

# Cockroach Allergen Biology and Mitigation in the Indoor Environment

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## Key Words

Blattella germanica, insect allergy, asthma, indoor air, *Blattella germanica*

## Abstract

For nearly a half century, cockroaches have been recognized as a major cause of asthma morbidity in the urban, inner-city environment. Several cockroach-produced allergens have been identified and characterized, and a few have been produced as recombinant proteins. Recent research has moved beyond clinical, patient-based investigations to a more entomological perspective that addresses the production, physiological regulation, and developmental expression of cockroach allergens, thus providing insight into their functional biology and their relationship to current cockroach control strategies. Although successful removal of cockroach allergens from the infested environment has been difficult to accomplish with remedial sanitation, large-scale reductions in cockroach allergens below clinically relevant thresholds have recently been realized through suppression of cockroach populations. Here we review the current understanding of cockroach allergen biology and the demographics associated with human exposure and sensitization. We also critically evaluate allergen mitigation studies from an entomological perspective, highlighting disparities between successful and failed attempts to lessen the cockroach allergen burden in homes.

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**Atopic:** genetically predisposed to develop allergic diseases, such as asthma, allergic rhinitis, and dermatitis

**Allergen:** any substance that produces an allergic response by sensitized individuals

**Isoallergen:** allergens derived from a single species having similar molecular size, identical function, and  $\geq 67\%$  amino acid sequence identity

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## INTRODUCTION: ASTHMA AND INDOOR ALLERGENS

Asthma is a multifactorial, chronic lung disease generally defined as an inflammation and narrowing of small airways, resulting in variable airway obstruction and reduced airflow in or out of the lungs (95). In atopic individuals, bronchial inflammation leads to recurrent episodes of breathlessness, wheeze, cough, tightness or pain in the chest, and hyperresponsiveness to a variety of stimuli. Asthmatic events can vary in occurrence and severity from person to person. In the United States, asthma affects approximately 30 million people, 9 million of whom are children under the age of 18 (35), and it is one of the most costly diseases, estimated at \$12.7 billion annually (143).

Asthma has been known for thousands of years, dating back to Hippocrates' Corpus Hippocraticum (85a), yet its prevalence has increased dramatically over the past 40 years (100) ostensibly as a result of changes in housing design and more time spent indoors, resulting in prolonged exposure to perennial allergens and other environmental triggers (77). The U.S. Institute of Medicine recently identified eight indoor agents involved in the development and/or exacerbation of asthma: cockroaches, dust mites, cats, dogs, respiratory syncytial virus, fungi, nitrogen dioxide, and environmental tobacco smoke (63). Approximately 43% of the U.S. population, aged 6 to 59, is allergic to at least one common indoor allergen, and 26% are sensitive to German cockroaches (*Blattella germanica* L.) (3).

## COCKROACH ALLERGENS

Cockroaches, first linked to allergic disease by Bernton & Brown in 1964 (17), are major sources of indoor allergens; exposure and sensitization to them is associated with the development of acute asthma morbidity (22, 47, 67, 68, 111). Although allergens have been identified in several cockroach species, only allergens from the German

and American cockroaches (*Periplaneta americana* L.) have been officially recognized and named according to World Health Organization/International Union of Immunological Societies (WHO/IUIS) nomenclature (64). Allergens are named according to their taxonomic source and an Arabic number that indicates the order of their identification for that species (70). Isoallergen variants, which are similar allergens from a single species and are often observed in cDNA clones, show close to 100% homology and are referred to by suffixes of a period followed by four Arabic numbers. The first two numbers refer to the isoallergen and the second two refer to the variant. Therefore, Bla g 1.01 refers to isoallergen 1 of *Blattella germanica* allergen 1 (Bla g 1). An official list of allergens is maintained by the IUIS Allergen Nomenclature Sub-Committee in an online database (<http://www.allergen.org/>). Discussion of the molecular biology, sources, and diagnosis of cockroach allergens can be found in several recent review articles (7, 8, 10, 24, 103, 131).

Fewer than 1% of the >4000 described cockroach species worldwide are pestiferous to humans. The German and American cockroaches are economically and medically important synanthropic pests with worldwide distribution (20, 125). The German cockroach is intimately associated with human-built structures, especially in food-preparation areas. The American cockroach is usually a peridomestic pest, preferring warm, humid environments such as sewers, but also can be the predominant indoor cockroach pest in tropical regions. Pathogenic microbes have been isolated from these cockroach species (16, 20), and both species can mechanically vector microbes (75, 158), but there are no documented cases directly linking cockroaches as the definitive vector of any human or animal disease.

To date, six *B. germanica*-produced allergens have been identified and characterized, and aqueous extracts of several cockroach tissues, including the intestinal tract,

Malpighian tubules, ovaries, ootheca, exuvia, and feces, are allergenic to sensitized individuals (50, 94, 101, 110, 159). Seven *P. americana*-produced allergens have been identified and characterized.

### Bla g 1 and Per a 1

Nucleotide sequences of Bla g 1 isoallergens show 74%–95% homology to a previously described 4-kb nucleotide sequence, Bla g Bd90K (57, 105) (Table 1). Bla g 1 and Per a 1 have variable molecular weights (89, 101, 127), share 70%–72% amino acid sequence homology, and are antigenically cross-reactive; together they comprise a family of structurally and antigenically related Group 1 allergens that consist of several tandem repeats of approximately 100 amino acids (89, 105). Proteins cross-reacting with the Group 1 allergens have also been found in the smokybrown cockroach, *Periplaneta fuliginosa* (Serville), the oriental cockroach, *Blatta orientalis* L., and the brownbanded cockroach, *Supella longipalpa* (Fabricius) (113, 126). Bla g 1 contains two duplexes, each consisting of two consecutive amino acid repeats that share only 26%–29% homology; a single duplex comprises a distinct molecular unit of Bla g 1 (106). Despite proteolytic cleaving of Bla g 1 into multiple molecular forms, only one duplex is necessary for immunoglobulin E (IgE) binding to occur, suggesting that allergen integrity may not be essential for allergenicity.

Exposure to Bla g 1 is a strong risk factor for sensitivity to German cockroaches (38, 102), and approximately 30%–77% of cockroach-allergic individuals have detectable IgE antibodies to purified Bla g 1 extract or recombinant Bla g Bd90K, with as little as  $10^{-3}$  to  $10^{-4}$   $\mu\text{g ml}^{-1}$  resulting in positive skin reactivity (12, 57, 101, 127). Likewise, skin reactivity to natural Per a 1 and its isoallergens is also high, ranging from 55% to 93% in patients with confirmed sensitivity to American cockroach (142, 149, 154). Recently, Wu et al. (154) identified two linear epitopes in Per a 1.0104 involved in IgE binding; synthe-

sized peptides corresponding to the two epitopes reacted with 80% and 100% of atopic sera.

Bla g 1 is associated primarily with the cockroach alimentary tract, mainly the midgut, and Northern hybridization of various gut tissues demonstrated that Bla g 1 is produced only by midgut cells (50). Quantitative analyses of Bla g 1 mRNA expression and Bla g 1 protein levels in adult females showed that both are closely modulated in relation to the reproductive cycle of the female cockroach (51). Both peak in vitellogenic females 3 to 5 days after eclosion and decline considerably after day 5. Modulation of Bla g 1 production thus appears related to food intake, which also peaks around day 2–4. Bla g 1 titers plummet after day 5, as the female continues to provision her oocytes, produces an ootheca, and incubates the embryos for ~20 days. Bla g 1 levels remain low during this protracted gestation, as the female feeds little and only sporadically (34, 80, 96, 124, 128). The central role of food intake was demonstrated experimentally, as starvation arrested both reproduction and the cyclic modulation of gut Bla g 1 levels, whereas refed females resumed mRNA expression and Bla g 1 production (51). Thus, the production of Bla g 1 is upregulated by food intake or events associated with it.

