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Cockroach-specific IgE antibodies in allergy

L. YMAN¹, I. HOLMQUIST¹, R. PAGANELLI²

SUMMARY

The prevalence of IgE antibodies to cockroach is high but varies with climate and housing conditions, from 0 % in a dry, high altitude region to 70 % in asthmatic urban populations. Several cockroach species are widely distributed and still expanding by accidental introduction to new areas. Common genera have been shown to share allergens but also to contain genus- and possibly species-specific allergenic epitopes. Similar high correlations between IgE antibody concentrations to *Blattella* and *Periplaneta* have been observed in Japan and in Italy. A study on Japanese asthma patients showed high prevalence of IgE antibodies also to other insects, like chironomid midges (flies) and moth (butterflies). A subgroup of the patients detected allergens shared with cockroach. A similar situation was observed in Italian patients where high correlation was seen between cockroach, common earwig, and sowbug, a widespread landliving crustacean. No relations were observed between cockroach and house dust mite. The relative importance of cockroach is bound to vary between regions depending not only on the exposure to cockroaches but also on the exposure to other arthropod allergens. Conclusions from regional studies may not necessarily have global relevance and further studies on potential constituents of inhaled dusts and their contribution to allergic disease can be expected to give important information improving diagnosis and management of indoor allergy.

KEY-WORDS: IgE. – Allergy. – Cockroach. – Insect. – Arthropod.

RÉSUMÉ

Anticorps IgE spécifiques des blattes en allergie. – La prévalence des anticorps IgE aux blattes est élevée mais variable selon le climat et les conditions de l'habitat, de 0 % dans une région sèche en altitude jusqu'à 70 % dans des populations urbaines d'asthmatiques. Plusieurs espèces de blattes sont largement répandues et continuent à se propager par introduction accidentelle dans de nouvelles zones. On a montré que les genres communs ont les mêmes allergènes, mais contiennent aussi des épitopes allergéniques spécifiques du genre - et peut-être de l'espèce. On a observé au Japon et en Italie de grandes similitudes entre les concentrations d'anticorps IgE pour *Blattella* et *Periplaneta*. Une étude sur des asthmatiques japonais a montré aussi une haute prévalence d'anticorps IgE contre d'autres insectes comme les moucheron chironomides et les papillons nocturnes. On a détecté, dans un sous-groupe de patients, des allergènes communs avec les blattes. Une situation analogue a été observée en Italie où de fortes corrélations ont été constatées entre les blattes, les perce-oreilles communs, et les «sowbugs», crustacé terrestre répandu. Aucune parenté n'a pu être mise en évidence entre les blattes et l'acarien de la poussière de maison : l'importance relative des blattes varie nécessairement selon les régions, en fonction, non seulement de l'exposition aux allergènes de blattes, mais aussi d'autres arthropodes. Les conclusions d'une étude régionale ne peuvent constituer une référence générale et de nouvelles études sur les composants potentiels des poussières inhalées et sur leur contribution aux maladies allergiques devraient aboutir à des connaissances importantes, permettant d'améliorer le diagnostic et la thérapeutique de l'allergie domestique.

MOTS-CLÉS: IgE. – Allergie. – Blatte. – Insecte. – Arthropode.

