been studied in this laboratory.^{13, 14} An attempt to treat pollen hay fever and asthma with aerosols of pollen extracts seemed to be a logical sequel to this experimental background.

This report is an analysis of the observations made on twenty-one adult patients treated with aerosols of pollen extracts. Ten were treated during the late summer of 1953. Three of these and eleven others were treated during the 1954 fall pollen season.

Although obviously introductory, the data presented are sufficiently clear-cut to leave little doubt that some cases of pollen hay fever and asthma can be treated effectively by aerosols of pollen extracts.

Apparatus and Materials.—A DeVilbiss No. 40, or other, nebulizer with a special attachment for nasal inhalation by hay fever patients, plus an adjustable flow of compressed air of about 5 liters per minute, is all that is needed. An electric room air compressor is satisfactory.

A pollen extract mixture of seven parts ragweed and one part each of goldenrod, cocklebur, and corn was used arbitrarily. This is used in injection treatment at this clinic. Stock 1:33 weight by volume extracts, made by extracting 3 grams of dry pollen with 100 ml. of buffered glycerosaline, were diluted with normal saline to provide the weaker concentrations noted in the case reports.

Precautions.—Syringes with needles attached, 1:1,000 aqueous epinephrine, ampules of aminophylline and antihistamines for intravenous administration, and a spare nebulizer preloaded with 1:200 Isuprel were at hand. A physician was in attendance at all times. The patients were required to remain for at least thirty minutes after each treatment. Antihistamines, aminophylline suppositories, and sympathomimetics to control delayed reactions were provided.

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Treatment Details.—Deviations from the following details, as shown in the tables, were dictated by the progress of the individual cases and by the absence of prior experience.

The scratch, intracutaneous, and conjunctival reactions were titrated with the pollen mixture to provide some indication of the degree of the patient's sensitivity. The concentration of the initial inhalation was selected arbitrarily for each patient, 1:400,000 or weaker. Case 6 (1953) and Case 10 (1954) were exceptions. In general, treatment was started with a weaker concentration than that which gave a faintly positive intracutaneous reaction; 1.0 ml. was finally found to be the most convenient volume to use for each treatment.

The transoral route of inhalation was used to treat asthma and the nasal route was used for hay fever. In the transoral route, the lips were closed around the nebulizer tip to insure inhalation of the full 1.0 ml. of extract. For the nasal route, both nares were plugged with the tips of the nasal attachment which comes with the DeVilbiss No. 40 nebulizer. Three to five inhalations were given initially, and the patient was observed for fifteen minutes. The remainder was then inhaled without letup unless hay fever or cough occurred. One to three treatments were given daily. Arbitrary increments in concentration were given at each treatment. If symptoms occurred, the dose was reduced.

The nose should be inspected for patency before nasal treatments are given. When obstructed, the nares should be opened by bland decongestant sprays.

In the 1953 season, six patients received all treatments in the laboratory. Four other patients were allowed to take inhalations from a DeVilbiss No. 40 hand-pumped nebulizer at home, after fairly strong extracts were well tolerated in the laboratory. Compressing the bulb thirty times was shown to deliver about 0.1 ml. The daily dose at home was usually thirty to forty inhalations three to five times daily, or approximately 0.3 to 0.5 ml.

In 1954, all treatments were started in the laboratory. When improvement was noted, all fourteen patients were allowed to continue inhalations at home.

The results presented are based on periodic interviews and on postseason questionnaires. It is an old and familiar story that this method of interpreting results is fallible. For purposes of this report, it is unimportant whether an individual case or symptom was relieved 65 per cent, 75 per cent, or 85 per cent. It is important and accurate to state that all those who reported 65 per cent or more relief were highly pleased with the results.

Selection of Cases.—There were only three requirements: (1) hay fever and/or asthma limited to, or markedly accentuated during, the ragweed season; (2) positive skin and/or conjunctival reactions to the fall pollen extracts; (3) availability to the laboratory several times daily.

The ten 1953 cases are presented in some detail. The essential data on the 1954 cases are summarized in a table, plus some relevant comments.

1953 CASE REPORTS

Case 1 (Coseasonal Aerosol Alone).—The patient was a 39-year-old nurse with typical perennial hay fever accentuated markedly during the fall pollen season for twenty-three years. She was greatly relieved by injections of fall pollen plus other inhalant extracts from June, 1946, until she discontinued them early in the summer of 1952. However, she had little difficulty during the 1952 ragweed season. She was next seen on Sept. 1, 1953. Her hay fever had been troublesome for one week. There were strong skin and conjunctival reactions to the fall pollen mixture. She was treated by the aerosol schedule shown in Table I.

