

Association of aeroallergen sensitization and atopic disease in the Sonoran Desert

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ABSTRACT

Background: Numerous aeroallergens have been associated with the development of asthma, including *Alternaria*, house-dust mite, and pet dander. Tucson, Arizona, is located in the Sonoran Desert, which has the highest diversity of vegetation of any desert in the world. Given the unique pollen profile in this region, we sought to identify the most common aeroallergens associated with rhinitis and asthma diagnosis in the local adult population.

Objective: To identify the prevalence of aeroallergen sensitivity in the Tucson adult population and to identify which aeroallergens are associated with a diagnosis of asthma.

Methods: We conducted a retrospective electronic chart review of 226 consecutive adult patients who underwent aeroallergen skin-prick testing for rhinitis at The University of Arizona Adult Allergy and Immunology Clinic over the course of 1 year. All the subjects were tested to a standard panel of tree, grass, weed, mold, house-dust mite, animal dander, cockroach, and feather extracts. Asthma was diagnosed by using the Expert Panel Report 3 guidelines.

Results: Skin testing results were most commonly positive to mesquite (54%), Bermuda (48%), palo verde (47%), olive tree (43%), and chenopodium (43%). Compared with the subjects without asthma, those subjects with asthma were more often sensitized to molds (odds ratio [OR] 2.25 [95% confidence interval {CI}, 1.22–4.14]; $p = 0.005$), including *Alternaria alternata* (OR 2.58 [95% CI, 1.23–5.39]; $p = 0.011$), and cat hair and/or pelt (OR 2.13 [95% CI, 1.24–3.69]; $p = 0.006$).

Conclusion: Regional pollens contributed significantly to allergic disease in this unique climate. Sensitization to *Alternaria* and other nonregional aeroallergens were related to asthma, which supported the current practice of testing and treating patients for allergy to both locally significant and ubiquitous aeroallergens.

(Allergy Asthma Proc 38:370–375, 2017; doi: 10.2500/aap.2017.38.4077)

Aeroallergen sensitization is relatively common in the general population. In the United States, monosensitization has been reported as 15.5% and polysensitization as 38.8%.¹ Other studies found polysensitization to range from 31 to 74.3% in patients who presented for evaluation of allergic rhinitis.^{2–4} Aeroallergen sensitization is associated with a number of atopic diseases, including allergic rhinitis, atopic dermatitis, and asthma.⁵ Due to significant regional differences in aeroallergen exposures, allergy/immunology specialists must take into account the locally significant aeroallergens when considering how to appropriately and effectively diagnose and treat atopic disease.⁶

Asthma is a common disorder, characterized by variable airflow obstruction and accompanied by bronchial

inflammation and hyperresponsiveness.^{7,8} The development of asthma has been associated with genetic and environmental factors, including environmental exposures, viruses, and allergens.⁹ House-dust mite (*Dermatophagoides* species) allergen exposure has been correlated with the development of asthma in children in the United Kingdom and in the United States.¹⁰ In addition to house-dust mite, other allergens have been associated with asthma, including cat hair and/or pelt.¹¹ Mold allergy, particularly to *Alternaria alternata*, is related to the development and severity of asthma; this was well documented in the longitudinal birth cohort of the Tucson Children's Respiratory Study.¹²

Tucson, Arizona, is located in the Sonoran Desert, which has the greatest diversity of vegetation of any desert in the world and features an abundance of grasses, trees, and weeds.¹³ Many plant species prominent in this area are not present elsewhere in the United States. For example, the range of the palo verde tree (*Parkinsonia* species) extends across Arizona, including only a small portion of southeastern California. The mesquite tree (*Prosopis* species) is a major source of aeroallergens and is the most prevalent tree in Arizona.^{14–16} Given the unique pollen profile in this region and the long, overlapping pollen seasons, identification of pollen aeroallergens for each patient is not possible through medical history alone.¹⁷ Further, with

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Abstract presented at the American Academy of Allergy, Asthma and Immunology Scientific Meeting, Los Angeles, California, March 3–7, 2016

