

IgE-Mediated Sensitization to Mould Allergens among Patients with Allergic Respiratory Diseases in a Desert Environment

C.I. Ezeamuzie^a S. Al-Ali^c M. Khan^c Z. Hijazi^b A. Dowaisan^c
M.S. Thomson^a J. Georgi^c

^aDepartment of Pharmacology and Toxicology and ^bDepartment of Pediatrics, Faculty of Medicine, Kuwait University and ^cAl-Rasheed Allergy Centre, Ministry of Public Health, Kuwait

Key Words

Asthma · Moulds · Sensitization · IgE · Desert · Kuwait

Abstract

Background: The importance of fungal allergens in the development of allergic diseases in a desert environment is uncertain. This study evaluated the prevalence of IgE sensitization to moulds among patients with allergic respiratory diseases in Kuwait – a desert country. **Methods:** A total of 810 patients (male:female ratio 1.4) with a mean age of 32.3 years (range 2–76 years) with extrinsic asthma or allergic rhinitis were studied. Sera from the patients were tested by the CAP-RAST method for specific IgE to 6 fungi (*Penicillium*, *Cladosporium*, *Aspergillus*, *Candida*, *Alternaria* and *Helminthosporium*). For comparison house dust mite and Bermuda grass were also assessed. **Results:** The overall positivity to at least one mould was 20.9%. Among 120 matched control subjects, the value was 5.8%. The value was much higher among patients with asthma alone (45.8%) or both asthma and rhinitis (28.3%) than those with rhinitis alone (11.8%; $p < 0.001$). Asthmatic children had the highest sensitization rate (66.0% in the 7- to 12-year age group), which declined sharply with age. Among asthmatics,

Candida and *Aspergillus* had the highest sensitization rates (23.1 and 21.3%, respectively), followed by *Helminthosporium* (18.8%), *Cladosporium* (15.9%), *Alternaria* (14.6%) and *Penicillium* (13.9%). The values for mite and Bermuda grass were 41.2 and 54.6%, respectively. Among asthmatic children, severe asthma was significantly more frequent among mould-positive (51.6%) than mould-negative patients (17.5%; $p < 0.0001$). **Conclusions:** Even in this desert environment, sensitization to moulds is quite common among patients with allergic respiratory diseases, with a striking preponderance among children with asthma. Mould allergy could also be an important factor determining asthma severity in this environment.

Copyright © 2000 S. Karger AG, Basel

Introduction

Allergic diseases occur worldwide and their prevalence appears to have been on the increase in the last 2 decades [1–3]. Reports from different geographical areas have shown that sensitization to moulds through exposure to airborne fungal allergens is common among patients with respiratory allergic diseases [4–6]. However, the associa-

tion of mould sensitization with allergic symptoms, especially of the respiratory tract, is only beginning to be appreciated. In a recent study involving 6-year-old children with persistent asthma, *Alternaria* was the allergen most closely associated with the development of asthma [7]. Exposure to airborne spores of *Alternaria* has been shown to be a trigger for severe asthma and a risk factor for respiratory failure, especially in children with bronchial asthma [8, 9]. In a recent large study involving 4,295 subjects, Gergen and Turkeltaub [10] showed a strong independent association of *Alternaria* sensitization with bronchial asthma and allergic rhinitis. A similar conclusion was reached for *Cladosporium* [11]. More directly, bronchial challenge of sensitized individuals with mould extracts readily induced acute bronchospasm [12].

Kuwait is a small desert country northeast of the Arabian Peninsula. The climate is dry and very hot in summer with an average daytime temperature of around 42°C and a mean annual relative humidity of about 30%. The average annual rainfall is less than 15 cm, and there is little or no vegetation in most parts of the country. Such conditions are often considered unfavorable for the occurrence of aeroallergens such as pollens, house dust mites and moulds, yet asthma and allergic rhinitis are quite common [13–15]. The role of moulds as causative allergens of allergic diseases in a desert environment has received limited attention. The pattern of allergic sensitization and the type of fungal species are likely to be different in different climatic conditions. For example, in an Australian study, Peat et al. [16] showed that *Alternaria* was the major asthma-associated allergen in the desert region, unlike at the seacoast where the house dust mite was the major allergen. A similar result was obtained in a recent study in another desert environment in Tucson, Ariz., USA [7]. On the other hand, Sporik et al. [17] found that animal danders rather than house dust mites were the allergens most frequently associated with asthma in the dry, high-altitude areas of New Mexico. Although the spores of some of the ubiquitous moulds such as *Cladosporium*, *Penicillium* and *Aspergillus* have been regularly trapped from the outdoor air of Kuwait [18], their role in allergic sensitization and association with allergic respiratory diseases have not been studied,

The objective of this study was, therefore, to determine the prevalence and pattern of IgE-mediated sensitization to moulds among Kuwaiti patients with allergic respiratory symptoms and to assess its relationship to disease severity among asthmatics.

