

Changes in severity of symptoms of asthma and allergic rhinitis due to air pollutants

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A total of 314 patients with allergic rhinitis, asthma, or both were observed from August 1 to November 1, 1963. Of these, 225 were sensitive to ragweed as well as other inhalants. The mean severity of symptoms was related to 10 measurements of air pollution, weather data, and mold and pollen counts. Of these, ragweed pollen was the only variable that was significantly related to severity of symptoms. Those patients who were allergic to ragweed had increased symptoms with the rise in pollen count. There also was a significant rise in symptoms in those patients who were not believed to have ragweed allergy. Chemical air pollution and mold counts showed inconsistent relationships, as did measures of humidity. Temperature changes showed a negative correlation, which is interpreted as a fortuitous happening.

The purpose of this study was to register the severity of symptoms of chronic sufferers of asthma, rhinitis, or both in a given area over a three month period from August 1 to November 1, 1963. Simultaneously, records are given for certain climatologic variables: daily counts of molds and ragweed pollen, daily measurements of certain chemical and physical air pollutants (SO₂, particulate matter, and smoke shade measurements), and daily meteorological data.

The Montefiore Hospital Group, because of its unique organization, affords numerous advantages for a study such as this. The insured persons are provided comprehensive medical care on a prepayment insurance basis through group practice. The structure permits the removal of economic barriers to treatment.^{1, 2}

Subjective evaluation of symptoms has many drawbacks.³ However, it was

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the only practical method we had available in 1963 to study this large group of people. To minimize the errors for this clinical study, only patients who had been proven to be fairly reliable in previous studies⁴⁻⁶ were chosen. These patients have been accustomed to keeping the diary cards through years of reporting symptoms. This system has been in use at this clinic since 1953. The importance of the diary has been repeatedly emphasized by the physician's referring to it in discussing the patient's progress. As some of the past work involved the use of placebos^{7, 8} where reports could be more fully evaluated, we were of the impression that these patients were as good a group as we could gather for the purpose of this study.

In order for appropriate scoring to be meaningful the results should be consistent with sound experience.⁹ In ragweed pollinosis a statistically significant correlation has been shown between daily ragweed counts and severity of symptoms graded on a simple four point scale.¹⁰ In addition to those patients who were known to be sensitive to ragweed, others were included who were sensitive to other allergens. The statistical analysis will primarily demonstrate the degree of correlation between pollen counts and symptom severity in the different disease manifestations and different allergen groups and explore whether other variables of weather and air pollution are determinants in the variation of symptom severity.

METHODS

Population sample

The 314 persons had all been patients of the allergy service for a minimum of 14 months. All were instructed to record daily their symptoms from August

FORM MG-3335

DAILY RECORD OF HAY FEVER SYMPTOMS

CARD No.

PATIENT'S NAME _____ NUMBER _____ AGE _____ SEX _____

ADDRESS _____ BOROUGH _____

DIAGNOSIS _____

MONTH OF _____ 19 _____

Date	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Severe																															
Moderate																															
Slight																															
None																															
Medication																															

MONTH OF _____ 19 _____

Date	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Severe																															
Moderate																															
Slight																															
None																															
Medication																															

HAY FEVER means sneezing; running nose; itching eyes, palate or nose; and/or nasal blockage.

ASTHMA - If you have any asthma (tightness in chest or cough) put the letter A in the appropriate space for the day to indicate if it was severe, moderate or slight.

MEDICATION - In the spaces opposite this write in the number of pills taken each day to keep comfortable (0 = none).

Table I

<i>Allergen (A)</i>	<i>Number of patients</i>		
	<i>Not allergic to A</i>	<i>Allergic to A only</i>	<i>Allergic to A and others</i>
Ragweed	55	34	225
Molds	257	0	57
Dust	111	4	199
Aggravated by infection	200	2	112
Grass	148	2	164
Trees	250	0	64

Table II

<i>Persons</i>	<i>Total days observed</i>	<i>Sum of scores</i>	<i>Mean score for person</i>	<i>Score on day 10</i>	<i>Deviation on day 10</i>
A	50	84	1.70	2	+0.30
B	65	91	1.40	1	-0.40
C	80	108	1.35	2	+0.65
D	40	30	0.75	1	+0.25
E	90	216	2.40	3	+0.60
					+1.40

1 to November 1, 1963, on a card (Chart 1). A check mark was to be made on the appropriate calendar day in either of the four rows signifying severe, moderate, mild, or no symptoms. The cards were collected every 2 or 3 weeks by the attending physician or nurse. All patients had a thorough allergy work-up, including their medical history, physical examination, and intracutaneous testing, and had been studied over a sufficiently long time to warrant the diagnosis. Children's records were kept by their mothers.