T. F. Carr has served on advisory board for AstraZeneca and receives royalties from Wolters Kluwer. The remaining author has no conflicts of interest to declare pertaining to this article

No external funding sources reported

Supplemental data available at www.IngentaConnect.com

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Table 1 Demographic characteristics of the study population

	Asthma (<i>n</i> = 95)	No Asthma (<i>n</i> = 131)
Women, % (no.)	70.5 (67)	63.4 (83)
Age, mean $\pm$ SD (range), y	40 $\pm$ 14 (18–69)	43 $\pm$ 13 (19–69)
Smoking status, % (no.)		
Never	73.7 (70)	72.5 (95)
Former	18.9 (18)	20.6 (27)
Current	7.4 (7)	6.9 (9)
Rhinitis, % (no.)	97.9 (93)	93.9 (123)

SD = Standard deviation.

the availability of standardized, U.S. Food and Drug Administration approved sublingual allergen-specific immunotherapy, we questioned the prevalence of sensitivity to the common, nationally prevalent pollens for which these tablets are specific. We, therefore, sought to identify the most common aeroallergens associated with allergic rhinitis and asthma diagnosis in our local adult population.

METHODS

We performed a retrospective electronic medical record chart review of consecutive patients evaluated at The University of Arizona Adult Allergy and Immunology Clinic in Tucson, Arizona. This review was approved by The University of Arizona Institutional Review Board (1412594114), and consent was waived due to the retrospective nature of the study. Subjects met inclusion criteria if they were at least 18 years of age and had skin-prick testing (SPT) performed at The University of Arizona Adult Allergy and Immunology Clinic between December 1, 2013, and December 1, 2014, to evaluate aeroallergen sensitivity in the setting of rhinoconjunctivitis or asthma.

Demographic information from all the patients was extracted from the electronic medical record. Atopy was determined by skin reactivity to 48 locally significant aeroallergens, including tree pollens (alder, ash, beech, birch, box elder, cottonwood, cyprus, elm, hickory, mesquite, mountain cedar, mulberry, oak, olive, palo verde, pecan, privet, walnut), grass pollens (bahia, Bermuda, Johnson; northern grass mix), weed pollens (carelessweed, cocklebur, dock/sorrel, chenopodium, ragweed, sagebrush), molds (*Alternaria*, *Aspergillus*, *Candida*, *Cladosporia*, *Curvularia*, *Epicoccum*, *Fusarium*, *Helminthosporium*, *Mucor*, *Penicillium*, *Phoma*, *Pullularia*, *Rhizopus*, *Trichophyton*), house-dust mites (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), cat hair and/or pelt, dog pelt, cockroach, and feather mix by using commercially available extracts (Allermed Laboratories, Inc., San Diego, CA) with histamine and saline solution controls. SPT was performed by using the ComforTen Skin Test System (HollisterStier Allergy, Spokane, WA). A

prick that induced a wheal of ≥ 3 -mm diameter with surrounding flare or a wheal of ≥ 3 mm in diameter than the negative control was considered a positive result. Asthma was diagnosed by the physician by using guidelines-based criteria.⁸ The subjects were excluded if they did not meet the inclusion criteria or if the histamine positive control test was nonreactive.

The χ^2 tests were performed on variables to assess their relationship to asthma. Logistic regression for the diagnosis of asthma was adjusted for variables as described in the Results section. A principal components analysis for a diagnosis of asthma included all tested antigens. The components analyzed were included due to the high proportion of effect represented (>0.10). Data were analyzed by using Stata version 10.0 (StataCorp, College Station, TX).

RESULTS

A total of 226 subjects met inclusion criteria. Demographic information for patients with and without a diagnosis of asthma is included in Table 1. There was no significant difference of sex, age, or smoking status between the group with asthma and the group without asthma. Of the total cohort, 184 (81.4%) had positive test results to at least one aeroallergen on SPT. The mean number of positive aeroallergen test results was 15, with a median of 12. A frequency graph of the number of individuals with the number of positive test results is shown in Fig. 1. The five most prevalent specific allergens in the cohort were mesquite (54.4%), Bermuda (47.8%), palo verde (47.3%), olive (42.5%), and chenopodium (42.5%). The most prevalent allergens by group were as follows: tree, mesquite (54.4%); grass, Bermuda (47.8%); weed, chenopodium (42.5%); mold, *A. alternata* (15%); and animal, cat (38.1%). These findings are presented in Table 2. Of the total cohort, 95 (42%) had a diagnosis of asthma. Of the subjects with a diagnosis of asthma, 80 (84.2%) were allergic to at least one allergen, with 18 (18.9%) allergic to 1–5, 33 (34.7%) allergic to 6–20, and 29 (30.5%) allergic to 21–40 dis-

