

The natural history of mountain cedar pollinosis

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*During the winter months, pollen from the mountain cedar (MC) (*Juniperus sabinoides*) causes severe respiratory tract allergy in central Texas. We have been impressed with the fact that many of our MC-allergic patients had only allergic rhinitis and were only sensitive to MC pollen. We therefore studied 234 unselected MC-allergic patients at the end of the MC season. The main criteria for inclusion into the study was a bona fide history of MC pollinosis confirmed by a positive skin test. All patients completed a detailed history questionnaire, were prick skin tested by using 1:20 w/v, extracts, and had a total IgE determined with commercially available reagents (PRIST). Thirty-four percent of patients were found to be allergic only to MC and 66% were allergic to MC and other aeroallergens. As a group, patients allergic only to MC had significantly lower total IgE levels (84 IU/ml vs. 360, $p < 0.001$) (normal < 180), required much longer exposure intervals to cedar pollen before developing MC pollinosis (14.4 yr vs. 5.69, $p < 0.001$), had less of a family history of allergic disease (43% vs. 88%, $p < 0.001$), had less of a history of asthma or eczema (11% vs. 39%, $p < 0.001$), and developed allergic disease at a later age (39 yr vs. 13, $p < 0.001$) when compared to patients with multiple allergies. These results suggest that the MC pollen may be unique in causing allergic rhinitis in patients who have no other sensitivities. A possible explanation may lie in the carbohydrate nature of the main allergen of the MC pollen, which may facilitate allergen transport through the respiratory tract mucosa and subsequent sensitization. (J ALLERGY CLIN IMMUNOL 73:88-93, 1984.)*

MC pollinosis has been recognized as a clinical entity in central Texas, New Mexico, and northern Mexico for many years.^{1, 2} The MC (*Juniperus sabinoides*) pollinates very heavily during the months of December, January, and February and somewhat less so in November and March,³⁻⁵ depending on yearly weather conditions. Within the city limits of San Antonio, there are few MCs, and yet in the winter months the pollen from the MC blows in with "northern fronts" and is the only pollen present in significant amounts in the air during this time.³ The *J. sabinoides* tree belongs to the cypress-juniper (Cupressaceae) family. The MC has received the greatest

attention as an allergen source, although other junipers may also have clinical importance.^{2, 17} This family contains many species that grow naturally or are cultivated as ornamental plantings throughout the United States and other parts of the world.

In a previous report from our institution, which studied the effectiveness of immunotherapy for MC pollinosis,⁶ over a third of the patients (37.5%) had no other sensitivities except MC allergy. We have also been recently impressed that many of our MC-allergic patients were sensitive only to MC and that among this population there was a paucity of patients with asthma and/or atopic dermatitis. Since this population appeared to differ from our usual allergic patients, we embarked on a clinical investigation protocol of 234 patients who were allergic to MC. This study was performed at the end of the 1981-1982 MC pollinating season. All patients were active duty or retired military personnel and their dependents currently residing in San Antonio or its vicinity.

MATERIALS AND METHODS

The 234 patients who consented to participate in this study were all selected from the Allergy-Immunology Clinic population (both new and old) at Brooke Army Medical

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Abbreviations used

MC: Mountain cedar
PRIST: Paper radioimmunosorbent test

Center in San Antonio, Texas. The main criterion for inclusion into this study was a bona fide history of MC pollinosis confirmed by a positive prick skin test. All patients who entered the study completed a detailed history questionnaire which reviewed (1) the patient's age and sex; (2) the presence (or absence) of allergic rhinitis, asthma, atopic dermatitis, food allergy, hymenoptera hypersensitivity, and/or contact dermatitis; (3) family history of atopic disease; (4) age at the onset of allergic disease; (5) age at the onset of MC allergy; (6) the number of winters of residence in areas known to have natural growth of MC (years of exposure); and (7) a review of all places of residence in chronological order.

For comparison, we examined 100 additional clinic records of patients with ragweed sensitivity. Our main interest was to compare these patients with the MC-allergic patients as to the prevalence of a sensitivity to only one allergen (ragweed vs. MC).