Of the 314 persons, there were 127 females and 187 males. The sex ratio was independent of all other variables in the study. Of these, 86 were under 15 years of age.

Some 204 suffered from perennial allergic rhinitis (AR) or hay fever alone, 40 from asthma alone, and 70 from both. Half of those suffering from asthma alone were children, while children only represented 22 per cent of those in the rhinitis or combined rhinitis and asthma group. Forty-eight of the children and 8 of the adults had symptoms since infancy. Average age of adult asthma patients was 43.7 years, of other adults 44.3 years.

In 251, or 80 per cent, the symptoms had lasted for more than 5 years. The causative allergens as determined by clinical observation corroborated by skin testing are given in Table I together with the number of patients in the given category.

It was noted that 38 persons were allergic to only one specific allergen, and 6 patients were allergic to all six groups of allergens. There was no particular association between ragweed and other allergens, but molds, dust, and infection were highly correlated and so were grass and trees. Ragweed allergy was equally

Table III. *Distribution of patients by allergen and symptom*

	<i>Rhinitis only</i>	<i>Rhinitis and asthma</i>	<i>Asthma only</i>	<i>Total</i>
Not ragweed	38	10	7	55
Ragweed and others	139	54	32	225
Ragweed only	27	6	1	34
Total	204	70	40	314

frequent in children and adults; 225 of our 314 patients were sensitive to ragweed, while 57 were sensitive to molds as well.

The length of observation of any given patient was not related to any of the above variables. The average length of observation was 54.7 days out of a possible 90 day period.

Air measurements

The following meteorological data was obtained from the United States Weather Bureau Monthly Summary Reports for the New York City area: daily average temperature, daily departure from normal temperature, relative humidity (24 hour average), and aqueous pressure in millimeters of mercury computed from temperature and relative humidity. The City of New York Department of Air Pollution Control (courtesy of Mr. M. M. Braverman) generously supplied daily measurements of three air pollutants: SO₂ (parts per million), particulate matter (micrograms per cubic meter), and smoke shade (COH units per 1,000 linear feet).^{*} These are commonly used in air pollution measurements employed both by New York City and the National Air Surveillance Network. The reported data are believed to present no unusual features for the season. Daily counts of ragweed pollen, *Alternaria* molds, and *Hormodendrum* molds were obtained from the Brooklyn Jewish Hospital and Dr. David Merksamer.

The gravity slide method¹¹ used to count ragweed and molds has some major disadvantages.¹² The collection is influenced by both wind velocity and direction. There can be non-uniform deposition of particles on the slide. The slide preferentially samples large particles. However, over the years we have found that ragweed patients' symptoms occur mainly in September when the count is usually reported to be at its highest.⁴⁻⁶

Computation of disease severity measurement

There were two problems confronting the measurement of variation in severity. First was the fact that on each day there was a different number of

^{*}Smoke shade is measured by drawing air through a filter paper for a measured period of time. The optical densities of the clean paper (I_0) and the soiled paper (I) are compared.
1 COH unit = $100 \times \log (I_0/I)$. L = 1,000 linear feet =
$$\frac{\text{flow (cubic feet per minute)} \times \text{sampling time (minutes)}}{1,000 \times \text{area of spot (square feet)}}$$

The standard unit used to express smoke concentration is COH units per 1,000 linear feet = COH/L.

persons observed. Each person was asked to register the severity of his symptoms on the 0 to 3 scale daily. If he failed to register on a particular day, he was not counted as observed. Neither was he counted if he indicated that he had been away from the observation area (New York City) on certain days. Not all persons started exactly on August 1, and several persons did not return reports for the latter part of the period. This accounts for the over-all observed length of 54.7 days, out of a possible 90 day period. The second problem was the arbitrary choice of scoring for mild, moderate, and severe. It is believed that each person has his own level of recognition in addition to his actual level of illness. For that reason, we computed the average score for each person over the days that he had been observed. On a given day, the deviation from this average was computed, and the mean deviation for all the persons observed was then calculated. For example, suppose 5 persons were observed on day 10. Table II gives the process of computing the mean deviation for that day. First, the total days that each person was observed is divided into the sum of scores for each person, thereby obtaining (in the fourth column) the mean score for that person. The fifth column gives the score noted by the persons on the day in question;