Materials and Methods

Patients

A total of 810 patients [male:female ratio of 1.4; mean age 32.3 years (range 2–76 years)] with a diagnosis of extrinsic asthma or allergic rhinitis participated in the study. They were recruited randomly (by random numbers of patients meeting the selection criteria) from patients with asthma and/or rhinitis who attended the Kuwait Allergy Centre or the allergy clinic of the Mubarak Al-Kabir Hospital (children) between January 1997 and December 1998. A comparable number of patients (30–50) was recruited per month throughout the period of study so as to avoid seasonal bias. The mean duration of disease was 7.4 years (range 1–33.6 years). The diagnosis of asthma was confirmed using the American Thoracic Society criteria [19]. Asthma was classified as severe if the peak expiratory flow rate at the time of the visit was less than 60% of the predicted value and/or the patient had had 4 or more attacks in the preceding 12 months. Allergic rhinitis was established by a combination of clinical history, examination of nasal discharges, and viewing of the mucus membrane of the nose and sinuses. All patients had either a documented positive skin prick test (SPT) reaction (wheal diameter ≥ 3 mm) to at least one of 5 test aeroallergens: *Dermatophagoides pteronyssinus*, grass pollen mix, tree pollen mix, date palm pollen and *Aspergillus fumigatus*, or a positive CAP-Phadiatop test (for children under 4 years of age). In addition, a study questionnaire covering demographic data, family history of atopy, smoking habits and respiratory symptoms was given to each patient. Asthma alone occurred in 165 patients (20.4%) while allergic rhinitis alone occurred in 353 (43.6%). In the remaining 291 patients (35.9%), both diseases coexisted. According to the criteria used, in the asthmatic group, asthma was considered mild to moderate in 384 patients (84.2%) and severe in 72 (15.8%). In the total patient population, 241 (29.8%) had a clear family history of atopy while 468 (57.8%) claimed they had not. The rest were equivocal or did not know. Only 85 patients (10.5%) were active smokers. Native Kuwaitis comprised 50.2% of the patient population, the rest being mainly other Arabs and Asians who had resided in Kuwait for a minimum of 1 year (mean 5.4 years).

In addition, 120 normal subjects (without any allergic disease) matched for sex and age were also studied. They were recruited from healthy blood donors at the Central Blood Bank (adults) and from patients visiting the outpatient clinics (including the pediatric one) of the Mubarak Al-Kabir Hospital for other complaints. All patients and control subjects (or the parents of children) gave informed consent before entering the study.

Venous blood samples were taken once from each patient or control subject, and the separated serum stored at -43°C for less than 3 months before antibody determination.

IgE Antibody Determination

The Pharmacia CAP-FEIA[®] test system, comprising the CAP-RAST, CAP-IgE and CAP-Phadiatop tests, were employed to measure the allergen-specific IgE, total serum IgE and atopy, respectively. Total and allergen-specific IgE assays were calibrated against the WHO reference serum 75/502. The working ranges of the assays were 0.35–100 kU/l for CAP-RAST and 2–2,000 kU/l for CAP-IgE. The Phadiatop test collectively measures the presence of specific IgE in a balanced mixture of common allergens. The test has been widely validated for the diagnosis of atopy [20, 21]. Specific IgE values greater than 0.35 kU/l (or CAP-RAST class ≥ 1) were regarded as positive.

All samples were screened for specific IgE to the following 6 moulds (*Penicillium notatum*, *Cladosporium herbarum*, *A. fumigatus*, *Candida albicans*, *Alternaria alternata* and *Helminthosporium halodes*) as well as 2 nonmould allergens, house dust mite (*D. pteronyssinus*) and Bermuda grass pollen (*Cynodon dactylon*). These were thought to be relevant to this environment by aerobiologic criteria or local SPT experience.

Analysis of Data

All data were analyzed with SPSS on a PC. For statistical purposes, total IgE values less than 2 kU/l were assigned a value of 1 kU/l. The severity of sensitization to individual allergens was expressed in CAP-RAST classes of 0–6. Data were expressed mainly as percent frequency and the difference between groups was tested by the χ^2 analysis or Fisher’s exact test as appropriate. Significance was set at $p < 0.05$.