Large amounts of Bla g 1 are excreted in cockroach feces. Feces production, in turn, follows closely the patterns of food consumption in *B. germanica*, and the Bla g 1 content of female feces follows a similar cyclic rise and fall associated with food intake and feces production (51). In general, females eat more and produce much more Bla g 1 than males do. Following oviposition, however, fecal Bla g 1 dramatically declines and remains low during pregnancy. Adult males, on the other hand, have no discrete feeding patterns, eat less than females do (34, 55), and produce nearly an order of magnitude less feces and Bla g 1 than females do (51).

Bla g 1 might serve at least two interesting physiological functions, both of which are

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IgE:  
immunoglobulin E

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**Table 1 Summary of cockroach allergens and isoallergens**

Allergen	MW (kDa)	cDNA size (bp)	Amino acids	IgE prevalence (%)	Protein family or deduced function	Accession no.	References
<i>Blattella germanica</i>							
Bla g 1	33–37	—	—	30–50	Digestion		12, 101, 127
Bla g 1.0101	46	1429	412	—	—	AF072219	105
Bla g 1.0102 <sup>a</sup>	90	4058	192	77	—	L47595	57
Bla g 1.0103	21	715	188	—	—	AF072221	105
Bla g 1.02	56	1791	492	—	—	AF072220	105
Bla g 2	36	1056	328	60	Inactive aspartic protease; digestion	U28863	12
Bla g 4	21	546	182	40–60	Lipocalin; reproduction	U40767	11
Bla g 5	23	1140	203	70	Glutathione S-transferase; detoxification	U92412	13
Bla g 6	25	580	38	14	Troponin C; muscle	—	8
Bla g 6.0101	—	—	—	—	—	DQ279092	59
Bla g 6.0201	—	—	—	—	—	DQ279093	59
Bla g 6.0301	—	—	—	—	—	DQ279094	59
Bla g 7	33	1115	284	16	Tropomyosin; muscle	AF260897	66
<i>Periplaneta americana</i>							
Per a 1	33–37	—	—	30–50	—		101, 127
Per a 1.0101	26	870	231	—	—	AF072222	89
Per a 1.0102	26	890	228	—	—	U78970	149
Per a 1.0103	45	1432	395	—	—	U69957	89
Per a 1.0104	31	1024	274	—	—	U69261	149
Per a 1.0105	13.8	579	124	—	—	AY259514	35a
Per a 1.02	51	1630	446	—	—	U69260	142
Per a 2 <sup>b</sup>	38	1056	351	53	Inactive aspartic protease; digestion	AY792947	97a
Per a 3	72	—	—	73–83	Arylphorin-like protein; storage		150, 151, 155
Per a 3.01	79	2418	685	—	—	L40818	151
Per a 3.0201	76	2274	631	—	—	L40820	151
Per a 3.0202	56	1410	470	—	—	L40819	153
Per a 3.0203	47	1179	393	—	—	L40821	153
Per a 4 <sup>b</sup>	—	552	183	—	—	AY792948	
Per a 5 <sup>b</sup>	—	651	216	—	—	AY792949	
Per a 6	17	456	151	—	Troponin C; muscle	AY792950	59
Per a 7	37	—	—	50	Tropomyosin; muscle	Y14854	15, 116
Per a 7.0101	33	855	284	—	—	Y14854	15
Per a 7.0102	33	1325	284	—	—	AF106961	116

<sup>a</sup>According to the WHO/IUIS nomenclature, Bla g Bd90K is now designated Bla g 1.0102.

<sup>b</sup>Not currently recognized by the WHO/IUIS.

associated with food intake. Pomes et al. (105) suggested that Bla g 1 is secreted from the midgut epithelium through the rough endoplasmic reticulum and that it could have a role in digestion. Bla g 1 shares 35%–40% deduced amino acid sequence identity with ANG12 of *Anopheles gambiae* (Giles) (accession no. Q17040) and AEG12 of *Aedes aegypti* (L.) (accession no. AY038041), both of which are produced in the midgut of the female mosquito and undergo temporal changes in expression relative to the acquisition of a blood meal (92). An alternative hypothesis is that Bla g 1 serves a structural rather than an enzymatic role in the midgut. Bla g 1 shares 37% amino acid sequence identity with the *Tenebrio molitor* cockroach allergen-like protein (accession no. AY327800), which, like AEG12 in a recent report (130), has been described as a microvillar membrane protein. This might account for the observation that the Bla g 1 concentration in feces is highest as feeding subsides. It suggests that microvilli might be sloughed off after large food boluses pass through the midgut. The function of Per a 1 is likely similar to that of Bla g 1, but it has not been investigated.

### Bla g 2 and Per a 2

Bla g 2 is an aspartic protease (Table 1) with sequence similarity to an *Ae. aegypti* lysosomal protease, *Drosophila melanogaster* aspartic protease, and an active human aspartic protease (12, 25, 104). Nevertheless, Bla g 2 lacks proteolytic activity, has critical amino acid substitutions around the catalytic residues, and resembles the pregnancy-associated glycoproteins of mammals in its primary structure (104). Unlike classical aspartic proteases, Bla g 2 has a zinc-binding site and five disulfide bridges that may contribute to its environmental stability and persistence (53, 155). Per a 2 also has been described as an inactive aspartic protease, but it shares only 44% amino acid sequence identity to Bla g 2 (97a). Similar to Bla g 1, the highest concentrations

of Bla g 2 are associated primarily with the alimentary tract (12), and it is also found in the feces, which is likely the source of environmental dissemination (61). A recent study suggests that exposure to or intake of boric acid, a slowly acting inorganic insecticide, may elevate Bla g 2 production in the German cockroach (157).

Bla g 2 is a potent allergen with a high prevalence of IgE among cockroach-allergic patients (12) (Table 1). Moreover, as little as 0.33  $\mu\text{g}$  Bla g 2  $\text{g}^{-1}$  of dust can induce an IgE response in allergic individuals (132).

### Per a 3

Unlike other known cockroach allergens, Per a 3 is a species-specific protein (150) (Table 1) with significant amino acid sequence identity to several insect arylphorin-type storage proteins, juvenile hormone-suppressible proteins, and arthropod hemocyanins (151). Per a 3 and its four isoallergens elicit high positive skin reactions in American cockroach-allergic individuals, ranging from 47% to 95% (150, 151, 153). Recently, Wu et al. (152) identified four IgE-binding epitopes from recombinant fragments of Per a 3.01 that bound 62%–87% of allergic sera.

### Bla g 4

Most animal allergens—including dog, cow, and horse epithelial allergens, and rat and mouse urinary allergens—are lipocalins (85). Lipocalins serve diverse roles in invertebrates, including nutritive (145), nitric oxide transport (14), colorant (45), and embryonic nervous system development (115). Korchi et al. (76) found a lipocalin-like cuticular surface protein secreted by the epidermis of the adult male tergal glands in the cockroach *Leucophaea maderae* (Lma-P22) and thought to be involved in sexual behavior. Although Bla g 4 (Table 1) shows low homology to Lma-P22 and other lipocalins that serve as pheromone transport proteins, sequence and structural

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**GST:** glutathione  
S-transferase

**HDM:** house dust  
mite

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similarities suggested that Bla g 4 might serve as a pheromone binding protein in the German cockroach (11, 25).