TABLE I. COSEASONAL INTRANASAL INHALATIONS

DATE		AMOUNT (ML.)	CONCENTRATION OF FALL POLLEN MIXTURE*	REACTION	COMMENTS
9/1/53	A.M.	0.5	1:400,000	None	
	P.M.	0.5	1:40,000	None	
9/2/53	A.M.	1.0	1:40,000	None	
	P.M.	1.0	1:20,000	None	
9/3/53	A.M.	1.0	1:8,800	None	90% Improved
	P.M.	1.0	1:4,000	None	
9/4/53	A.M.	1.0	1:2,000	None	90% Improved
	P.M.	1.0	1:1,100	None	
9/5/53	A.M.	1.0	1:800	None	90% Improved
	P.M.	1.0	1:400	None	
9/6/53-9/9/53					
	Once daily	1.0	1:400	None	90% Improved
9/29/53-10/2/53					
	Once daily	1.0	1:400	None	90% Improved

*This is the ragweed concentration. The other pollen extracts in the mixture are weaker (see text).

Comment: The only therapy was aerosol desensitization. Relief was striking by the third day. There were no complications of the therapy. Antihistamines were not necessary. She estimated 90 per cent relief. Multiple perennial inhalant problems did not prevent excellent relief from aerosol therapy. The patient was treated successfully by aerosol again in 1954 (Case 3, Table VIII).

Case 2 (Coseasonal Aerosol Alone).—The patient was a 29-year-old physician with typical ragweed hay fever for nine years, but no asthma. When first seen on Sept. 2, 1953, symptoms were unusually severe and were becoming refractory to the antihistamines which had been effective previously. There was some obstruction from a deviated nasal septum. His skin and conjunctivae reacted strongly to the fall pollen mixture. Aerosol treatment was given as shown in the protocol (Table II).

Comment: Some relief was noted within forty-eight hours. Treatment was discontinued on Sept. 18, 1953, because he had no symptoms. An acute upper respiratory infection on Sept. 8, 1953, subsided soon after Gantrisin

was started. He wheezed a little after one aerosol treatment at the peak of the infection. The aerosol was omitted for three days. Symptomatic remedies were not needed after aerosol therapy was stopped. The deviated nasal septum did not prevent the good response to therapy. He estimated 100 per cent relief of rhinorrhea, pruritus, and nasal stuffiness and 75 to 80 per cent relief from sneezing. Relief seemed clearly due to aerosol therapy.

TABLE II. CASE 2. COSEASONAL INTRANASAL INHALATIONS

DATE	AMOUNT	CONCENTRATION OF FALL POLLEN MIXTURE*	REACTION	COMMENTS
9/2/53	1.0 ml.	1:800,000	None	Symptoms $\pm$ 10 days
9/3/53	A.M. 1.0 ml.	1:80,000	None	
	P.M. 1.0 ml.	1:40,000	None	
9/4/53	1.0 ml.	1:20,000	None	Definite relief
9/5/53-9/7/53		None		
9/8/53	1.0 ml.	1:20,000	None	A cold
9/9/53		None		
9/10/53	A.M. 1.0 c.c.	1:20,000	None	
	P.M. 1.0 c.c.	1:8,000		Mild wheeze in 6 to 8 hours
9/11/53	1.0 c.c.	1:8,000		Tight chest; pus in nose; started on sulfa
9/12/53-9/14/53	None			
9/15/53	1.0 ml.	1:8,000	None	Cold O.K.
9/16/53		None		
9/17/53	1.0 ml.	1:4,000	None	
9/18/53	1.0 ml.	1:2,000	None	No symptoms; no antihista- mines needed

*See footnote, Table I.

Case 3 (Pre- and Coseasonal Aerosol Alone).—A 22-year-old woman had had severe hay fever and asthma in August and September and mild perennial hay fever from house dust for nearly twenty years. Benadryl and epinephrine, her only prior treatment, had been only partly effective. Preseasonal physical findings included a pale, boggy nasal mucosa, enlargement of the left inferior turbinate, and a few symptomless expiratory wheezes during forced expiration. There were positive scratch reactions to the fall pollens and plantain, plus many positive intracutaneous reactions to routine foods and inhalants. The fall pollen conjunctival tests were strongly positive in high dilution. Her aerosol treatment schedule is shown in Table III.