Results

Among the 810 patients with allergic respiratory disease, the overall frequency of positive specific IgE to any of the 6 mould allergens was 20.9% (table 1). The corresponding value for the control group was 5.8%. The values for the individual moulds were: *Candida* (16.9%), *Aspergillus* (15.2%), *Helminthosporium* (13.3%), *Cladosporium* (11.4%), *Alternaria* (10.1%) and *Penicillium* (9.0%). The corresponding values for the control group were 4.2, 5.0, 3.3, 4.2, 3.3 and 2.5%, respectively. In com-

parison, the frequency of sensitization to the 2 nonmould allergens, house dust mite and Bermuda grass, among allergic patients was 38.4 and 56.5%, respectively. The corresponding values in control subjects were 14.9 and 15.8%, respectively.

Results in table 1 also show that mould sensitization was clearly associated with asthma rather than rhinitis. In all cases, the frequency of sensitization was highest among patients with asthma alone, intermediate in those with both asthma and rhinitis and very low in patients who had only rhinitis. For example, among patients who had asthma alone, the prevalence of sensitization to any mould was as high as 45.8% compared with 11.9% for patients with rhinitis alone and 28.3% for all asthmatic patients with or without rhinitis. The prevalence rates for the individual allergens among patients with asthma alone were: *Candida* (37.6%), *Aspergillus* (29.7%), *Helminthosporium* (35.1%), *Cladosporium* (31.5%), *Alternaria* (26.7%) and *Penicillium* (25.5%). The corresponding values for the group with rhinitis alone were: 8.8, 7.1, 6.5, 5.4, 4.2 and 3.1%, respectively. For the group that had both diseases or had asthma with or without rhinitis, the values were intermediate. The differences in the prevalence rates for the individual allergens between the group with asthma alone (or asthma with or without rhinitis) and the group with rhinitis alone were highly significant ($p < 0.0001$ in each case). There was no significant difference in the sen-

Table 1. Frequency of IgE sensitization to moulds among all patients and the relationship with disease presentation

Allergens	Frequency of sensitization				controls (n = 120)
	patients				
	all patients (n = 810)	asthma ± rhinitis (n = 456)	asthma alone (n = 165)	rhinitis alone (n = 354)	
<i>Candida</i>	16.9***	23.1***	37.6***, ++	8.8	4.2
<i>Aspergillus</i>	15.2**	21.3***	29.7***, ++	7.1	5.0
<i>Helminthosporium</i>	13.3**	18.8***	35.1***, ++	6.5	3.3
<i>Cladosporium</i>	11.4*	15.9**	31.5***, ++	5.4	4.2
<i>Alternaria</i>	10.1*	14.6**	26.7***, ++	4.2	3.3
<i>Penicillium</i>	9.0*	13.9**	25.5***, ++	3.1	2.5
Any mould	20.9***	28.3***	45.8***, ++	11.9	5.8
House dust mite (<i>D. pteronyssinus</i>)	38.4***	41.2***	46.7+, ***	35.0**	14.9
Bermuda grass	56.5***	54.6***	58.2***	58.5***	15.8
Total IgE (GM)	325.5***	324.1	378.3	327.3	65.8

Values represent % with the exception of total IgE where they represent kU/l. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. controls; + $p < 0.05$, ++ $p < 0.0001$ vs. rhinitis alone. GM = Geometric mean.

sitization rates between patients with rhinitis alone and control subjects, either with respect to the individual moulds or to any mould ($p > 0.05$). In contrast, the differences between the asthmatic groups and the controls were statistically significant ($p < 0.05$ – 0.001). House dust mites, but not Bermuda grass, also had a higher prevalence rate in the group with asthma alone (46.7%) than in the group with rhinitis alone 35.0% ($p < 0.05$). However, unlike for the moulds, the prevalence rates for the two allergens were significantly higher in patients with rhinitis alone than in controls ($p < 0.01$ – 0.001). The total serum IgE levels were not influenced by the disease presentation (geometric means: 378.3, 324.1 and 327.3 kU/l for asthma alone, asthma with or without rhinitis and rhinitis alone, respectively) (table 1). The values were, however, significantly higher than that for the controls (65.8 kU/l; $p < 0.001$ in each case).

As shown in table 2, sex had no significant effect on the rate of sensitization to mould allergens except for *Cladosporium* and *Aspergillus* for which males had significantly higher rates than females: *Cladosporium*: 13.0 versus 7.8% ($p < 0.05$) and *Aspergillus*: 17.4 versus 11.4% ($p < 0.05$). For the 2 nonmould allergens, males had significantly higher rates than females – house dust mite (42.5 vs. 31.4%, $p < 0.01$) and Bermuda grass (61.5 vs. 47.3%, $p < 0.001$). Males also had significantly higher total serum IgE values than females (geometric mean 411.4 vs. 243.1 kU/l, $p < 0.005$), and both values were significantly higher than the corresponding values for the controls