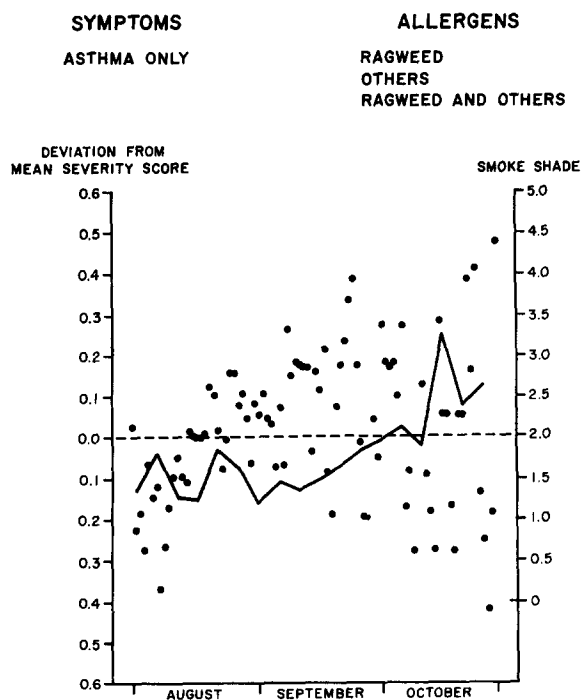


Fig. 1

Each plot represents the mean reaction for persons registering on a given day. The values are obtained by subtraction of the mean value for each person over the whole period in which he registered from his score for the day in question, and then these deviations for all persons with asthma, but no allergic rhinitis, were averaged. The broken line at 0.0 indicated the expected mean if no change in symptoms had accrued during the study period. The solid line represents 5 day means of *smoke shade* for New York City.

and in the final column the deviation is obtained by subtracting column 5 from column 4. Finally, the deviations are added and divided by the number of persons, in this case 5, to obtain a mean deviation for day 10 equal to +0.280.

A positive mean score, therefore, indicated that the group as a whole felt worse than average on that particular day, and a negative score indicated a lessening of symptoms below the average. For computer purposes, punch cards were marked for each of the 90 days and each of the various categories of patients that will be discussed further on. On the "day card" were introduced the values of each of the 10 independent variables observed on that day (air pollution, weather, etc.) together with the mean score and the number of persons observed on that day. The latter number served as a weight for each variable included.

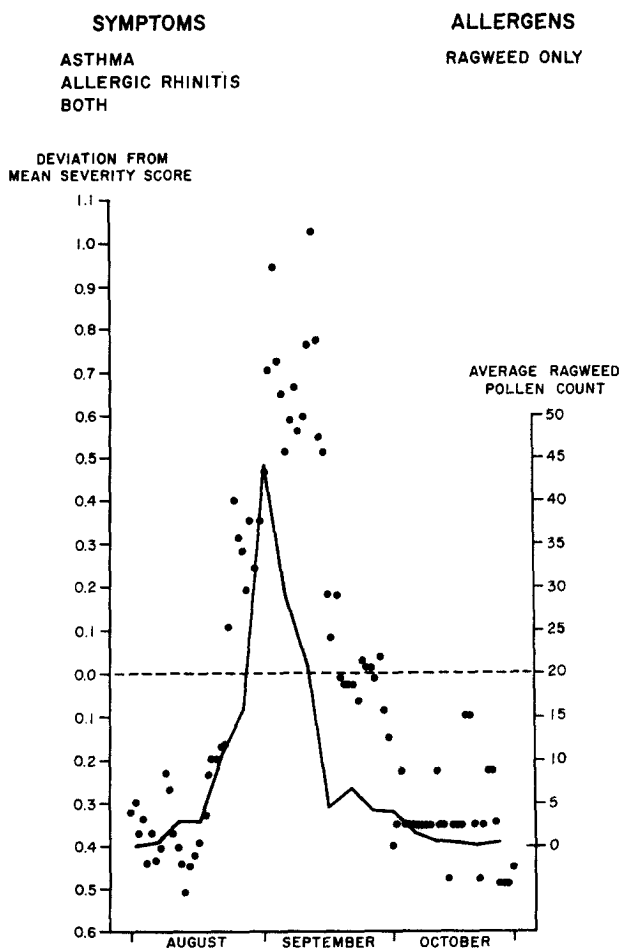
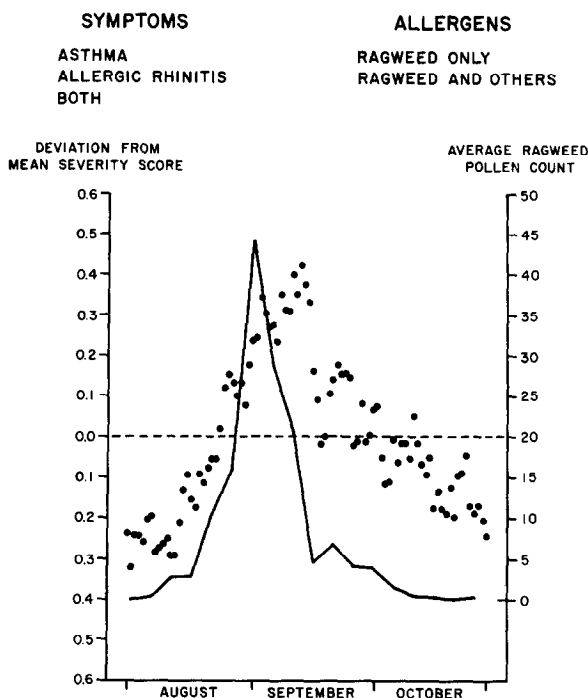


