
Incidence of cockroach allergy in atopic Italian children

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Background: Recent studies suggest that sensitization to cockroach allergens is common in urban areas and highlight the importance of cockroach allergens as a risk factor for asthma.

Objective: To elucidate the prevalence of cockroach allergy in atopic Italian children and to evaluate the correlation between cockroach allergens and other major indoor allergens.

Methods: Four hundred eighty two children with at least one positive skin test response to a common allergen and with personal history of atopic diseases, were investigated. A questionnaire was administered in order to obtain data on epidemiologic and clinical characteristics of the population. Skin tests to 24 common allergens (including extracts of two cockroach species) were carried out and serum total and cockroach specific IgE were evaluated.

Results: 61/482 (12.7%) children had positive skin test to cockroach extracts. Among them the frequency of children living in urban areas was higher ($P < .05$). In addition, a significant correlation between results of skin tests to cockroach and mite allergens was observed ($P < .009$). No correlation between cockroach allergy and the clinical characteristics of the study population was found.

Conclusions: The results show that cockroach allergy affects a small portion of atopic Italian children and suggest that it is related with living in urban areas and with sensitization to other indoor allergens, such as dust mite.

Ann Allergy Asthma Immunol 1999;83:167-171.

INTRODUCTION

Recent studies have highlighted the clinical relevance of cockroach (CR) hypersensitivity in allergic subjects, in particular those living in urban areas and in crowded multifamily dwellings.¹⁻⁸ In USA and Europe the most common CR species are the German (*Blattella germanica*) and the American (*Periplaneta americana*) CR.⁹⁻¹³

It is known that CR components such as body parts and feces disintegrate and become incorporated into respirable house dust acting as inhalant allergens.¹⁴

In the USA almost 50% of urban atopic population, belonging to a particular subgroup (overall poor, Hispanic or black), have positive skin prick tests (SPTs) to CR allergens.¹⁵ In addition, it was reported that asthmatic patients who are CR positive (CR+) are sicker and more steroid-dependent than CR negative (CR-) subjects.⁷

So far, few data have been reported about the prevalence of CR hypersensitivity in countries different from USA and the study populations were mainly represented by adult patients. In this paper we investigated the prevalence of CR allergy in a population of atopic Italian children.

MATERIALS AND METHODS

Patients

We recruited 482 children (aged 10 to 192 months; median 99 months) consecutively referred to our Unit (Unit of Allergy and Clinical Immunology, De-

partment of Pediatrics, University of Florence, Italy) by primary care physicians for respiratory (asthma, rhinoconjunctivitis) and/or dermatologic (urticaria, atopic dermatitis) disorders related to allergy. Only patients with confirmed diagnosis of atopic diseases were included in the study.

All subjects were skin prick test (SPT) positive to at least one of the tested allergens. A questionnaire addressing familial and personal history of atopic diseases, age at the onset of atopic disease, place of residence (rural or urban), housing characteristics (age of building older or less than 50 years, presence of pets, presence of smokers in the residence) and history of previous admissions in hospital for asthma or other allergy-related disorders (urticaria-angioedema, severe dermatitis), was used.

At the time of evaluation all the subjects were healthy and had not assumed drugs interfering with the skin testing for at least 15 days.¹⁶ The parents gave their informed consent to their children's participation.

Skin Testing

Skin testing technique, nature of allergens and controls, allergen dilution and reaction grading have been described previously.¹⁷ A positive skin test was defined according to the recommendations of European Academy of Allergy and Immunology.¹⁸ The average diameter of each wheal was established by measuring the longest diameter and the diameter perpendicular to it. Positivity was rated 4+ in the presence of a wheal double the size of the wheal induced by histamine, 3+ in the presence of a wheal of the same diameter as the wheal induced by histamine, and 2+ if the average diameter was half that of the wheal induced by

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Received for publication December 17, 1997.