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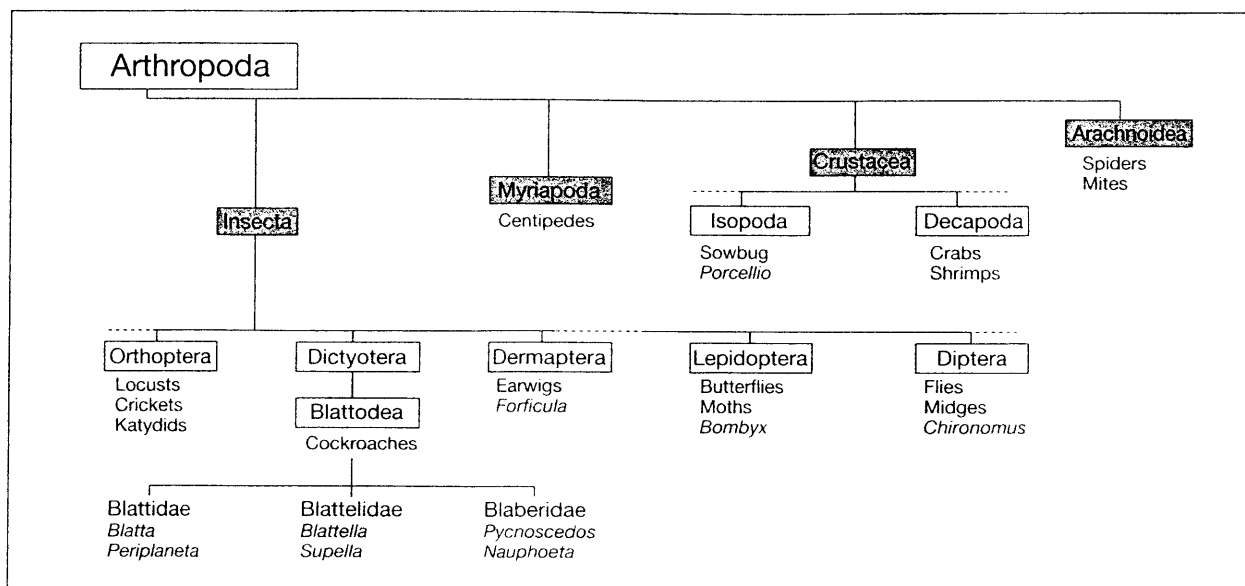


Fig. 1. - Summary of the relations between some common arthropods.

Indoor allergens are frequently involved in the appearance of perennial and periodical allergic symptoms. The roles of mites and animal epithelia as house dust allergens are well documented and testing with house dust extracts is slowly being replaced by measurement of sensitization to defined allergens emanating from standardized sources. Although allergy to insects, and particularly to cockroach, is well documented since 1964 [9], it is only recently that their importance as triggers of allergy has been fully recognized. Insects are arthropods with an external skeleton. Lobsters, centipedes and house dust mites are other members of this large animal group (fig. 1). Several of the 20 orders of insects include indoor or outdoor pests potentially contributing to the allergenicity of dusts on general or local level.

IgE antibodies to cockroach were demonstrated by Morita *et al.* in 1975 [30] and have been measured routinely since almost 20 years. The data generated around the world have contributed to the understanding of the importance and the complexity of this important cause of asthmatic disease.

The distribution of insects in the world differs with geography, climates and cultures but many, including cockroaches, are widespread and are still accidentally introduced into new areas.

There is a clear relation between the density of insects and the prevalence of sensitization in asthmatic patients.

This presentation discusses recent data on the role and distribution of IgE antibodies to allergens from cockroaches and related arthropods and reports some new results from studies with Pharmacia CAP System™ and UniCAP®.

Cockroaches discussed

<i>Blatta orientalis</i>	Oriental
<i>Blattella asahinai</i>	Asian
<i>Blattella germanica</i>	German
<i>Nauphoeta cinerea</i>	Lobster
<i>Periplaneta americana</i>	American
<i>Periplaneta australasiae</i>	Australian
<i>Periplaneta brunnea</i>	Brown
<i>Periplaneta fuliginosa</i>	Smokey brown
<i>Pycnoscelus surinamensis</i>	Surinam
<i>Supella longipalpa</i>	Brownbanded

Other arthropods

<i>Bombyx mori</i>	Silk moth
<i>Chironomus yoshimatsui</i>	Midge
<i>Forficula spp.</i>	Earwigs
<i>Porcellio spp.</i>	Sowbugs (woodlice)
<i>Dermatophagoides pteronyssinus</i>	House dust mite

QUANTITATIVE MEASUREMENTS OF IGE ANTIBODIES

Specific IgE antibodies in serum were, unless otherwise stated, measured with Pharmacia CAP System or UniCAP [36]. Prototype ImmunoCAP

reagents were made for *Periplaneta fuliginosa*, *P. americana*, *Blatta orientalis*, *Forficula* and *Porcellio*. Other insects, ie *Blattella germanica*, and all other reagents were commercial material (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden).

ALLERGENIC SIMILARITIES AND DIFFERENCES BETWEEN COCKROACH GENERA OR SPECIES

Studying asthmatic subjects from two North American cities, Kang *et al.* [22] found IgE antibodies to 2-12 allergen components of *P. americana*, *B. germanica* and *Blatta orientalis*. Data suggested presence of at least one common allergen detected by most patients. Cockroach sensitivity seemed to be a more common cause of asthma in one of the cities (Chicago). Antibodies to *P. americana* were the least prevalent although all three species were considered common in both locations.