Fig. 2

Each plot represents one day's mean deviation from personal mean score (see text and Fig. 1) for all persons allergic to *ragweed only*. The solid line indicates 5 day means of *ragweed pollen counts*.

**Fig. 3**

Each plot represents one day's mean deviation from personal mean score (see text and Fig. 1) for all persons allergic to *ragweed only* or to *ragweed and other* allergies. The solid line indicates 5 day means of *ragweed pollen counts*.

RESULTS

Pattern of symptom severity

The heterogeneous group of patients was subdivided into 9 categories as displayed in Table III, where the rows represent classification by allergens and the columns classification by symptoms. Ragweed was the predominant allergen, and it was hardly possible to use other categorization. For example, of the 57 patients sensitive to molds, 45 were also sensitive to ragweed and the remaining 12 to other antigens. It is meaningful, however, to separate the 55 patients who were not allergic to ragweed. The subdivision by symptoms has been mentioned before. Other subgrouping was not informative because it led to too small samples. The smallest sample, that of "asthma only," has a certain bias because of the larger number of children than in any other group.

While 9 subgroups were studied individually, the main findings are best displayed in presenting the 6 groups represented by the column totals and row totals in Table III, namely, the 3 symptom groups for all allergens and the 3 allergen groups for all symptoms.

Figs. 1 through 5 present the average severity score for each day of study plotted as mean deviation from the over-all level for each patient.

The predominant pattern is that of a maximal rise in severity of symptoms by early September. This phenomenon is most distinct in Figs. 2 and 5, represent-

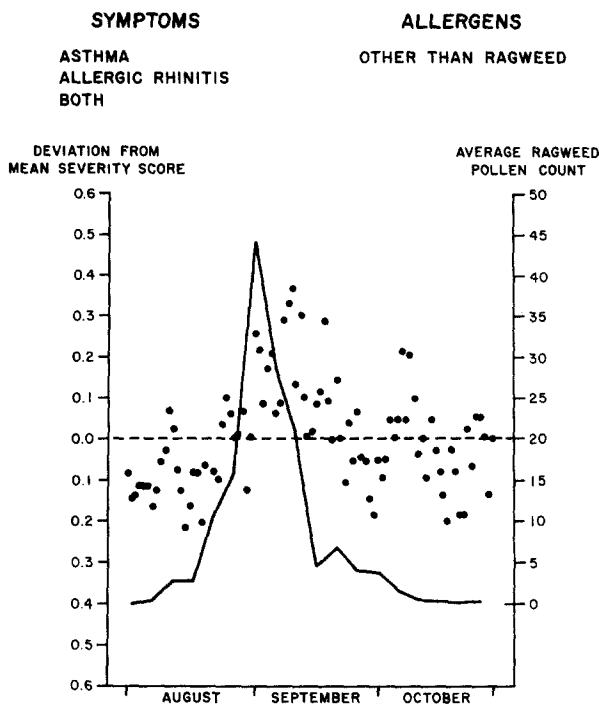


Fig. 4

Each plot represents one day's mean deviation from personal mean score (see text and Fig. 1) for the balance of persons not included in Fig. 3 (not allergic to ragweed). The solid line indicates 5 day means of *ragweed pollen counts*.

