

THE INHALATION TEST AS A DIAGNOSTIC PROCEDURE WITH SPECIAL EMPHASIS ON THE HOUSE DUST ALLERGEN

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INDUCED asthmatic attacks can be readily detected by the attending decrease in vital capacity and slowing in the expiratory rate and, in many subjects, these changes follow the inhalation of aerosolized allergenic extracts.^{1, 2, 3} The method has been useful for the study of changes in the mechanics of respiration in bronchial asthma as well as for the study of drugs active in preventing or relieving symptoms.^{4, 5, 6} The present report describes our experience with the inhalation method as a diagnostic procedure in a group of 75 asthmatic patients.

METHODS

The patients ranging in age from 6 to 62 years, with mild to severe asthma, were questioned carefully regarding the time of year in which symptoms occurred and the existence of precipitating factors. Skin tests were done by the intracutaneous method. All patients were exposed to aerosolized allergenic extracts in the manner described elsewhere,^{2, 3} at a time when they were free, or almost free of asthma. The materials used included freshly prepared 5 per cent extracts of birch, oak, timothy, and ragweed pollens and the molds, *alternaria*, and *hormodendrum*. House dust extract,* prepared by the method of Boatner, Efron, and Dorfman,^{7, 8} was used in a concentration of 1-400. Dosage was easily controlled by decreasing or increasing the number of inhalations. A satisfactory procedure was to give a single inhalation, followed in five minutes if no reaction occurred by three inhalations, and five minutes later by six inhalations, making a total of ten. Measurements of the vital capacity and expiratory rates were made at 1 or 1½ minute intervals during the test. A reduction in vital capacity of 10 per cent or more and/or a clearcut slowing in the rate of expiration accompanied or unaccompanied by symptoms and signs of asthma has been considered by us to be indicative of bronchial or pulmonary sensitivity to the substance inhaled. Care was taken to avoid nonspecific pulmonary reactions due to irritating extracts and a control consisting of the extracting solution was always included. If glycerinated extracts are used, it may be necessary, with certain patients, to dilute the extract and increase the number of inhalations. Induced pulmonary reactions may be readily relieved by the administration of a drug such as nebulized Isuprel. Very infrequently a pronounced induced pulmonary reaction, though promptly relieved, was followed later by

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asthma lasting for a few hours. Such an occurrence underscored the importance of the responsible allergen. Apprehensive patients may be upset by this, therefore they should be forewarned and should have suitable medication available.

RESULTS

The 75 patients were divided, as shown in Table I, into three groups: Group I including all those reacting to dust by inhalation, Group II including those reacting to other allergens but not dust, and Group III, those failing to react by inhalation to any of the allergens used. Group I was further divided into (A) those reacting to dust only and (B) those reacting to dust and one or more of the other allergens. Of the 75 patients, there were 57 who reacted to one or more allergens by inhalation. Dust caused reactions in 43 patients, ragweed in 22, birch in 5, and oak, timothy, alternaria, and hormodendrum in 3 each. The incidence of skin reactions was much greater than that of pulmonary reactions and the occurrence of a pulmonary reaction on exposure to an aerosolized allergen could not be satisfactorily predicted on the basis of skin tests. We were especially impressed, on the other hand, by our failure to produce pulmonary reactions with allergens which did not give skin reactions.

The time of year in which symptoms of asthma were aggravated as judged by the patient's statements and medical record is represented by the heavy bars in Figs. 1 to 4. As seen in Figs. 1 and 2, among the 43 patients reacting to dust by inhalation, in 25 asthma tended to be aggravated in the fall, especially during the month of October. On the other hand, patients failing to react to dust by inhalation but who reacted to other allergens (Fig. 3) showed a predominance of symptoms in September and earlier. Those who failed to react by inhalation to any of the 7 allergens used (Fig. 4) tended to have an aggravation of symptoms during the colder months.