Similar results were obtained in a skin test study on 46 atopic asthmatics from the New Orleans area showing that 22/38 cockroach sensitive patients reacted to both *P. americana* and *Blattella germanica*. RAST inhibition confirmed presence of common allergens in bodies and feces of the two species [29].

Helm *et al.* [17] found IgE antibodies to 8 allergens (18-92 kD) of *B. germanica* and demonstrated high degree of cross-reactivity to *B. asahinai*, a close relative to *B. germanica*, recently introduced into Florida. The allergenic relation between the two *Blattella* species was stronger than between the genera *Blattella*, *Periplaneta*, and *Blatta*.

Presence of common as well as species/genus-specific allergens in the three genera was also suggested by the results of immunoblotting studies on 16 patients showing heterogenous IgE reactivity to 20 components in the molecular weight range 15-260 kD [45].

An additional species of *Periplaneta* (*P. fuliginosa*) is commonly found in Japan. The prevalence of specific IgE antibodies (Pharmacia CAP System) in Japanese asthmatic children was 16 %, the same as to *B. germanica* [35]. The measured IgE antibody concentrations indicate a close relationship between the allergens of the two species (fig. 2).

Antigenic relationship between cockroaches and other insects, like beetles, moths, chironomid midges and silverfish, have been proposed [2, 6, 37, 52]. Cockroach allergens do not seem to cross-react with house dust mites (*Dermatophagoides*) to any significant extent [21, 35, 55]. Triopomyosin,

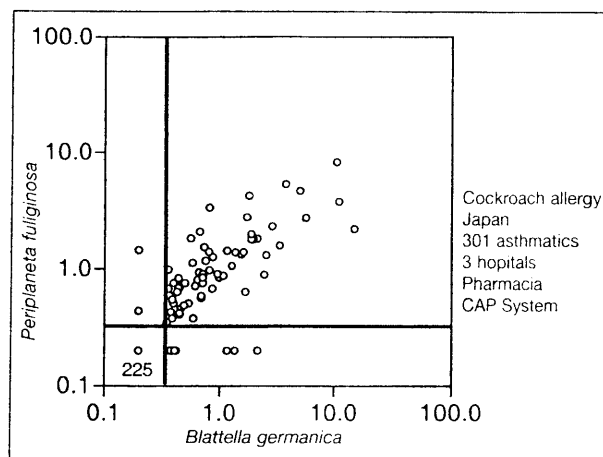


Fig. 2. - Specific IgE antibodies to *Blattella* and *Periplaneta* in Japanese asthmatic patients (Pharmacia CAP System). The prevalence was 25 %. Specimens from Toyama Red Cross Hospital (Dr G. Murakami), National Institute of Health (Dr M. Sakaguchi), and National Sagamiyara Hospital (Dr H. Yasueda).

a muscle protein, has been shown to carry epitopes common to crustaceans, mollusks, and insects [12, 28]. However, an immunoassay for shrimp tropomyosin was unable to detect any counterpart in oyster, cockroach or house dust mite [20].

IGE ANTIBODIES TO DEFINED ALLERGENIC PROTEINS

Cockroach allergens seem to emanate from the intestinal tract and other internal organs [55]. The whole insect body is an adequate allergen source.

About half of an American patients group skin reactive with whole body extracts of American or German cockroach were skin test positive to a major cross-reactive allergen [44]. Although the homologous proteins of the two species are very closely related they were shown to contain also epitopes that were not shared. The allergens, Per a 1 and Bla g 1, were recognized by 100 % and 70 %, respectively, of the patients.

Human IgE antibodies binding to Bla g 1 (25 kD) from *Blattella germanica*, considered as the major cockroach species in USA, were strongly reactive with allergens from the related species *B. asahinai* and did also show cross-reactivity to members of the genera *Periplaneta*, *Supella*, *Leucophea*, and *Blatta* [38].

Bla g 2, a digestive tract enzyme (36 kD) of *Blattella*, was much less cross-reactive [38] and was

not detected in *Periplaneta* [3]. IgE antibodies to Bla g 1 and Bla g 2 were detected in 30 % and 58 %, respectively of 106 asthmatic cockroach allergic patients living in different areas of North America. Skin test reactivity correlated with the serum IgE antibody.

