

***Alternaria* as a Major Allergen for Asthma in Children Raised in a Desert Environment**

MARILYN HALONEN, DEBRA A. STERN, ANNE L. WRIGHT, LYNN M. TAUSSIG, and FERNANDO D. MARTINEZ

Respiratory Sciences Center (Westend Laboratories), Departments of Pharmacology and Pediatrics, University of Arizona Health Sciences Center, Tucson, Arizona; and National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado

The relationships of asthma and allergic rhinitis with individual immediate skin test responses were examined for preferential associations and for changes with age in children raised in a semiarid environment. Prevalence of physician-diagnosed asthma was 9.8% at age 6 (n = 948) and 15.5% at age 11 (n = 895). Immediate skin test responses to Bermuda grass were the most prevalent among children with allergic rhinitis and control subjects, whereas responses to the mold, *Alternaria alternata*, were the most prevalent among asthmatics. Skin test responses for crude house dust, *Dermatophagoides farinae*, and cat had low prevalences in all groups. By logistic regression, *Alternaria* was the only allergen independently associated with increased risk for asthma at both ages 6 and 11. Allergic rhinitis showed independent association with sensitization to Bermuda grass and mulberry tree pollen at age 11 but did not show an independent relation to any single allergen at age 6. Logistic regression further revealed that persistent asthma (diagnosed before age 6) was independently associated with *Alternaria* skin tests at both ages 6 and 11, whereas new asthma (diagnosed after age 6) was associated with *Alternaria* skin tests at age 6 but not at age 11. We conclude that *Alternaria* is the major allergen associated with the development of asthma in children raised in a semiarid environment and that skin test responses at age 6 are more closely linked to asthma than those at age 11. Halonen M, Stern DA, Wright AL, Taussig LM, Martinez FD. *Alternaria* as a major allergen for asthma in children raised in a desert environment.

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It is well established that asthma and allergic rhinitis are associated with increased IgE levels for specific local aeroallergens (frequently assessed by immediate skin test reactivity). Several recent studies have sought to determine if responses to certain allergens are more closely associated with asthma than are those to other allergens. The general method has been to determine if sensitization to a particular allergen occurs significantly more frequently among asthmatics compared with the general (non-asthmatic) population. Most of these studies have implicated house dust mite as a major allergen in many environments worldwide (1-3).

House dust mite is not the only allergen showing strong associations with asthma. Additional studies have implicated molds, allergens shed from pets, and cockroaches (4-8). These allergens contrast with common tree, weed, and grass pollens that have not shown significant independent associations with asthma (5, 9). Although chemical similarities have not been identified among the asthma-related allergens, they have been grouped and identified as perennial allergens present indoors. Such findings have led to the suggestion that susceptibility to sensitization early in life to those allergens most frequently encountered may be the common factor linking this group of allergens to individuals susceptible to asthma.

A few recent studies also provide support for the notion that the pattern of allergic sensitization in asthma likely differs in different environments. Peat and coworkers (10) recently described differences in asthma/allergen associations between the seacoast and desert regions in Australia, showing that house dust mite was the major asthma-associated allergen at the seacoast but, in the desert, *Alternaria alternata* was the major allergen. Sporik and associates found that animal-shed allergens but not house dust mite were associated with asthma in a high altitude, nonhumid region in New Mexico (11).

Differences in the symptom complex and prognosis of asthma have been identified in relation to the age of asthma onset (12, 13) but whether asthma developing at different ages differs in regard to which allergens are asthma-associated has not been examined. To identify the allergens associated with asthma in a U.S. southwestern desert region and to determine if those associations change with age of asthma onset, we carried out the study described here in which the relations of asthma and allergic rhinitis prevalence with skin test reactivity to aeroallergens are determined at ages 6 and 11 in children born and raised in Tucson, Arizona.

METHODS

Subjects

The subjects of this report are participants in a longitudinal prospective study of childhood respiratory health (14). A total of 1,246 infants whose families were members of a health maintenance organization (HMO) in Tucson, Arizona, were enrolled at birth between May 1980 and October 1984.

Detailed health questionnaires were completed at regular intervals. Total serum IgE levels were assayed and allergy skin prick tests were per-

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Correspondence and requests for reprints should be addressed to Marilyn Halonen, Ph.D., Professor of Pharmacology, Respiratory Sciences Center, University of Arizona Health Sciences Center, Tucson, AZ 85724.

