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Cockroach allergy

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Cockroaches represent one of the most primitive insects and date back some 340 million years according to fossil records. More than 3500 species exist worldwide, and new species are added to the list each year. Most species are concentrated in a broad band 30° north and 30° south of the equator in the warm, photosynthetically rich forests. In the continental US cockroaches represent 31 genera and 74 species, most of which were introduced from other parts of the world. Although most species exist in the wild (feral species), approximately 50 are considered domestic (live indoors) or peridomestic (live around artificial structures) [1].

Cockroaches adversely may affect human health through food contamination, transmission of bacterial and viral pathogens, psychologic stress, and allergic sensitization [2]. This article provides an overview of cockroach allergy and discusses taxonomy, allergen characterization and cross-reactivity, and cockroach-induced allergic disease and treatment.

Taxonomy

Cockroach evolution often has been linked to a common ancestry with termites because of the presence of gut-associated symbiotic protozoa; however, this interpretation has been criticized [3]. Although there is some disagreement about the taxonomic classification of cockroaches, most schemes place the organisms in the phylum Arthropoda, class Insecta, order Blattaria, and the 5 families Blaberidae, Blattidae, Blattellidae, Polyphagidae and Cryptocercidae. Most household cockroaches belong to the Blattidae (American, Oriental, smokey-brown) or Blattellidae (German, brown-banded; Fig. 1) family. The two most common dom-

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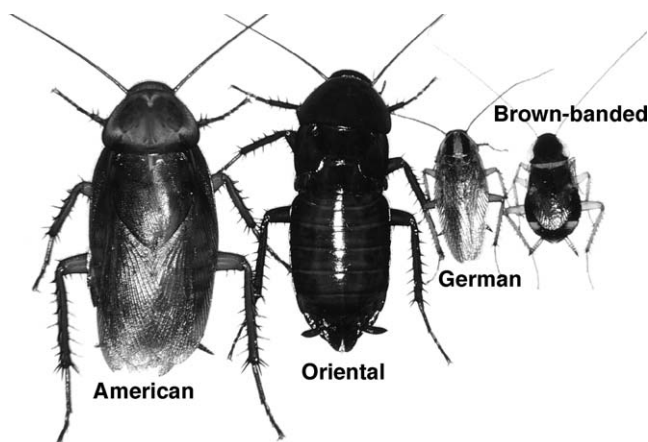


Fig. 1. Relative size comparison of common cockroach species. (Courtesy of Jim Kalisch, University of Nebraska.)

iciliary species, which are associated with allergic disease, are the American (*Periplaneta americana*) and German (*Blattella germanica*) cockroaches.

Cockroach characterization

The American cockroach is the largest of the household roaches, averaging 1.5 inches in length with fully developed wings. The wings extend 0.16 to 0.31 inches over the end of the abdomen, and the species can fly. The adults are reddish-brown to dark brown in color. The female produces eggs that are carried in a bean-shaped capsule (oothecae) containing approximately 16 eggs. Each female is capable of producing up to 14 egg cases, which generally are deposited in sheltered areas near the floor. The capsule protrudes from the body until an opportune location is available for deposit. The average number of young or nymphs that emerge from each capsule is 13.6 (Fig. 2). The newborn nymphs molt up to 13 cycles a month until they reach maturity. The numerous shedding cycles create an abundance of body castings, which can be a source of allergen and lead to a significant load of aerosolized allergenic proteins. The American cockroach is a peridomestic species that maintains its habitat around buildings in moist areas. They infest basements and sewers, move outdoors in warmer temperatures (around 84°F), and do not tolerate the cold. They often are found in restaurants, grocery stores, bakeries, and facilities where food is plentiful. These insects can be transported into homes and apartments through items from infested establishments [4].