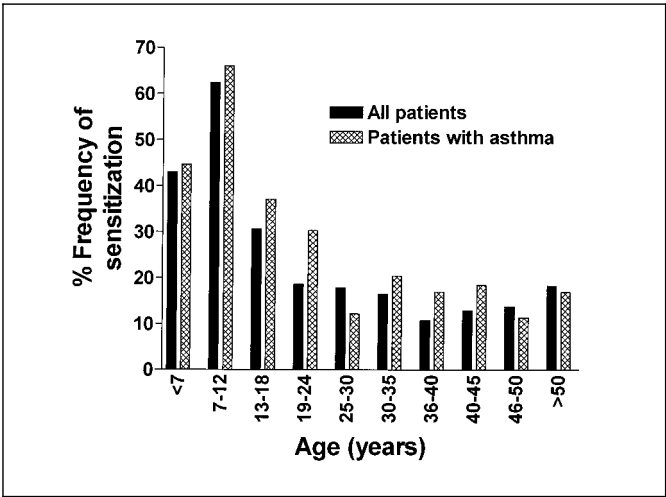


Fig. 1. Frequency of allergic sensitization to any mould according to age groups. The total number of patients per age group ranged between 40 and 112 for all patients and between 38 and 56 for patients with asthma.

(76.8 kU/l for males and 48.6 kU/l for females; $p < 0.001$ in each case).

The analysis of the prevalence of sensitization to any mould with respect to age (fig. 1) showed a clear age-dependent frequency distribution with an overwhelming preponderance among young patients (≤ 18 years). The peak rate of 62.4% (66.0% among asthmatics) occurred in

Table 2. Influence of sex on IgE sensitization to mould allergens and total IgE among all patients and controls

Allergens	Frequency of sensitization			
	patients		controls	
	males (n = 476)	females (n = 334)	males (n = 69)	females (n = 51)
<i>Candida</i>	18.1	13.8	4.3	3.9
<i>Aspergillus</i>	17.4*	11.4	5.8	3.9
<i>Helminthosporium</i>	14.9	10.2	4.3	2.0
<i>Cladosporium</i>	13.0*	7.8	4.3	3.9
<i>Alternaria</i>	11.6	7.2	2.9	3.9
<i>Penicillium</i>	9.9	6.9	1.9	2.0
Any mould	23.1*	17.1	5.8	5.9
House dust mite (<i>D. pteronyssinus</i>)	42.5**	31.4	18.8	9.8
Bermuda grass	61.5***	47.3	20.3	9.8
Total IgE (GM)	411.4***	243.1	76.8*	48.6

Values represent % with the exception of total IgE where they represent kU/l. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. females. GM = Geometric mean.

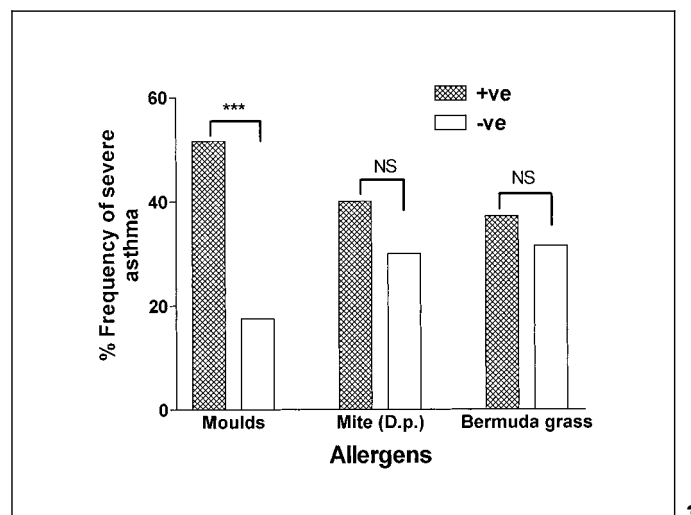
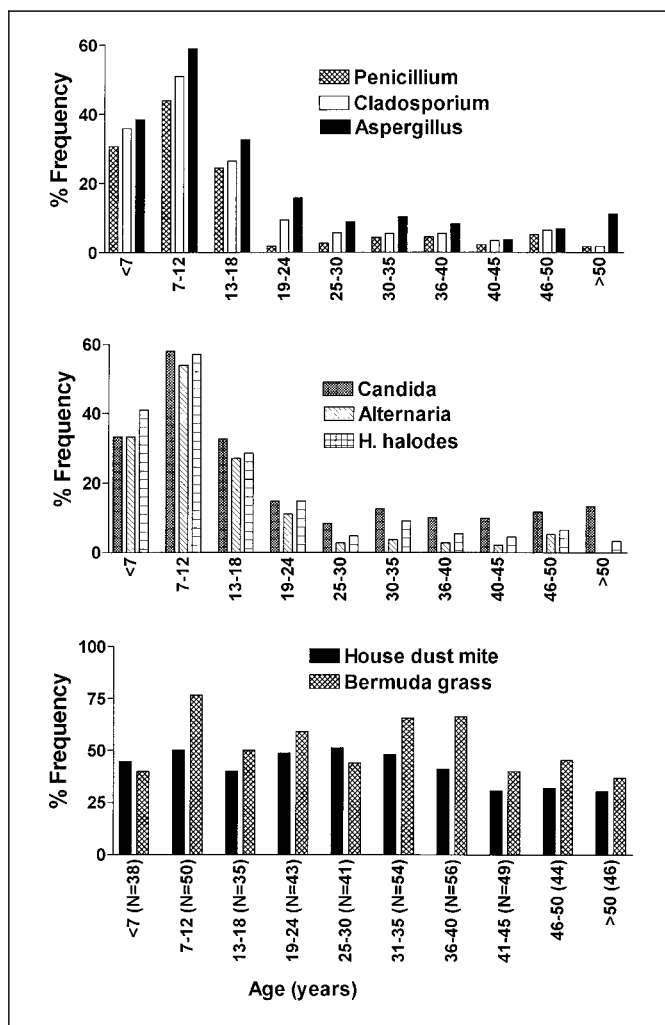