Fan et al. (43) reported, however, that Bla g 4 is produced only in the adult male accessory reproductive glands, structures responsible for supplying seminal fluids, structural and secretory materials for spermatophore formation (27, 49, 56), and, in the case of the uricose glands, storage and excretion of uric acid (93, 112). More specifically, Bla g 4 is produced in the conglobate gland and the apical utricles of the male reproductive system, packaged in the spermatophore, and transferred to the female's genital tract during copulation. Although the fate and function of Bla g 4 in females remains to be investigated, Bla g 4 immunoreactivity disappears from the mated female 24 h after mating, and a substantial amount of Bla g 4 remains in the discarded spermatophore, suggesting that Bla g 4 may be a component of the spermatophore and not of seminal secretions.

Conglobate gland proteins gradually increase following eclosion of adult male *B. germanica* (141). Bla g 4 undergoes a similar age-related increase in adult males between day 0 and day 8, after which it plateaus by day 14 (43). This age-related production of accessory gland proteins, including Bla g 4, is modulated by juvenile hormone (44, 99, 140, 141). Topical administration of juvenile hormone III to newly eclosed adult males causes significant increases in Bla g 4 levels by day 6 in both the conglobate gland and the utricles.

Production of Bla g 4 only by adult male *B. germanica*, and its subsequent excretion from females in the form of the expelled spermatophore after copulation, might at first suggest that Bla g 4 should be a less pervasive environmental allergen. However, serum IgE prevalence to Bla g 4 in cockroach-sensitized patients is high (11) (Table 1). It is not known whether greater human exposure to this protein is a result of the broad foraging range of adult male cockroaches or the environmental stability of Bla g 4.

## Bla g 5

Bla g 5 has been identified as a glutathione S-transferase (GST) (Table 1) on the basis of its ability to bind glutathione, 42%–45% amino acid sequence homology to GSTs of other insects, and 28% homology to the GST allergen, Der p 8, of the European house dust mite (HDM), *Dermatophagoides pteronyssinus* (Trouessart) (13). IgE antibody prevalence for Bla g 5 is high among cockroach-allergic patients (Table 1), with as little as 3 pg resulting in immediate positive response in skin tests (13). Three enzymatically active GST isoforms, one major (GST-1) and two minor (GST-2 and GST-3), isolated from insecticide-susceptible adult male *B. germanica* bind IgE antibody from serum of cockroach-allergic individuals (156). Amino acid sequence analysis showed that GST-1 and Bla g 5 share the same first 15 residues in the N-terminal region. Nevertheless, it will require complete sequence verification to determine whether GST-1 and Bla g 5 are indeed identical.

Future research into environmental Bla g 5 may affect pest management practices. GSTs are important detoxification enzymes linked to insecticide resistance in *B. germanica* (138, 139). Carbamate and organophosphorus insecticide resistance in *B. germanica*, resulting in elevated GST activity, might result in a disproportional accumulation of environmental Bla g 5 in homes infested with insecticide-resistant *B. germanica*.

## Bla g 6 and 7 and Per a 6 and 7

Bla g 6 and Per a 6 have been identified as troponin C (9, 59) (Table 1), a calcium-binding subunit of the troponin complex that regulates contraction in striated muscle. Despite its ubiquity, sensitization to Bla g 6 is only 14% among cockroach-allergic patients, suggesting a relatively minor role in allergic disease (59).

The deduced amino acid sequence of Bla g 7 (Table 1) has a high degree of similarity to tropomyosin from other invertebrates,

including 97% identity to the antigenically cross-reactive *P. americana* tropomyosin (Per a 7) (15, 66, 116). Furthermore, Per a 7 shares 99% identity with its homolog Per f 7 from *P. fuliginosa* (65). Monoclonal antibodies raised against HDM react to shrimp (*Crangon crangon* L.) (147) and cockroach tropomyosin Per a 7 (116), which in turn is cross-reactive with protein extracts of *B. germanica* and *Blatta orientalis*, as well as tropomyosin from another shrimp (*Pandalus borealis* Kroyer) (15). The tropomyosins are thus considered pan-allergens because they are cross-reactive in many invertebrates (109).

Nevertheless, IgE antibodies to Bla g 7 and Per a 7 exhibit substantially different reactivity among allergic individuals. Only 16% of sera from cockroach-allergic patients show positive IgE reactivity to Bla g 7 (66), suggesting that, like Bla g 6, it may not be a major allergen. IgE antibodies to Per a 7 have been detected in as many as 50% of persons allergic to cockroaches (116). Interestingly, only 16% of cockroach-sensitive patients with high prevalence of IgE to HDM had rPer a 7-reactive IgE (122). The same cohort of patients also exhibited a high prevalence of IgG to rPer a 7 in the absence of Per a 7-specific IgE, suggesting that simultaneous exposure to HDM and cockroach tropomyosin, not antigenic cross-reactivity, may explain cosensitization. A more detailed review of tropomyosin as a pan-allergen is given by Reese et al. (109).

### ***P. americana* Arginine Kinase**

An arginine kinase (pI 6.3 and a molecular mass of 40.57 kDa) was recently identified from an extract of *P. americana* (131a). IgE antibodies of all 25 tested cockroach-sensitive Thai patients reacted with the native protein in Western blots, suggesting that arginine kinases may be major cockroach allergens. Because these proteins are cross-reactive invertebrate pan-allergens, this recent finding should stimulate research on the *B. germanica* homolog.

## **ALLERGEN SAMPLING METHODOLOGY**

There are no standardized sampling procedures for environmental allergens, but three general approaches have been used: (a) vacuum sampling of settled dust, (b) sampling of airborne allergens, and (c) solvent-assisted wipe sampling of surfaces. Arthropod allergens are thought to act as aeroallergens, or inhaled allergens, and although they have been collected in air under undisturbed conditions (33), cockroach allergens usually depend on disturbance to become airborne (32, 90). Bla g 1 and Bla g 2 are carried principally by dust particles with a diameter >10  $\mu\text{m}$  and remain airborne for ~30 min after disturbance (32, 33). Airborne concentrations of allergens probably represent the best index of inhalant exposure, and airborne allergen sampling should therefore be pivotal in research and clinical efforts. However, few studies have utilized airborne allergen sampling, and only a few studies have used intranasal samplers and pumps to collect particulates (33, 58, 69, 90). Nonetheless, it appears that little to no correlation exists between airborne and settled dust sampling methods (69), clearly of concern because most studies use vacuum sampling of settled dust as proxy for assessing exposure.

In general, settled dust is sampled with a modified vacuum cleaner fitted with a reservoir for collecting dust. Dust samples are generally sieved to remove large particulates, extracted, and assayed by ELISA or similar methods. This method allows for the collection of large quantities of crude dust over a large surface area, as well as the ability to remove allergens embedded in carpets (54). The vacuuming equipment, supplies, and the time and area of sampling vary considerably among studies, and no single method appears superior to others (84). Settled dust may also be sampled by collecting dust that settles on open petri dishes (69).