Comment: Aerosol treatment was begun about fifteen days before the onset of the ragweed season. It was continued coseasonally.

It was difficult to regulate the patient's aerosol dosage. There were some cough and purulent sputum for a few days at the end of August. She was given a supply of extract to use in the hand nebulizer one week before the pollen season. Two weeks after the pollen season began, she reported annoying asthma on two occasions only. In previous years, she had been uncomfortably asthmatic almost constantly at this stage of the season. Frequent stuffy nose but little sneezing were noted. The aerosol hand nebulizer treatments were continued. An occasional transient mild wheeze was the only sign of asthma during the last three weeks of the season.

Her postseason evaluation of aerosol therapy was 90 per cent relief or rhinnorrhea, nasal pruritus, and lacrimation. She estimated 80 per cent relief of the nasal stuffiness, sneezing, and sluggishness, and about 80 per cent relief of the asthma. She took antihistamine pills three or four times daily at first, but discontinued them about the middle of September.

Several reactions to the preseasonal treatments were severe enough to require one or two doses of Adrenalin. It is interesting that the early reactions

TABLE III. CASE 3. PRE- AND COSEASONAL TRANSORAL PLUS INTRANASAL INHALATIONS

DATE	AMOUNT	CONCENTRATION OF FALL POLLEN MIXTURE*	REACTION	COMMENTS
8/ 4/53 A.M.	0.25 ml.	1:40,000,000	None	
P.M.	0.25 ml.	1:4,000,000	None	
8/ 5/53 A.M.	0.25 ml.	1:400,000	None	
P.M.	0.25 ml.	1:40,000	Delayed wheeze	
8/ 6/53 A.M.	0.4 ml.	1:40,000	None	
P.M.	3.0 ml.	1:400,000	Delayed wheeze	
8/ 7/53	3.0 ml.	1:200,000	Delayed wheeze	
8/ 8/53	3.0 ml.	1:100,000	Delayed wheeze	
8/10/53 A.M.	3.0 ml.	1:50,000	None	
P.M.	3.0 ml.	1:25,000	Mild immediate wheeze	
8/11/53 A.M.	3.0 ml.	1:20,000	Mild immediate wheeze	
P.M.	3.0 ml.	1:8,000	Immediate wheeze and cough	
8/12/53	1.0 ml.	1:8,000	Immediate wheeze and cough	
8/13/53 A.M.	1.5 ml.	1:8,000	Immediate wheeze and cough	
P.M.	3.0 ml.	1:50,000	Immediate wheeze and cough	
8/14/53 A.M.	3.0 ml.	1:25,000	Immediate wheeze and cough	
P.M.	2.0 ml.	1:25,000	Immediate wheeze and cough	
8/15/53	3.0 ml.	1:30,000	None	Mild cough
8/16/53-8/28/53	20 inhalations 4 or 5 times daily	1:2,000	None	Hand nebulizer at home. No wheezing, mild cough with purulent sputum, hay fever improved 50%
(August 21-22—Season started)				
8/29/53-8/30/53	30 inhalations 3 times daily	1:2,000	None	Occasional mild asthma
9/ 1/53-9/ 5/53	30 inhalations 3 times daily	1:2,000	None	Annoying asthma twice
9/ 5/53-9/30/53	30 inhalations 3 times daily	1:2,000	None	Mild daily wheeze

*See footnote, Table I.

to the weaker concentrations of pollen extract were delayed. When the concentration was increased, the reactions were prompt. Some of the reactions to pollen aerosol may have been intensified by the low-grade bronchitis a few days before the season began. The delayed and prompt reactions, in contrast to Herxheimer's⁸⁻¹⁰ cases, did not necessitate interruption of aerosol treatment. Instead, the concentration of the inhaled extract was reduced markedly

after the second episode of delayed wheezing. The increments thereafter consisted of doubled doses instead of the greater increases given in other cases in which there were no reactions.

Her improvement seemed clearly the result of aerosol therapy, since no other treatment was used except antihistamines, which had been only partially effective before. Her polyvalent perennial allergy did not prevent good results from pollen aerosol treatment.

She was treated successfully by aerosol again in 1954 (Case 2, Table VIII).