Blattella-specific IgE antibodies were found in 37/37 asthmatic patients (USA) with positive skin test results to cockroach. Immunoblotting analysis of the sera showed binding to 23 allergens in the range 11 kD to > 100 kD. Four components with molecular weights higher than 40 kD showed reactivity with 50-80 % of the subjects tested [34]. Allergens prepared from whole body and feces showed equivalent patterns of IgE antibody reactivity.

Also Bla g 4 (21 kD) is a *Blattella*-specific allergen. The prevalence of serum IgE antibody in asthmatic cockroach allergic patients (USA) was about 50 % [4].

The same seems to be true for Bla g 5 (23 kD) which, despite its general function as a glutathion

S-transferase (GST) and its sequence relations to GST of other insects, have not been found in *Periplaneta* [5]. The prevalence of Bla g 5-specific IgE antibodies in cockroach-allergic patients (USA) was 70 %.

Per a 3 (72-78 kD), isolated and cloned from *Periplaneta americana*, was found to be a major cockroach allergen in the central parts of Taiwan, and one of nine *P. americana* allergens, but did not have an IgE binding counterpart in *Blattella* [53, 54].

IGE ANTIBODY IN ALLERGIC DISEASE

Recent studies on the prevalence of IgE antibodies to cockroach (table I) confirm data generated by in vivo testing. The influence of climate and socioeconomic status of the patients is clear. The prevalence was 0 (zero) % in asthmatic patients in Los Alamos, New Mexico, USA, where the dry conditions at high altitude prevent cockroach and mite infestation and where asthma instead is cau-

Tableau I. - Prevalence of cockroach sensitization.

Country	Prevalence (%)	Patient selection	Allergy test	Reference
America				
USA, 8 inner city areas	37	Asthma, child	Skin test	40
USA, San Diego Cal	22	Asthma, child	Skin test	11
USA, Baltimore Md	41	Asthma, child	Skin test	42
USA, Louisville Ky	37	Asthma	Skin test	16
USA, Chigago Ill	48	Asthma	Skin test	23
USA, New York NY	68	Asthma	Phadebas RAST	46
USA, Shreveport La	70	Asthma	Skin test	29
USA, Los Alamos NM	0	Asthma, child	Pharmacia CAP System	19
Mexico	27	Allergy	Skin test	51
Dominican Republic	16	Asthma/rhinitis, child	Skin test	7
Brazil	31	Atopic	Skin test	8
Europe				
Portugal	17	Atopic	Skin test	13
Spain	26	Asthma/rhinitis	Skin test	43
Italy	13	Asthma/rhinitis	Skin test	39
France	24	Respiratory symptoms	Pharmacia CAP System	14
France	5	General population	Pharmacia CAP System	10
The Netherlands	16	Respiratory symptoms, child	Pharmacia CAP System	50
Switzerland	6	Asthma/rhinitis, non-season	Phadezym RAST	31
Africa				
Morocco	25	Allergy	Skin test	1
Asia				
Turkey	26	Asthma	Skin test	3
Saudi Arabia	35	Asthma/rhinitis	Skin test	47
India	35	Asthma/rhinitis	Skin test	48
Thailand	44	Asthma, child	Skin test	26
Malaysia	21	Suspected allergic rhinitis	Skin test	18
China (south east)	73	Atopic	Skin test	27
Taiwan	36	Asthma	Pharmacia CAP System	49
South Korea	12	General population	Skin test	24
Japan	16	Asthma	Pharmacia CAP System	35, 41