As may be seen in Table II, there were no significant differences between the groups shown in Table I with regard to sex, age, and duration of asthma. However, patients in Group I and Group II had a high incidence of allergic manifestations other than asthma, as compared to Group III and this difference, statistically significant, is largely attributable to the high incidence of hay fever in the first two groups.*

DISCUSSION

The possibility that the observed pulmonary reactions are merely nonspecific and irritative in character must be considered. Nonspecific irritability of the lung, as measured by responsiveness to histamine or mecholyl, varies widely among asthmatic subjects and tends to be greatest among those having severe asthma.⁹ However, the severity of asthma in our patients has not correlated well with the pulmonary responsiveness to inhaled aerosolized allergens, some of the patients with mild asthma having exhibited very marked pulmonary reactions. On the other hand, most of the patients falling in Group III, all of

*To test the data for statistical significance, we find Chi-square = 10.9 which, for 2 degrees of freedom, is significant at approximately the .005 level. Since better than 60 per cent of the total Chi-square was contributed by Group III, we conclude that this group shows a real difference in behavior from the other two.

TABLE I. CORRELATION OF SKIN AND INHALATION RESPONSES IN 75 ASTHMATIC SUBJECTS
EXPOSED TO AEROSOLIZED ALLERGENIC EXTRACTS

ALLERGEN USED	PATIENTS REACTING TO DUST BY INHALATION										PATIENTS NOT REACTING TO DUST BY INHALATION															
	GROUP I										GROUP II										GROUP III					
	A					B					TOTAL PATIENTS A AND B					PATIENTS REACTING TO MISC. ALLERGENS					PATIENTS FAILING TO REACT TO ALLERGENS					
	PATIENTS REACTING TO DUST ONLY		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST		PATIENTS REACTING TO MISC. ALLERGENS AS WELL AS DUST							
	SKIN	LUNG	RE- TESTED	ACTED	RE- TESTED	ACTED	SKIN	LUNG	RE- TESTED	ACTED	SKIN	LUNG	RE- TESTED	ACTED	SKIN	LUNG	RE- TESTED	ACTED	SKIN	LUNG	RE- TESTED	ACTED	SKIN	LUNG	RE- TESTED	ACTED
Birch	20	4	9	0	10	6	8	3	30	10	17	3	11	5	8	2	12	1	12	1	7	0	12	1	7	0
Oak	21	3	9	0	11	6	7	3	32	9	16	3	11	3	7	0	12	1	12	1	7	0	12	1	7	0
Timothy	25	14	12	0	10	8	10	2	35	22	22	2	12	6	10	1	14	0	14	0	8	0	14	0	8	0
Alternaria	24	9	13	0	10	4	4	2	34	13	17	2	11	4	10	1	15	3	15	3	9	0	15	3	9	0
Hormodendrum	20	7	13	0	7	2	2	2	27	9	15	2	11	4	9	1	13	1	13	1	6	0	13	1	6	0
Ragweed	28	21	28	0	13	13	13	12	41	34	41	12	14	14	14	10	16	9	16	9	16	0	16	9	16	0
House Dust	30	30	30	30	13	13	13	13	43	43	43	43	14	10	14	0	16	12	16	12	18	0	16	12	18	0
No. of pa- tients in each category	30				13				43		43		14		14		18									

GROUP I.(A)
DISTRIBUTION OF PATIENTS REACTING TO AEROSOLIZED
DUST ONLY, INDICATING TIME OF YEAR
WHEN ASTHMA IS AGGRAVATED

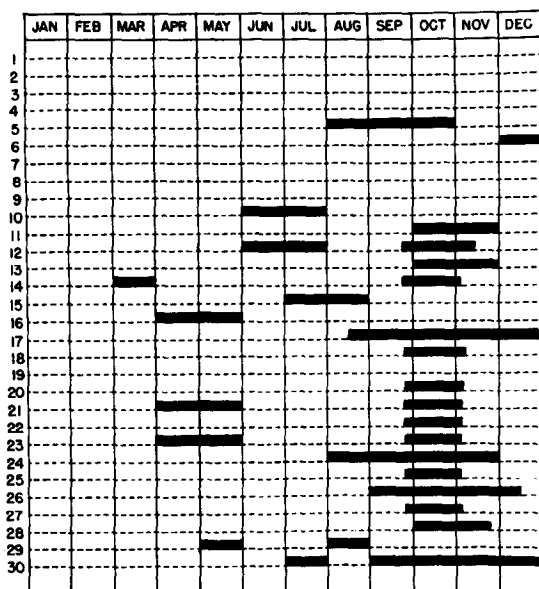


Fig. 1.