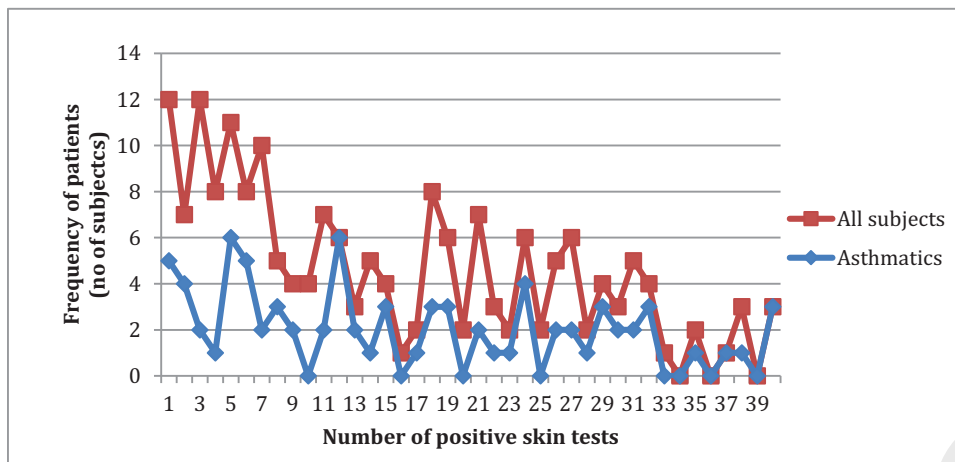


Figure 1. Frequency of the number of positive skin test results.

Table 2 Allergen sensitivity patterns

	Total Cohort, % (no.) (n = 226)	Patients with Asthma only, % (no.) (n = 95)
Top 5 allergens		
Mesquite	54.4 (123)	60.0 (57)
Bermuda	47.8 (108)	51.6 (49)
Palo verde	47.3 (107)	48.4 (46)
Olive	42.9 (97)	48.4 (46)
Chenopodium	42.5 (96)	48.4 (46)
Top 2 trees		
Mesquite	54.4 (123)	60.0 (57)
Palo verde	47.3 (107)	48.4 (46)
Top 2 grasses		
Bermuda	47.8 (108)	51.6 (49)
Bahia	42.5 (96)	48.4 (46)
Top 2 weeds		
Chenopodium	42.5 (96)	44.2 (42)
Carelessweed	40.7 (92)	43.2 (41)
Top 2 molds		
<i>Alternaria</i>	15.5 (35)	22.1 (21)
<i>Cladosporium</i>	10.0 (23)	16.8 (16)
Dog	25.2 (57)	26.3 (25)
Cat	38.1 (86)	48.4 (46)
House-dust mite	36.3 (82)	43.2 (41)
<i>Dermatophagoides farinae</i>	31.4 (71)	36.8 (35)
<i>Dermatophagoides pteronyssinus</i>	33.6 (76)	40.0 (38)
Cockroach	23.0 (52)	25.3 (24)
Negative skin-prick testing results	18.6 (42)	15.8 (15)

tinct antigens. Fifteen patients (15.8%) were not sensitized to any antigens.