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formed at ages 6 and 11. The prevalence of asthma, wheezing, and rhinitis were determined from questionnaires completed around the time of the child's sixth and eleventh birthdays (median age 6.2 yr. and 10.7 yr, $n = 1,025$ and 912 , respectively).

The diagnosis of allergic rhinitis included a parental affirmative to the question, "Has your child ever had hay fever or any other condition that makes your child's nose stuffy, itchy or runny apart from colds?" and a physician confirmation that the "symptoms were due to allergies." Active allergic rhinitis was determined by a parental report that the symptoms were "still present" at the time the questionnaire was completed or, since allergic rhinitis can be seasonal, by the use of medication for "nasal symptoms" in the past year. Those children whose rhinitis was not active during the year preceding the questionnaire, who had nonallergic rhinitis, or who did not see a physician for their symptoms were included with the no rhinitis group.

Physician-diagnosed active asthma included a "yes" answer to "Has your child ever had asthma (reactive airways disease)?", an age at which the physician diagnosed the child with asthma and a parental report of "asthma attacks or episodes" during the past year. These attacks were coded according to severity: "a few (1-3)" attacks in the past year, "several (4-12)" attacks in the past year, or "almost every day."

If a child had been diagnosed with asthma before age 6 and the parent did not report an asthma attack or episode during the previous year but did report active wheezing, the child was considered an active asthmatic. Mild asthma was defined as 1 to 3 episodes in the previous year, moderate/severe asthma as 4 or more episodes in the previous year. Children whose parents reported their child as "ever" having asthma but who were without any asthmatic attacks/episodes or wheezing during the previous year or were without a physician diagnosis were included with the nonasthmatic group.

For purposes of comparison, the children were divided into two groups based on parental ethnicity ($n = 1,246$); those with Hispanic parents (10.5%) and those with at least one Anglo parent (81.1%) (the other being Anglo or Hispanic). Children with other multiethnic backgrounds (8.4%), including mixes of Anglo, Hispanic, African American, American Indian, and Asian ancestry were not included in the ethnicity analyses because of small numbers in each group.

Informed consent was obtained from parents of participating subjects and the study was approved by the Human Subjects Committee of the University of Arizona.

Serum IgE Concentrations

Serum IgE levels were assayed by Phadebas radioimmunosorbent test (PRIST) using commercially available kits (Pharmacia Diagnostics, Piscataway, NJ) as previously described (15). At age 6 and 11, peripheral blood samples for total serum IgE determinations were drawn from participating children ($n = 534$ and $n = 462$, respectively). All samples were assayed in duplicate and results expressed as IU/ml.

Allergy Skin Prick Tests

For the age 6 skin tests, extracts of seven aeroallergens common in the Tucson area and diluents were obtained from Hollister-Stier Laboratories (Everett, WA). Allergens included house dust mix (1:10 wt/vol), *Alternaria alternata* (1:100 wt/vol), Bermuda grass (1:20 wt/vol), careless weed (1:20 wt/vol), and olive, mesquite, and mulberry trees (each 1:20 wt/vol). Allergy skin prick tests were performed at age 6 in 760 children (except mulberry tree antigen, which was applied to 731 subjects). The same allergens were repeated at age 11 in 622 children, except cat hair (10,000 BAU/ml) was added and house dust mix was replaced by *Dermatophagoides farinae* (*D. farinae*, 30,000 AU/ml). Cat hair and *D. farinae* were applied to 539 children. All tests were read at 20 min and the sizes of the wheals elicited by each allergen were recorded as the sum of the two diameters at right angles to each other (in mm). Wheal sizes of 3 mm or greater were considered positive.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for UNIX version 4 (SPSS Inc. Chicago, IL). Total serum IgE values were log-normally distributed and results expressed in IU/ml as geometric mean with SEM or 95% confidence intervals. Statistical analyses including IgE were performed using standard parametric techniques. Analysis of variance in conjunction with Duncan multiple

range test was used to compare group means. Logistic regression analysis was used to examine the independent effects of skin tests, IgE, and gender on asthma or rhinitis. A p value < 0.05 (two-tailed) was considered statistically significant for all tests. All analyses concerning skin test reactivity were repeated using a wheal size of 4 mm or greater as a positive reaction and no differences were found in the relations reported in RESULTS.