Evaluation

All participants in this study were skin-tested on the volar surface of their forearms by the prick technique with 1:20, w/v, extracts in 50% glycerin obtained from commercial sources (Hollister-Stier Laboratories, Spokane, Wash.) comprising the following panel of 32 allergens common in central Texas:

<i>Trees</i>	
Cottonwood	Arizona ash
Pecan	Mesquite
Elm	Sycamore
Oak	<i>Ligustrum</i>
Mountain cedar	Hackberry
<i>Weeds</i>	
Ragweed	Sage
Pigweed	Russian thistle
Franseria	Marsh elder
<i>Grasses</i>	
Bermuda	Johnson
Red top	June
Rye	Timothy
<i>Molds</i>	
<i>Alternaria</i>	<i>Helminthosporium</i>
<i>Hormodendrum</i>	<i>Aspergillus</i>
<i>Penicillium</i>	<i>Fusarium</i>
<i>Environmental</i>	
House dust	Dog dander
Mite	Cat dander
<i>Controls</i>	
Saline	Histamine

Reactions were read after 20 min. Wheals and erythema

TABLE I. Profile of patient study groups

	Group A	Group B
Total No. of patients	80	154
Native	26	37
Sex (M/F)	28/52	56/98
Age at study (yr)	46.8	39.4
Mean IgE (IU/ml)	84	360
Asthma/atopic dermatitis (%)	11	39
Family history (%)	43	88
Mean No. years exposed to MC	14.4	5.69
Mean age at onset of allergic symptoms	39 (MC)	13 (any)

greater than 3 mm over a saline control were considered positive. All patients had a total IgE determined by using commercially available reagents in duplicate (PRIST) (Pharmacia Diagnostics, Piscataway, N. J.).

Statistical methods

Patients were divided into groups A and B. Group A consisted of patients who were allergic only to MC, as defined by a bona fide history of allergic symptoms only in the winter months of San Antonio, and had one isolated positive prick skin test to the MC extract. Group B consisted of patients with multiple sensitivities confirmed by history and skin testing, including sensitivity to MC. Present in groups A and B is a subset of patients who were born and raised in central Texas or in areas known to contain natural growth of MC. This subset is labeled "native." For the purposes of the present investigation, central Texas, New Mexico, and northern Mexico were considered to be the only areas with natural growth of MC.⁷ Years of exposure were calculated as the number of winters of residence in any of the above areas.

The two-sample t test was used to determine the significance of differences observed between the two groups in (1) the total IgE levels, (2) the age of onset of allergic disease, and (3) the years of exposure before developing MC pollinosis. The significance of the differences observed in the years of exposure was further analyzed by the f test for variances. The χ^2 test was used for determining the significance of the differences observed in (1) family histories of allergic disease, (2) the prevalence of asthma, atopic dermatitis, and other allergies, and (3) the number of native persons present in both groups.

RESULTS

Out of a total of 234 patients, 80 patients (34%) were found to be allergic only to MC and constituted group A. This compares with only 5 out of the 100 ragweed-allergic patients who were allergic only to ragweed extract.

Characteristics of patients in study groups A and B are summarized in Table I. There were no statistically significant differences in sex, present age, percentage