The German cockroach is the most common species and tends to be smaller than its American counterpart. It is light tan to brown and approximately 0.50 to 0.63 inches long. Two dark bands run lengthwise on the dorsal side of the head. Males and females are winged but cannot fly (Fig. 3). The German cockroach produces more eggs per capsule than do other species. The female carries the

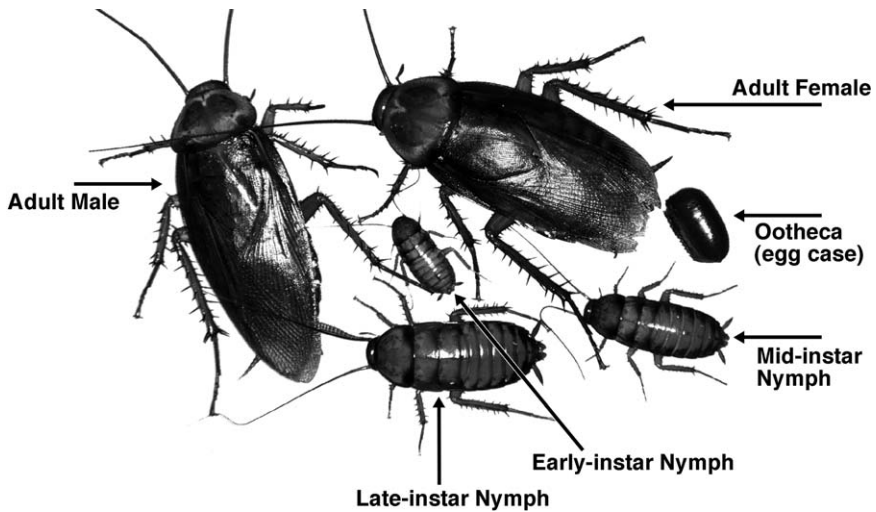


Fig. 2. Life stages of the American cockroach. (Courtesy of Jim Kalisch, University of Nebraska.)

capsule until full maturation, in contrast to the American cockroach, which sheds the capsule at inconspicuous locations. The number of eggs per capsule ranges between 30 to 40. The German cockroach generally is spread through domestic transportation in cartons and food items. The roaches move from building to building during warmer temperatures. Their most common habitats are kitchens, bathrooms, and other sites close to a water source [4].

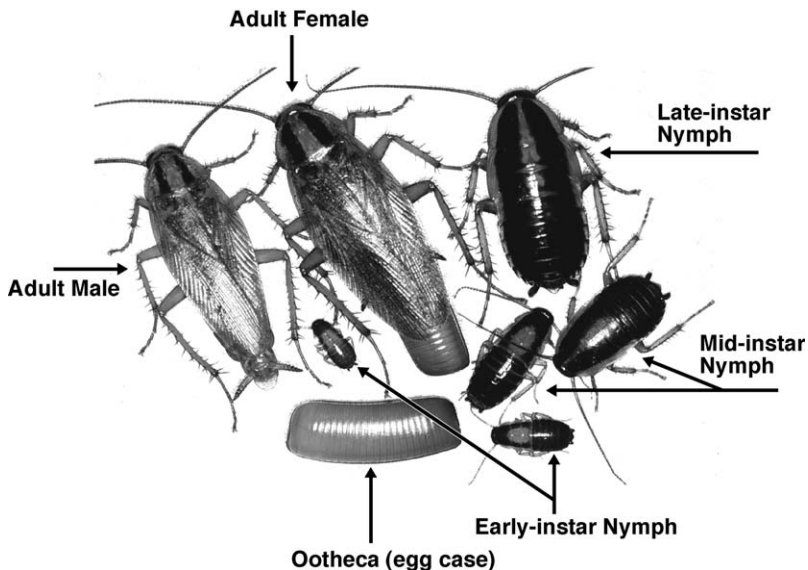


Fig. 3. Life stages of the German cockroach. (Courtesy of Jim Kalisch, University of Nebraska.)

Cockroaches are omnivorous, feeding on a variety of foods ranging from cereals, starches, and sugars to leathers and book bindings. Most species are aggressive foragers and in the process release unpleasant odors emanating from regurgitated food, excrement, and fluid exuded from the abdominal scent glands [4]. Such a release of fluid from a numerous roaches in a heavily infested area is another source of large amounts of allergenic protein.

The Oriental cockroach, also known as the “water bug,” is prevalent throughout the United States and all of Europe. The Oriental cockroach prefers damp basements, crawl spaces, and areas beneath refrigerators, and travels through sewer pipes. It feeds on decaying organic matter and is considered the filthiest of the house-infesting cockroaches. The Oriental cockroach is dark brown to black in color and often referred to as the black beetle (Fig. 1). The male has fully developed functional wings while the female has short stubs. The female will produce 1 to 18 egg capsules, each containing up to 16 eggs. The capsule is carried 12 hours to 5 days before it is deposited in a sheltered location. These roaches are found outdoors during warmer weather and may migrate indoors when cooling occurs [42].