Accepted for publication in revised form March 1, 1999.

histamine. Only wheals 2+ or more were considered positive. The following allergens were tested: *Dermatophagoides pteronyssinus* and *D. farinae*, skin derivatives of cat and dog, molds (*Alternaria alternata*, *Cladosporium herbarium*, *Penicillium notatum*, and *Aspergillus fumigatus*)⁶ pollen of grasses, weeds (*Parietaria officinalis*, *Artemisia vulgaris*, and *Taraxacum officinalis*), trees (*Olea europea* and *Cupressus sempervirens*), and eight food allergens. In addition all subjects were prick skin tested with extract of American and German CR (Lofarma, Milan, Italy). Each allergen was tested at 1/20 (wt/vol) dilution. Histamine 10 mg/mL was included as positive control.

Total IgE and Cockroach-Specific IgE Antibodies

Total IgE and levels of specific IgE to American and German CR were determined in 440/482 (91.3%) children by a radioimmunoassay technique (PRIST and RAST, respectively, Pharmacia Diagnostics AB, Uppsala) according to the test procedure instructions. Total IgE levels were calculated as IU/mL, whereas CR-specific IgE were expressed as a percentage of total counts added.¹⁹

Statistical Analysis

Ages were expressed as median and range, and differences were calculated by the non-parametric Mann-Whitney's test. Because serum IgE levels vary according to age, differences were evaluated by Student's *t* test on means $\pm$ SD of z-scores. Z-scores were calculated using normal values according to age previously obtained in our laboratory as reference.¹⁷ Chi-square and Fisher's exact test were employed for differences between proportions. Probabilities of developing asthma over time were calculated by Kaplan-Meier product-limit method and the differences in curves were tested by the non-parametric Cox-Mantel test.

RESULTS

Sixty-one out of 482 children studied (12.7%) had positive SPT responses to

CR allergens; among them 36 (59%) were positive to American CR, 9 (14.8%) to German CR, and 16 (26.2%) to both the species. The age and gender distribution of CR+ children are shown in Table 1. The percentage of CR+ subjects increased with age up to 8 years, thereafter it stabilized around 15%.

The number of children with positive family history of atopic diseases was almost the same among CR+ and CR−, 33/61 (54%) and 210/421 (50%) respectively. Analysis of environmental data showed no differences in the housing characteristics (age of building older or less than 50 years, presence of pets, presence of smokers in the residence), whereas the frequency of children living in urban areas was significantly higher ($P < .05$) among CR+ (45/61 = 73.8%) than among CR− (255/421 = 60.5%). On the other hand when the data were analyzed on the basis of urban versus suburban location of the individuals, there was no significant difference in the housing characteristics (including the age of house building), rate of asthma (66% and 67.3% in urban and suburban children, respectively), and sensitivity to indoor allergens (including mite: 56.6% and 55.6% in urban and suburban children, respectively).

An equal distribution of respiratory and dermatologic manifestations was found in the two groups (Fig 1). The number of missing school days, nights with lost sleep and days of wheezing, was not different between CR+ and CR− children (data not shown). Sim-

ilarly no significant differences were observed in the history of previous admissions in hospital between CR+ (14/61) and CR− (86/421) children. The time of onset of atopic symptoms was very similar: 36 months and 42 months in CR+ and CR−, respectively.

When we considered only the subpopulation of patients affected by asthma (321/482), the onset of asthma was 28 ± 4 months and 35 ± 2 months in CR+ and CR− subjects, respectively. Using the Kaplan-Meier product-limit method, we observed that the onset of asthma was earlier in CR+ than in CR− subjects, but without significant differences (data not shown). The prevalent skin test positivities were to grass pollen (67.2%), *Dermatophagoides* (56.2%), tree pollens (40.4%), *Parietaria officinalis* (30.7%), *Artemisia* (29.2%), cat dander (27.8%), and molds (23.2%).

A statistically significant association was found between positive SPT responses to CR allergens and *D. pteronyssinus* ($P < .009$) and *D. farinae* ($P < .03$) (Table 2).

In contrast, no relationship between hypersensitivity to CR allergens, molds and cat was found (Table 2). Similarly, no significant difference between CR+ and CR− patients in the prevalence of positive SPTs to the other tested inhalant and food allergens was observed (data not shown).

