

## Chapter 7

# **The ABC's of Indoor Health:**

## **Allergens, Baits, and Cockroach Mitigation Strategies**

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The German cockroach, *Blattella germanica*, is a major structural pest, and cockroach allergens have been linked to the development and exacerbation of allergic disease and asthma in cockroach sensitive individuals. The inner-city residential environment often supports large cockroach infestations, which expose residents to high levels of allergens. This review summarizes information on the public health and veterinary importance of the German cockroach. It then presents a brief overview of the current status of various pest control options, with particular emphasis on insecticide baits and the role of horizontal transfer of active ingredient among cockroaches. Finally, I summarize experimental efforts to both eradicate cockroach infestations and to reduce allergen levels. Field studies show that intensive, targeted cockroach control with reduced-risk gel baits can lead to both dramatic reductions in cockroaches and clinically significant declines in cockroach allergens.

Human population growth and industrial development continue to lead to urbanization, especially in developing countries, where people move in large numbers from rural provinces to urban centers. The resulting urban mix of densely packed and crowded residences, centralized large-scale food processing and distribution, and a network of plumbing and sewer lines provides several

commensal indoor pests easy access to, and dispersal within, the human-built environment.

While most indoor pests, including ants, bed bugs, beetles, fleas, flies, and termites are facultative commensals with humans, the German cockroach, *Blattella germanica*, stands alone as the only indoor pest with an obligate relationship with humans and human-built structures. A handful of the approximately 4,000 described cockroach species are considered pests – including *Supella longipalpa* (brownbanded), *Periplaneta americana* (American), *Periplaneta fuliginosa* (smokybrown), *Periplaneta australasiae* (Australian or Australasian), *Periplaneta brunea* (brown), *Blatta orientalis* (oriental), and *Eurycotis floridana* (Florida) – but the German cockroach remains the most important and is becoming so in more developing countries as indoor temperature and humidity are more ubiquitously managed in residential and other structural environments.

## **The German Cockroach: Public Health and Veterinary Pest**

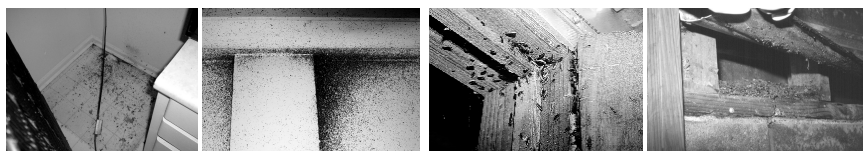
The German cockroach poses both direct and indirect hazards to humans and animals. The major reasons for suppressing indoor cockroach infestations and the choice of control options include public health, veterinary and aesthetic concerns, the harmful effects of insecticides to humans, pets and the environment, and regulatory requirements.

### **Cockroaches as Producers of Allergens**

The prevalence and severity of asthma have been increasing dramatically over the past 40 years (1), and in the United States, asthma affects approximately 30 million people, 9 million of whom are children under the age of 18 (2); it is one of the most costly diseases, estimated at \$12.7 billion annually (3). Although triggers of allergies and asthma are multifactorial, it is thought that the same changes in housing design that support cockroach infestations, as well as changes in human behavior (e.g., more time spent indoors) have resulted in prolonged human exposure to indoor aeroallergens of biological origins, including from cockroaches.

Because cockroach infestations can reach extremely high levels in homes and in industrial and agricultural situations (Figure 1), they pose risks from inhalant allergens. Approximately 26% of the U.S. population, aged 6 to 59, is sensitive to German cockroach allergens (4), and evidence suggests that exposure to cockroach allergen might be the most important risk factor for asthma in inner-city households. The National Cooperative Inner-City Asthma Study (NCICAS) found that asthma morbidity was highest in children with *both* a positive skin-test response and a high exposure to the cockroach allergen (5). Detectable levels of this cockroach allergen were found in 85% of the bedrooms tested, and 50% of the bedrooms had levels above the proposed threshold for allergic sensitization. The same study showed that 37% of inner-city children were allergic to cockroaches because of chronic exposure to cockroaches (5). Of