Whole-body and fecal cockroach allergens

Cockroach infestation of a living space depends on the cleanliness of the environment, degree of adequate pesticide use, and condition of housing structures. Infestation creates large amounts of allergenic proteins, which can be measured in dust samples from bedding, furniture, carpeting, bedroom floors, and kitchens. The highest levels are found in the kitchen, where an ample supply of food is available [5,6]. These proteins derive from saliva, fecal material, secretions, cast skins, egg cases, and dead bodies. An early study by Richman using RAST inhibition concluded that cast skin and whole-body extracts (WBEs) from German cockroaches contained clinically relevant allergens, whereas extracts from fecal material and egg casings had similar, but less potent, proteins [7]. Western blot inhibition and immunoelectrophoresis showed that only 1 of 15 bands in fecal extract was unique; the other 14 bands showed a high degree of similarity to WBE. The fecal proteins were a subset of WBE, and overlap primarily was in the acidic region (isoelectric point [pI], 4.7) [8]. Using RAST, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), and Western blot inhibition, Musmand and colleagues established that fecal extracts possessed an allergenicity similar to that of WBEs by showing near-complete inhibition by the heterologous WBE [9]. A study using two site ELISA experiments reported that fecal extracts contain six times more major allergen than WBE and that fecal matter may be a more important source of allergens than is WBE. [10]

Characterization of cockroach allergens

Extracts from American and German cockroaches have revealed antigenic proteins with molecular weights in the ranges of 6 to 120 kDa and 25 to 200 kDa,

respectively [11–13]. Early work by Twarog and co-workers reported purification of three proteins (molecular weight, < 10 kDa, 25 kDa, 65 kDa) that were cross-reactive between the two species [14]. Wu and Lan described 29 protein fractions in a crude American-cockroach extract using crossed radioimmuno-electrophoresis (CRIE). Based on sera from seven cockroach-sensitive asthmatics, they defined four principal allergens in the range of 26 to 120 kDa. Two proteins of 72 kDa and 78 kDa bound 100% of the sera from atopic subjects [13]. The authors named these two proteins the major allergens of *P americana*, and the 72-kDa protein was characterized as Per a 3. Schou et al showed the presence of 45 antigens in *P americana* and 29 in *B germanica*. Using sera from 30 patients with cockroach allergies, the investigators showed that immunoglobulin E (IgE) bound to seven *P americana* precipitates and three *B germanica* precipitates. One homologous, 25-kDa allergen bound IgE in 100% (*P americana*) and 70% (*B germanica*) of the sera from sensitized patients. [12]. This allergen was found to be the major group 1 allergen from German cockroach Bla g1. Kang and colleagues evaluated extracts from American, German, and Oriental cockroaches. Using Western blotting, they identified a common 40- to 45-kDa protein that reacted to most of the sera from atopic subjects. The same authors also described other low-molecular-weight proteins (28, 32, 45 kDa) as potentially important allergens in American cockroach extracts [15]. The proteins described in these reports were purified using protein chemistry techniques such as CRIE, SDS-PAGE, immunoelectrophoresis, and Western blotting. The varied use of these methods makes it difficult to compare allergenic fractions between studies, because the exact molecular weight of a protein may vary depending on the isolation technique used. Allergens from German and American cockroaches have been identified over the past decade using immunoelectrophoretic techniques in combination with monoclonal antibodies (Table 1). Several antigens listed have been sequenced, cloned, and produced as recombinant antigens.

Table 1
Cockroach allergens from German and American species

Species	Molecular weight (kDa)	Function
<i>Blattella germanica</i>		
Bla g 1	20–25	Unknown
Bla g 2	36	Aspartic protease
Bla g 4	18–20	Lipocalin
Bla g 5	23	GST
Bla g 6	18	Troponin C
<i>Periplaneta americana</i>		
Per a 1	~25	Unknown
Per a 3	72	Arylphorin
Per a 7	33	Tropomyosin