Fig. 2. Age dependency of allergic sensitization to the individual moulds among patients with asthma (with or without rhinitis). Data for house dust mite and Bermuda grass are included for comparison.

Fig. 3. Prevalence of severe asthma among asthmatic children (<18 years old) who were positive (+ve) or negative (-ve) to moulds: comparison with house dust mites and Bermuda grass. *** $p < 0.001$. NS = Not significant; D.p. = *D. pteronyssinus*.

the age range of 7–12 years and declined rapidly thereafter, reaching below 15% at the age of 25 and over. The analysis of the individual allergens among asthmatics revealed a strikingly similar age-dependent prevalence pattern (both in magnitude and distribution) for the 6 moulds (fig. 2). The sensitization rates for each mould rose steeply from around 35% in the <7-year-olds to peak at around 58% in the 7- to 12-year age group before declining sharply with increasing age. By the age of 25 years and over, the rates had decreased to between 0 and 7% in most cases. Among the 120 controls (42 children under 18 years of age and 78 adults) mould sensitization was also higher among children [5 out of 42 (11.9%)] than adults [2 out of 78 (2.6%); $p < 0.05$]. In contrast, the rates for the house dust mite and Bermuda grass were more or less independent of age up to 35 years of age, after which a gradual decrease with age was seen. Smoking habits had

no significant effect on the frequency of mould sensitization as 21.7% (18 out of 85) of smokers and 18.9% (116 out of 614) of nonsmokers were sensitized ($p = 0.616$).

Because of the preponderance of mould sensitization among asthmatic children (<18 years), this subgroup was analyzed further for the relationship between mould sensitization and asthma severity (estimated as the % frequency of severe asthma cases). As shown in figure 3, severe asthma was significantly more common (51.6%) among mould-positive asthmatic children than among those that are mould-negative (17.5%; $p < 0.001$). In contrast, there was no significant difference in the prevalence of severe asthma between mite-positive and mite-negative asthmatic children, nor between Bermuda grass-positive and Bermuda grass-negative asthmatic children. The propensity of the individual allergens to cause severe asthma or severe sensitization (% frequency of cases with

Table 3. Frequency of severe asthma and severe sensitization among asthmatic children (n = 120; <18 years) sensitized to the various moulds

Positive allergens	Frequency, %	
	severe asthma (clinical criteria)	severe sensitization (CAP-RAST ≥ 4)
<i>Penicillium</i>	50.0	2.8
<i>Cladosporium</i>	48.3	7.5
<i>Aspergillus</i>	47.5	7.5
<i>Candida</i>	49.2	15.8
<i>Alternaria</i>	49.2	40.8*
<i>Helminthosporium</i>	50.0	31.71*
Any mould	51.7	–
House dust mite (<i>D. pteronyssinus</i>)	40.0	7.5
Bermuda grass	36.7	27.5

* p < 0.05 compared with similar values for the other moulds.

CAP-RAST class ≥ 4) was also examined. As shown in table 3, the frequency of severe sensitization was by far higher for *Alternaria* (41.2%) and *Helminthosporium* (32.1%) than for the other moulds (2.3–17.1%, p < 0.05–0.001). However, the frequency of severe asthma (47.4–50.0%) was similar in asthmatic children positive for the individual mould allergens. Polysensitization was found to be particularly common with 113 out of the 129 mould-positive asthmatic patients (87.6%) sensitized to more than 1 mould, and as much as 38.0% sensitized to all 6 moulds. The median number of sensitizing moulds per patient in this group was 5.

