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Cockroach Allergy and Asthma in a 30-Year-Old Man

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A growing body of evidence has implicated allergens derived from cockroaches as an important environmental factor that may aggravate asthma in sensitized persons. We present the case of a 30-year-old man with asthma and a cockroach allergy. Allergy skin testing confirmed hypersensitivity to cockroach extract, and a home visit revealed visual evidence of infestation and the presence of *Bla g* 1 German cockroach allergen in vacuumed dust. As is typical of patients with a cockroach allergy and asthma, multiple factors in addition to cockroach allergen appeared to aggravate the patient's asthma. A multimodality therapeutic regimen, which included medications as well as cleaning of the home, integrated pest management, and professional application of chemical controls, resulted in substantial clinical improvement. The pathophysiology, epidemiology, and clinical features of cockroach-allergic asthma are reviewed, and an approach to diagnosis and management is suggested. *Key words*: allergy, asthma, cockroach, indoor allergens. *Environ Health Perspect* 107:243–247 (1999). [Online 10 February 1999]
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Case Presentation

A 30-year-old Puerto Rican man with a history of asthma was referred for allergy skin testing at his own request. The patient reported a history of asthma since infancy. He had been hospitalized twice for asthma exacerbations, most recently 3 years earlier, and he had had several asthma-related emergency room visits in the past year. He reported ongoing symptoms of intermittent wheeze, dyspnea, productive cough, and chest tightness. His sleep was disturbed by these symptoms several nights per week. His current medications were a flunisolide metered-dose inhaler (MDI), four inhalations twice daily, and an albuterol MDI, two inhalations as needed, which he had been requiring twice daily on most days of the week.

The patient, who had a strong family history of asthma, voiced his suspicion that allergy to cockroaches might have something to do with his asthma. He reported living in a severely cockroach-infested apartment, a situation about which his landlord was refusing to take any action. He sometimes noticed red bumps on his skin after getting out of bed in the morning, and he wondered whether this might relate to cockroaches, which he saw frequently in his bedroom and throughout the apartment. In the past, he had noticed itchy, watery eyes after exposure to dogs or cats, but he denied having pets or visiting homes with pets. The patient had smoked cigarettes for the past 14 years, and currently smokes seven cigarettes per day.

Review of systems was notable for frequent symptoms consistent with gastroesophageal reflux. The patient was employed in the housekeeping department at a local university, where his job involved the maintenance of classroom facilities. He denied exposure to dust, fumes, or animals in his job.

On examination, the patient appeared well. Vital signs were unremarkable, and the skin was without rash. The nasal mucosa was slightly edematous and erythematous bilaterally, but the nasal passages were clear. Chest auscultation revealed faint expiratory wheezes at both lung bases. The heart and abdomen were normal. Extremities showed no clubbing or edema. Peak expiratory flow rate was 520 l/m (95% of predicted).

Allergy testing by the epicutaneous (skin prick) technique showed a positive reaction to cockroach extract, with a wheal diameter of 6 mm and a flare diameter of 30 mm. Other positive skin tests included mixed ragweed, maple tree pollen, cat, dog, and dust mite (*Der f*) extracts. There was a borderline reaction to *Aspergillus fumigatus*. The patient was instructed to increase his flunisolide MDI to six puffs twice daily. He was educated about the need for and methods of reducing his exposure to cockroach and dust mite allergens. He was given smoking cessation counseling. He was educated on how to prevent gastroesophageal reflux and treated with oral omeprazole.

A visit was made to the patient's home as part of a pilot research project. He and his wife lived on the top floor of a four-story wood-frame building in a low-income neighborhood in Boston, Massachusetts. On inspection, their small one-bedroom apartment had severe cockroach infestation. Living cockroaches were seen in numerous locations in the kitchen and entryway of the apartment. Dead cockroaches were seen in all cabinets, and roach stains were noted in numerous locations. The bedroom had low-pile carpeting, and the patient's mattress and pillows did not have allergen-impermeable covers. Dust specimens were collected according to a standard research protocol and sieved to separate the fine dust, which was extracted and assayed for the cockroach allergen *Bla g* 1 by a monoclonal antibody enzyme-linked immunosorbent assay (ELISA). The concentration of *Bla g* 1 in the bed, bedroom floor, and kitchen floor were 0.77, 3.3, and 29 U/g of dust, respectively. In dust vacuumed from the bed, the concentration of the dust mite allergens *Der f* 1 and *Der p* 1 were low (0.073 µg/g of dust) and undetectable, respectively. Dust from the bedroom floor had a moderate concentration of *Der f* 1 (1.3 µg/g of dust).