German cockroach allergens

Bla g 1 was the first group 1 allergen to be defined and was shown to be a protein with a pI of 3.5 and a molecular weight of approximately 25 kDa [12]. The protein consists of tandem repeats, each of which are approximately 100 amino acids in length [16]. Molecular sequencing of Bla g 1 revealed that the protein contains an amino acid sequence that is analogous to a sequence in Bla g bd90k, as reported by Helm [17]. The Bla g 1 also showed homology to a digestive protein precursor (ANG12) from the African malaria mosquito (*Anopheles gambiae*). Bla g 2, the second German cockroach allergen, is a 36-kDa protein, has a pI of 5.2, and initially was isolated using monoclonal antibodies [18]. Arruda and co-workers cloned the protein and showed that high concentrations were found in the cockroach esophagus, gut, and proventriculus [19]. In terms of allergenic importance, 30% to 50% of patients with cockroach allergies have serum IgE to Bla g 1, and 60% to 68% have serum IgE to Bla g 2 [20]. The mechanism of IgE sensitization from these allergens is unknown; however, as in bee venom and dust mite, enzymatic activity may be responsible for promoting IgE production. Pomes et al studied Bla g 2 for enzymatic activity and found that the allergen was an inactive aspartic proteinase that was related to a family of mammalian pregnancy-associated glycoproteins. Because of its inactive enzymatic state, it was concluded that the allergenicity must be influenced by other genetic and exogenous factors [21].

Similar to many animal allergens, Bla g 4 belongs to the lipocalin family of proteins. Lipocalins are small (approximately 20 kDa), ligand-binding proteins that can bind and transport small hydrophobic chemicals. Three-dimensional modeling has revealed a conserved tertiary structure with an N-terminal α -helix and an antiparallel β -strand barrel that provides the pocket for ligand binding. Other important allergens in the lipocalin group include the mouse urinary Mus m1, rat urinary Rat n1, dog Can f 1 and Can f 2, cow Bos d 2 and Bos d 5, cow's milk β -lactoglobulin, and equine Equ c 1 and Equ c 2. Bla g 4, an 18-kDa protein, has been cloned and expressed in a *Pichia pastoris* vector; in one study, it showed strong IgE binding with 44 of 73 (64%) sera samples [22,23].

Blg g 5 is a 23-kDa protein and a glutathione S transferase (GST) that has elicited IgE antibody in approximately 70% of patients with cockroach allergies [24]. The sequence homology between Bla g 5 and GST protein from Der p was 27%, but the sequence homology between Bla g 5 and GST protein from *Anopheles gambiae* was 51%. Bla g 6 is an 18-kDa troponin C, which is a minor protein component of thin filaments of striated muscle.

American cockroach allergens

The American cockroach has three well-characterized allergens. Per a 1 is a 20- to 25-kDa acidic protein of unknown function that initially was isolated from crude American cockroach extract and has been shown to elicit IgE responses in 30% to 50% of sera from allergic individuals [12,13,15]. Monoclonal antibodies were

developed for screening cDNA libraries, which enabled the identification of clones and the sequencing and characterization of Per a 1 [25]. The allergen was shown to have a high degree of homology to Bla g 1 and is similar to the mosquito protein ANG12 [16,26–28]. Per a 3, a 72-kDa protein, originally was characterized using immunochemical studies and is an important allergenic protein in Taiwan [13,29]. With molecular sequencing, Per a 3 was shown to be a species-specific allergen that is related to an insect hemolymph protein arylphorin [25,30,31]. Per a 3 has three isoallergic variants with skin reactivities ranging between 26% and 95% [32]. Santos et al characterized the third American cockroach allergen, Per a 7. This 33-kDa tropomyosin showed 50% reactivity with sera from allergic patients [33]. Tropomyosin is a structural protein that is involved in muscle contraction and first was reported in shrimp. It has been identified as the major allergen in other arthropods, such as crab, lobster, and mites [34].

Cross-reactivity among cockroach allergens

The cross-reactivity among cockroach and other insect allergens initially was studied using immunochemical technology and later with molecular cloning. Schou demonstrated IgE binding to a 25-kDa protein that is present in crude extracts from American and German cockroaches [12]. Pollart showed species-specific binding of monoclonal antibodies to German cockroach allergens; however the antibodies for Bla g 1 also bound a cross-reacting protein (Per a 1) in crude American cockroach extract [18]. Melen et al noted strong binding with anti-Per a 1 and anti-Bla g 1 monoclonal antibodies and with known levels of anti-Bla g 1; strong binding did not occur between IgE and control antibodies (control monoclonal antibodies and IgE sera against Bla g 2). Two groups cloned the Per a 1 allergen and demonstrated sequence identity with Bla g 1. These findings conclusively showed cross-reactivity between Per a 1 and Bla g 1 [27,35]. Bla g 1 and Per a 1 are the only German and American Cockroach allergens that show extensive cross-reactivity. These two allergens are called group 1 allergens. An inhibition assay, in which Bla g 2 cross-reactivity was evaluated using high-titer polyclonal mouse anti-Bla g 2 antibodies, revealed less than 5% inhibition by *P americana* extracts. In the same study, Northern blot analysis showed that mRNA that encodes Bla g 2 was not detectable in *P americana*, lending further evidence that group 1 allergens are the only cross-reacting epitopes [19].