Cockroach allergens have also been monitored using spatial swab sampling with cotton-tipped applicators (4, 21). The advantage over

## DEFINITION OF UNIT

U is unit and is an arbitrary designation, per detection assay manufacturer's calibration, for allergen measurement. There are as yet no national or international reference standards for cockroach allergens.

### Sensitization

**threshold:** level of environmental allergen that sensitizes atopic individuals to an environmental allergen

### Morbidity

**threshold:** level of environmental allergen causing the onset or exacerbation of asthmatic symptoms

**SES:** socioeconomic status

**NCICAS:** National Cooperative Inner-City Asthma Study

**ICAS:** Inner-City Asthma Study

other techniques is that swabbing does not require specialized equipment and allows for the detection of allergen in multiple locations over a smaller spatial area (4). However, this method has limited quantitative ability, greater sample variability, and collection efficiency that is sensitive to factors such as solubility of the allergen, surface area and type, contact pressure, and the efficiency of extraction of the swabbing material (87).

## DEMOGRAPHICS OF COCKROACH ALLERGEN EXPOSURE AND SENSITIZATION

A combination of sensitization and exposure to high levels of cockroach allergens is associated with asthma morbidity in children and the elderly. Furthermore, the risk of sensitization is significantly greater in children living in homes with detectable cockroach allergen than in allergen-free homes (62). There are generally agreed upon levels that result in sensitization and asthma exacerbation for other allergens, but these levels have not been defined for cockroach allergens. Nonetheless, limited results from dose-response research suggest that exposure to 2–4 Units (U) Bla g 1 g<sup>-1</sup> of vacuumed and sieved house dust cause sensitization to cockroaches, and therefore 2 U Bla g 1 g<sup>-1</sup> dust may be considered a sensitization threshold (38); the onset or exacerbation of asthmatic symptoms is thought to occur at approximately 8 U Bla g 1 g<sup>-1</sup> dust, a level referred to as the morbidity threshold (111) (see side bar).

Asthma disproportionately affects children, minority populations, and persons of

low socioeconomic status (SES) (135). Factors associated with asthma include biological features, such as the type of allergens, age, ethnicity, and genetic predisposition. More important predictors of arthropod-induced asthma, however, include the asthmatic's lifestyle, housing type and condition, geographic location, and financial disposition. Several studies have addressed these disparities in relation to asthma and allergen exposure. However, unraveling the interrelationship between the contributing factors has proven difficult and complex. Comprehensive coverage of socioeconomic indices as they relate to public health is provided by Evans & Kantrowitz (41).

### Inner-City Residence as a Predictor for Cockroach Allergen Exposure and Sensitization

A recurring theme in studies relating cockroaches to asthma has been the high frequency of exposure and sensitization to cockroach allergens among inner-city residents. This is not surprising, because both the incidence and severity of cockroach infestations are greatest in inner-city homes (72, 123). Children living in urban areas of Maryland and Kentucky, for instance, were significantly more sensitive to cockroach allergens than were suburban children (46, 117). Therefore, most demographic and allergen mitigation studies have been conducted in inner-city neighborhoods.

The National Cooperative Inner-City Asthma Study (NCICAS) found that 37% of asthmatic children in eight major U.S. cities were allergic to a mixed extract of German and American cockroach allergens (111). They also had significantly more incidences of medical utilizations (e.g., asthma-related hospitalization and unscheduled physician office visits) and asthma-related morbidity (e.g., wheezing and school absenteeism) than other groups. More recently, the Inner-City Asthma Study (ICAS), which expanded the study population of the NCICAS to also include children from southwestern and western

cities, found a high prevalence of cockroach sensitivity (68.6% overall), similar to earlier studies (68), and nearly identical morbidity outcomes to those of NCICAS (52). However, significant differences among study sites suggested that exposure and sensitivity to cockroach allergens predominates in the northeastern United States.

The findings from these and other studies demonstrate an association between inner-city residence and sensitization to cockroaches. However, chronic cockroach infestations can be found in suburban and rural residences as well, and therefore it is not surprising that cockroach-provoked allergic disease can be found in both types of communities. Matsui et al. (86) contends that sensitization in suburban, middle-class asthmatic children in counties surrounding Baltimore, Maryland, may be more common than previously thought. Sensitivity rates among infants and small children (26%) in rural West Virginia (146) and children and adults (43%) of rural Kentucky (46) also imply cockroach allergen exposure rates similar to those of inner-city residents.

Although cockroach allergens are generally considered to be of residential importance, children may be exposed to them in schools and day-care facilities, where long periods of exposure in close proximity to the allergens may occur (2, 5, 29, 31, 120, 136, 137). It remains to be determined whether children in inner-city schools experience greater exposure to cockroach allergens than do children in suburban schools.

### **Demographic and Socioeconomic Factors as Predictors of Cockroach Allergen Exposure and Sensitization**

Several studies have attempted the difficult task of unraveling the complex interrelationship of factors associated with cockroach allergen exposure among allergic inner-city youth. In 1967, Bernton & Brown (18) first documented differential rates of cockroach sensi-

tization among ethnic groups. Of 755 allergy clinic patients, 44% were cockroach sensitive; sensitization rates were highest among Puerto Ricans (59%), followed by African Americans (47%), Italians (17%), and those of Jewish descent (5%). They concluded that economic disparities among the groups, and thus different degrees of infestation, likely resulted in greater intensity and duration of allergen exposure among Puerto Ricans and African Americans compared with the other two groups (18). A more recent study confirmed that African American children were 15.8 times more likely to be exposed to cockroach allergens in their bedroom—and 16.4 times more likely to become sensitized to these allergens—than were Caucasian children (117). Within these groups, children in a low SES group were nearly 12 times more likely to become sensitized to cockroach allergen than were children of moderate or higher SES groups. Similar studies in the northeastern United States concluded that homes of African Americans and Hispanics had a much greater risk of having higher cockroach allergen levels compared with Caucasian and Asian American residences, and homes in high poverty areas (<\$30,000 annual family income), which more frequently included less educated minorities, were at greater risk for having Bla g 1 or Bla g 2 levels  $\geq 2 \text{ U g}^{-1}$  dust (71, 79).

The disparities found at the local or regional level have also been observed nationally. In a representative sample of children from the third National Health and Nutrition Examination Survey (1988–1994), 43% of children were sensitive to at least one of four indoor allergens studied and 20% were sensitive to German cockroach extract (134). Racial-ethnic (these studies reflect the U.S. Census Bureau's social definition of race that does not conform to any biological, anthropological, or genetic criteria) differences in cockroach allergen sensitivity were significant and independent of other socioeconomic factors, with African American and Mexican American

children more likely to be cockroach sensitized compared with Caucasian children. As in other studies, however, a significant interaction of race and living in the inner-city again highlights the overriding effect of exposure to chronic cockroach infestations (134). Interestingly, a multi-city study found that African Americans and Hispanics continued to have higher reactivity than Caucasians to mixed American and German cockroach allergen extracts (53%, 46%, and 17%, respectively), even when an adjustment was made for site differences (81), suggesting genetic differences.

Housing type and condition appear to play a major role in the risk of exposure and sensitization to cockroach allergens. Because children living in high poverty areas are more likely to live in multi-unit apartment buildings (79), which are considered more conducive to cockroach infestations (72, 123), this environment would contribute to a higher allergen burden (28, 30, 52). Cockroach infestations in multi-unit apartment buildings can easily spread, making pest control especially challenging. Unsanitary apartments whose residents do not use pest control may harbor cockroach populations that can spread to neighboring units. Furthermore, deteriorated conditions in homes, such as leaky drainpipes, may contribute to infestations; and homes in disrepair are significantly associated with elevated Bla g 2 levels (108).