Total serum IgE was evaluated in 55/61 CR+ and in 385/421 CR− children and the IgE level z-score (mean $\pm$ SD) resulted equal in the two groups. Specific IgE to American and/or German CR was found in 40/55 CR+ children (72.7%).

DISCUSSION

The prevalence of cockroach allergy, defined by skin tests and/or blood tests (RAST), varies widely in different countries^{20–22} and from study to study but is usually high.^{7,23}

Prevalence of cockroach hypersensitivity among atopic children in our study was equal to 12.7% (positive skin test results); this prevalence is slightly lower than that found in other

Table 1. Age and Sex Distribution of Cockroach Positive Children

	Atopic Population (N = 482)	CR Positive (N = 61)
Gender		
Males	311	43
Females	171	18
Age (mo)	n	%
0–48	48	3 6.3
48–96	174	19 11.0
96–144	83	28 15.3
144–192	78	11 14.1

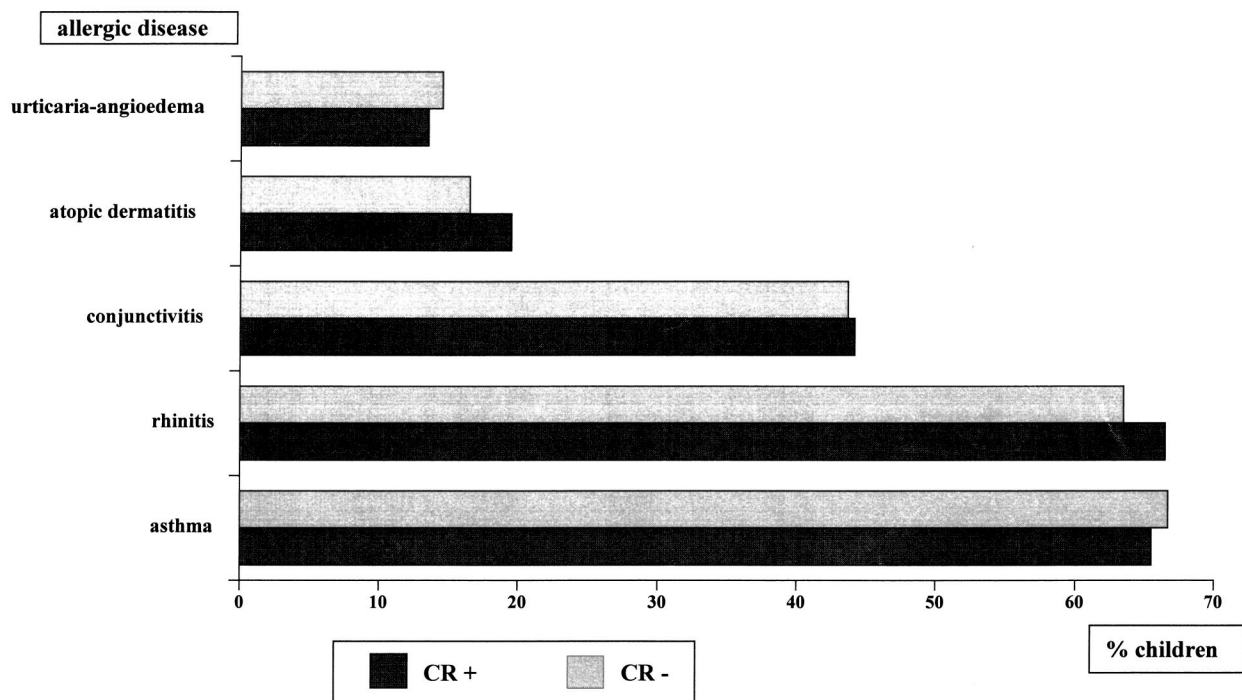


Figure 1. Prevalence of atopic diseases in cockroach (CR) positive (n = 61) and CR negative (n = 421) children. Data are expressed as percentage of children affected by different allergic diseases.