We then compared patterns of atopy between the patients with asthma and the patients without asthma. Compared with those without asthma, the patients in the cohort with asthma were more likely to be allergic to any of the tested molds (57.9 versus 50.4%; $p = 0.005$). Specific molds related to asthma were *Alternaria*

(odds ratio [OR] 2.58 [95% confidence interval {CI}, 1.22–5.45]; $p = 0.01$), *Candida* (OR 5.40 [95% CI, 1.88–15.48]; $p = 0.0017$), *Cladosporium* (OR 3.59 [95% CI, 1.41–9.11]; $p = 0.0072$), *Epicoccum* (OR 7.59 [95% CI, 1.62–35.49]; $p = 0.01$), *Fusarium* (OR 6.75 [95% CI, 1.42–32.00]; $p = 0.0162$), *Helminthosporium* (OR 4.00 [95% CI, 1.37–11.63]; $p = 0.011$), *Pullularia* (OR 4.93 [95% CI, 1.00–24.31]; $p = 0.049$), and *Trichophyton* (OR 3.3 [95%

Table 3 Allergens and asthma

	Asthma, % (no.) (<i>n</i> = 95)	No Asthma, % (no.) (<i>n</i> = 131)	Asthma diagnosis, OR (CI)	<i>p</i> Value
Any allergen	84.2 (80)	79.4 (104)	1.39 (0.69–2.78)	0.36
Any tree	76.8 (73)	64.1 (85)	1.79 (0.99–3.26)	0.0545
Any grass	57.9 (55)	50.4 (66)	1.35 (0.80–2.31)	0.26
Any weed	67.4 (64)	55.7 (73)	1.64 (0.95–2.84)	0.08
Cocklebur	41.4 (39)	21.4 (28)	2.56 (1.43–4.60)	0.0016
Any mold	42.1 (40)	24.4 (32)	2.25 (1.28–3.98)	0.005
<i>Alternaria</i>	22.1 (21)	9.9 (13)	2.58 (1.22–5.45)	0.0134
<i>Aspergillus</i>	8.4 (8)	9.2 (12)	0.91 (0.36–2.33)	0.85
<i>Candida</i>	15.8 (15)	3.8 (5)	5.40 (1.88–15.48)	0.0017
<i>Cladosporium</i>	16.8 (16)	5.3 (7)	3.59 (1.41–9.11)	0.0072
<i>Curvularia</i>	8.4 (8)	3.1 (4)	2.92 (0.85–10.0)	0.09
<i>Epicoccum</i>	10.5 (10)	1.5 (2)	7.59 (1.62–35.49)	0.0100
<i>Fusarium</i>	9.5 (9)	1.5 (2)	6.75 (1.42–32.00)	0.0162
<i>Helminthosporium</i>	13.7 (13)	3.8 (5)	4.00 (1.37–11.63)	0.0110
<i>Mucor</i>	10.5 (10)	5.3 (7)	2.08 (0.76–5.70)	0.15
<i>Penicillium</i>	10.5 (10)	9.9 (13)	1.07 (0.45–2.55)	0.88
<i>Phoma</i>	6.3 (6)	3.1 (4)	2.14 (0.59–7.81)	0.25
<i>Pullularia</i>	7.4 (7)	1.5 (2)	4.93 (1.00–24.31)	0.0499
<i>Rhizopus</i>	3.2 (3)	0.8 (1)	4.24 (0.43–41.40)	0.21
<i>Trichophyton</i>	13.7 (13)	4.6 (6)	3.30 (1.21–9.04)	0.0200
Cat	48.4 (46)	30.5 (40)	2.14 (1.23–3.69)	0.0066
Dog	26.3 (25)	24.4 (32)	1.10 (0.60–2.03)	0.75
Any house-dust mite	43.2 (41)	31.3 (41)	1.67 (0.96–2.89)	0.0681

OR = Odds ratio; CI = confidence interval.

CI, 1.21–9.04]; $p = 0.02$). Patients with asthma were also more likely to be allergic to cat hair and/or pelt (OR 2.14 [95% CI, 1.23–3.69]; $p = 0.0066$) and to cocklebur (OR 2.56 [95% CI, 1.43–4.60]; $p = 0.0016$). These results are presented in Table 3.