Cockroach-triggered allergic disease is not limited to the United States. Similar high prevalence of sensitivity to cockroach allergens among asthmatics has been documented in temperate, tropical, and subtropical climates, including Brazil, 55%–79% (116); Taiwan, 51%–58% (78); Thailand, 44%–60% (74, 107); Malaysia, 44% (114); and Nigeria, 45% (1). Interestingly, sensitivity to cockroaches appears to be less frequent in Europe, for example, Spain, 25.7% (121); France, 24.5% (19); Poland, 24.3% (133); Italy, 12.7% (98); Norway, 7.5% (83); and Germany, 4.2% (60).

## COCKROACH ALLERGEN MITIGATION: PIVOTAL ROLE OF PEST CONTROL

Most allergic disease and asthma result from sensitization and perennial exposure to allergens. It follows, then, that a central tenet of asthma intervention should be to minimize exposure through environmental allergen reduction (63). Two obvious components of this approach are suppression of cockroach populations and removal of residual cockroach allergens (10, 36, 82). Indeed, reducing exposure to HDM reduces asthma morbidity in asthmatic individuals (40). Until recently, however, there has been sparse evidence that environmental intervention could attain long-term, clinically relevant reductions of cockroach allergens in infested homes.

Most cockroach allergen mitigations have used a mix of intervention strategies, most commonly pest control coupled with cleaning. The first such effort combined sprays of residual insecticides (**Supplemental Table 1**, follow the Supplemental Material link from the Annual Reviews home page at <http://www.annualreviews.org>) and weekly vacuuming of college dormitories (119). Although Bla g 2 levels declined by 85% within two weeks after insecticide treatment, reductions were apparently short-lived and Bla g 2 levels increased throughout the subsequent year. Because the cockroach population size was not estimated, the relative importance of the two interventions (pest control or cleaning) could not be discerned.

Other studies have attempted to improve upon this two-pronged approach, with limited efficacy. The NCICAS homes, for example, received two insecticide bait treatments by a professional pest control service and residents were requested to thoroughly clean their homes and to attend educational sessions (48) (**Supplemental Table 1**). Despite a statistically significant reduction in Bla g 1 levels after two months, reductions were again short-lived and Bla g 1 in house dust remained well above clinically acceptable levels.

Because this and related allergen mitigation studies tacitly assumed that pest control was effective, especially when performed by professional pest control services, unsatisfactory results were attributed to poor resident compliance (48, 119, 148).

Similar intervention approaches also employed professional cleaning services to remove allergens. In a study in inner-city Baltimore intervention was performed three times during four months with insecticide baits and cleaning, and residents were asked to continue pest management and cleaning for four more months (39) (**Supplemental Table 1**). These efforts resulted in substantial reductions in Bl a g 1 levels, but allergens remained well above clinically relevant thresholds throughout the study. Unlike previous trials, however, three traps were deployed overnight in the kitchen to estimate the size of the cockroach population. Although the median catch per trap declined from 5 to 0, similar ranges at zero, four, and eight months indicated that (a) some residences were only lightly infested with cockroaches at the onset of the study, and (b) that pest control was relatively ineffective in some homes. Moreover, without a nonintervention control group, this study, like the concurrent NCICAS study (48), could not relate the reduction in cockroach allergen to successful pest control and thus concluded that "housecleaning procedures are only partially effective in removing residual allergen over 8 months" (39).

A similar study, but with the inclusion of sodium hypochlorite, which causes fragmentation of some indoor allergens, including Bl a g 1, and reduces IgE and IgG binding capabilities (26), reached similar conclusions (148). As before, the median trap catch per home declined from 3 to 0 (102 to 105 in three control homes), but allergens remained above the proposed morbidity threshold level (**Supplemental Table 1**).

The latter two intervention studies, and a preliminary trial in North Carolina (144), used traps to infer large pest control-imposed reductions in cockroaches and extensive re-

ductions in Bl a g 1 levels, up to 93% in the kitchen and 78% in the bedroom (**Supplemental Table 1**). Although these results were considered to be of only limited efficacy because allergens persisted above clinically relevant morbidity thresholds after treatment, they documented that pest control could effect substantial allergen reductions, even without cleaning (144), and suggested a need to improve the pest control efforts.

Three concurrent studies made significant inroads into separating and quantifying the relative efficacy of each of several approaches—pest control, education, cleaning, and resident involvement in allergen mitigation—but reached dramatically different conclusions. A study in inner-city Los Angeles (88) used a no-treatment control group and two treatment groups, one that received pest control (baits) and professional cleaning and the other received sham baits (without active ingredient) and cleaning; treatments were provided 1 and 7 weeks after the study began and all residents received instructions about mechanical and cultural cockroach control. Cockroaches were also extensively monitored with 24 traps per home.

In this 11-week study median cockroach counts declined by 90% in insecticide-treated homes and did not change in homes that received sham baits (**Supplemental Table 1**). Yet median Bl a g 2 levels declined by only 51% in homes that received insecticide baits and cleaning, and by 88% in homes that received only cleaning, leading to the conclusion that cleaning was as effective, or more so, than cleaning coupled with pest control. McConnell et al. (88) point out, however, that allergen sampling comprised two composite vacuumed samples from multiple surfaces in the kitchen and bedroom, and dead cockroaches from normally inaccessible places (e.g., behind the refrigerator) might have contributed to higher allergen loads; cleaning is expected to reduce allergen loads when it—and allergen sampling—include areas of little consequence (bioavailability) to human

exposure. Other confounding factors merit consideration, including the enrollment of homes with only a single cockroach trapped at baseline and a highly uneven allocation of homes to the three treatment groups (**Supplemental Table 1**).

Significant cockroach and allergen reductions were demonstrated in a six-month intervention that combined integrated cockroach control, resident education, and professional cleaning in Raleigh, North Carolina, homes (4). Reductions in cockroach allergen levels below the sensitization threshold occurred in beds, ostensibly the most relevant site for exposure (38, 52, 117), and below the asthma morbidity threshold on bedroom floors and living room floors and sofas in several study homes (4) (**Supplemental Table 1**). Unlike previous studies, pest control in homes was extensive, targeted with reduced-risk bait formulations, and performed by university personnel at frequent intervals throughout the study. Unfortunately, this experimental design could not separate which of the three intervention strategies was key to the observed effects.

Therefore, in a six-month continuation of the first study, the nonintervention control homes now received the intensive, targeted insecticide bait treatment, while the intervention homes continued to receive this treatment on an intermittent, as-needed basis; neither treatment group received cleaning or resident education and untreated control homes were not included (6). As expected, low allergen levels persisted for another six months in the original intervention homes with only minimal, cockroach monitoring-guided intervention (**Supplemental Table 1**). This design, in contrast to previous studies, attributed the *Bla g 1* reductions in the previous control homes to significant reductions in the cockroach populations. Both the cockroach populations and environmental *Bla g 1* levels declined dramatically, and at the conclusion of the study the allergen levels in homes receiving only pest control were not different from those attained over

six months in homes receiving the combined intervention in months 0–6. These surprising results showed that monitoring-guided pest control alone could reduce environmental allergens below the proposed exposure thresholds. These findings have important public policy implications because pest control is generally much less costly and less intrusive than other approaches, such as professional cleaning.