Case 4 (Coseasonal Aerosol Plus Injections).—The patient was a 38-year-old white woman with typical severe hay fever starting Aug. 12, 1953, for the first time. She had been given daily injections of penicillin for one week and large doses of a variety of antihistamines, elsewhere, without benefit. There

TABLE IV. CASE 4. COSEASONAL INTRANASAL INHALATIONS PLUS INJECTIONS

DATE	AMOUNT	CONCENTRATION OF FALL POLLEN MIXTURE*	REACTION	COMMENTS
8/26/53-9/2/53	Coseasonal pollen injections given here			Onset of symptoms, August 12
8/26/53	0.25 ml.	1:400,000	None	Preliminary dose
		Aerosol program		
9/ 3/53 10 A.M.	0.5 ml.	1:400,000	None	
2 P.M.	0.5 ml.	1:40,000	None	
4 P.M.	0.5 ml.	1:20,000	None	
9/ 4/53 10 A.M.	1.0 ml.	1:20,000	None	
12 P.M.	1.0 ml.	1:8,000	None	
3 P.M.	1.0 ml.	1:4,000	None	
9/ 5/53-9/ 9/53	30 inhalations 3 times daily	1:1,000	None	Improved Hand nebulizer at home
9/10/53-9/17/53	30 inhalations 3 times daily	1:500	None	75% improved
9/17/53-10/ 2/53	40 inhalations 3 times daily	1:500	None	More improvement

*See footnote, Table I.

were purulent flecks in both nares, plus partial obstruction by a deviated nasal septum. Intracutaneous reactions were positive to ragweed and several other inhalants. Conjunctival tests with goldenrod and cocklebur pollen were strongly positive and precipitated acute hay fever within five minutes. Daily coseasonal injections of fall pollen extracts, started Aug. 26, 1953, plus symptomatic therapy, provided little relief in one week. Because of this, treatment with fall pollen aerosol was started on Sept. 3, 1953. She had been given a preliminary aerosol dose on August 26. The schedule of aerosol treatments is shown in Table IV.

Comment: Her postseason evaluation of aerosol therapy was 100 per cent relief from stuffy nose and lacrimation, 90 per cent relief of rhinorrhea, nasal

pruritus, and sluggishness, and 60 per cent reduction of sneezing. She continued to receive an injection of weak fall pollen extract once a week during the season.

The severe hay fever was not benefited by antibiotics (naturally), nor by antihistamines plus daily coseasonal injections of fall pollen extract. Improvement was noted on the fourth day of aerosol therapy and was estimated at 75 per cent relief within one week. Symptomatic remedies, which had been used until September 17, were not needed during the last two weeks of the season. There were no disagreeable effects from the aerosol.

Aerosol desensitization seemed to be the chief factor in her improvement, since seven days of coseasonal injections of pollen extract failed to provide relief. Coseasonal injections are usually effective within the first five days, if at all.¹⁵ The possibility of improvement from the coseasonal injections cannot be dismissed, however.

Case 5 (Pre- and Coseasonal Aerosol Plus Injections).—The patient was a 26-year-old man with perennial hay fever and asthma, accentuated in grass and ragweed seasons. Complications were marked deviation of nasal septum, chronic sinusitis and bronchitis, emphysema, postpolio kyphoscoliosis, and funnel breast. Antihistamines and injections of grass pollen extract, elsewhere, had provided little relief. There were strongly positive skin reactions to the fall pollens plus numerous other inhalants. Conjunctival reactions were positive to the fall pollen mixture, grass, and plantain.

He was free of symptoms when preseasonal aerosol therapy was begun on July 29, by the schedule shown in Table V.

Comment: Reactions to aerosol inhalations were so troublesome the first two trials that they were discontinued both times. Five injections of fall pollen extract were given between August 7 and 21. No more injections were given.

Aerosol treatment was resumed, for the third trial, on August 13 with weaker extracts for two days. On August 16 the patient was given some extract to inhale daily from a hand nebulizer at home. On August 28 another treatment was given in the laboratory. The hand nebulizer was used from August 28 to September 4. By that time he had become essentially asymptomatic. On October 20 he reported only two mild attacks of asthma during September. One of these was precipitated by a typical respiratory infection. The pollen aerosol accentuated his asthma during the respiratory infection.

It seems fortunate that aerosol treatment was begun three weeks pre-seasonally. The difficulty in adjusting the dose was nearly solved by the beginning of the season. The possibility of Herxheimer's⁸⁻¹⁰ hypersensitive state induced by reactions to aerosols must be considered here, but the reduced tolerance for antigen aerosols in the presence of bronchitis seems a more likely explanation for the reactions early in the course of aerosol therapy.