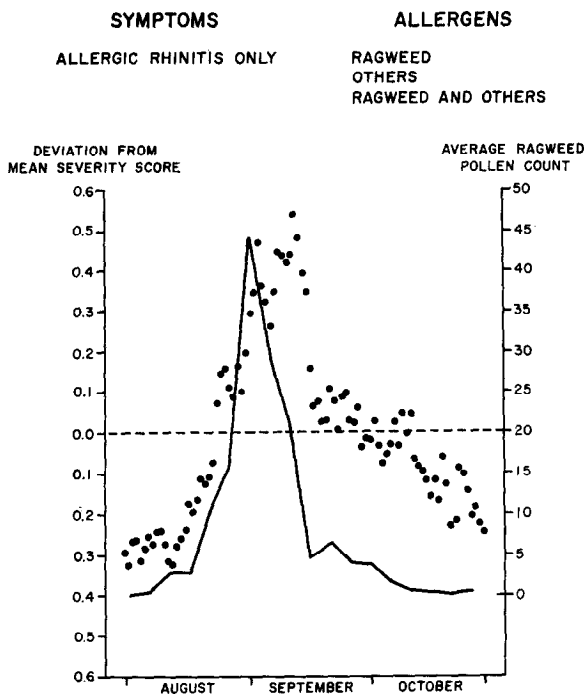
ing sensitivity to ragweed and hay fever, respectively. The group of asthma patients (Fig. 1) is the least distinct.

Pattern of air contamination

Air pollutants are shown in Fig. 6. The somewhat erratic behavior during August and September is followed by a simultaneous rise of all 3 measurements in the later part of October. Particulate matter deviates from the 2 others by a temporary peak in September while the others show relatively lower values.

Biological pollutants (molds and ragweed) are quite different (Fig. 7). Ragweed rises from a zero count in the first weeks of August to a distinct peak around the first of September and is almost absent in October. While *Alternaria* molds oscillate at random around the same level, there was a clearly high count of *Hormodendrum* in the first part of August, after which it follows the *Alternaria* count.

The temperature pattern (Fig. 8) during the 3 months of observation was marked by somewhat lower than normal temperatures in August, a seasonally cold September, and a seasonally warm October, as compared to the average temperatures in prior years. Negative departures from normal were especially pronounced in September. Relative humidity has no systematic pattern, and

**Fig. 5**

Each plot represents one day's mean deviation from personal mean score (see text and Fig. 1) for persons suffering from *allergic rhinitis only* but allergic to one or more of all types of allergens. The solid line indicates 5 day means of *ragweed pollen counts*.

aqueous pressure is highly correlated to temperature. Neither of these two variables is presented graphically.

Primary correlation

Table IV serves to present the crude linear correlation that can be obtained by computing correlation coefficients between the severity of symptoms of all patients and the 10 independent variables. There is only one highly significant correlation which will be elaborated later, namely, the positive association between ragweed counts and severity of symptoms. The 3 air pollutants have no significant bearing. *Hormodendrum* molds show a significant negative correlation due to the high counts of *Hormodendrum* in the beginning of August where most symptoms were below normal severity. Temperature and absolute aqueous pressure are indirectly correlated and have a significant negative correlation on patient symptoms, probably due to the fact mentioned above that the coldest weather prevailed at the height of the ragweed season, the first weeks of September.

Independent effect

A computer program was designed to solve for partial correlations of the 10 independent variables on the severity score. Table V presents the results of the