The paradox of cockroach allergen mitigation studies is why numerous interventions involving professional and residential pest control have generally resulted in only modest reductions in allergens, yet large reductions in both cockroaches and cockroach allergens were evident in several recent investigations (4, 6). To address this, we recently designed a study to distinguish between the efficacy and effectiveness of pest control. That is, when conducted by researchers or academic urban entomologists, the efficacy of cockroach control (i.e., treatment effect) is measured in full compliance with all study procedures and insecticide label directions. Residents and pest management professionals (PMPs), in contrast, consider the cost of intervention and therefore might use less—or less effective— insecticides, and they might limit treatment to only certain locations (e.g., kitchen only, ignoring the rest of the residence). Thus, the same general strategy may reveal high efficacy in controlled investigations but lower effectiveness in “real world” populations. To evaluate the effectiveness of professional pest management in reducing cockroach allergens, we used untreated control homes and two intervention groups of homes: one treated with insecticide baits applied by research personnel following previously established protocols (4, 6), and the other provided with professional pest control (129).

Yet again, the intensive, targeted approach was highly efficacious, reducing cockroach populations by 97% within six months. These data show, however, that the PMPs were substantially less effective at reducing cockroach infestations (53% reduction after six

months), but comparable to most intensive environmental interventions that employed PMPs and reported trap catches (37). This disparity similarly manifests in the magnitude of allergen reduction in several rooms of the home; for example, allergen levels on the kitchen floor were reduced 8% over six months in PMP-treated homes and by 90% in homes treated by researchers. Our collaborative studies with the National Institute of Environmental Health Sciences underscore that although pest control is a pivotal strategy in allergen mitigation, the specific tactics employed to suppress pest populations significantly affect cockroach control and consequently the level of environmental allergens. These studies also highlight the importance of effective collaborations among entomologists, environmental scientists and clinicians.

Four concerns should be considered in future studies on the implementation of cockroach control and allergen reduction in homes. First, the goal of cockroach control in an allergen mitigation program must be to eliminate the allergen source, not to reduce or manage it. With few exceptions, professional pest control has largely failed to reduce cockroach populations to a sufficiently low level to reduce cockroach allergens below clinical thresholds. Pest control service contracts, which are often written only to suppress cockroaches rather than eradicate them from a structure (73), need to be modified. Nevertheless, properly trained PMPs are vital to the implementation of comprehensive allergen avoidance programs. Involvement of PMPs requires an industry-wide commitment to regard cockroach control as a public health need and to reevaluate the intensity and scope of the services they provide in cockroach-infested homes. Likewise, in-house pest control services in inner-city housing will require a major upgrade if the goal of intervention is redefined from reducing nuisance cockroaches to affecting health outcome variables.

Second, mitigation studies are still conducted without appropriate control groups. Placebo controls, while desirable, might not

be appropriate. For example, sham baits (without active ingredient), as used by McConnell et al. (88), could not only inflate the cockroach population beyond the effect of an untreated control, but might also increase allergens that are upregulated by feeding (51). Untreated controls, on the other hand, must be included in mitigation studies; otherwise it becomes difficult to attribute results to an intervention effect because of seasonal and other changes in both cockroaches and allergens (30, 90, 118).

Third, a major shortcoming of several allergen mitigation studies is a lack of objective measures of cockroach populations (23, 42, 48, 119). Even some of the most thorough clinical interventions have failed to link environmental and clinical outcomes to specific intervention components, mainly because pest populations were not monitored. Several approaches monitor cockroach populations (97), but relatively low cockroach infestations, which are the subject of most intervention studies, require that many traps be deployed throughout the home, possibly for multiple nights.

Fourth, most allergen mitigation studies, including ours, have selected study homes from randomized lists of infested homes, without regard to the incidence of cockroach sensitivity among the study population. This was a reasonable tactic in the quest for approaches that would reduce allergens. Now that effective procedures have been reported for both cockroach elimination and allergen reduction, it is imperative that the next generation of mitigation studies use asthmatics' homes and evaluate the health benefits of intervention. Presumably, these subjects would also represent more motivated study participants.

## **COCKROACH ALLERGEN MITIGATION: HEALTH OUTCOMES**

Ultimately, the goal of allergen mitigation programs is to eliminate, or at least reduce,

exposure to allergens to a degree that results in significant reductions in asthma morbidity. Little work has been performed to quantify morbidity outcomes as a function of cockroach allergen mitigation and, until recently, the few cited examples have provided limited evidence that reducing cockroach allergens in an infested home improves morbidity. Studies that examine health outcomes tend to combine behavioral interventions, including caregiver education and encouraging proactive involvement, and environmental interventions that incorporate allergen-impermeable bedding and various forms of pest control. Moreover, morbidity outcomes are confounded when intervention targets a specific allergen source (e.g., HDM) while patients may be sensitized to multiple antigens, including those from cockroaches.

The NCICAS study tailored intervention strategies to the specific risk profiles of 5- to 11-year-old inner-city asthmatic children; families were provided an asthma counselor to facilitate caretaker education and involvement, pillow and mattress covers, and, if the child was cockroach sensitive, instructions for reducing cockroach food sources and two visits by a PMP (42). Of the measured morbidity and medical utilization outcomes during this two-year study, only the maximum number of symptom days was significantly reduced 0.5 days per 2 weeks (42). As before, the contribution of individual intervention components remains unknown because this study did not quantify indoor allergen levels or the efficacy of pest control. Indeed, it is not clear whether cockroach-sensitive individuals were positively affected by this intervention.

Recent studies have relied largely on caretakers to implement low-cost interventions aimed at improving asthma morbidity among inner-city asthmatic children. In the first study, conducted in Atlanta, Georgia, 43% of the enrolled children had been sensitized and exposed to cockroach allergen; homes were randomized into three groups: (a) an active-

intervention group provided with allergen-impermeable bedding covers, instructions for washing bedding, and cockroach "bait traps" (presumably bait trays or stations) to be placed by the residents; (b) a placebo intervention group given allergen-impermeable bedding covers, "ineffective cockroach traps" (presumably empty bait trays or stations), and instructions to wash bedding as they normally would; and (c) a no-treatment control group that was visited one year after enrollment (23). Similar marginal allergen (Bla g 2) reductions were found after one year in both the active-intervention and placebo homes, but results were not reported for the no-treatment control houses. Because both active and placebo interventions resulted in significant declines in the number of acute hospital and clinic visits for asthma compared with the no-treatment controls, and there was no correlation between reduced cockroach allergen in the home and the number of acute visits, these results suggest a Hawthorne effect (an experimental effect in the direction expected but without causal basis in the theoretical motivation for the intervention, apparently due to behavioral changes in the participants). Again, the cockroach populations were not monitored.

In the past two years, two studies similar in design reported very different outcomes; unfortunately, pest populations—and hence efficacy of the cockroach intervention—were not monitored in either study. In Baltimore, 100 asthmatic children, 42% of whom were cockroach sensitive, were randomized between an untreated control group and an environmental intervention group that included bedding covers, a room-sized HEPA filter for the child's bedroom, and insecticide bait applied as needed (84% of homes were treated) throughout the home by a professional pest control service for the first six months (37). Bedroom Bla g 1 levels, which were relatively low at baseline (median  $4.7 \text{ U g}^{-1}$  dust), declined in the intervention group by 41%, and as many as 55% of the children reported no

daytime symptoms in the two weeks prior to evaluation, a modest but significant change compared with controls; all other health outcomes (spirometry, acute asthma visits, and hospitalizations) remained unchanged in the intervention group. The decline in Bla g 1 levels in intervention homes was due likely to the pest control service because allergen levels in control homes increased 2.5-fold during the same period. However, because the intervention targeted multiple indoor allergens, it is plausible that the health benefits were due largely to interventions targeting HDM (bedding covers and HEPA filters).