Intensive cleaning and professional pest control were carried out in the patient's apartment as part of the pilot research project. The patient was educated in the methods of integrated pest management. Chemical controls included gel baits, bait stations, and boric acid powder inside wall voids. The patient's mattress and pillows were encased in allergy-proof covers.

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One month later he returned to the clinic. He reported a large reduction in cockroaches in his home after the intervention. He had stopped smoking and was using the inhaled corticosteroid as prescribed. He was taking omeprazole daily and reported that his symptoms of gastroesophageal reflux had resolved. He reported that his symptoms of wheezing, dyspnea, cough, and chest tightness were much less frequent, although he was still requiring albuterol about 3 days/week.

Discussion

The evaluation of the patient with asthma should always include a search for environmental factors that may cause or aggravate this condition. These factors include inhaled or ingested allergens, inhaled irritants, and medications such as aspirin or beta blockers, which aggravate symptoms in some asthmatics by pharmacologic mechanisms. Inhalational exposure to allergens and irritants may occur in the home, in the workplace, out of doors, or in any combination of these. Examples of potentially harmful exposures in the home include cat and dust mite allergens (*1*), environmental tobacco smoke (*2*), and household cleaners that release irritating fumes. Workplace exposures that may cause or aggravate asthma are numerous (*3*): some common examples include flour dust in bakeries, isocyanates and other components of spray paint in auto body shops, and quarternary ammonium compounds in the antiseptic cleaners used by hospital housekeeping workers. Outdoor exposures that may aggravate asthma include Alternaria spores and the ambient pollutants ozone (*4*) and fine particles (*5*).

Cockroach Allergy and Asthma

Immunoglobulin E-mediated (type 1) hypersensitivity plays a central role in the pathogenesis of many cases of asthma. In genetically susceptible persons, exposure to allergenic substances derived from animals and plants is often a critical environmental factor influencing the development and severity of this condition, and a growing body of evidence has implicated allergens derived from cockroaches as being particulary important in this regard.

Following early reports (*6,7*) that some allergy patients displayed immediate cutaneous hypersensitivity to cockroach extract, Bernton and Brown (*8,9*) systematically evaluated cockroach sensitivity among allergy clinic patients. In Washington, DC, they observed that 28% of 114 unselected allergy patients had positive allergy skin tests to German cockroach (*Blattella germanica*) extract, compared with only 7.5% of 253 healthy control subjects (*8*). In New York City, 44% of 589 patients seen at hospital-based allergy clinics had positive skin test reactions to German cockroach extract (*9*). Analysis by ethnic subgroup revealed striking variation in the prevalence of skin test reactivity to cockroach extract, with a prevalence of 59% among Puerto Rican patients. The authors concluded that the high prevalence of skin test reactivity among Puerto Rican patients in New York was related to the high prevalence of cockroach infestation in the homes of this group, consistent with the observation that atopic persons tend to develop sensitization to the allergens most common in their environment.

Subsequent reports have revealed moderate to high rates of immediate cutaneous hypersensitivity to cockroach extract among asthma and allergy patients in other U.S. cities (*10–14*) and in other parts of the world (*15–17*). For example, data from the National Cooperative Inner-City Asthma Study (NCICAS) indicated that 36% of 1,286 asthmatic children living in low-income communities in six northeastern U.S. cities had a positive allergy skin test to German cockroach extract (*13*). In a study of asthmatic children in metropolitan Baltimore, Maryland, urban children were more likely to have a positive skin test to cockroach extract than were suburban children, and African–American race and low socioeconomic status were independently associated with skin test reactivity to cockroach extract (*18*).

The potential relevance of cockroach hypersensitivity to asthma has been supported by specific bronchial provocation studies. Most asthma patients with positive skin tests to cockroach extract develop an acute asthmatic response upon inhalation of cockroach extract aerosol in the laboratory (*19,20*). Most of these patients also display a late asthmatic reaction (dual response) hours later (*20*). Cockroach skin test-negative asthmatics, in contrast, do not react upon inhaling aerosols of cockroach extract (*19,20*).