The allergenicity of the Oriental cockroach proteins has not been well characterized. Earlier studies showed IgE binding to crude extracts but individual allergenic proteins have not been cloned and sequenced. Cross-reactivity between crude American, German, and Oriental cockroach is due to group 1 allergens and Per a 7 [36]. Currently, most extract companies do not manufacture an Oriental extract.

Species cross-reactivity also has been studied between Per a 7 and the tropomyosin from other arthropods. The cockroach Per a 7 shares an 80% identity with mite Der p 10 and Der f 10 and shares an 82% identity with shrimp

Pen a 1 [36–38]. Similar reports have shown IgE cross-reactivity between cockroach, shrimp, and crustacea allergens using RAST inhibition [34,39].

Cockroach allergen and disease

Sensitization

Cockroach allergy is associated with exposure in areas of heavy infestation. The risk for clinical disease in the form of hypersensitivity reactions or asthma is dependent on a combination of sensitization and level of exposure. The National Cooperative Inner City Asthma Study (NCICAS) revealed that asthma severity in children from large US cities was linked to the presence of IgE and a certain level of allergen exposure. The study evaluated the Bla g 1 levels in homes of inner-city children with asthma. Investigators found detectable allergen levels in 85% of samples from bedding and bedroom floor dust. Bla g 1 levels crossed the 8-U/g threshold in 50% of bedrooms, and this level of allergen was associated with increased hospital admissions. In comparison, cat and mite levels were only high in 12.6% and 9.7% bedrooms, respectively [40]. Sarpong and colleagues studied the homes of 87 asthmatic children aged 5 to 17 years and found that more than 80% of children with bedroom Bla g 1 or Bla g 2 levels of 1 U/g or greater demonstrated skin reactivity to mixed cockroach extract [41]. Eggleston and co-workers reported similar findings in their study of 500 inner-city children who were a subset from the NCICAS study. The investigators noted that the proportion of sensitized subjects increased up to 44% when the level of Bla g 1 increased from 2 U/g to more than 4 U/g, confirming a dose–response relationship between allergen level and sensitization. This study also found that the strongest correlation between sensitization and level of exposure occurred in the bedroom, even though the highest allergen levels occurred in the kitchen [42]. This finding suggests that duration of exposure and proximity to allergens (eg, face in pillows) are determinants of sensitization. Litonjua et al have shown that early life exposure to Bla g 1 or Bla g 2 at a level greater than 2 U/g poses a markedly increased relative risk for asthma [43]. These data have been the basis for determining which allergen exposure levels can result in sensitization and clinical disease. The cutoff level for sensitization to Bla g 1 is 2 U/g, and exposure to 8 U/g of this allergen increases the risk for asthma. Allergen exposure within homes can occur through normal domestic activity that stirs up allergen particles and through undisturbed dust that releases particles into the air. Airborne cockroach allergens are carried on irregularly shaped particles that are 3 to 350 μm in size. More than 80% of such particles eluting allergen are greater than 10 μm in size. Because of their irregular shape, these particles can behave in a manner that is aerodynamically similar to that of smaller particles, enabling allergens to enter the lower respiratory tract [44]. These particle dynamics may explain the abundance of data showing a worsening of asthma in heavily infested areas.

Cockroach-induced allergic disease primarily manifests as rhinitis and asthma. The prevalence of cockroach allergy in the US ranges from approximately 6% in asymptomatic control subjects to 42% in atopic individuals [40,42,45,46]. The prevalence ranges from 3.9% to 24.5% in Europe [46–50] and is reported to be as high as 55% in atopic children and adults in South America [33]. The prevalence figures are influenced by the presence or absence of asthma, living conditions, degree of cockroach infestation, type of extract used for testing, and study-inclusion criteria. Figures are not comparable between studies. US studies involved individuals from selected groups, such as those with allergic histories, rather than a random sample from the general population.