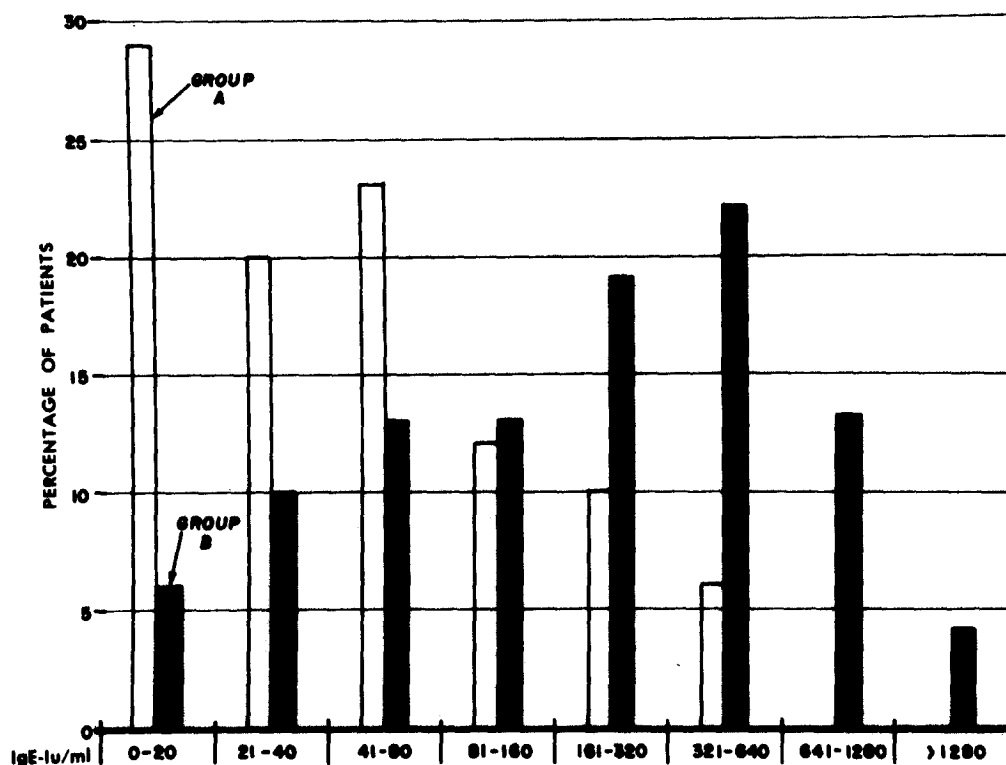


FIG. 1. Total IgE levels.

of native patients in group A vs. group B or in the prevalence of food allergy, Hymenoptera hypersensitivity, or contact dermatitis. Sixty-five percent of our study patients were women, which approximates the overall sex ratio in our clinic (64%).

The distribution of total IgE values in all patients studied is shown in Fig. 1. The mean total IgE level in group A was 84 IU/ml (range 6 to 395). Therefore the majority of group A patients would be considered to have normal total IgE levels (<180 IU/ml). By comparison, the mean total IgE level of group B was much higher (360 IU/ml) (range 6 to 1625). The difference in the IgE levels was highly significant between groups A and B at $p < 0.001$ level. As mentioned, this study was performed at the end of the MC pollinating season, which would have boosted the IgE level of both groups. In spite of this, the total IgE level for group A was normal, which makes this finding even more significant. There was no difference in the total IgE values when the subsets of native patients in both groups were compared with then nonnative patients in their corresponding groups.

In general agreement with the findings of the IgE levels, which suggest a lower atopic tendency for group A patients, were the prevalence rates for asthma and/or atopic dermatitis and for a family his-

tory of allergic disease. As shown by the data illustrated in Fig. 2, group A participants had lower prevalence rates for asthma and/or atopic dermatitis (11% vs. 39%) ($p < 0.001$) and had less of a family history of allergy (43% vs. 88%) ($p < 0.001$) than group B participants. These sets of data confirm our initial impression that prompted this investigation.

Most of our study patients could define with reasonable certainty the year MC began causing symptoms. Illustrated in Fig. 3 is the number of winters of exposure to MC pollen prior to onset of allergic symptoms. For the total population of groups A and B, there was a significant difference ($p < 0.001$) in the number of years exposed: 14.4 yr for group A and 5.69 yr for group B. Thus patients with a lower atopic tendency required more years of exposure before developing symptoms than patients with a higher atopic tendency.

After initial scanning of population data of both groups, it appeared that patients native to MC areas required a greater number of years of exposure to develop symptoms than nonnatives. As depicted in Table I, the majority of our patients were not native to central Texas or to other areas with natural growth of MC. Analysis of the means of the numbers of years exposed showed that there was a difference among the subsets of groups A and B (Table II). For native group

	GROUP A	GROUP B		GROUP A	GROUP B
Positive	9	60	Positive	35	135
Negative	71	94	Negative	45	19
(1) ATOPIC DERMATITIS/ASTHMA			(2) FAMILY HISTORY OF ALLERGY		

FIG. 2. Prevalence of atopic dermatitis/asthma and family history of allergy.