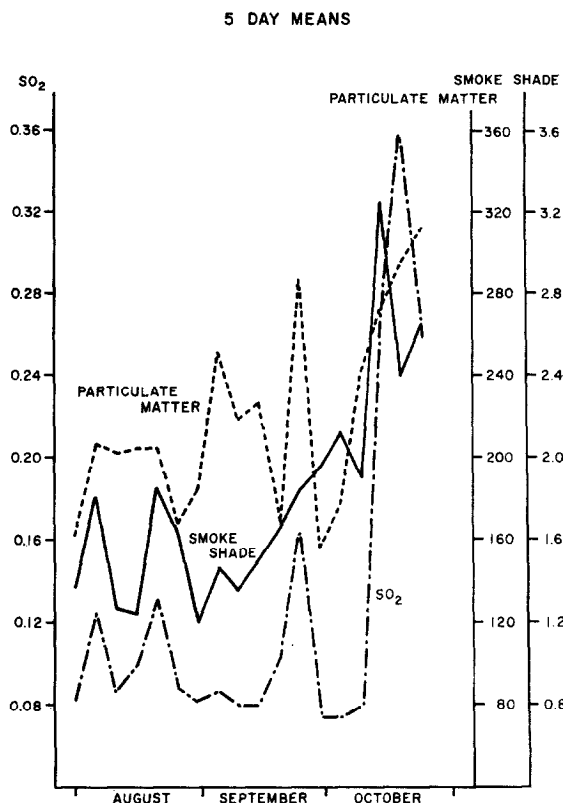


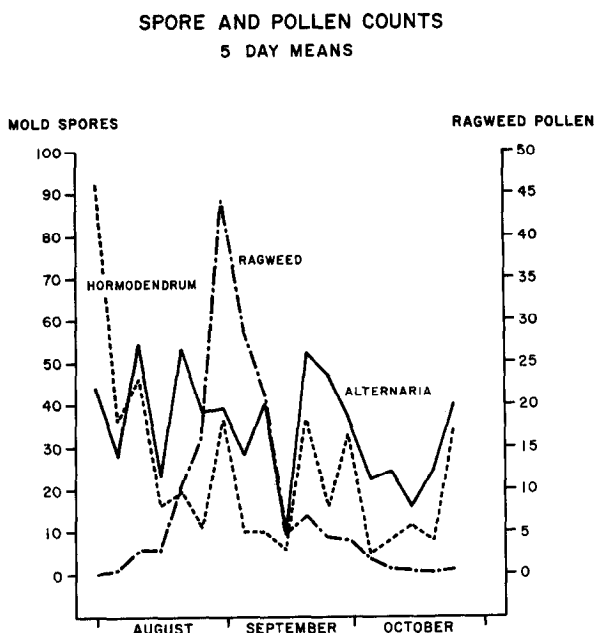
Fig. 6

Comparison of change in three principal air pollutants, 5 day means. The solid line denotes *smoke shade*; the dot-dash line denotes *SO₂*; the dashed line, *particulate matter*.

6 patient groups whose severity patterns are shown in Figs. 1 through 5. The result is that only ragweed remains a significant determinant for all groups. There is no independent effect of the three air pollutants. The negative correlation of *Hormodendrum* is only apparent in the rhinitis group. Temperature and other climatologic measurements are reduced to nonsignificance.

Relationship of ragweed count to severity symptoms

Table VI shows that the strength of association between ragweed count and severity of symptoms varies according to kind of disease and allergic sensitivity. The first 3 lines represent patient groups on whom tests show no allergy to ragweed. Nevertheless, there is a positive correlation of ragweed count and severity of symptoms of these patients. It is particularly noticeable among patients with presumed allergic rhinitis by clinical evaluation whose intradermal skin test was negative to ragweed, 1,000 protein nitrogen units per milliliter. In the group of rhinitis combined with asthma, the coefficient is positive but not significant (0.137), and asthma patients who are not allergic to ragweed have a correlation of only borderline significance (0.281).

**Fig. 7**

Comparison of 5 day mean count of *ragweed pollen* (dot-dash line) and *Hormodendrum* (dashed line) and *Alternaria* spores (solid line).

There are several possible explanations for the association of ragweed count and symptoms in patients who are not expected to react to ragweed. First, the skin and ophthalmic test may not be sensitive enough to disclose all patients with ragweed allergy. The other possibility is that they are allergic to some unregistered air pollutant that occurred simultaneously with ragweed pollen (molds did not peak at this time). None of the measured pollutants accounts for the reaction of these first 3 patient groups. Generally, however, the association is less strong between ragweed counts and severity in these patients than in other groups where ragweed allergy has been clinically demonstrated. The association is equally strong whether patients are allergic to ragweed only or ragweed and other allergies.

Most important, however, is the low association of ragweed exposure and symptoms of asthma patients in contrast to rhinitis patients. This lower value of the correlation coefficients exists whether the asthma patients are clinically allergic to ragweed or not. Thus the algebraic analysis confirms the notion afforded by the graphic presentations of symptom severity.