RESULTS

Prevalence of Asthma and Allergic Rhinitis at Ages 6 and 11

The prevalence of active physician-diagnosed asthma was 9.8% at age 6 ($n = 948$) and 15.5% at age 11 ($n = 895$). The prevalence of allergic rhinitis without asthma was 26.2% at age 6 and 23.2% at age 11. Among asthmatics, the prevalence of allergic rhinitis was 67.7% at age 6 and 66.9% at age 11, giving a prevalence for allergic rhinitis (with or without asthma) of 32.8% at age 6 and 33.6% at age 11. Overall, 36.0% of children at age 6 and 38.8% at age 11 had one or both of these conditions.

Boys had significantly more asthma than girls at age 6 (12.3% versus 7.5%, OR = 1.7, 95% CI = 1.1 to 2.7). At age 11, asthma prevalence had increased in both groups and the gender difference remained (20.6% versus 10.9%, OR = 2.1, 95% CI = 1.5 to 3.1). Prevalence of asthma among Hispanics was not different from Anglos at either age. Prevalence of allergic rhinitis at age 6 and 11 was not related to gender or ethnicity at either age.

Relation of Asthma and Allergic Rhinitis to Specific Allergen Skin Tests

Children with asthma reacted significantly more frequently to each of the individual allergens tested at both age 6 and 11 compared with the control group (with neither asthma nor allergic rhinitis diagnoses; Table 1). In addition, the rank order for response prevalence was different for asthma: at age 6, responses to *Alternaria* were the most prevalent among asthmatics, whereas Bermuda responses were most prevalent among the allergic rhinitis group and the group with neither diagnosis. At age 11, the prevalence of the *Alternaria* responses was less prominent among asthmatics (third in rank behind Bermuda and olive) but had fallen in rank even further for the allergic rhinitis and asymptomatic groups (from second to fifth; Table 1).

Because of the strong tendency for individuals to show multiple sensitivities, the individual skin tests may show association with asthma or rhinitis that is not necessarily independent. To assess the independent relation of the individual allergens to asthma, logistic regression analysis was performed. Gender and total serum IgE (in 5 half-log intervals) were also examined for independent influences. At age 6, only *Alternaria* and careless weed skin test responses and total serum IgE showed significant independent associations with the prevalence of asthma at the same age (Table 2). When the *Alternaria*-sensitive subjects were excluded from the regression, the prevalence of asthma was unrelated to reactivity to any of the individual aeroallergens at age 6. At age 11, only the *Alternaria* skin test and serum IgE provided increased risk for asthma.

In addition to being associated with the *Alternaria* skin test prevalence, asthma was also strongly related to the *Alternaria* skin test wheal size at age 6 (Figure 1A). Indeed, among those with a skin test of 11 mm or greater, 87.5% of the subjects were asthmatic. Also, asthmatic children with the largest *Alternaria* wheal sizes were much more likely to have moderate/severe (rather than mild) asthma. At age 11, the relationship of asthma to *Alternaria* wheal size was not as striking (Figure 1B) although it was still significant. The association between millimeter wheal size and asthma was not present for any of the other allergens.

TABLE 1
PREVALENCE OF POSITIVE SKIN TESTS TO INDIVIDUAL
ALLERGENS IN SUBJECTS WITH ASTHMA, ALLERGIC RHINITIS,
AND CONTROLS AGES 6 AND 11

Diagnosis*	n†	Alt	Berm	C Weed	Olive	Mesq	Mulb	Dust	D.f.	Cat	Any
Skin test allergens age 6 (% positive)											
Asthma	80	50.0‡	43.8‡	31.3‡	27.5‡	21.3‡	25.3‡	11.3‡	—	—	65.0‡
Rhinitis	191	19.4§	34.0‡	15.2§	17.8‡	12.0	11.1§	5.2	—	—	47.6‡
Controls	431	10.2	20.9	7.2	8.6	7.7	4.6	2.8	—	—	28.3
Skin test allergens age 11 (% positive)											
Asthma	106	40.6‡	51.9‡	32.1§	47.2‡	33.0‡	23.6‡	—	22.5	10.1‡	84.0‡
Rhinitis	143	27.3‡	51.0‡	28.0	37.8§	34.3‡	18.2‡	—	15.6	8.6§	69.9‡
Controls	359	14.5	25.1	19.8	23.7	16.7	7.8	—	12.2	2.3	46.8

Definition of abbreviations: Alt = *Alternaria alternata*; Berm = Bermuda grass pollen; C Weed = careless weed; Mesq = mesquite tree pollen; Mulb = mulberry tree pollen; Dust = house dust mix; D.f. = *Dermatophagoides farinae*.