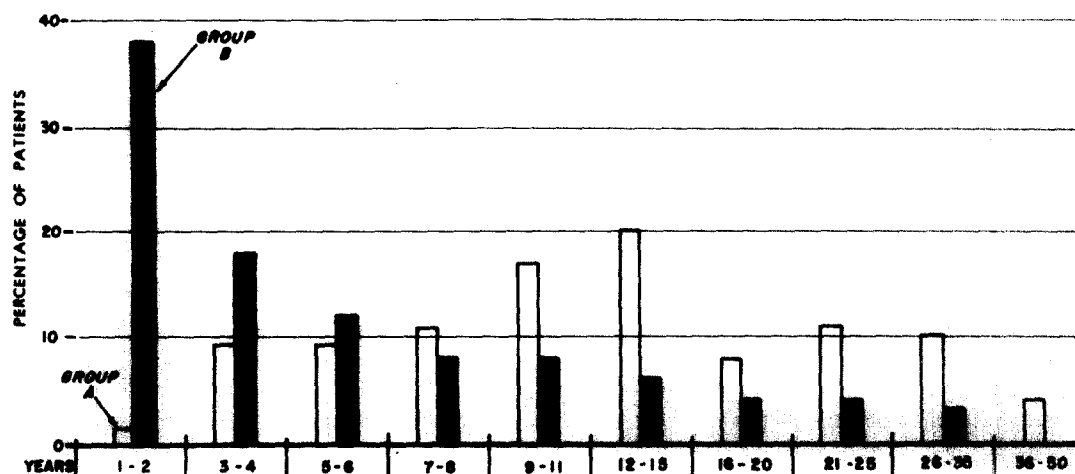


FIG. 3. Number of seasons exposed to MC pollen.

B patients, the age of onset of MC allergy (and therefore the number of winters exposed) coincided with the onset of their sensitivities to other pollens, molds, danders, etc.—13 yr. This value was not significantly different from the age of onset of other non-MC sensitivity in nonnative group B patients. However, non-native group B patients developed MC allergy after a mean of only 3.8 winters after moving into an area with natural MC growth. Seventeen percent of non-native group B patients reported symptoms the first year of MC exposure. This occurred at a mean age of 32.7 yr for nonnative patients. Of perhaps even greater interest is the difference in the number of seasons exposed in the subsets of group A. Native patients had a mean number of 22 yr of exposure vs. 9.9 yr for nonnatives. The age of onset of MC allergy also differed in the subsets of group A as expected, since for nonnatives, MC exposure first occurred as adults. The native patients had a mean age of onset of 24 yr as compared to 45.8 yr for nonnative patients. The difference of 2 yr in the number of seasons exposed and the age of onset for native group A patients was due to moving to and from areas endemic with MC.

DISCUSSION

Our initial impression confirmed in this study was that many of our MC-allergic patients differed in several ways from our usual clinic population. These patients appeared to develop hypersensitivity later in life, had mostly rhinitis and conjunctivitis as their only symptom complex, had lower total IgE levels, and were only allergic to a single pollen, MC. Slightly over one third of patients allergic to MC fit this description.

It is the experience of most allergists that most atopic patients have a genetic tendency to sensitize IgE to many inhalant allergens. Smith,⁸ in a study of 1106 patients found that 99% of patients with the onset of allergic disease before the age of 30 had three or more markedly positive skin tests. In that same study, only 1% of patients with the onset of allergic disease past the age of 30 had multiple positive skin tests. In another study by the same group,⁹ 85% of patients with a positive family history of allergy had the onset of allergic disease before the age of 20, as compared to only 49% of patients with a negative family history. Our population sample, which consti-

TABLE II. Differences between native and nonnative participants in both study groups

	Group A		Group B	
	N	N/N	N	N/N
Mean No. years exposed to MC pollen	22.0	9.9	13.0	3.8
Mean age at onset of MC allergy	24.0	45.8	13.0	32.7
Mean age at onset of other non-MC sensitivity (yr)	N/A	N/A	13.0	13.9

N = native; N/N = nonnative; N/A = not applicable.

tutes group B patients, correlated with these findings in age of onset of allergic disease (13.9 yr), family history of allergy (88%), and the number of strongly positive skin tests (>3). Our group A patients can also be viewed as being in general agreement with Smith's studies to the extent that they had less of a family history of allergy (43%), their mean age of onset of allergic disease occurred later (39 yr), and they were sensitive to only one allergen. The isolated discrepancy found in this investigation appears to be the absolute percentage and number of patients with sensitivity to a single allergen (34% of patients allergic to MC).

There have been numerous studies correlating skin test reactivity and total IgE.¹⁰⁻¹⁴ Most recently, Brown et al.¹⁴ evaluated 311 subjects from a general population and confirmed that increasing IgE levels are positively correlated with increasing skin reactivity by prick skin testing. However, the range of values for IgE varied greatly for a given skin test reactivity. In the present study, the mean total IgE value for group A patients was 84 IU/ml, which was statistically different from the 360 IU/ml value of our group B patients who had greater skin test reactivity. A value of 84 IU/ml is within the limits of normal for IgE in a nonatopic population.¹⁴ In further agreement with the low atopic tendency of our group A patients is the relatively low prevalence of asthma and atopic dermatitis in this population (11%). By comparison, our group B patients had a prevalence rate of asthma and/or atopic dermatitis of 39%, which agrees with a reported rate of 38% in an investigation¹⁵ of 1125 patients with allergic rhinitis.