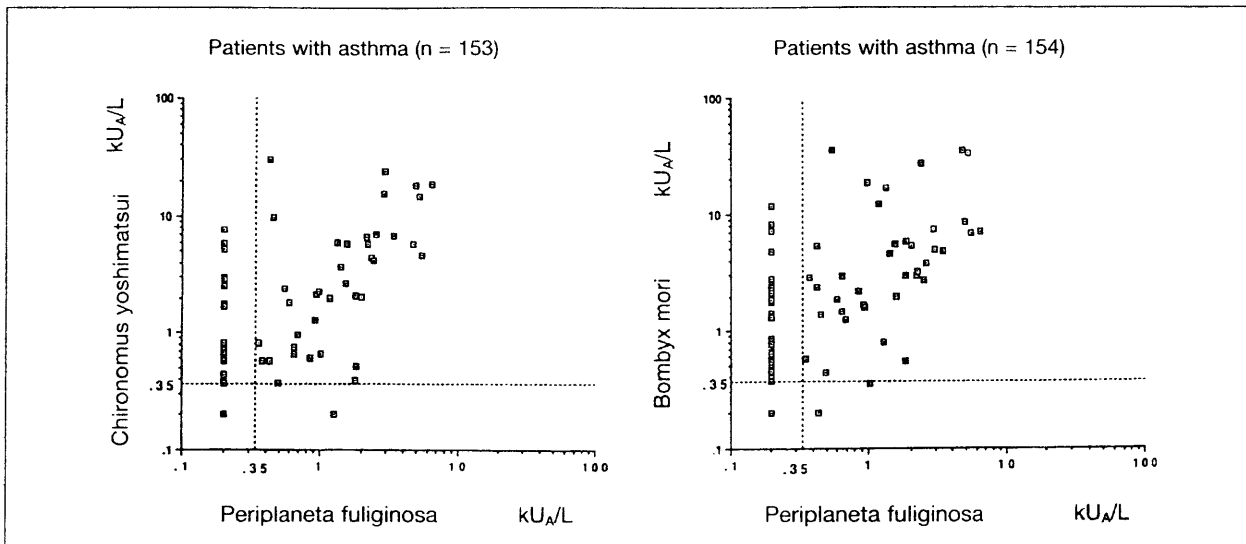


Fig. 3. - Specific IgE antibodies to midge and moth wings compared to IgE antibodies to cockroach in Japanese asthma patients (Pharmacia CAP System). Specimens from Tokyo University (Dr K. Ito), Toyama Red Cross Hospital (Dr G. Murakami), and National Sagami Hospital (Dr H. Yasueda).

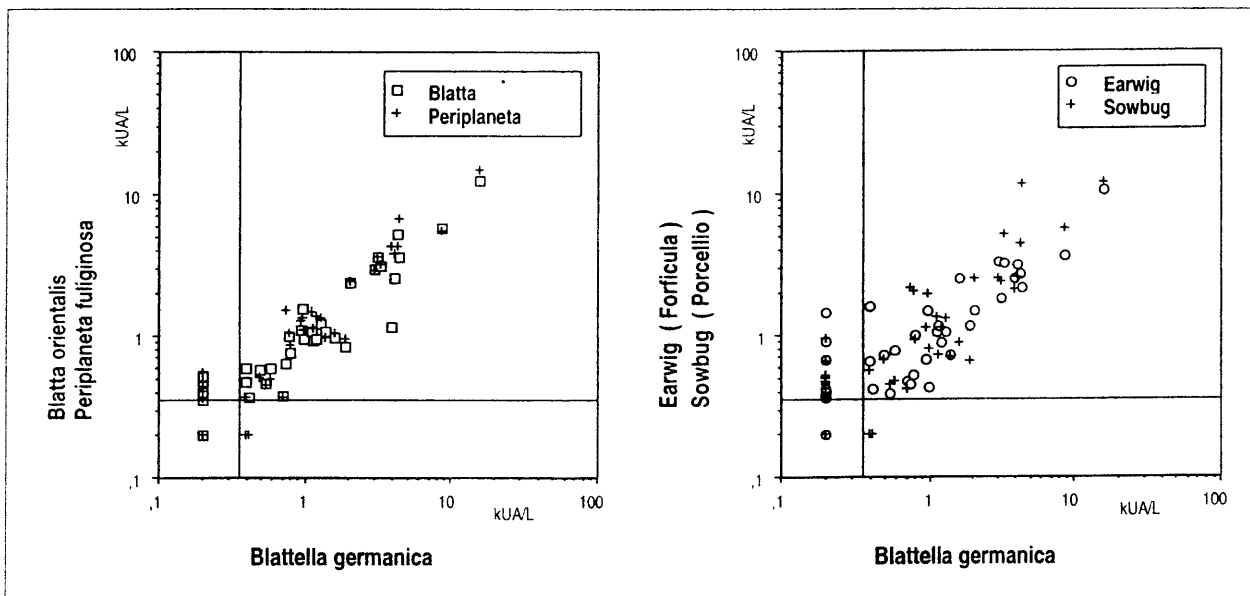


Fig. 4. - Specific IgE antibodies against selected cockroaches, another insect and a crustacean in 159 consecutive patients with suspected allergy visiting an allergy clinic in Rome, Italy (R. Paganelli).

sed by cats (62 %) and dogs (67 %) kept indoor [19]. On the other hand, the prevalence was 68 % in New York City in an asthmatic inner-city population where the prevalence of IgE antibodies to mite, dog and cat was only 24 %, 28 %, and 38 %, respectively [46]. Despite the differences in selection criteria, allergen quality, and test techniques, the data summarized in table I provide an overview of the situation in the areas represented.