GROUP I. (B)
DISTRIBUTION OF PATIENTS REACTING TO MISCELLANEOUS
ALLERGENS AS WELL AS DUST, INDICATING TIME OF YEAR
WHEN ASTHMA IS AGGRAVATED

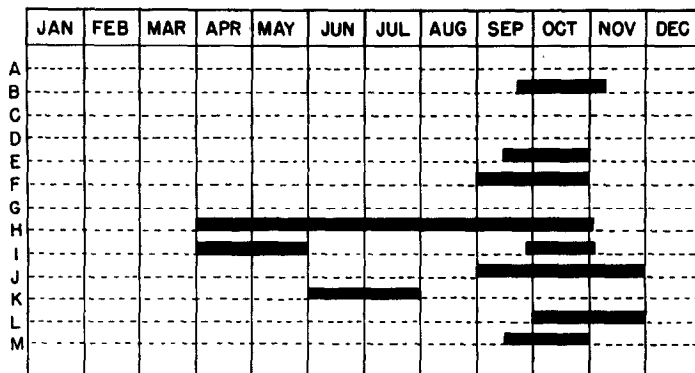


Fig. 2.

TABLE II. CLINICAL DATA ON 75 SUBJECTS WITH BRONCHIAL ASTHMA EXPOSED TO AEROSOLIZED ALLERGENIC EXTRACTS

	PATIENTS REACTING TO DUST BY INHALATION			PATIENTS NOT REACTING TO DUST BY INHALATION	
	GROUP I			GROUP II	GROUP III
	A PATIENTS REACTING TO DUST ONLY	B PATIENTS REACTING TO MISC. ALLER- GENS AS WELL AS DUST	TOTAL PATIENTS REACTING TO DUST	PATIENTS REACTING TO MISC. ALLERGENS	PATIENTS FAILING TO REACT TO ALLERGENS
Numbers of cases	30	13	43	14	18
Males	17	4	21	7	8
Females	13	9	22	7	10
Age (Years)	6-58	14-49	6-58	8-62	6-62
Average Age (Years)	28	31	29	33	34
Duration (Years)	2-30	2-22	9 mos.-30	6 mos.-20	1 mo.-15
Average Duration (Years)	11	10	10	7	6
Pts. with Other Symp- toms*	23	11	34	13	7
Hay Fever	18	9	27	11	4
Eczema	5	1	6	1	2
V.M.R.	2	4	6	3	2
Nasal Polypi	1	0	1	0	0
Urticaria	1	2	3	0	2
Family History Allergy	13	8	21	11	13

*Manifestations that may be of an allergic nature, past or present.

whom failed to exhibit pulmonary reactions to the inhaled allergens used by us, had severe asthma. These arguments also militate against the presence of histamine-like or acetyl-cholinelike substances in the extracts. Finally, pulmonary reactions to the inhaled allergens occurred only in those patients exhibiting skin sensitivity as well. We feel justified in concluding, therefore, that the occurrence of pulmonary reactions following the inhalation of aerosolized allergens cannot be ascribed to nonspecific reactions occurring in the lung.

In attempting to assess the value of the inhalation method as a means of diagnosis we are faced with the need for fixed points from which to take our bearings. We turn quite naturally to the two well-tried aids to diagnosis, the history and skin test. They are the best we have and, in a general way, these seem to be fairly trustworthy. In the individual case, however, we may be dependent on incomplete, and in some degree erroneous data buttressed by astute guessing, intuition, faith, and perhaps even bravado. Careful questioning revealed that our patients had symptoms intermittently throughout the year, that respiratory infections complicated the allergic picture in a disastrous manner, and that aggravation of asthma occasionally occurred in the absence of recognizable allergic or infectious causes. We quickly reached the conclusion that the methods of studying asthma and our understanding of the disease leave much to be desired. We are inclined to believe that we are not alone in this opinion.

We can not expect, therefore, to derive conclusive support for or evidence against the value of the inhalation method of diagnosis by consideration of the history and skin tests alone. We have derived some comfort, on the other hand,

GROUP II.