As mentioned, this investigation was performed with the participation of active duty and retired military personnel and their dependents. Because of this, the majority of our patients are nonnative to areas with natural growth of *Juniperus sabinoide*s. Review of the exposure times of groups A and B seems to

suggest that subjects native to the MC-endemic areas need longer exposure intervals to develop symptoms than subjects who move into a MC area. One possible explanation is that children may be less susceptible to developing MC allergy. However, the fact that the age of onset of non-MC allergy and MC allergy in native group B patients was the same argues against this possibility. A more reasonable explanation is that subjects not native to MC-endemic areas may have been sensitized in other geographic areas with pollen of other cross-reacting Cupressaceae. Several reports in the literature have suggested cross-reactivity between MC (*J. sabinoide*s) and Port Orford cedar (*Chamaecyparis lawsoniana*),¹ red cedar (*Juniperus virginiana*),² and western red cedar, western juniper, and Pfitzer juniper,¹⁶ by skin testing, by the favorable outcome of immunotherapy, or by immunodiffusion with rabbit antisera. These other members of the Cupressaceae family have a very wide territorial distribution throughout the United States and other parts of the world. Few of them have been linked to the pathogenesis of allergic disease, with possible exception of *J. virginiana* and the pollen from the Japanese cedar.¹⁷ It is, nevertheless, possible that pollen from some, if not all, of these cross-reactive species may sensitize patients so that they would manifest symptoms only when living in an area of high pollen exposures as with the MC in central Texas. The fact that 17% of our nonnative group B patients noticed symptoms of MC pollinosis during their first winter in San Antonio is in agreement with this hypothesis (Fig. 3).

What is a possible explanation if indeed pollens from the Cupressaceae family, especially when present in high concentrations, can sensitize a population with a low atopic threshold? A tenable explanation may lie in the chemical nature of the MC pollen allergen. Suvurungsi and Sullivan¹⁸ recently showed that there appears to be a single allergen in MC with a molecular weight of 40,000 daltons, which is a glycoprotein having 80% to 90% carbohydrate content. This contrasts with the majority of known allergens in pollen grains,¹⁹⁻²¹ which tend to be a mix of allergenic glycoproteins having less than 10% carbohydrate content and with molecular weights ranging from 5000 to approximately 42,000 daltons. Maybe the combination of the high density of pollen with a single, mostly carbohydrate allergen can sensitize by natural mucosal exposure otherwise nonallergic subjects to produce an IgE response. In partial agreement with this hypothesis are the studies by Salvaggio and associates,²²⁻²⁴ who showed that atopic patients could be sensitized intranasally with bovine ribonuclease,²² aerosolized dextran²³ and keyhole-limpet hemocyanin.²⁴ Nonatopic patients, however, could not be

sensitized with the bovine ribonuclease but could be sensitized to a lesser extent than atopic patients to aerosolized dextran (molecular weight 1,940,000 daltons)²³ and also to the high-molecular-weight protein keyhole-limpet hemocyanin.²⁴ This effect was not thought to be due to a more rapid absorption of allergens by atopic subjects.²⁵ The sensitizing potential or the mucosal absorption and clearance of a low-molecular-weight carbohydrate allergen introduced by natural exposure is unknown. Allergens that are usually injected, including penicillin,²⁶ pollen extracts,^{27, 28} or Hymenoptera venoms,²⁹ can induce IgE responses in atopic and nonatopic patients. It is attractive to speculate whether a carbohydrate inhalant allergen can behave in a similar manner due to either rapid absorption or to the delivery of the allergen to the necessary immunocompetent cells.

The results of the present study therefore suggest that the pollen of *Juniperus sabinoides* may be unique in causing allergic rhinitis in patients who have no other sensitivities. These findings should be of special interest to allergists in areas with natural growth of MC in central Texas, New Mexico, and northern Mexico. If the artificial cultivation of *J. sabinoides* and other cross-reacting Cupressaceae as landscaping shrubs is continued in greater numbers, the findings of this study may have wider application throughout the United States.

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