The immunologic and molecular characterization of major cockroach allergens has greatly facilitated the clinical and epidemiologic investigation of cockroach allergy and asthma. Much of this work has focused on allergens derived from the German cockroach (see Fig. 1), the most common cockroach species infesting homes in cities in the United States and many other parts of the world. Multiple allergens have been observed in extracts of German cockroach, some specific to the German cockroach and some cross-reactive with allergens from other species such as the American cockroach (*Periplaneta americana*; see Fig. 2) (*21–26*). Two major German cockroach allergens, so defined on the basis of the high prevalence of specific IgE against them among cockroach-allergic patients, have been designated *Bla g* 1 and *Bla g* 2 (*24,25*). *Bla g* 1 is a 25- to 35-kd protein that has been purified from both German and American cockroaches (*24*). Approximately 30% of cockroach-allergic patients in Virginia were found to have IgE specific for this allergen (*25*). *Bla g 2* is a 36-kd protein specific to the German cockroach (*25*); approximately 60% of cockroach allergic patients in Virginia had IgE specific to this allergen. Molecular cloning of the *Bla g* 2 allergen has revealed sequence homology to aspartic proteases, and a high concentration of *Bla g* 2 has been observed in the cockroach digestive system, suggesting that the allergen may be a digestive enzyme (*27*). Another recently characterized German cockroach allergen, *Bla g* 4, is a 21-kd protein for which 40–60% of cockroach-allergic patients in Virginia had specific IgE (*28*). Sequence homology suggests that this protein may be a calycin (*28*).

ELISAs for major cockroach allergens, particularly *Bla g* 1 (*29,30*) and *Bla g* 2 (*29*), provide a method for measuring the levels of these allergens in the home and other environments. Both monoclonal (*29*) and monospecific polyclonal (*30*) antibodies have been employed in these assays. Usually applied to vacuumed dust samples, these measurements provide estimates of exposure

Figure 1. German cockroach (*Blattella germanica*) male (A) and female (B). Reproduced from *Urban Entomology* [W Ebeling. Berkeley, CA:Division of Agricultural Sciences, University of California Berkeley, 1978;Plate III] with permission from the University of California Board of Regents.

that are presumably more accurate and more relevant to biologic effects than are exposure estimates based on observations of the number of cockroaches seen or trapped in a particular environment. A high proportion of low-income urban homes have detectable cockroach allergen in vacuumed house dust (*18,29,31*). For example, 27 (71%) of 38 of urban homes sampled in Atlanta, Georgia, had detectable *Bla g* 1 in vacuumed dust (range 4–1,340 U/g of fine dust) (*29*). In NCICAS, the homes of 406 (85%) of 476 urban asthmatic children had detectable *Bla g* 1 allergen in bedroom dust, and 239 (50%) of the homes had levels exceeding 8 U/g of dust (*31*). In the northeastern United States, high levels of *Bla g* 1 or *Bla g* 2 in vacuumed dust are associated with urban residence, African–American race, and low socioeconomic status (*18,32*). Within a given home, the highest cockroach allergen levels are usually in the kitchen, where food and moisture promote infestation, although substantial levels of allergen are also measurable in bedding, bedroom floors, and upholstered furniture (*29,32*). In a study in Wilmington, Delaware, 20% of homes with no visible evidence of cockroach infestation had detectable levels of *Bla g* 2 in at least one room (*29*). Cockroach allergens appear to be associated with relatively large particles that remain airborne in detectable quantities for only a short time after disturbance (*33*).

Studies employing ELISA measurements of cockroach allergens have suggested that exposure to these allergens in the home may promote allergic sensitization to cockroaches. Among 81 asthmatic children in Baltimore, the levels of cockroach allergen (*Bla g* 1 or *Bla g* 2) in the bedroom were significantly associated with skin test reactivity to cockroach extract, even after adjustment for covariates including age, race, and socioeconomic status (*18*). Of the 22 asthmatic children with a bedroom level of *Bla g* 1 or *Bla g* 2 exceeding 1 U/g of dust, over 80% had a positive skin test to cockroach extract. Cross-sectional studies of current hypersensitivity and exposure status are unable to elucidate the temporal and dose–response aspects of the relation of exposure to the development of allergic sensitization. The hypothesis that exposure to cockroach allergen is an independent risk factor for the initial development of asthma is untested, although it is currently being evaluated by longitudinal birth-cohort studies.

Several studies have addressed the hypothesis that exposure to cockroach allergen may be an independent risk factor for exacerbation of existing asthma. Case–control studies of children in Atlanta (*34*) and adults in Wilmington (*32*) revealed that subjects presenting with acute asthma exacerbations were substantially more likely than nonasthmatic controls to have the combination of sensitivity to an indoor allergen (cockroach, dust mite, or cat) and significant exposure to that allergen in their home. Most of this association, however, was explained by the association between asthma and allergic sensitization per se, and these studies do not establish with certainty whether the level of exposure to cockroach and other indoor allergens is related to the risk of asthma exacerbation among sensitized asthmatics.