Table 2. Relationship Between SPT* Responses to Cockroach (*Blattella germanica* and/or *Periplaneta americana*) and Other Indoor Allergens (*D. pteronyssinus*, *D. farinae*, molds and cat)

SPT Response to Cockroach	Positive SPT Response			
	Dpt† (%)	Dfa‡ (%)	Mold (%)	Cat (%)
Negative (n = 421)	53.9	52.2	23.5	28.0
Positive (n = 61)	72.1	67.2	21.3	26.2
Significance	$P < .009$	$P < .03$	NS§	NS

* SPT = skin prick tests.

† Dpt = *Dermatophagoides pteronyssinus*.

‡ Dfa = *Dermatophagoides farinae*.

§ NS = not significant.

European studies.^{11–13,24} Very recently, however, a multicenter study performed in Italy on adults showed a prevalence of sensitization to CR allergens corresponding to 13%.²⁵ Comparing this finding with our results, we suggest that in our areas CR allergy starts in early childhood, but it stabilized with age.

It may seem surprising that sensitization to American CR was more common compared with German CR, especially considering that the former species is rare in Southern Europe.¹¹

It is well known, however, that a large extent of cross-reactivity exists among different CR species.^{26,27} In this context, the high rate of sensitization to American CR may actually be due to a cross-reactive response to other CR species commonly found in Italy, such as *Blattella orientalis*. Many factors such as the geographic area, the place of residence, the socio-economic status and the living-habits may play an important role in the development of sensitization to CR allergens. In the study population the number of children liv-

ing in urban area was significantly higher among CR+ patients.

A number of reports showed a causal relationship between CR allergy and asthma.²⁸ In our study only 12.5% (40/321) of asthmatic patients had positive SPT to CR derivatives and considering the age of onset of asthma, we did not observe any significant difference among CR+ and CR- subjects.

It is known that indoor allergens such as *Dermatophagoides* and house dust play an important role in the pathogenesis of childhood asthma and a prospective study suggested that exposure of infants to high levels of indoor allergens could lead to earlier onset of asthma.^{28,29} CR antigens are a major component of indoor allergens especially in patients of lower socio-economic status and may be involved in the etiology of house dust allergy.^{6,14,30–33}

Since CR+ children had in more than 70% of cases positive SPT response to *Dermatophagoides* allergens, the clinical effects of CR sensitization are very likely the effect of other more

dominant allergens. In fact, we found a positive correlation between positive SPTs response to *Dermatophagoides* (*pteronysinus* and *farinae*) and CR allergens.

The rationale for a high concordance of sensitization to CR and *Dermatophagoides* is unclear. Although more information about RAST inhibition experiments are needed, cross-reactivity between mite and CR allergens cannot be ruled out.

Positive correlation found between SPTs with CR, mite, mosquito larvae, and shrimp are in favor of this hypothesis. Furthermore, Witteman et al³⁴ identified tropomyosin as a cross-reactive allergen among members of the classes of Crustacea, Arachnida (*Dermatophagoides pteronyssinus*) and Insecta (chironomid, mosquito and *Blattella germanica*). Recently, Crespo et al³⁵ showed cross-reactivity of IgE-binding components between boiled Atlantic shrimp and German CR.

On the other hand, several studies suggested the possibility that *Dermatophagoides* and cockroaches commonly coexist in the same environment and in houses without apparent CR, the levels of CR allergens might be sufficient to induce a sensitization in atopic patients.²⁴

In this context, the observation that in this study the sensitivity to CR allergens is higher in urban children compared with rural, whereas no difference in mite sensitivity was observed between the two groups, suggests that the CR SPT positivities are not uniquely due to cross-reactivity with mite antigens.

In spite of the lack of evidence of CR infestations in the homes in Florence, it is likely that the children living in inner-city are more exposed to CR allergens. In fact, according to published studies, CR allergy is predominantly a disorder of individuals living in the inner-cities where the CR infestation is more common.^{36,37}

Whatever is the true hypothesis, it seems to us that CR allergy affects a small number of atopic patients, but together with other indoor allergens may play a role in the induction of

respiratory symptoms. Thus, the addition of CR extract to standard SPT panels might be considered as tool to better individuate the allergen/s responsible of allergic diseases.

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