* Asthma = subjects with current physician-diagnosed asthma. Rhinitis = subjects with current physician-diagnosed allergic rhinitis. Controls = subjects without a diagnosis of asthma or rhinitis.

† Values for n are as shown except for mulberry at age 6 (79 asthma, 189 rhinitis, 415 controls), and cat and *D. farinae* at age 11 (89 asthma, 128 rhinitis, and 311 controls).

Comparison of subject with asthma or rhinitis to controls: ‡p < 0.001, §p < 0.01, ||p < 0.05.

Allergic rhinitis (without asthma) at ages 6 and 11 was associated with significantly increased skin test reactivity to several of the allergens (Table 1). At both ages, the rank order of prevalence was essentially the same as that in the group with neither diagnosis. Logistic regression analysis was also performed for this group and revealed that, at age 6, total serum IgE but no single skin test reaction was independently related to allergic rhinitis (Table 2). Using logistic regression to test the relation of the prevalence of allergic rhinitis with serum IgE and any positive skin test (rather than include each of the individual skin tests) revealed significant independent relations of both of these variables to allergic rhinitis. At age 11, total serum IgE and responsiveness to mulberry pollen showed significant independent contributions to the risk for allergic rhinitis, with a contribution of Bermuda sensitization of borderline significance ($p = 0.06$, Table 2).

Relation of Age of Diagnosis of Asthma with Skin Test Responses at Age 6 and 11

The longitudinal nature of these data allowed separation of the children into those with persistent (present asthma at ages 6 and

11), remitting (asthma at age 6 but not at age 11), or new asthma (asthma at age 11 but not at age 6). Of 822 children with data at both ages, 6.9% developed persistent asthma, 7.7% new asthma, and 2.3% remitting asthma (this last group being too small for further separate analysis). Boys had significantly more persistent (16.9% versus 8.0%, OR = 2.3, 95% CI = 1.2 to 4.2) and new asthma (16.9% versus 10.0%, OR = 1.8, 95% CI = 1.1 to 3.1) than girls.

Children with either persistent or new asthma were more likely to be skin test positive to all the allergens at age 6 compared with the control subjects (Table 3). At age 11, children with persistent asthma were significantly more reactive to *Alternaria*, *D. farinae*, cat, Bermuda and olive compared with control subjects. In contrast children with new asthma were not more reactive to *D. farinae* and cat but showed significant increases to all other allergens (Table 3).

By logistic regression analysis, persistent asthma was associated with age 6 positive skin tests for *Alternaria* and mulberry with gender and total IgE or borderline significance ($p = 0.06$ and 0.07, respectively; Table 4). Analyses with the age 11 data were similar to the age 6 data for persistent asthma: *Alternaria*

TABLE 2
LOGISTIC REGRESSION ANALYSIS OF THE ASSOCIATION OF
ASTHMA OR ALLERGIC RHINITIS WITH ALLERGEN SKIN TEST
REACTIVITY, IgE, AND GENDER AT AGES 6 AND 11

Allergen	Risk for Asthma				Risk for Allergic Rhinitis (No Asthma)			
	Age 6 Yr		Age 11 Yr		Age 6 Yr		Age 11 Yr	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
<i>Alternaria</i>	2.3	(1.4–3.6)*	2.7	(1.2–6.0)†	1.2	(0.9–1.7)	0.8	(0.4–1.8)
Bermuda grass	0.5	(0.3–0.9)†	1.8	(0.8–4.0)	1.0	(0.8–1.4)	1.9	(1.0–3.8)
Olive tree	0.9	(0.5–1.6)	1.4	(0.7–3.2)	1.2	(0.8–1.8)	1.0	(0.5–2.1)
Mesquite tree	0.9	(0.4–1.7)	1.0	(0.4–2.3)	1.1	(0.7–1.7)	1.8	(0.9–3.8)
Careless weed	1.8	(1.1–3.1)†	0.4	(0.2–1.0)	1.0	(0.6–1.5)	0.5	(0.2–1.0)†
Mulberry tree	1.8	(0.9–3.6)	1.6	(0.6–4.6)	1.3	(0.8–2.2)	2.9	(1.1–7.7)†
House dust mix	1.0	(0.5–2.1)	—	—	1.0	(0.6–1.9)	—	—
Cat	—	—	3.1	(0.7–14.3)	—	—	2.4	(0.6–9.1)
<i>Dermatophagoides farinae</i>	—	—	1.1	(0.5–2.5)	—	—	0.5	(0.2–1.2)
IgE	1.8	(1.3–2.5)*	1.5	(1.1–2.1)‡	1.2	(1.0–1.5)†	1.5	(1.2–1.9)*
Gender	1.6	(0.8–3.3)	1.5	(0.8–3.0)	0.9	(0.6–1.4)	1.3	(0.7–2.2)

Definition of abbreviations: OR = odds ratio; CI = confidence interval.