We then used logistic regression analysis to clarify any interactions among these variables. In a model that included the antigens significantly related to asthma on χ^2 testing, all of the antigens except cocklebur lost their effect. We, therefore, chose to analyze the antigens in antigenic groups, such as mold, tree pollen, grass pollen, weed pollen, house-dust mite, and pet. For example, we defined an individual as sensitized to “mold” if he or she had at least one positive skin test result to a mold. In a logistic regression, including the antigenic groups, only mold allergy was related to an asthma diagnosis (OR 1.23 [95% CI, 1.04–1.47]; $p = 0.015$). Further, when distinguishing those with positive test results to one ($n = 30$), or two or more ($n = 45$) mold species, the effect of mold allergy was limited to those with multiple mold sensitization (OR 3.29 [95% CI, 1.49–7.27]; $p = 0.003$).

To test the observation that sensitization to antigenic groups may be more indicative of an asthma diagnosis

than sensitization to any individual antigen, we performed a principal component analysis for the diagnosis of asthma by using each individual antigen. Two components (1 and 2) were analyzed further due to the high proportion of effect represented (0.3440 and 0.1044, respectively). The principal components analysis plot is shown in Fig. 2, and the list of variable coefficients for each component is shown in Online Supplemental Table 1. Most of the seasonal pollens, including cocklebur but with the exception of mountain cedar and cypress, were noted to cluster in component 1. Molds and other perennial exposures, including house-dust mite, cat, dog, cockroach, and feather clustered in component 2. Logistic regression adjusted for age, sex, and components 1 and 2 revealed a significant association of only component 2 with asthma (OR 1.22 [95% CI, 1.05–1.42]; $p = 0.009$).

DISCUSSION

Our analysis showed that allergic sensitization was common in the total population of patients seen at The University of Arizona Adult Allergy and Immunology Clinic for rhinoconjunctivitis and/or asthma symp-

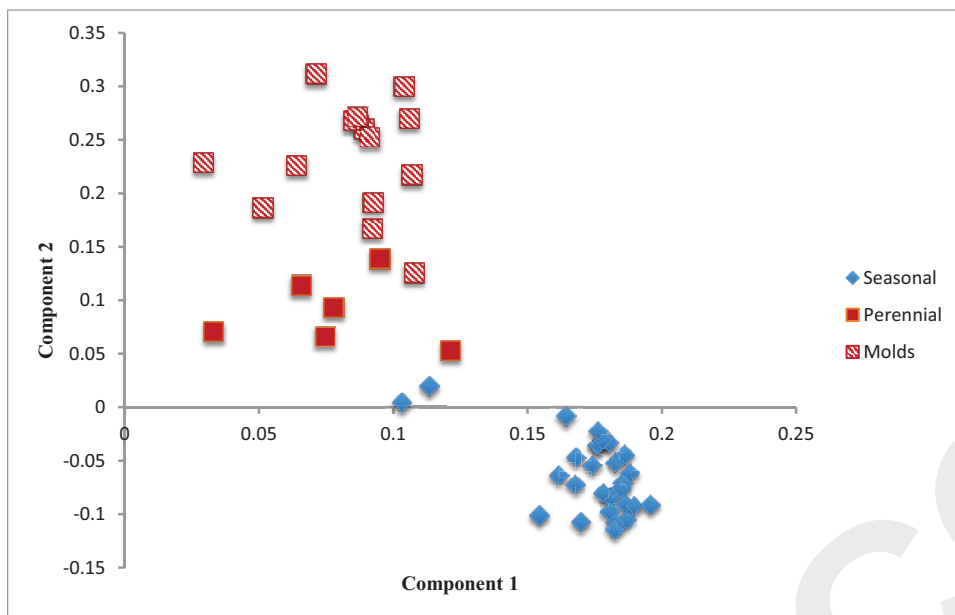


Figure 2. Principal component analysis of the aeroallergens.

toms, with >80% of patients allergic to at least one allergen, with a mean of 15 allergens. The most common allergens are locally prevalent mesquite, Bermuda, palo verde, olive trees, and chenopodium. Further, among the tested antigens, the molds were most strongly and consistently related to asthma in a logistic regression analysis and clustered with other perennial antigens in a principal components analysis. Although very common in this cohort, allergy to tree, grass, or weed pollen was not strongly associated with a diagnosis of asthma.