It is impossible to assess the role of aerosol in his improvement, estimated at more than 50 per cent, because he received some preseasonal injections of pollen extract.

TABLE V. CASE 5. PRE- AND COSEASONAL TRANSORAL INHALATIONS PLUS INJECTIONS

DATE		AMOUNT	CONCENTRATIONS OF MIXTURES		REACTION	COMMENT
			FALL POLLEN	GRASS AND PLANTAIN		
7/29/53	A.M.	1.0 ml.	1:8,000,000	1:2,000,000	None	
	A.M.	1.0 ml.	1:800,000	1:200,000	None	
	A.M.	1.0 ml.	1:80,000	1:20,000	Asthma in 5 hours	
7/30/53	A.M.	1.0 ml.	1:8,000	1:2,000	Immediate asthma	
	P.M.	1.0 ml.	1:16,000	1:4,000	Asthma in 1 hour	
8/ 5/53		3.0 ml.	1:16,000	1:4,000	Immediate tight chest	
8/ 6/53		3.0 ml.	1:20,000	1:6,000	Immediate and delayed asthma	
8/ 7/53			Started fall pollen injections			
8/13/53		3.0 ml.	1:200,000	1:60,000	None	
8/14/53		3.0 ml.	1:50,000	1:15,000	Delayed wheeze	
8/16/53-8/30/53	30 inhalations 3 times a day		1:4,000	1:1,000	Hay fever and asthma, 2 nights	Hand nebulizer at home
8/21/53			Pollen injections discontinued			Season began
8/28/53		3.0 c.c.	1:20,000	1:6,000	Delayed wheeze	
9/ 1/53-9/30/53	30 inhalations 3 times a day		1:2,000	1:600		Occasional transient wheeze, 2 mild attacks
10/ 1/53-10/20/53	30 inhalations 3 times a day		1:2,000	1:600		O.K.

This case is presented in detail to illustrate the problems of adjustment of dosage, rather than as an example of striking improvement from aerosol therapy. It also shows that, with care, aerosol therapy is not contraindicated in complicated cases.

Case 6 (Coseasonal Aerosol Plus Injections).—The patient was a 44-year-old man with fall hay fever for twenty-two years and fall asthma for twelve years. He got satisfactory relief from coseasonal pollen injections in 1942 and 1943. Thereafter, his symptoms were controlled satisfactorily by symptomatic remedies until 1952, when hay fever and asthma became troublesome again.

Mild hay fever began on Aug. 17, 1953. There were positive intracutaneous and conjunctival reactions to the fall pollen mixture. Coseasonal fall pollen extract injections were started then. On Aug. 27, 1953, he complained of local reactions and abdominal pain after each injection. There were no reactions to five subsequent smaller daily doses. Hay fever had not

been relieved by coseasonal injections and antihistamines, but was worse when aerosol treatment was started on Aug. 27 by the schedule shown in Table VI.

Comment: Note that he was given a fairly strong vial of extract to take at home from a hand nebulizer. When he returned on Sept. 10, 1953, he was essentially symptom-free. Definite improvement was noted by September 1, three days after (1) starting aerosol, (2) reducing the coseasonal injection doses, and (3) changing antihistamines.

Through an error, a vial of strong fall pollen extract was given to him on September 10. A few inhalations of this caused immediate severe hay fever and moderately severe asthma. He recovered promptly. On September 13, 1:2,000 fall pollen mixture was started by aerosol at home. He had no more trouble during that season.

TABLE VI. CASE 6. INTRANASAL INHALATIONS OF COSEASONAL AEROSOL PLUS INJECTIONS

DATE	AMOUNT	CONCENTRATION OF FALL POLLEN MIXTURE	REACTIONS	COMMENTS
8/18/53- 8/27/53	(Coseasonal daily)	pollen injections	Local and gastro- intestinal	Onset of hay fever, August 17
8/27/53	0.25 ml.	Aerosol started 1:8,000	None	
8/28/53- 9/ 3/53	40 inhalations 3 times a day	1:4,000	None	Hand nebulizer
	(Smaller coseasonal pollen injections daily)		None	Better by Septem- ber 1
9/ 3/53- 9/10/53	40 inhalations 3 times a day	1:4,000	None	90% relief; no anti- histamines
9/11/53	"Few inhala- tions"	1:40	Immediate hay fever and asthma	
9/13/53-10/ 2/53	40 inhalations 3 times a day	1:200	None	No symptoms
10/ 2/53-10/10/53	40 inhalations 3 times a day	1:200	Aggravated the cough of acute respiratory infection	

The original plan was to have him continue the aerosol perennially. However, he developed an acute respiratory infection in October. Aerosol aggravated the cough markedly, so it was stopped.