* $p < 0.001$.

† $p < 0.05$.

‡ $p < 0.01$.

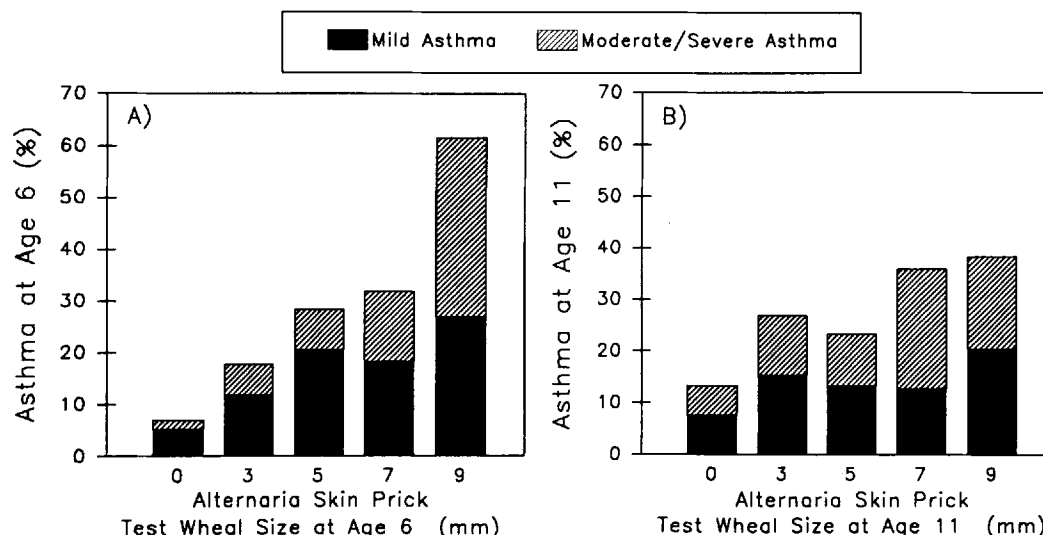


Figure 1. Asthma at (A) 6 yr and (B) 11 yr in relation to *Alternaria* skin prick test wheal size (mm) at ages 6 and 11 yr. Group sizes for ages 6 and 11, respectively: for the ≤ 2 mm group $n = 581$ and 474 , ≥ 3 mm $n = 34$ and 26 , ≥ 5 mm $n = 39$ and 30 , ≥ 7 mm $n = 22$ and 39 , and ≥ 9 mm $n = 26$ and 39 . Asthma at both ages was significantly associated with *Alternaria* skin test wheal size ($p < 0.0001$).

skin test and gender provided significant independent increased risk for persistent asthma (Table 4). New asthma was similar to persistent asthma in regard to independent associations with *Alternaria* responses and with total IgE assessed at age 6. No single allergen tested at age 11 showed an independent relation to new asthma and the total serum IgE contribution was of borderline significance ($p < 0.06$; Table 4).

DISCUSSION

Examining immediate skin test reactivity and its relation to allergic respiratory diseases in different environments provides the opportunity to characterize the influence of those environments on the relation of specific allergens to the prevalence of allergic diseases. We herein report such relations for children raised in a semiarid environment. Because the study was longitudinal, changes in disease and skin test reactivity related to age could also be examined.

The prevalence of active physician-diagnosed asthma at ages 6 and 11 in this population was 9.8% and 15.5%, respectively. Thus, asthma prevalence in our study appears to be more than twice that in the U.S. as a whole for data obtained in 1981: 6.7% for children 3 to 17 yr of age (16). As previously reported (17), asthma prevalence in this environment is known to be high, stem-

ming in part from immigration of subjects moving to a dry climate on advice of their physicians. In addition, however, the limited recent data available indicate that prevalence rates are increasing both in the U.S. (18) and other western societies (19). Reports of higher prevalence in boys versus girls (16, 20) was confirmed in this population: boys demonstrated significantly higher prevalence of asthma but not allergic rhinitis than girls.