Discussion

Kuwait is a small Arabian desert country where the prevalence of allergic diseases is unexpectedly high. Moulds are ubiquitous in nature, but the comparative study of the different moulds as causative allergens in allergic respiratory diseases has not been previously addressed in this environment nor, to our knowledge, in any other desert environment. In this study, we evaluated the prevalence of mould allergen sensitization and its relationship to disease severity among the entire age spectrum of Kuwait patients with extrinsic asthma and allergic rhinitis. IgE sensitization to moulds was found to be common, being present in 20.9% of all patients with respiratory

allergic disease and 28.3% asthmatics, compared with 5.8% nonallergic controls. The sensitization pattern revealed that mould allergy was extremely common among children with asthma, especially in the age group of 7–12 years, where the prevalence peaked at 66.0%. Beyond this age group, the prevalence declined rapidly with increasing age, falling to below 15% at age 25 and over. This shows that mould allergy in this environment, unlike mite and pollen allergy, is essentially a feature of childhood asthma. Age dependency of mould sensitization has been previously reported. In the age group of 14–19 years, Kauffman et al. [22] reported a prevalence rate of 20 and 18.8%, respectively, for *Alternaria* and *Cladosporium* among asthmatics, which decreased sharply to below 6.5% at the age of 30 years. As their study did not include patients younger than 14 years, it might have missed the peak prevalence. The corresponding prevalence rates for the two moulds in the 13- to 18-year-old asthmatics in the present study were higher (32.3 and 32.4%, respectively). Using SPT and standardized mould extracts, Aas et al. [23] reported a positive reaction rate of 60% for *Cladosporium* among 8- to 15-year-old asthmatic children. This is comparable to the rate of 54.3% obtained for the 7- to 12-year-old asthmatics in the present study. In other studies that covered the full age spectrum as the present study, essentially similar results (both in magnitude and age-dependent distribution) were reported [7, 24].

A clear preponderance of mould sensitization among asthmatics compared with rhinitics has previously been observed [7, 25]. It suggests an important role for fungal sensitization/lung infection in the development of asthma. On the other hand, it could be that the bronchial inflammation of asthma predisposes for sensitization to inhaled fungal spores.

The reason for the early sensitization to mould allergens and its rapid decline after puberty is still uncertain. It has been suggested that the relative capacity of the airways to eliminate fungal spores, which may be low in early childhood, probably surges during adolescence, thus limiting the access of the spores to the immunocompetent cells [26]. However, how children that are already sensitized can outgrow their sensitization remains unknown. One possibility is that the hormonal changes that accompany puberty may play a role, but this remains to be clarified.

Sex seemed to have little effect on sensitization to moulds. Although males generally had higher rates than females, only for *Cladosporium* and *Aspergillus* were the differences significant. These sex differences were much more pronounced for house dust mite and Bermuda grass.

This confirms our recent data showing highly significant differences in the sensitization to nonmould aeroallergens among asthmatics in this environment [25]. The reason for the overall tendency for sensitization rates to be higher in males than females is uncertain. There is no evidence to suggest that a differential exposure of the sexes to aeroallergens may occur. It is also unlikely to relate to the higher rate of smoking among males, since in the present study the rates were similar in smokers and nonsmokers. It may rather be a reflection of the generally higher total IgE values in males than females as seen in this and other studies [24, 25], which may in turn depend on hormonal differences.

The relatively high sensitization rate to house dust mites in this desert environment was unexpected. Mites tend to require a minimum relative humidity of 60% and moderate temperatures (around 25°C) to thrive [27], whereas the mean relative humidity in Kuwait is about 30% and the average summer temperature may exceed 42°C. It is likely that the extensive use of air conditioners in Kuwait in recent times may well have created indoor climatic conditions conducive for the growth of mites, and indeed moulds as well.