He estimated 90 per cent relief of nasal stuffiness, pruritus, and sneezing. He had no asthma except after the inhalation of the concentrated fall pollen mixture.

This case suggests that aerosol may be an effective supplement to coseasonal injections of pollen extract. The patient had troublesome reactions and no relief after nine coseasonal injections of relatively weak extract plus antihistamines. There are the same problems of accurate appraisal of aerosol as in Case 4.

The chief reasons for including this case are: (1) the troublesome reaction to an inadvertent overdose of aerosol, (2) failure to develop the "hypersensitive state" of Herxheimer, and (3) marked aggravation of the cough of bronchitis after the season by the aerosol.

Routine perennial injections of fall pollen extracts were given until the 1954 season started, when he promptly developed severe hay fever. Aerosol therapy relieved him again in 1954 (Case 1, Table VIII).

Case 7.—The patient had polyvalent perennial hay fever and frequent respiratory infections plus fall pollen hay fever. Coseasonal treatment with injections of fall pollen extract plus dust had not helped. Supplementary aerosol treatment produced an estimated 25 per cent relief. The following winter was her best one for years.

Case 8.—Treatment of uncomplicated fall pollen hay fever by injections and aerosol immediately before and during the season provided 90+ per cent relief. There were no undesirable reactions to the injections or to the aerosol. Evaluation of aerosol versus injections as factors in the marked relief is impossible.

Case 9.—A 20-year-old woman with perennial and ragweed hay fever developed severe, acute bronchitis during the aerosol treatments. She developed asthma on the fifth day of treatment and refused further aerosol. This is a clear-cut example of failure and is another illustration of the aggravation of bronchitis by aerosol therapy.

Case 10.—A 51-year-old woman with perennial, grass, and fall hay fever and asthma had been well controlled for about ten years by perennial allergen injections. Early in the 1953 season, she developed severe hay fever in spite of continued injections of fall pollen extract, an air-filtered room, and large doses of antihistamines. Aerosols of fall pollen extracts seemed to provide marked relief within a week. Injection and aerosol treatments were continued. Later in the season, however, asthma developed for the first time in ten years. This coincided with a period of acute, severe, emotional stress. Emotional episodes had previously precipitated asthma. Fall pollen extract aerosol apparently relieved the hay fever but did not prevent what seemed to be psychogenic asthma.

COMMENTS ON THE FOURTEEN 1954 CASES

The 1954 cases were treated by a more uniform schedule than were the 1953 cases. The pollen mixture, precautions, technique of administration, and criteria for selection of cases were the same as in 1953.

The treatments were given by the technicians by the routine outlined in Table VII. The essential clinical data on the fourteen 1954 cases are summarized in Table VIII and in the following comments:

All the patients had hay fever. Five had asthma, but it was quite mild in four patients. All but two (Cases 3 and 11) were treated only co-seasonally with the aerosol. Those two patients had pre- and coseasonal aerosol therapy.

TABLE VII. 1954 ROUTINE FOR POLLEN AEROSOL TREATMENT

1. Sequence of aerosol strengths		
1—1:4,000,000	fall pollen (= ragweed concentration)	
2—1:400,000	fall pollen	
3—1:40,000	fall pollen	
4—1:24,000	fall pollen	
5—1:12,000	fall pollen	
6—1:4,000	fall pollen	
7—1:2,400	fall pollen	
8—1:1,200	fall pollen	
9—1:400	fall pollen	
2. A treatment = 5 whiffs, 15 minutes' observation, then inhale rest of 1.0 ml.		
3. Two or 3 treatments daily at $\pm$ three-hour intervals until relieved. Use above dose sequence.		
4. Stop the inhalation at the first suggestion of tight chest, cough, wheeze, or hay fever.		
5. Maintain relief by hand nebulizer.		

Eleven patients obtained striking relief, estimated at 65 per cent or better. All the symptoms were relieved to about the same degree. One patient (Case 14) developed an obstinate virus infection of the upper and lower respiratory tracts about one week after starting the aerosol. It was impossible to evaluate the result of aerosol therapy.