Our study demonstrates that sensitization to *Alternaria* is closely associated with asthma. Several studies have led to the hypothesis that asthma prevalence is strongly associated with sensitization to indoor allergens. In one sense, our data provide support for this hypothesis, but they also emphasize that the hypothesis should not be limited to allergens that are present only or even mainly indoors. Monitoring studies have shown that *Alternaria* is present in similar concentrations both indoors and outdoors and suggest that *Alternaria* indoors may be mainly from outdoor sources (21, 22). Others have also found a significant association of *Alternaria* with asthma (9, 10, 16), although these investigators found house dust mite to be a significantly related allergen as well. In a recent study of schoolchildren from New Mexico, no association of asthma and house dust mite was evident; however, neither *Alternaria* nor other mold allergens were tested (11, 23).

Given studies in many parts of the world implicating house

TABLE 3
PREVALENCE OF POSITIVE SKIN TESTS TO INDIVIDUAL ALLERGENS IN SUBJECTS WITH PERSISTENT OR NEW ASTHMA AND CONTROLS

Diagnosis	n	Alt	Berm	C Weed	Olive	Mesq	Mulb	Dust	D.f.	Cat	Any
Skin test allergens age 6 (% Positive)											
Persistent asthma	51	60.8*	47.1*	33.3*	31.4*	21.6*	31.4*	11.8*	—	—	72.5*
New asthma	53	30.2*	41.5*	15.1†	18.9*	15.1†	12.0‡	5.7*	—	—	64.2*
Controls§	306	8.2	15.4	6.2	5.6	5.6	2.7	0.3	—	—	23.5
Skin test allergens age 11 (% Positive)											
Persistent asthma	43	55.8*	48.8‡	27.9	44.2‡	27.9	16.3	—	29.3‡	17.1*	88.4*
New asthma	48	27.1†	54.2*	39.6‡	45.8‡	35.4‡	29.2*	—	16.2	5.4	79.2*
Controls§	272	14.0	25.7	19.1	24.3	17.6	7.7	—	10.5	2.5	47.1

For definition of abbreviations, see Table 1.

Comparison of persistent or new asthma to controls: * $p < 0.001$, † $p < 0.05$, ‡ $p < 0.01$.

§ Control group includes subjects without a diagnosis of asthma or rhinitis.

TABLE 4
LOGISTIC REGRESSION ANALYSIS OF THE ASSOCIATION
OF PERSISTENT OR NEW ASTHMA WITH ALLERGEN SKIN TEST
REACTIVITY, IgE, AND GENDER AT AGES 6 AND 11

Allergen	Risk of Asthma with Age 6 Allergens				Risk of Asthma with Age 11 Allergens			
	Persistent Asthma		New Asthma		Persistent Asthma		New Asthma	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
<i>Alternaria</i>	3.4	(1.7–6.6)*	2.2	(1.3–3.6)†	5.6	(1.7–18.9)†	1.2	(0.4–4.0)
Bermuda grass	0.6	(0.3–1.3)	1.1	(0.7–1.7)	1.4	(0.4–5.1)	1.6	(0.5–5.2)
Olive tree	1.3	(0.6–2.8)	1.0	(0.6–1.9)	1.9	(0.6–6.2)	0.8	(0.2–2.8)
Mesquite tree	0.7	(0.2–2.2)	1.3	(0.6–2.7)	0.6	(0.2–2.3)	1.2	(0.4–3.8)
Careless weed	0.9	(0.4–2.2)	0.6	(0.2–1.4)	0.3	(0.1–1.4)	1.1	(0.3–3.8)
Mulberry tree	3.9	(1.3–11.8)‡	2.0	(0.8–5.1)	0.7	(0.2–3.3)	2.4	(0.5–12.2)
House dust mix	2.3	(0.5–10.4)	2.4	(0.6–10.2)	—	—	—	—
Cat	—	—	—	—	4.1	(0.7–23.2)	1.1	(0.1–12.8)
<i>D. farinae</i>	—	—	—	—	2.4	(0.8–7.7)	0.6	(0.1–2.7)
IgE	1.5	(1.0–2.4)	1.4	(1.0–1.9)‡	1.7	(1.0–2.9)	1.6	(1.0–2.6)
Gender	2.8	(1.0–8.5)	1.1	(0.5–2.4)	3.3	(1.1–9.6)‡	0.8	(0.3–2.1)

* $p < 0.001$.