The NCICAS examined skin test sensitivity, bedroom dust allergen levels, and asthma morbidity among 476 asthmatic children (*31*). Children with the combination of a positive skin test reaction to cockroach extract and a bedroom level of *Bla g* 1 exceeding 8 U/g of dust had significantly more hospitalizations for asthma, unscheduled medical visits, and parent-reported wheezing than other children. Neither cockroach skin test reactivity in the absence of exposure nor cockroach allergen exposure in the absence of skin test reactivity was associated with increased morbidity. In this population, exposure to dust mite and cat allergens was much less common than exposure to cockroach allergen, and neither cat nor dust mite allergen exposure was significantly related to asthma morbidity.

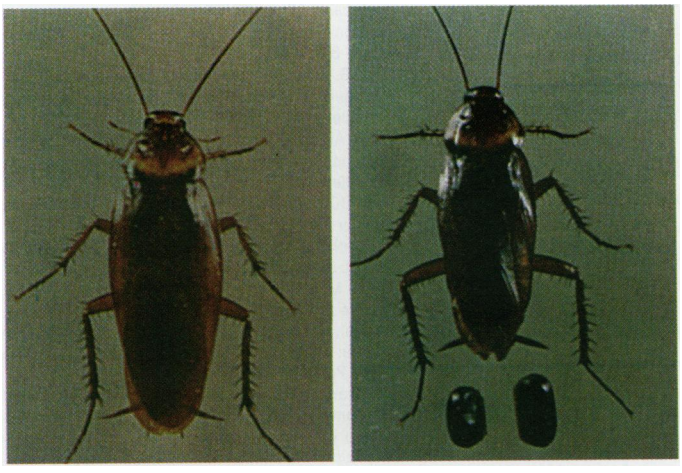

Figure 2. American cockroach (*Periplaneta americana*) male (A) and female (B). Reproduced from *Urban Entomology* [W Ebeling. Berkeley, CA:Division of Agricultural Sciences, University of California Berkeley, 1978;Plate III] with permission from the University of California Board of Regents.

It has been suggested that cockroach allergy is associated with particularly severe and chronic asthma (*35,36*). While it is indeed possible that cockroach allergen is more likely than other allergens to induce severe and chronic asthma symptoms, the severity and persistence of asthma in cockroach-sensitized residents of the inner city may relate to the effects of cockroach allergen exposure combined with other factors associated with poverty, including limited access to medical care and medications, low birth weight, prematurity, obesity, dietary factors, and smoking.

Evaluation and Management of the Patient

The clinical presentation of cockroach-allergic asthma is typically nonspecific. Occupational asthma in a laboratory worker who reported symptoms whenever working with a certain species of cockroaches has been reported (*19*), but such cases are unusual. More typically, exposure is related to infestation of the home or workplace, and is not recognized by the patient to be an environmental factor relevant to asthma. Because the exposure is chronic and the source of the allergen may not be apparent to the patient, there is often no clear history of asthma symptoms having been precipitated by exposure. Instead, there is usually a nonspecific history of perennial asthma, possibly worse in the winter, when more time is spent indoors (*36*). Patients may report aggravation of asthma symptoms by household cleaning activities, particularly in areas with visible evidence of cockroach infestation, and rare patients may even have experienced a rash at sites where cockroach bodies contacted their skin during cleaning. Occasionally, as in the case reported here, a patient may voice suspicion of cockroach allergy, but more often cockroach allergy becomes a consideration because of a physician inquiry about cockroach infestation or because of a positive allergy skin test result. Because cockroaches spend most of their time hidden from sight in small harborages, infestation and significant allergen exposure may be present in a home in which cockroaches are rarely seen by the occupants.

Patients with poorly controlled asthma and possible cockroach exposure should undergo allergy skin testing with either German cockroach extract or mixed German and American cockroach extract. Commercially available cockroach extracts have been reported to vary considerably in the concentration of major cockroach allergens (*25*), but the impact of this variability on test sensitivity has not been defined. When allergy skin testing is not possible, serum IgE specific for cockroach allergens can be measured by the radioallergosorbent test (RAST). A positive skin test or serum

RAST in the context of poorly controlled asthma and reported cockroach infestation should be taken as evidence of cockroach-allergic asthma. In some cases, cockroach may be the only identifiable allergen (*7,12*), but more often, patients are sensitized to multiple indoor and/or outdoor aeroallergens (*12*), as in the case of the patient described.