This study also revealed that among all patients with respiratory allergic diseases, the rank order of sensitization rates was: *Candida* > *Aspergillus* > *Helminthosporium* > *Cladosporium* > *Alternaria* > *Penicillium*. This prevalence pattern may contrast with those from European countries where *Alternaria* and *Cladosporium* seem to be the most prevalent sensitizing moulds [28]. The reason for the prominence of sensitization to *Candida* is presently unclear. This yeast-like fungus, which unlike the other fungi produces no airborne spores, is a common commensal of the mucous membranes of man. One possibility is that its prominence reflects an inappropriate use of antibiotics in the community which might have led to their proliferation and hence increased sensitization. This is being further investigated. For the other fungi, the results appear to be consistent with local aerobiologic data which showed that the spores of *Cladosporium*, *Aspergillus* and *Alternaria* are most frequently trapped in Kuwait [18, 29] with two seasonal peaks in March to April and November. In one study, the mean daily spore count was reported to range from 1,200/m³ air for *Cladosporium* to 200/m³ air for *Alternaria* [29]. Nevertheless, it is to be noted that among asthmatic children aged 7–12, the prevalence rates for *Candida*, *Aspergillus*, *Alternaria* and *Cladosporium* were essentially similar (59.6, 59.3, 57.4 and 54.3%, respectively). In fact in this age group the moulds had higher sensitization rates than mites, and

only slightly less than Bermuda grass. The result for *Alternaria* is consistent with that of another study conducted in a desert environment in Tucson, Ariz., USA, in which Halonen et al. [7] showed that among asthmatic children aged 6 *Alternaria* had a much higher prevalence of sensitization (50%) than house dust mites. The other moulds were not investigated in that study.

Our results further showed a high rate of polysensitization to the moulds, with 87.6% of all mould-positive asthmatics sensitized to more than 1 mould. In fact, the median number of mould allergens per patient was 5, with 38.0% being sensitized to all 6 moulds. Whether this reflects intergenera allergen cross-reactivity or a case of 1 sensitizing mould predisposing the airways to others is currently uncertain.

A number of studies have shown that mould sensitization is a strong risk factor for the development of asthma and its exacerbation [8–10]. In the present study we examined the possible relationship of mould sensitization with asthma severity by determining the frequency of severe asthma among mould-positive and mould-negative groups. Among asthmatic children, severe asthma was by far more common among those who were positive for at least 1 mould (51.6%) than those who were not (17.5%). No such significant relationship was seen with mites and Bermuda grass allergens. Analysis of the individual moulds revealed that while *Alternaria* and *Helminthosporium* caused the severest sensitization, perhaps due to their possession of more potent allergens, their ability to cause severe asthma was comparable to those of the other moulds, though higher than those of nonmould allergens. The reason for these differences is not immediately clear, but underscores the fact that the presence of IgE is only one component of an apparently complex process of clinical manifestation of allergic disease, in which the inflammatory reactions associated with fungal colonization may even be more relevant. However, unlike severe sensitization, the analysis of the propensity of individual moulds to cause severe asthma may be less informative because of the extensive polysensitization among the moulds. Thus, although moulds may generally have lower sensitization rates than other allergens, they may cause more severe sensitization and more severe asthma. In one population study, it has been reported that skin reactivity to moulds, especially *Alternaria*, increased the risk of asthma 5-fold as compared with 2- to 3-fold for sensitization to other aeroallergens [10]. Similar conclusions were also reached by Peat et al. [16] who showed that *Alternaria* was the most asthma-associated allergen in a study in the Australian desert.

In summary, these results have shown that in Kuwait, a desert country, mould sensitization is common among patients with allergic respiratory diseases, but with an overwhelming preponderance in young children with asthma. Furthermore, mould allergy may be an important factor determining the severity of childhood asthma in this environment.

Acknowledgment

This work was supported by grant No. 95-07-06 from the Kuwait Foundation for the Advancement of Sciences (KFAS).

We are grateful to the Ministry of Public Health, Kuwait, for the permission to source our patients from Government Health Institutions and to Mrs Elizabeth Philips for the technical assistance.