Relationship of temperature and humidity to severity of symptoms

Although the independent effects of temperature and relative humidity are negligible when corrected for all variables, there are reasons to investigate whether there is some possible association between symptom severity and temperature and humidity when these variables are corrected for the effect of rag-

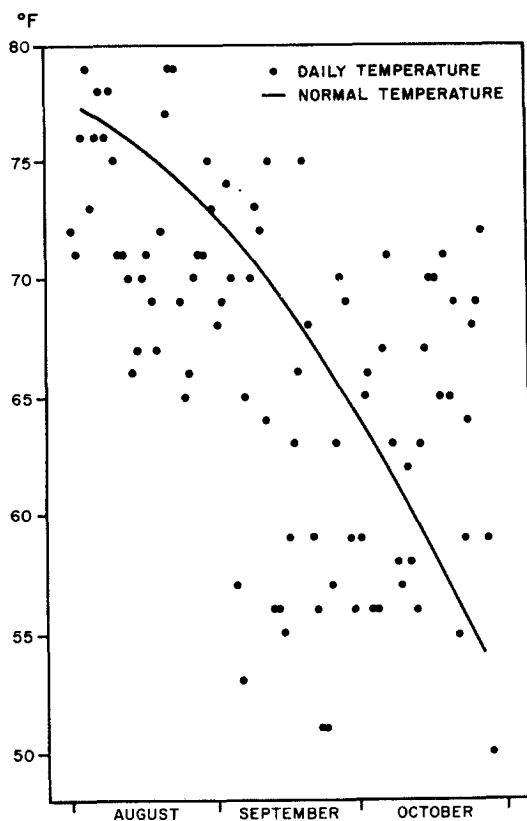


Fig. 8

Mean daily temperature (degrees Fahrenheit) in New York City compared to 60 year mean (normal temperature) for each day of the study period.

weed only. Table VII presents these partial correlation coefficients in the same subgroups that are displayed in Table VI.

Those for relative humidity are quite small, and none reaches a noteworthy level of significance. The positive and negative values do not follow any of the parameters delineated by the subgroups.

The coefficients for temperature corrected for ragweed are mostly on the negative side, and some are decidedly significant at the 1 per cent level. There is considerable variation among these negative coefficients but none that can be ascribed to factors associated with the subgroups. For example, it cannot be said that asthma is more affected by low temperature than is rhinitis.

It would be unwise to ascribe a causative element to the association between temperature and severity of symptoms. The fact remains that September happened to be a colder part of the observation period in which fell the major portion of the "ragweed season." An association of high severity and lower temperature may be a phenomenon entirely peculiar to the particular place and time of observation. In a pilot study¹⁰ in 1962, of some 50 patients with ragweed pol-

Table IV. *Primary correlation coefficients of independent* variables on mean severity score of all 314 patients*

<i>Independent variable</i>	<i>Primary correlation coefficients</i>
SO ₂	-0.174
Particulate matter	+0.032
Smoke shade	-0.169
Alternaria molds	-0.001
Hormodendrum molds	-0.295†
Ragweed	+0.670†
Average temperature	-0.264‡
Temperature departure from normal	-0.202
Aqueous pressure	-0.296†
Relative humidity	-0.130

*"Independent" signifies the partial correlation of the 2 variables that remain after the adjustment for the 9 other independent variables.

†Significant at the 1 per cent level.

‡Significant at the 5 per cent level.

Table V. *Independent* correlation coefficients of air measurements on mean severity score by patients grouped according to allergens and to symptoms*

<i>Independent variable</i>	<i>All allergens</i>			<i>All symptoms</i>		
	<i>Rhinitis only</i>	<i>Rhinitis and asthma</i>	<i>Asthma only</i>	<i>Ragweed only</i>	<i>Ragweed and others</i>	<i>No ragweed</i>
SO ₂	-0.21	-0.12	+0.12	-0.07	-0.18	-0.14
Particulate matter	+0.07	-0.02	-0.07	+0.03	+0.04	+0.11
Smoke shade	+0.13	+0.03	+0.13	+0.03	+0.18	+0.03
Alternaria molds	-0.19	-0.13	-0.07	-0.20	-0.18	-0.15
Hormodendrum molds	-0.29†	-0.15	-0.00	-0.22‡	-0.27‡	-0.08
Ragweed	+0.80†	+0.64†	+0.37†	+0.78†	+0.77†	+0.59†
Average temperature	-0.22‡	-0.11	-0.08	-0.13	-0.21	-0.05
Temperature departure from normal	+0.08	-0.11	-0.13	-0.05	-0.05	+0.14
Aqueous pressure	+0.10	+0.08	-0.03	+0.11	+0.08	-0.02
Relative humidity	-0.03	-0.08	+0.08	-0.04	-0.02	+0.06

*"Independent" signifies the partial correlation of the 2 variables that remain after the adjustment for the 9 other independent variables

†Significant at the 1 per cent level.