In addition to therapy with antiinflammatory and bronchodilator medications, the management of cockroach-allergic asthma should include efforts to reduce exposure to cockroach allergens in the home or work environment. Avoidance of dusty jobs in cockroach-infested buildings and the use of respiratory protection when undertaking such jobs are logical steps to recommend. Exposure in the home will be optimally reduced by moving out of the infested home and into a noninfested one, but this is rarely feasible. For more patients, avoidance measures will consist of efforts to reduce cockroach infestation and cockroach allergen levels in the home. Cockroach infestation in the home can usually be greatly reduced or even eliminated by combining the approach of integrated pest management (IPM) with the use of modern chemical controls. IPM is a strategy for making the environment as inhospitable as possible for cockroaches by sealing entry points and small enclosed spaces (harborages) and eliminating sources of water (e.g., leaking pipes) and food (e.g., sealing all open food in plastic or glass and rigorously cleaning crumbs from the floor). Chemical controls favored by most pest-control authorities include hydramethylnon or abamectin gel baits and bait stations, sometimes combined with the application of boric acid powder in harborages before they are sealed or in other areas not accessible to gel baiting. Hydroprene, an insect growth retardant, is also favored by some authorities as an additional component of an aggressive cockroach control program. In cases of a heavy infestation, cockroaches may be flushed out of harborages with hot air and then removed by a vacuum cleaner to achieve a quick reduction in their population. Insecticide sprays are not recommended, both because they are less efficacious than gel baits and because inhalation of these products may provoke asthma symptoms (*37*).

Unfortunately, cockroach allergens are persistent in the indoor environment and are still measurable in vacuumed dust even after the cockroach population has been greatly reduced. One study of an urban dormitory chronically infested with German cockroaches showed that the professional application of pesticide followed by vacuuming was associated with significant reductions in the concentration of the *Bla g 2* in dust vacuumed from kitchen and bedroom floors as well as from bedding (*38*). Preliminary data from recent studies in urban homes, however, have revealed disappointingly little rapid impact of professional pest control and cleaning on dust concentrations of cockroach allergens (*39*). It is possible that pest control combined with rigorous cleaning may reduce the total amount of allergen in a home, although the concentration of allergen in vacuumed dust may decline more slowly. Research efforts are under way to determine the optimal methods of reducing cockroach allergen in infested homes as well as the optimal metric for quantifying exposure.

Immunotherapy with cockroach extract has been reported to lead to a beneficial change in immunological and clinical parameters in one small study (*40*), but the role of immunotherapy in asthma remains controversial, and immunotherapy for cockroach-allergic asthma is not generally considered a modality of proven efficacy at this time.

An aspect of this case that is typical of patients with cockroach allergy and asthma is that the cockroach allergy was not the only factor influencing the severity of asthma symptoms. Skin testing revealed hypersensitivity to multiple indoor and outdoor allergens, and dust mite avoidance measures were recommended along with cockroach remediation. Although bed levels of dust mite allergen were low, encasement of the mattress and pillows may have reduced exposure to dust mite as well as cockroach allergens. The patient was smoking cigarettes upon initial presentation, and he subsequently succeeded in quitting, which may have contributed to his clinical improvement. In addition, he initially reported symptoms of gastroesophageal reflux, a common condition that can aggravate asthma. Education and medical treatment led to improvement of his reflux symptoms, which in turn may have contributed to the improvement of his asthma. Finally, he was treated with a higher dose of inhaled corticosteroid. Asthma is a complex, multifactorial condition, and the management of patients with poorly controlled asthma often involves multiple modalities of environmental and medical intervention.

Conclusion

A growing body of evidence indicates that cockroach allergy is a major environmental risk factor for the aggravation of asthma. The symptoms of patients with cockroach-allergic asthma, as in this case, are nonspecific, and questioning by the clinician about infestation accompanied by allergy skin testing or serum RAST are crucial to making the diagnosis. In addition to asthma medications, management should include efforts to reduce exposure to cockroach allergens. The combination of cockroach control measures, including IPM techniques and chemical controls, and thorough cleaning is a logical step to reduce exposure to cockroach allergen, but the clinical efficacy of such an intervention has yet to be demonstrated. Although modern cockroach-control approaches can greatly reduce the level of infestation in a home, it appears to be difficult to achieve rapid reductions in cockroach allergen levels. Immunotherapy with cockroach extract is of uncertain clinical benefit at this time. Although the proportion of asthma morbidity in the inner city attributable to cockroach allergy is not known, it may be substantial. Cockroaches do not respect the borders between apartments, and reducing asthma morbidity related to cockroach allergy may require a focus that extends beyond the individual patient to neighborhood and community efforts to improve housing conditions.

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