PATIENTS NOT REACTING TO DUST BY INHALATION BUT REACTING TO MISCELLANEOUS ALLERGENS, INDICATING TIME OF YEAR WHEN ASTHMA IS AGGRAVATED

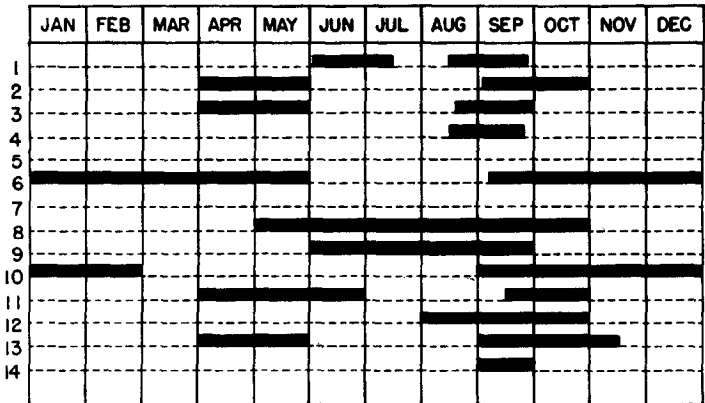


Fig. 3.

GROUP III.

PATIENTS FAILING TO REACT TO ALLERGENS BY INHALATION, INDICATING TIME OF YEAR WHEN ASTHMA IS AGGRAVATED

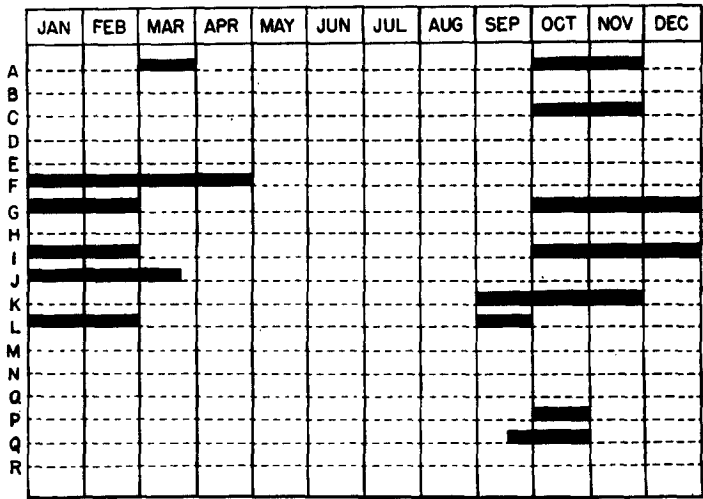


Fig. 4.

from the following considerations: first, that the procedure involves exposing a patient to a substance which might reasonably be expected to cause asthma in some subjects; second, that the reaction produced is indistinguishable from spontaneously occurring asthma except that it is usually much milder; and finally, that the reactions obtained, as mentioned above, cannot logically be ascribed to nonspecific irritation or due to the presence of histamine-like substances in the extracts.

Early in the course of this study our attention was centered on house dust because of the frequency of pulmonary reactions following exposure to this allergen in the laboratory among those who had increasing asthma in the latter part of September or in October, and the lack of such reactions when exposed to other allergens. Inspection of Figs. 1-4 clearly shows that, in patients who reacted to house dust by inhalation (Group I), house dust, among other possible excitants yet to be discovered, is a factor to be reckoned with in late September and October. The distribution of the patients in the other two groups was not unexpected. This "dust season," following so closely the period during which ragweed pollinates, at least in the New England area, has contributed to the confusion in the management of patients. This confines the dust season to a shorter period than that which has been considered to extend from late fall through the winter. Our findings have not only impressed us with the importance of dust as an allergen but have given us an understanding of those patients having exacerbations of asthma in the early fall.

SUMMARY AND CONCLUSIONS

1. Seventy-five asthmatic patients, studied from the point of view of history, skin reactions, and inhalation tests with pollen extracts of birch, oak, timothy, and ragweed, extracts of alternaria and hormodendrum and house dust extract, were divided into three groups: (a) patients in whom asthmatic attacks could be induced by inhalation of house dust extract; (b) patients in whom attacks could be induced with allergens other than house dust; (c) patients in whom attacks could not be induced by inhalation of the allergens.

2. The time of year when symptoms in each patient increased in severity was delineated month by month.

3. The clinical characteristics of the three groups are presented.

4. Support is given for the view that among the available methods for determining symptom-producing inhalants in bronchial asthma, the inhalation test is most valuable.

5. Sensitivity to house dust may be readily confused with ragweed pollen sensitivity. The results of this study indicate that, at least in the New England area, asthma occurring in the period between mid-August and mid-September is usually caused by ragweed pollen, whereas house dust is frequently the cause of symptoms from late September to the end of October. Asthma occurring from mid-August to the end of October probably arises from sensitivities to both ragweed pollen and house dust.

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