Relief was usually apparent by the fourth day and maximal by the tenth day.

The initial concentrations of aerosols were weaker than those given in 1953, in general. 1:4,000,000 was the usual arbitrary starting dose. Patient 10 (who received striking relief) was the exception.

The final concentration varied. In each case it was approximately that concentration which was reached about the time that definite improvement was noted. This was the usual strength used at home.

All the 1954 patients completed treatment at home with a hand nebulizer. A few supplementary office treatments were given to three, in whom the hand nebulizer seemed not to maintain relief. In two of these, the over-all result was excellent.

There were no severe or prolonged reactions. Six patients had transient intensification of nasal symptoms either from the first few doses or, later, when stronger extracts were used. Four had mild bronchial reactions in the form of cough or wheezing.

All the patients had used antihistamines, with only fair relief, prior to treatment. During the last three weeks of the season, only six required symptomatic treatment. Of these six, one or two antihistamine doses per day provided almost complete relief to four patients.

Only one patient (Case 1) had had perennial or preseasonal injections of pollen extracts. He got no relief from them. Patient 7 was given some co-seasonal injections to attempt to increase the degree of relief from aerosol. No additional improvement was obtained from these injections.

Eight patients had had injections of pollen extracts in previous years. Seven felt that the results of aerosol therapy were better. One thought that the results were the same.

TABLE VIII. ESSENTIAL DATA ON AEROSOL TREATMENT, 1954 FALL POLLEN SEASON

	CASE NUMBER													
	1*	2†	3‡	4	5	6	7§	8	9	10	11	12	13	14
Diagnosis: pollen asthma (all had hay fever also)	0	+	0	0	0	0	0	+	0	+	+	0	0	+
Date aerosol started	9/2	8/21	8/5	9/13	9/1	9/2	8/31	9/15	9/8	9/8	8/11	9/7	9/9	8/31
Relief started (number of days)	4	2	Pre-seasonal	1	2	1	3	3	1	3	18	3	3	2
Relief maximal (number of days)	10	5	0	5	5	20	10	8	2	6	30	7	7	3
Aero. route: per oral plus nasal (all used nasal route also)	0	+	0	0	0	0	0	+	0	0	0	+	0	+
<i>Aerosol dilutions</i>														
Initial = 1:(In millions)	4.0	4.0	0.4	4.0	4.0	4.0	1.2	4.0	4.0	0.04	4.0	4.0	4.0	4.0
Final = 1:(In thousands)	4.0	40.0	0.4	0.4	2.4	4.0	2.4	40.0	1.2	4.0	0.4	0.8	4.0	1.2
Hand nebulizer effective (all used hand nebulizer)	+	+	±	+	+	+	+	±	+	+	+	+	+	0
More laboratory aerosol needed	0	0	+	0	0	0	+	+	0	0	0	0	0	0
<i>Estimated relief (per cent)</i>														
Total	80	90	80	75	65	80	40	90	85	90	85	85	50	P
Stuffy nose	100	50	80	100	60	75	40	80	65	85	85	80	50	O
Rhinorrhea	100	85	80	75	50	75		85	80	95	90	85	50	O
Sneezing	50	85	80	75	60	100	50	90	100	95	85	80	50	O
Ocular	85	98	80	75	45	90		100	100	95	85	85+	50	R
Cough	75	100						90	90	90	80	90		
Wheezing		95						100	100	90+	100			
Malaise		85	80	90		90+		95	65		85	85	50	
<i>Reactions</i>														
Nasal	0	0	+	0	0	+	+	+	0	0	0	+	+	0
Bronchial	+	0	0	0	0	+	+	0	0	0	+	+	0	0
<i>Antihistamines needed</i>														
Early	++	++	++	++	++	++	++	++	++	++	++	++	++	++
Late (after maximal relief)	0	0	0	+	0	0	+	0	0	0	+	+	+	+
Compared with injection Rx	B	B	S	B	B	B	B	B	B	B	B	B	B	B
Compared with no Rx	B	B	B	B	B	B	B	B	B	B	B	B	B	S

*Case 6, 1953. Had ineffectual preseasonal injections of pollen extract.

†Case 3, 1953.

‡Case 1, 1953.

§Had ineffectual coseasonal injections of pollen extract.

||B, Better; S, same.

The over-all results were better in 1954 than in 1953, perhaps because more of the cases were simple hay fever and/or asthma with fewer complications than in several of the 1953 patients, or because smaller doses were used to start treatment.