The much larger, multi-city ICAS similarly evaluated the effectiveness of environmental interventions customized to the allergic sensitization and environmental risk profile of inner-city asthmatic children (91). As in the Baltimore study (37), participants received either no treatment or an environmental intervention that included bedding covers, a vacuum equipped with a HEPA filter, a HEPA air purifier, and, if sensitive and exposed to cockroaches, professional pest control. The intervention resulted in a 51% reduction in Bla g 1 on the bed and 64% on the bedroom floor, but control homes also experienced an inexplicable 46%–47% decline in Bla g 1. Nevertheless, environmental intervention led to a significant reduction in the number of self-reported symptom days per 2-week period, extrapolated up to 34 fewer days with reported wheeze during the two-year study. The environmental intervention also led to significant reductions in disrupted caretaker plans, lost sleep, missed school days, and unscheduled asthma-related visits to health care providers (91), outcomes associated with cockroach sensitivity (111). This study shows that inner-city asthmatic children can benefit from a multifaceted intervention tailored to their specific needs, and therefore underscores that more efficacious pest control should result in greater allergen reductions and further improvements in asthma morbidity.

## FUTURE DIRECTIONS

Since the link was first made with allergic disease in 1964, several cockroach allergens have been identified and characterized. Surprisingly, however, cockroach allergens have received only scant attention from entomologists. Although great strides have been made in developing our understanding of the molecular biology and environmental fate of cockroach allergens, much remains unclear about their basic biology and function. Nevertheless, recent work has provided insight into the developmental and tissue-specific production of several allergens, their physiological regulation, and patterns of excretion into the environment. Continued research, especially with modern proteomic approaches, will undoubtedly reveal many more cockroach allergens with diverse physiological functions, and this growing list of cockroach allergens requires extensive annotation of structure, function, prevalence in the environment, and impact on humans.

Sensitivity to cockroach allergens varies greatly, ranging from 14% to 93% of atopic individuals having serum IgE to cockroaches and/or reacting upon skin provocation. It is imperative to determine not only the immunological bases for this variation, but also the mechanisms by which each allergen is disseminated into the environment, its bioavailability and environmental stability, and how each aeroallergen reaches the respiratory system. In this context, comparative studies of allergen sampling methods are sorely needed.

We now know that cockroach control is a critical and likely the single most important component in reducing cockroach allergens in infested homes. But cockroach control requires site-specific tactics, some of which may inadvertently elevate environmental allergens (157). It is crucial therefore that we have a clear understanding of allergen biology so that we are better equipped to develop effective mitigation programs. Moreover, multi-treatment mitigation study designs are needed to evaluate the incremental benefits accrued

from adding other intervention tactics (e.g., cleaning, education, repair, caulking, and insect growth regulators) to an insecticide bait-based intervention.

Last, there is a need in environmental intervention to establish clear relationships among pest populations, allergen reduction, and symptom reduction in cockroach-sensitive asthmatics. Interestingly, symptoms in children with atopic asthma have been suc-

cessfully reduced with intensive, home-based interventions that resulted in only modest reductions in cockroach allergen levels. Now that procedures have been reported for cockroach elimination and much greater allergen reduction, it is essential that the next series of mitigation studies evaluate the health benefits of intervention in asthmatics' homes while monitoring environmental allergens and the pest population.

### SUMMARY POINTS

1. Cockroaches produce several allergens. Exposure and sensitization to these allergens are associated with the development of acute asthma morbidity, especially among inner-city, asthmatic youth.
2. Unraveling the complex interrelationship of factors contributing to asthma is difficult; however, being African American or Hispanic and of low socioeconomic position appear to be independent, significant risk factors for sensitization and exposure to cockroach allergens in the inner-city.
3. Pest control is a pivotal component in cockroach allergen mitigation programs; cockroach control alone can significantly reduce the level of cockroach allergen in infested homes.
4. Although the evidence is currently limited, reducing exposure to cockroach allergens in infested structures could lead to improvements in asthma morbidity among cockroach-sensitized individuals.

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43. Shows that Bla g 4 is produced only by adult male German cockroaches, is passed to the female during copulation, and is regulated by juvenile hormone.

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50. First study to address the biology of cockroach allergens, identifying the midgut as the tissue responsible for producing Bla g 1.

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51. Demonstrates that Bla g 1 production in *B. germanica* is modulated in relation to food intake.

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**89. Defines the molecular structure and antigenic relationships of the Group 1 cockroach allergens.**

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**91. The ICAS demonstrated that reducing environmental cockroach allergen exposure in the home can lead to significant improvements in reported asthma morbidity among inner-city asthmatic children.**

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111. A high-impact, NCICAS report linking cockroach allergen exposure to a higher frequency of asthma morbidity among inner-city children.

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117. Established African American race and low socioeconomic status as independent, significant risk factors for sensitization to cockroach allergen in asthmatic children.

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Table 1. Overview of cockroach and allergen mitigation studies