The association between mold allergy and asthma is well described in the literature, and our data were consistent with this.¹⁸ Specifically, our data were consistent with early findings of the Tucson Children's Respiratory Study, which found a significant correlation between *A. alternata* sensitization and the diagnosis of asthma in children.^{19,20} Interestingly, this cohort of individuals currently living in Tucson was unlikely to have entirely grown up in this region, which suggested that a relationship between mold allergy and asthma development was either not unique to this region or that mold allergy may have contributed to asthma in adulthood as well. The mold testing panel in this clinic was designed to capture sensitivity to molds implicated in allergic bronchopulmonary mycosis and allergic fungal sinusitis. The principal components analysis presented revealed a relationship with mold allergy and asthma but did not support a relationship between pollen allergy and asthma, which indicated that, in Tucson, mold allergy is important for the development or pathogenesis of asthma. These findings may be regional, however, and should be assessed in different climates. In the pet dander group, cat dander was associated with a diagnosis of asthma, whereas

dog dander was not. This is consistent with other studies that demonstrated the relationship between asthma and animal dander and the development or persistence of asthma.^{21,22}

We have unique allergens here in the Sonoran Desert, and our cohort demonstrated a high prevalence of allergy to these locally relevant pollens, including to the palo verde and mesquite trees, which underscored the importance of availability of these extracts for testing and immunotherapy in a commercial setting. Palo verde (*Cercidium*), mesquite (*Prosopis*), acacia (*Acacia*), and Australian pine (*Casuarina*) are all members of the Fabaceae (Leguminosae) family of the Rosales Order. There is evidence of cross-reactivity within the genus, specifically for mesquite and acacia tree pollens; however, there are few data specifically concerning palo verde cross-reactivity with these other pollens. In our cohort, of those who had positive results to SPTs for mesquite, 78.1% (96/226) also had positive results to palo verde. Further, of those who had positive SPT results to palo verde, 91.6% (98/107) had positive results to mesquite, which demonstrated potentially significant but incomplete cross-reactivity.

Regarding grass reactivity in our cohort, Bermuda was the most common (47.8%), followed by bahia (42.5%), Johnson (35.8%), and the northern grass mix (34.1%). Further, only 38.5% (87/226) were allergic to ragweed and 34.1% (77/226) were allergic to northern grasses, including Timothy grass. The Timothy grass family can be found in 47% of the counties (7/15) in Arizona, including Pima, and is a versatile grass that is used as feed for livestock.²³ Ragweed can be found in 100% of the counties (15/15). Despite the presence of these antigens, due to the relatively low proportion of patients with sensitivity, and potentially also due to

their polysensitization, the utility of the U.S. Food and Drug Administration approved sublingual immunotherapy tablets for the Timothy grass family pollen or ragweed pollen for these patients may be limited.

The strengths of this study were that it was a retrospective cohort study with consecutive sampling. All the patients received testing with the same standardized panel of aeroallergens, and the results were interpreted by the same allergy nurse and physician. There were several weaknesses to the study, including the retrospective nature of the study. Further, this cohort was biased toward allergic disease because all the patients, by inclusion criteria, had symptoms consistent with respiratory allergy. Therefore, the atopy patterns described were not necessarily representative of sensitization in the population at large. We were unable to investigate the relationship between specific allergens and asthma severity because asthma severity was not available for every patient selected for review. In addition, some of the population may have recently moved from other locations in the country, so the duration of exposure to our local pollens varied. We assumed that, for many of these patients, they had had enough exposure to induce allergy, but this information was not reliably available.

CONCLUSION

Our research showed that locally prevalent aeroallergens were a significant cause of allergic sensitization in patients with symptoms of rhinoconjunctivitis and/or asthma. Given the geographic differences in aeroallergen exposure across the United States, it, therefore, is important that clinicians are familiar with the local aeroallergens and continue to include them in SPT panels. We further demonstrated that, although we have unique aeroallergens in the Sonoran Desert, many of our patients are indeed sensitized to them at high frequencies. Also, this cohort found the allergens associated with a diagnosis of asthma to be both molds and perennial allergens, which underscored the importance of evaluation for sensitivity to these antigens in patients with respiratory disease.

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