DISCUSSION

The problems of local desensitization have been revived by Swineford^{13, 14} and by Herxheimer.¹² They have shown that sensitized guinea pigs can be desensitized locally by aerosols of haptens¹³ and whole antigens.¹² Herxheimer⁸ doubts the validity of estimating the sensitivity of organs, such as the lungs, by testing a distant organ, such as the skin. The data of Schiller and Lowell^{4, 5} support this doubt. Herxheimer⁸ suggests further that local desensitization of a shock organ might be a more logical therapeutic approach than are the current methods of parenteral administration of allergens.

The 1953 observations described here had already been made when Herxheimer's^{8, 10} reports of aerosol treatment of asthma and hay fever were found. The technique used here (consisting of a nebulizer, compressed air, and allergen extract) is much simpler and more suitable for routine clinical use than the closed circuit respirometer used by Herxheimer. The graduated increases in allergen aerosol concentration seem safer than the time increments of concentrated allergens used by him, in view of (1) the occasional fatal reaction in guinea pigs following a few seconds' exposure to hapten aerosols,^{13, 14} (2) prompt asthma from a few whiffs of strong extract in Case 6, and (3) the occasional observation of severe asthma or shock from an injection of perhaps 0.1 ml. of 1:10,000 pollen extract, remembering that the injected extract is further diluted several thousand times by plasma before it reaches the bronchi.

The fall pollen season lasts from about August 19 to October 1 in central Virginia. The 1953 season was an average one. The 1954 season was hot and was the driest in twenty-four years. It started a few days earlier, lasted about one week longer, and was more severe than the average.

The prime purpose of this study was to see if allergen aerosols would relieve fall pollen hay fever and asthma. They did. Numerous supplementary clinical experiments are suggested by these observations. Most of them could be done better in larger clinics than this.

The lack of controls is an obvious and basic omission. Certainly, the final role of specific aerosols in the treatment of inhalant allergy will not be assigned until extensive, controlled studies have been done. In spite of this omission, the background of this problem is sufficiently factual to lend validity to the observations reported here. Several examples will suffice to make this point: (1) the bronchi of guinea pigs are readily desensitized specifically by aerosols;^{13, 14} (2) Herxheimer's results⁶⁻¹² were in agreement with those reported here, although the techniques were quite dissimilar; (3) Schiller and Lowell,¹⁻⁵ Herxheimer,⁶⁻¹² and others have demonstrated repeatedly the specificity of aerosols in the production of respiratory symptoms in sensitized animals and man. It has become almost axiomatic that antigens which produce specific inhalant allergic reactions can be used effectively in treatment.

Furthermore, it seems significant that, of the eight 1954 cases treated previously by pollen injections, seven reported more relief from aerosol therapy than from injections and one thought that the two methods provided about the same degree of relief.

Aerosol treatment with pollen extracts obviously is not the panacea for pollinosis. It is neither claimed nor implied that it should replace established specific methods of treatment.

SUMMARY

Twenty-one patients with fall hay fever, eight of whom also had asthma, were treated with aerosols of pollen extract.

The initial concentration of pollen extract varied from 1:40,000,000 to 1:8,000. The final concentration varied from 1:40,000 to 1:200. A part of the treatment was carried out at home by fifteen patients using a hand-pumped nebulizer.

Four patients received aerosol both pre- and coseasonally. Seventeen were given aerosol during the season only.

In 1953, six patients received aerosol plus pollen injections before and/or during the season. In 1954, only two patients received injection therapy.

In 1953, wheezing followed the aerosol in six cases, in four of these only when bronchitis was present. In 1954, six of the fourteen patients had nasal and four had bronchial reactions. All of these were mild and of short duration.

Severe asthma was precipitated once by an aerosol which was too concentrated. Transient asthma was precipitated in two patients who had not recognized asthma previously.

Aerosol therapy should be used with particular care in the presence of bronchitis.

In 1953, relief was estimated at 90 per cent in four cases, 80+ per cent in two, 50 per cent in one, 25 per cent in two, and no relief in two.

In 1954, eleven of fourteen cases reported relief estimated at 65 per cent or better. Relief began by the fourth day in all but one of the cases treated coseasonally by aerosol alone.

In contrast to Herxheimer's experiences, coseasonal therapy seemed effective and simple, and no evidence of "induced hypersensitivity" was encountered.

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