References

- Burr M, Butland B, King S, Vaughan-Williams E: Changes in the asthma prevalence: Two studies 15 years apart. *Arch Dis Child* 1989;64: 1118–1125.
- Sibbald B, Rink E, D'Souza M: Is the prevalence of atopy increasing? *Br J Gen Pract* 1990; 40:338–340.
- Åberg N, Hasselmar B, Åberg B, Eriksson B: Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995;25:815–819.
- Koivikko A, Viander M, Lanner A: Use of the extended Phadebas RAST panel in the diagnosis of mould allergy in the asthmatic children. *Allergy* 1991;46:85–91.
- Lehrer SB, Hughes JM, Altman LC, et al: Prevalence of basidiomycete allergy in the USA and Europe and its relationship to allergic respiratory symptoms. *Allergy* 1994;49:460–465.
- Tariq SM, Matthews SM, Stevens M, Hakim EM: Sensitization to *Alternaria* and *Cladosporium* by the age of 4 years. *Clin Exp Allergy* 1996;26:794–798.
- Halonen M, Stern DA, Wright AL, Taussig LM, Martinez FD: *Alternaria* as major allergen for asthma in children raised in a desert environment. *Am J Respir Crit Care Med* 1997; 155:1356–1361.
- O'Hollaren MT, Yunginger JW, Offord KP, et al: Exposure to an aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. *N Engl J Med* 1991;324:359–363.
- Targonski PV, Persky VW, Ramekrishnan V: Effect of environmental moulds on risk death from asthma during pollen season. *J Allergy Clin Immunol* 1995;95:955–961.
- Gergen PJ, Turkeltaub PC: The association of individual allergen reactivity with respiratory disease in a national sample: Data from the second National Health and Nutrition Examination Survey, 1976–80 (NHANES II). *J Allergy Clin Immunol* 1992;90:579–588.
- Garret MH, Rayment PR, Hooper MA, Abramson MJ, Hooper BM: Indoor airborne fungal spores, house dampness and associations with environmental factors and respiratory health in children. *Clin Exp Allergy* 1998;28: 459–467.
- Horner WE, Lopez M, Salvaggio JE, Lehrer SB: Basidiomycete allergy: Identification and characterization of an important allergen from *Calvatia cyanthiformis*. *Int Arch Allergy Appl Immunol* 1991;94:359–361.
- Al-Awadi AA: Study of Allergy in Kuwait. 1. Prevalence and Role of Environmental Factors. Kuwait, Ministry of Public Health, 1973.
- Ellul-Micallef R, Al-Ali S: The spectrum of bronchial asthma in Kuwait. *Clin Allergy* 1984; 14:509–517.
- Strannegard IL, Stannegard O: Childhood bronchial asthma in a desert country. *Allergy* 1990;45:327–333.
- Peat JK, Tovey CM, Mellis CM, Leeder SR, Woolcock AJ: Importance of house dust mite and *Alternaria* allergens in childhood asthma: An epidemiological study in two climatic regions of Australia. *Clin Exp Allergy* 1993;23: 812–820.
- Sporik R, Ingram JM, Price W, Sussman JH, Honsigner RW, Platts-Mills TAE: Association of asthma with serum IgE and skin test reactivity to allergens among children at high altitude. *Am J Respir Crit Care Med* 1995;151:1388–1392.
- Moustafa AF, Kamel SM: A study of fungal spore population in the atmosphere of Kuwait. *Mycopathologia* 1976;59:29–35.
- American Thoracic Society: Standards for the diagnosis and care of patients with chronic obstructive pulmonary diseases and asthma. *Am Rev Respir Dis* 1987;136:225–244.
- Gustafsson D, Daniesson D: In vitro diagnosis of atopic allergy in children. A comparison between total IgE, conventional RAST and a new multi Rast (Phadiatop). *Allergy* 1988;43: 105–108.
- Eriksson NE: Allergy screening with Phadiatop and CAP Phadiatop in combination with a questionnaire in adults with asthma and rhinitis. *Allergy* 1990;45:285–292.
- Kauffman HF, Zuidema S, de Monchy JGR: Clinical significance of fungal allergy: Aerobiological and clinical studies; in Samson RA, Flannigan B, Flannigan ME, Verhoef A, Adan OOC, Hoekstra ES (eds): *Health Implications of Fungi in Indoor Environments*. Amsterdam, Elsevier, 1994, pp 221–228.
- Aas K, Leegaard J, Aukrust L, Grimmer O: Immediate type hypersensitivity to common moulds. Comparison of diagnostic material. *Allergy* 1980;35:443–445.
- Niemeyer NR, de Monchy JGR: Age-dependency of sensitization to aero-allergens in asthmatics. *Allergy* 1992;47:431–435.
- Ezeamuzie CI, Thomson MS, Al-Ali S, Dowaisan A, Khan M, Hijazi Z: Asthma in the desert: Spectrum of the sensitizing aeroallergens. *Allergy* 1999;55:1–6.
- Kauffman HF, Tomee JFC, van der Werf TS, de Monchy GR, Koeter GK: Review of fungus-induced asthmatic reactions. *Am J Respir Crit Care Med* 1995;151:2109–2116.
- Arlian LG: Biology and ecology of house dust mites, *Dermatophagoids* spp. and *Euroglyphus* spp. *Immunol Allergy Clin North Am* 1989;9: 339–356.
- D'Amato G, Spiekstra FTHM: Aerobiologic and clinical aspect of mould allergy in Europe. *Allergy* 1995;50:870–877.
- Halwagy MH: Fungal airspora of Kuwait City, Kuwait. *Grana* 1994;33:340–345.

Copyright: S. Karger AG, Basel 2000. Reproduced with the permission of S. Karger AG, Basel. Further reproduction or distribution (electronic or otherwise) is prohibited without permission from the copyright holder.