Cockroaches first were linked with immediate hypersensitivity reactions in 1943 when Lerner reported generalized urticarial rash secondary to roach exposure. Occupational surveys identified individuals with respiratory symptoms after working with cockroaches [2]. In 1964, Bernton and Brown reported positive skin tests in 44% of 755 patients. They also noted that 13% of patients were monosensitized to cockroach allergens [51]. The same authors also performed bronchial challenges in 10 sensitized subjects and found immediate responses in all subjects [52]. Kang et al confirmed these observations by performing inhalation challenges on 33 cockroach-positive and 13 cockroach-negative asthmatics. The challenges produced an acute-phase response in 30 of the 33 cockroach-positive subjects and produced a late-phase response in 16 of these sensitive subjects; none of the cockroach-negative subjects reacted to the challenge. These findings demonstrated that cockroach antigen can induce a dual-phase response after direct challenge. Peripheral blood eosinophilia also was noted in the skin tests of sensitive individuals, as were high total and antigen-specific IgE levels [53]. These data support the contention that atopic asthma in cockroach-sensitive subjects is an allergen-specific response.

Asthma

Kang and colleagues characterized the asthmatics with cockroach allergies and compared them with asthmatics without such allergies. The cockroach-sensitive patients had year-round symptoms, and their disease worsened during the winter months. These patients commonly lived in the inner city, where cockroach infestation is high. These patients tended to have more severe disease that required more steroid treatment compared with other atopic individuals. Cockroach-sensitive patients tended to have higher total and antigen-specific IgE levels than did ragweed-sensitive asthmatics and were sensitized to fewer antigens than were their atopic counterparts. These patients also had a higher incidence of associated allergic rhinitis [54,55].

Low socioeconomic status and race have been reported to be principal determinants for hospitalization and asthma morbidity [56,57]. Sarpong et al showed that low socioeconomic status, Bla g 1 or Bla g 2 exposure greater than 1 U/g, and being black were associated independently with sensitization to cockroach allergens in atopic asthmatics. Investigators found that a black child

had a 16 times greater likelihood of experiencing exposure and sensitization to allergen than did a white child [41]. The Third National Health and Nutrition Examination Survey also reported increased prevalence rates of sensitivity to indoor allergens among black and Mexican American children [58]. NCICAS reported that inner-city children with cockroach sensitization who were exposed to high levels of allergen in their bedrooms had more symptoms, greater number of hospitalizations per year, more days of wheezing, greater number of missed school days, increased number of nights with sleep loss, and greater use of healthcare services than other children in the study who either had low cockroach exposure or were not sensitized to cockroach. These data provide evidence of the association between cockroach allergy and clinical disease. Epidemiologic data have revealed higher morbidity and mortality from asthma in inner-city blacks than whites; many factors contribute to the increased health risks, and cockroach allergen is clearly one risk factor [59]. A study in Boston of allergic patients demonstrated a significant association between exposure to cockroach allergen in the first 3 months of life and wheezing in the first year of life [60]. These authors showed that indoor levels of cockroach allergen were associated with early wheezing and with doctor-diagnosed asthma [43]. This association was significant after adjustment for socioeconomic factors. Economic status, race, allergen levels, and age of exposure to allergen all seem to be important in the risk for asthma.

Lewis and colleagues reported results of a longitudinal study evaluating the effects of cockroach-allergen sensitization and exposure in asthmatic women from metropolitan Boston. Their results showed that allergic individuals who were exposed to Bla g 1 or Bla g 2 at levels greater than 2 U/g had a three times greater likelihood of needing steroids and seeking emergency-room care than the entire asthma cohort studied. These results were adjusted for poverty levels [61]. Weiss and co-workers studied the rate of decline in forced expiratory volume in 1 second (FEV₁) in relation to home allergen exposure and reported a direct relationship between exposure and accelerated decline in lung function. The greatest decline in FEV₁ occurred in patients with positive skin test results, regardless of the presence of underlying asthma [62]. These data show that cockroach exposure in sensitized individuals increases short-term asthma morbidity but also may result in a decline in lung function with long-term exposure.