‡Significant at the 5 per cent level.

linosis, the authors found a positive correlation between temperature and severity of symptoms after correction for ragweed. It so happened that in this study of the same area, there was a relatively cool August and warmer September, explaining the positive correlation in this case.

The nonbiologic air pollutants were not demonstrated as being statistically significant in aggravating the patients' symptoms. There was a notable trend, however, for the non-ragweed allergic rhinitis patients to have increased symptoms associated with more particulate matter in the air (Figs. 4 and 6) and the

Table VI. *Independent* correlation coefficients between ragweed and severity of symptoms by allergen and disease*

Allergic to:		Disease		Correlation coefficients
Ragweed	Others	Hay fever	Asthma	
0	+	0	+	0.281
0	+	+	+	0.137
0	+	+	0	0.653
+	+	0	+	0.332
+	+	+	+	0.630
+	+	+	0	0.760
+	0	0	+	(1 patient only)†
+	0	+	+	0.572
+	0	+	0	0.771

*"Independent" signifies the partial correlation of the 2 variables that remain after the adjustment for the 9 other independent variables.

†This patient kept records daily from August 1 through September 30. He recorded no symptoms up to September 1. From September 2 to 15, he recorded slight to moderate symptoms and none in the last half of September.

Table VII. *Partial correlation coefficients for temperature and for relative humidity on severity of symptoms*

Allergic to:		Disease		Relative humidity corrected for ragweed and temperature	Temperature corrected for ragweed
Ragweed	Others	Hay fever	Asthma		
0	+	0	+	-0.009	+0.259
0	+	+	+	-0.227	-0.094
0	+	+	0	+0.137	-0.207
+	+	0	+	+0.107	-0.550
+	+	+	+	+0.029	-0.279
+	+	+	0	[+0.236 -0.024 -0.067]	[-0.347 -0.512 -0.170]
+	0	0	+		
+	0	+	+		
+	0	+	0	+0.211	-0.218

asthmatic patients to be worse (Figs. 1 and 6) when the measurements of 3 of the charted nonbiological contaminants rose.

COMMENT

During the summer of 1960, Booth and colleagues¹³ studied epidemic asthmatic attacks in 9 cities. Tabulation of daily visits were made of asthmatic patient visits to the emergency clinics of 16 hospitals. Of the 16 hospitals, Cook County in Chicago and Harlem in Metropolitan New York showed a marked increase in emergency clinic visits in October and November, 1960. The authors could not ascribe any reasons for the increase of these clinic visits. Kenline¹⁴ likewise made a study of the emergency clinic visits of asthmatic patients to the Charity Hospital in New Orleans. He correlated the asthma visits with dust particle counts and found a rough association. No attempt was made

to identify the asthmatic patients or to determine an allergic diagnosis for any of the patients. He did find that an increase of small particles, that is, less than 10 $m\mu$ in size, correlated with increase in asthma, while those of larger size were identified with a lesser number of visits. Branscomb and colleagues¹⁵ attempted to study respiratory disease in the whole state of Alabama. The investigations depended upon random sampling, the cooperation of many volunteer workers, and the use of patients filling out questionnaires. This is an ambitious project, and if the study comes to fruition there might be some answers as to whether respiratory disease increases with air pollution. In view of the size of the study with so many participants, areas, and patients, it will probably take years to assess the results. Glasser, Greenburg, and Field¹⁶ observed a marked rise in the number of emergency clinic visits of patients suffering with asthma and bronchitis at 7 large New York City hospitals on the third day of air pollution in November, 1966.

Our investigation encompasses patients who have been followed for years prior to this study so that a definite allergic disease had been established. By referring to Fig. 1 it can be seen that apparently more patients suffered with asthma as the concentration of air pollutants increased. That this could not be statistically proved might be due to the relatively small number of asthmatic patients participating. Further study with more patients might conceivably associate symptoms with the increase of these air pollutants.

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