Study (duration; site)	Intervention			Cockroach counts; median (range)		Allergen mitigation	
	Cockroach control	Cleaning	Other	Baseline	Conclusion	Baseline	Conclusion
<b>Sarpong et al. 1996</b> (4 wks; dormitories)	Insecticide sprays <sup>a</sup>	Weekly vacuuming	N/A	ND	ND	5.2 (0–19.6) U Bla g 2/g dust	0.95 (0–4.2)
<b>Gergen et al. 1999</b> (48 wks; apartments)	<ul style="list-style-type: none"> <li>• Avert baits</li> <li>• 2X at start</li> <li>• KT &amp; rooms with signs of CR</li> </ul>	Families asked to clean prior to and after extermination	Resident education	resident reported sightings (67.6%)	resident reported sightings (42.2%)	KT = 68.7 LR = not given BR = 8.9 (mean U Bla g 1/g dust)	KT = 33.6 LR = not given BR = 11.1 (month 2)
<b>Eggleston et al. 1999</b> (32 wks; apartments)	<ul style="list-style-type: none"> <li>• Avert baits</li> <li>• 2X at start</li> <li>• 1X @ month 4</li> <li>• KT, LR, BR, basement</li> </ul>	<ul style="list-style-type: none"> <li>• Professional cleaning</li> <li>• 2X at start</li> <li>• 1X at month 4</li> <li>• all surfaces in KT, hard surfaces in other rooms</li> </ul>	N/A	<ul style="list-style-type: none"> <li>• 5 per trap (0–63)</li> <li>• 3 traps in KT for 24 hrs</li> </ul>	<ul style="list-style-type: none"> <li>• 0 per trap (0–37)</li> </ul>	KT = 745 (0–2333) LR = 65 (0–1908) BR = 82 (0–548) (median & range U Bla g 1/g dust)	KT = 36 (0–1576) LR = 15 (3–142) BR = 21 (0–87)
<b>Williams et al. 1999</b> (24 wks; apartments)	<p><b>A.</b> Combat baits</p> <ul style="list-style-type: none"> <li>• 10–15 in KT, 2–4 in BT, 2–4 other rooms</li> <li>• replaced @ month 4</li> </ul> <p><b>B.</b> Control</p>	N/A	N/A	<p><b>A.</b> 3.7 per trap (0.71–9.5)</p> <ul style="list-style-type: none"> <li>• 10–18 traps in KT, 2–4 traps BT for 24 hrs</li> </ul> <p><b>B.</b> 2.1 per trap (0.91–8.5)</p>	<p><b>A.</b> 0 per trap (0–0.07)</p> <p><b>B.</b> 1.8 per trap (1.15–2.36)</p>	<p><b>A.</b> Bla g 1 = 167 (88–248) Bla g 2 = 31.9 (10.3–110) (mean &amp; range U/g dust)</p> <p><b>B.</b> Bla g 1 = 127 (28.7–2107) Bla g 2 = 32.8 (12.6–201)</p>	<p><b>A.</b> Bla g 1 = 90 (52–120) Bla g 2 = 30.4 (8.9–140)</p> <p><b>B.</b> Bla g 1 = 220 (127–382) Bla g 2 = 69.3 (24–200)</p>
<b>Wood et al. 2001</b> (24 wks; apartments)	<p><b>A.</b> Avert baits; 2X month 1, 1X @ 12 wks in KT, LR, BR, basement</p> <p><b>B.</b> Control</p>	<p><b>A.</b> Professional cleaning 2X at start, 1X @ 12 weeks, bleach on hard surfaces</p> <p><b>B.</b> None</p>	N/A	<p><b>A.</b> 3 per home (0–24)</p> <ul style="list-style-type: none"> <li>• 3 traps for 24 hrs</li> </ul> <p><b>B.</b> 102 per home (58–127)</p>	<p><b>A.</b> 0 per home (0–2)</p> <p><b>B.</b> 105 per home (29–167)</p>	<p><b>A.</b> KT= 281 (28–4495) LR = 43 (1–1689) BR= 36 (15–875) (median &amp; range U Bla g 1/g dust)</p> <p><b>B.</b> KT= 467 (22–2063) LR = 232 (68–560) BR= 218 (50–370)</p>	<p><b>A.</b> KT= 26.5 (2–879) LR = 10 (0–177) BR= 8 (0–568)</p> <p><b>B.</b> KT= 1587 (465–1964) LR = 394 (219–1160) BR= 450 (262–1583)</p>

Table 1 (continued). Overview of cockroach and allergen mitigation studies

Study (duration; site)	Intervention			Cockroach counts; median (range)		Allergen mitigation	
	Cockroach control	Cleaning	Other	Baseline	Conclusion	Baseline	Conclusion
<b>McConnell et al. 2003</b> (11 wks; apartments)	<b>A.</b> 24 Fipronil bait stations + Maxforce	<b>A.</b> Prof. clean @ wk 6	N/A	<b>A.</b> 136 per home (14–1600)  • 24 traps in KT & BR for 1 wk	<b>A.</b> 14 per home (0–26)	<b>A.</b> KT = 136 (73–402) BR = 32 (11–83) (median & range U Bla g 2/g dust)	<b>A.</b> KT = 66 (26–197) BR = 19 (8–57)
	<b>B.</b> 24 sham bait + sham gel • trt @ wks 1 & 7	<b>B.</b> Prof. clean @ wk 6, surfaces cleaned with bleach and/or vacuumed		<b>B.</b> 55 (32–215)	<b>B.</b> 68 (31–244)	<b>B.</b> KT = 214 (13–1403) BR = 21 (4–41)	<b>B.</b> KT = 25 (5–197) BR = 7.3 (4–24)
	<b>C.</b> Control	<b>C.</b> None		<b>C.</b> 19 (7–298)	<b>C.</b> 22 (0–249)	<b>C.</b> KT = 104 (9.3–297) BR = 15 (5.3–79)	<b>C.</b> KT = 61 (18–247) BR = 10 (6.3–32)
<b>Arbes et al. 2003</b> (24 wks; apartments)	<b>A.</b> Maxforce & Pre-Empt • all rooms treated at start & months 1, 2 & 4 if roaches trapped	<b>A.</b> Professional cleaning • all rooms @ start & months 1, 2 & 4 if allergen detected	<b>A.</b> Resident education	<b>A.</b> KT = 113 (38–287) LR = 76 (3–204) BR = 78 (0–311) • 6 traps in each room for 3 days	<b>A.</b> KT = 0 (0–103) LR = 0 (0–26) BR = 0 (0–9)	<b>A.</b> KT = 633 (253–1585) LR = 25 (11–44) BR = 46 (21–103) bed = 6 (3–11) (mean & range U Bla g 1/g dust)	<b>A.</b> KT = 24 (10–60) LR = 4 (2–9) BR = 7 (3–16) bed = 1 (<1–2)
	<b>B.</b> Control	<b>B.</b> None	<b>B.</b> None	<b>B.</b> KT = 146 (87–347) LR = 58 (0–186) BR = 14 (0–124)	<b>B.</b> KT = 46 (0–319) LR = 10 (0–366) BR = 6 (0–204)	<b>B.</b> KT = 351 (136–906) LR = 28 (14–56) BR = 17 (8–39) bed = 5 (3–9)	<b>B.</b> KT = 287 (111–741) LR = 29 (15–57) BR = 27 (12–61) bed = 7 (4–13)

Table 1 (continued). Overview of cockroach and allergen mitigation studies

Study (duration; site)	Intervention			Cockroach counts; median (range)		Allergen mitigation	
	Cockroach control	Cleaning	Other	Baseline	Conclusion	Baseline	Conclusion
Arbes et al. 2004 (24 wks; apartments, continued from Arbes et al. 2003)	A. Intervention <sup>b</sup>	N/A	N/A	A. KT = 0 (0–103) LR = 0 (0–26) BR = 0 (0–9) • 6 traps in each room for 3 days	A. KT = 1 (0–193) LR = 0 (0–150) BR = 0 (0–48)	A. KT = 24 (10–60) LR = 4 (2–9) BR = 7 (3–16) bed = 1 (<1–2)	A. KT = 19 (6–59) LR = 5 (2–11) BR = 7 (3–18) bed = 2 (1–4)
	B. Crossed-over control <sup>c</sup>	• see methods for <i>Intervention</i>		B. KT = 46 (0–319) LR = 10 (0–366) BR = 6 (0–204)	B. KT = 2 (0–82) LR = 0 (0–4) BR = 0 (0–2)	B. KT = 287 (111–741) LR = 29 (15–57) BR = 27 (12–61) bed = 7 (4–13) (mean & range U Bla g 1/g dust)	B. KT = 14 (5–48) LR = 6 (3–14) BR = 5 (2–14) bed = 2 (1–5)

<sup>a</sup> Pest management company indicated using diazinon, Dursban (chlorpyrifos), Tempo (cyfluthrin), or Safrotin (propetamphos) biannually on a rotational basis.

<sup>b</sup> Intervention homes received insecticide bait application, professional cleaning, and resident education in previous 6 months.

<sup>c</sup> Crossed-over control homes received no interventions in previous 6 months.

Avert = gel bait (abamectin); Combat = bait stations (hydramethylnon); Maxforce = gel bait (hydramethylnon); Pre-Empt = gel bait (imidicloprid)

N/A - not applicable; ND - not determined; KT = kitchen, BT = bathroom, LR = living room, BR = bedroom