Allergen control

One major component of cockroach management involves reduction in allergen levels within living spaces. The first step in a comprehensive pest management strategy is monitoring. Stick traps can be used to quantify the number of roaches and provide an indirect indicator of the effectiveness of the cockroach management plan. An additional surveillance tool is the ELISA-based diagnostics that measure specific allergen levels in dust. In situations of health risk, such data can serve as useful adjuncts in monitoring the effectiveness of extermination [63]. Envi-

Table 2
Insecticides for cockroach control

Active ingredients	Products	Mechanisms	Effectiveness	Toxicity	Preparation
Organo-phosphates	Diazinon Chlorpyrifos (Dursban)	Cholinesterase inhibitor	Diazinon 40%–98% kill in 1 mo	LD ₅₀ , 135 mg/kg; CNS, flu-like, GI symptoms, short residual time	Liquid spray 1%–2% dust
Carbamates	Carbaryl (Sevin) Propoxur (Baygon)	Cholinesterase inhibitor	—	LD ₅₀ , 500 mg/kg; CNS, flu-like, GI symptoms	Granules, wettable powder emulsion
Pyrethrins	Permethrin Deltamethrine Fenvalerate Sumethrine	Inhibits ATP formation	Sumethrine 50%–80% kill in 2 wk	LD ₅₀ , 4000 mg/kg; tremor, choreoathetosis	Micro encapsulated wettable powder
Chlorinated hydrocarbons	Chlordane Lindane	CNS inhibitor	—	LD ₅₀ , 400mg/kg	
Avermectins	Abamectin (Avert, Raid)	GI, neurotoxin, ovulation inhibitor	Abamectin 92% kill in 1 mo	LD ₅₀ , 5000 mg/kg	0.05% gel granules, Bait stations
Miscellaneous	Fipronil Hydromethylnon (Combat, MaxForce) Sularamide	Fipronil blocks GABA-gated Cl _i ; is ATP inhibitor	92% kill in 1 mo	LD ₅₀ , 1500–5000 mg/kg	Gel bait stations
Growth regulators	Methoprene Hydroprene Fenoxycarb Biflubenarone Alsystin	Molting-hormone inhibitors; chitin synthase inhibitors	90% kill in 4–5 mo	LD ₅₀ , 10,000 mg/kg	0.125% liquid aerosol
Inorganics	Boric acid	ATP inhibitor	25%–50% kill in 2 wk	LD ₅₀ , 2500 mg/kg	1% spray, 30%–50% baits

Abbreviations: CNS, central nervous system; GABA, γ -aminobutyric acid; GI, gastrointestinal; LD₅₀, 50% lethal dose.

Adapted from Eggleston PA, Arruda LK. Ecology and elimination of cockroaches and allergens in the home. J Allergy Clin Immunol 2001;107:S422–9; with permission.

ronmental allergen levels are difficult to reduce because levels in cockroach-infested homes remain above the clinically important threshold for months after extermination.

Cockroach control consists of physical and chemical measures. Physical methods include reducing access to food sources (eg, grease, cooking debris, cooking waste disposed in garbage cans, open food containers, nonhuman food items with organic components) and water sources (eg, sink traps, pipe condensation, toilets, plumbing leaks, house plants). The food and water supplies should be targets for baiting and pesticide application. Repairs should be made to areas that may provide breeding and hiding locations for roaches, such as cracks.

Chemical treatment may be performed using residual insecticides (Table 2), such as inorganic compounds, chlorinated hydrocarbons, organophosphates, carbamates, pyrethroids, avermectin, insect-growth regulators, and the three new compounds fipronil, hydromethylnon, and sularamide. Gels are the preferred treatments, because they have a longer duration of effectiveness and because the pests carry the gels' toxic substances back to areas of heavy infestation. Bait traps that are impregnated with insecticides such as boric acid and hydromethylnon are also effective, but may require frequent replacement to provide long-term benefit. The earliest beneficial effect on population reduction occurs in 2 weeks; however, maximal effectiveness takes 4 to 6 weeks. The population remains under control for only 3 to 6 months, depending on the environment. An effective pest-control strategy involves vigorous cleaning of the infested area and application of insecticides. The environment should be cleaned before the application of pesticides. Once the pesticide has resulted in killing, the area should be cleaned again to remove cockroach debris. Sarpong et al evaluated the combination of pesticide and cleaning in urban dormitories and showed an 85% reduction in Bla g 2 levels in settled dust; however, the beneficial effect was lost within a few months [64]. NCICAS used a similar abatement strategy, and the results showed a slight decrease in the percentage of kitchens having living cockroaches (from 30% to 23%). The Bla g 1 level decreased from 69 U/g to 34 U/g over 6 months. At 1 year, the allergen levels returned to or exceeded baseline levels [65]. This study used only two applications of Abamectin, and compliance with cleaning was poor. Eggleston and colleagues used a more rigorous approach that involved professional pesticide application and professional cleaning. This study, conducted in inner-city Baltimore, showed a reduction in allergen levels by 78% to 93% during an 8-month period. The absolute levels still remained above 20 U/g, which is well above the 8 U/g associated with increased asthma morbidity [66]. This study seemed to be more successful at reducing allergen levels, but as in other studies, allergen levels did not remain low. The same authors confirmed these findings in another study that involved continual cleaning with sodium hypochlorite. Despite this change in approach, allergen levels often remained higher than the disease threshold level [67]. The best pest-management strategies seem to reduce allergen levels significantly but not to a level that is below the disease threshold level (8 U/g). One encouraging finding in NCICAS was that even though the cockroach