OBSERVATIONS ON REGIONAL DIFFERENCES AND SIMILARITIES

IgE antibodies to cockroach and other insects in Japan

Already the very early studies suggested that insects as a group may play a role in asthma [30]. Later investigations have confirmed that cockroach is a major sensitizer in asthma and that the

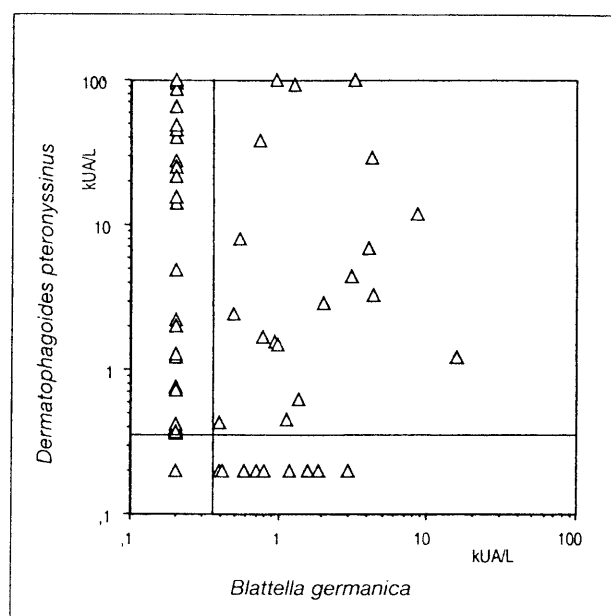


Fig. 5. - Comparison of IgE antibody concentrations against cockroach and house dust mite in 159 consecutive patients with suspected allergy visiting an allergy clinic in Rome, Italy (R. Paganelli).

majority of the patients studied react to *Periplaneta* as well as *Blattella* (fig. 2). However, they have also shown that IgE antibodies to silk worm wings and to chironomid midges are about twice as common as antibodies to cockroach in Japanese asthmatics [33]. The results of a multicenter study on the role of insects in asthma (fig. 3) suggest species-specific sensitization by inhaled allergens from midges and moths but also cross-reactivity between these [25] as well as crossreactivity with cockroach detected by a subgroup of the patients. For this Japanese patient population the cockroach is an important allergen but does not seem to be the major sensitizer.

IgE antibodies to cockroach and other arthropods in Italy

Preliminary data (UniCAP) from an investigation of a group of Italian patients (fig. 4 and 5) confirmed the extensive cross-reactivity between three genera of cockroaches but did also identify cases with species-specific sensitivity. Testing the same subjects with allergens prepared from earwig, a related insect widely spread around the world, and sowbug also called woodlouse, a common land living crustacean, supports the observations from Japan regarding the importance of additional insects and suggests very complex sensitization patterns involving also inhaled and possibly ingested crustacean allergens [15]. In this group there is no obvious correlation between the IgE antibody concentrations measured with cockroach and house dust mite (fig. 5).

CONCLUSIONS

Cockroach specific IgE antibodies are frequently found in patients with asthma and other allergic conditions all around the world. Data suggest good agreement between IgE antibody measurements, in vivo tests, and clinical sensitivity. Variations observed can be ascribed to variation of methods and allergen preparations. Clinical sensitivity to cockroach is not easy to define in a fully specific way with the overlap that exists in the form of cross-reactivity and multisensitization, probably also to insect sources not yet defined. The relative importance of cockroach is bound to vary between regions depending not only on the exposure to cockroaches but also on the exposure to other arthropod allergens. Conclusions from regional studies may not necessarily have global relevance and further studies on potential constituents of inhaled dusts and their contribution to allergic disease can be expected to give important information improving diagnosis and management of indoor allergy.

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