† $p < 0.01$.

‡ $p < 0.05$.

dust mite as a major allergen associated with asthma, it is of interest that reactivity to house dust at age 6 and *D. farinae* at age 11 did not show a statistically significant association with asthma in our study, after adjusting for the effects of the other skin test responses. This lack of association of asthma with house dust mite allergen in a setting that has high asthma prevalence puts some doubt on whether eradication of a major allergen from a given locale will be found to result in subsequent major decreases in asthma prevalence. This is not to say, however, that such efforts will not decrease symptoms (i.e., asthma episodes) for those already sensitized. Thus, it is important to segregate issues related to substances that initiate asthma attacks and those that may be related to the pathogenesis of the disease state.

Similar to the study in New Zealand of Sears and colleagues (6), our data demonstrate that asthma and allergic rhinitis show different specific allergen patterns of skin test reactivity. In the study by Sears and colleagues, allergic rhinitis was associated with grass pollen skin tests, and at age 11 both Bermuda and mulberry tree showed an association with allergic rhinitis in our population. However, in the Sears study the major allergens closely associated with asthma (in children of age 13) were house dust mite and cat allergen, whereas in our study of children in a semiarid environment, only *Alternaria* showed a consistent close association with asthma.

Although asthma was independently associated with *Alternaria* sensitization, individuals with asthma showed increased sensitization to a variety of allergens. Among the asthmatics, skin test reactivity at age 6 was 65% and increased further to 84% by age 11. These prevalences were markedly greater than those reported in the National Health and Nutrition Examination Survey (NHANES) study of 44.5% for asthmatics. The NHANES prevalence of 20.7% for nonasthmatics among U.S. children in 1981 (16) compares with 34.2% (at age 6) and 53.4% (at age 11) for nonasthmatics (rhinitis and control groups combined). Whether the differences are related to time frame (~1981 for the NHANES study) or region is difficult to determine. However, prevalences similar to those of our study have been recently reported for children in North Carolina (9), New Zealand (6), and Australia (10). Such data tend to support a purported ongoing increase in allergen sensitivity in many western societies.

To determine whether asthma diagnosed early and late showed different relationships to individual allergens, asthma was divided

into those with persistent asthma (diagnosed by age 6 and present at age 11) and those with new asthma (diagnosed after age 6). By logistic regression analysis, persistent and new asthma were significantly associated with *Alternaria* skin test responses at age 6. Thus, new asthma showed a temporal pattern in which *Alternaria* sensitization preceded asthma diagnosis, supporting the possibility of *Alternaria* being a causative agent of asthma, at least in this group. Our data set does not include skin tests before age 6 and thus a similar assessment for persistent asthma cannot be made.

Allergic rhinitis prevalence at age 6 showed an association with skin test reactivity in general, but the spectrum of sensitizing allergens was similar qualitatively to the group with neither diagnosis. It can be noted that allergic rhinitis (and asthma) diagnoses were made in this HMO pediatric group practice setting based on clinical symptoms and history data independent of any skin test data. The skin tests were performed by us expressly for the purpose of these studies. It is certainly possible that the children may have been sensitive to allergens not included in our panel. However, no significant independent relationship of allergic rhinitis with any one of the individual allergens by logistic regression was identified at age 6. Allergic rhinitis prevalence did not change from age 6 to age 11, whereas skin test prevalence increased in a pattern such that Bermuda and mulberry demonstrated detectable independent associations with allergic rhinitis at age 11.

In summary, our study demonstrates that *Alternaria* appears to be the major allergen associated with asthma in children raised in a desert environment and that this relationship was most evident from skin test responses assessed at age 6. At age 6, this allergen had the highest prevalence of sensitization among asthmatics, whereas Bermuda responses were the most prevalent among subjects with allergic rhinitis and control subjects. Prevalence of asthma was relatively high in this environment even though house dust mite sensitivity was low and did not show an independent relation to asthma. Boys had more asthma, but not allergic rhinitis, than did girls, and Hispanics did not differ from Anglos in these outcomes. Prevalence of asthma, but not allergic rhinitis, increased from ages 6 to 11. Those becoming asthmatic during this age period showed the independent association with *Alternaria* at age 6 but not at 11, whereas persistent asthma remained associated with *Alternaria* at age 11.

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