allergen levels remained above 30 U/g, the reported health problems decreased. The environmental levels may only be partly responsible for the noted asthma morbidity, and benefit in disease activity cannot be attributed solely to allergen reduction, which is difficult to achieve.

Diagnosis and treatment

The best management for patients with cockroach allergies is avoidance of exposure. This goal is difficult to achieve in situations where the sensitivity arises from exposure within the patient's home. In such cases, allergen immunotherapy may be an alternative. Immunotherapy for asthma has shown benefit for allergen-sensitized asthmatics whose symptoms worsen when challenged with the allergen [68]. Kang and co-workers reported improvement in symptom and medication scores in cockroach-sensitive asthmatics after treatment with immunotherapy. These authors also demonstrated an allergen-specific immune modulation by showing decreased release of basophil histamine in immunotherapy recipients [69]. One study evaluated 32 atopic patients with perennial rhinitis and asthma who were treated with cockroach immunotherapy for 3 years. This study, which did not evaluate changes in lung function, reported improvement in sneezing, rhinorrhea, and nasal obstruction. Serum IL-2 and IL-4 levels diminished by the third year of allergen-specific treatment [70]. There have been no other clinical studies of cockroach-specific immunotherapy and asthma.

Skin testing and immunotherapy have been performed with WBEs from various species. Most extracts have been nonstandardized, and units are reported as weight per volume or as protein nitrogen units. Patterson et al from the Food and Drug Administration reported highly variable total protein and allergen content (Bla g 1, 3503 U/g $\pm$ 1094 U/g) in 24 US cockroach extracts. Compared with previously characterized extracts, the relative potencies of these 24 extracts were variable (10–250 bioequivalent allergy units (BAU)/mL). The aqueous extracts contained no detectable allergen by competitive ELISA, and many extracts contained only small amounts of total protein. In glycerinated German cockroach extracts, the protein concentrations, relative potencies, and specific allergen levels were correlated significantly ($P < 0.001$) [71]. Until standardized products for cockroach immunotherapy are available, glycerinated products should be used. The variability in the extracts tested is not surprising, because the source material from which the extracts were developed may vary in its allergen content. Lehrer et al evaluated four different cockroach source materials and found that the materials had comparable activity, but the source material for American cockroach WBE was more variable than German cockroach WBE based on RAST inhibition activity [72]. The inconsistency in source materials can be a result of the lack of constant growth conditions, inconsistent protein extraction techniques, variable harvest times and inaccurate species identification. These data show that cockroach extracts need to be standardized to have a more consistent product between batches and manufacturers.

Summary

The ubiquitous existence of cockroaches and the large-scale domestic infestation seen in inner cities make cockroach proteins a significant indoor allergen and a risk factor for asthma among inner-city residents. Studies have shown that early exposure to high levels of allergen may lead to the development of asthma in individuals with a genetic predisposition to asthma. Although field trials at cockroach abatement do not yield promising results, integrated pest management still remains the best control strategy. In highly susceptible or symptomatic patients, allergen-specific immunotherapy may be beneficial, although data are limited. As molecular techniques improve and recombinant allergens are developed, a more novel form of T-cell-specific immunotherapy may prove to be efficacious without the anaphylactic side effects seen with traditional allergy vaccines.

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