the ~400,000 yearly emergency room admissions of adults with asthma, ~200,000 are associated with mite, cat, or cockroach allergens (6). In the NCICAS, children that were sensitive to cockroach allergens had a 3.4-times higher rate of hospitalization than other study cohorts, they made 78% more asthma-related unscheduled visits to health care providers, awoke more nights, and missed more school days (5). Other studies (e.g., 7) have confirmed that cockroach allergen level is a good predictor of repeated wheezing and asthma. These measures of morbidity due to asthma highlight the medical and economic costs of cockroach infestations to society.



**Figure 1.** Left to right: Cockroaches and cockroach “frass” behind the refrigerator of a cockroach-infested apartment; fecal smears on a wall in a cockroach-infested apartment (smears are laden with allergens); doorway of an infested pig farm in Eastern NC; and the wall void of an infested pig farm showing the large accumulation of cockroach feces and allergens.

### Cockroaches as Vectors of Pathogens and Antibiotic Resistant Microbes

Because cockroaches move freely between waste and food, they can acquire, carry, and transfer pathogenic bacteria, helminthes, fungi, protozoa, and viruses either mechanically or in their digestive system (8). A number of studies have implicated cockroaches as potential mechanical vectors of microbial pathogens to humans and animals (e.g., 9, 10). We recently screened the gastrointestinal microbial community of German cockroaches from several swine farms for antibiotic sensitivity in two clinically important bacterial species (Aqeel et al., unpublished). All isolates of *Enterococcus faecalis* and *Escherichia coli* were highly resistant to tetracycline. In addition, a high percentage of *E. faecalis* was also resistant to neomycin, erythromycin, chloramphenicol and vancomycin. *Escherichia coli* isolates were found to be resistant to streptomycin and cephalothin, two widely used antibiotics in medicine. In contrast, bacterial isolates from cockroaches collected in residences in Raleigh, North Carolina, exhibited only minor tolerance to tetracycline. Since cockroaches readily spread within the residential community, they could play a significant role in the epidemiology of antibiotic resistant strains.

We also examined the vector competence of German cockroaches for one of the most important bacterial pathogens of piglets, a verotoxigenic *Escherichia coli*. While most *E. coli* are non-pathogenic, several strains (containing specific virulence factors: toxins and pili/fimbriae) cause severe and sometimes life-threatening diarrhea, septicemia, or enterotoxemia in neonatal, young, and post-

weaning piglets as well as adult pigs (11). Using multiplex PCR for screening 4 virulence factors associated with this bacterial strain, we showed that this pathogen remained viable and virulent in the cockroach gut and feces for >8 days after the initial exposure (12). These preliminary results strongly implicate cockroaches in the mechanical dissemination of antibiotic resistant pathogenic microbes from places where they evolve antibiotic resistance (e.g., farms) to residential settings and potentially even to food processing.

### **Indirect Effects Related to Insecticide Use**

Cockroaches are generally controlled with broad-spectrum neurotoxic insecticides. Insecticide use targeting cockroaches is widespread in inner-city communities, resulting in extensive indoor exposures to pesticides (13). Recent studies in New York City reported that 72% of recent mothers reported indoor insecticide exposure during pregnancy, and urine samples collected during delivery showed that 55% had detectable levels of a metabolite of the organophosphate chlorpyrifos, and 37% had detectable levels of a metabolite of pyrethroid insecticides (14). Another study in New York showed that 100% of participants had detectable airborne exposures to organophosphate and carbamate insecticides and these insecticides were detected in up to 74% of blood samples collected from mothers and newborns at delivery, implicating placental transfer of these compounds (13). There are several more such studies, all indicating that neurotoxic insecticides might have detrimental effects in the indoor environment (see 15), including a recent examination of the relationship between household exposure to pesticides and the risk of childhood hematopoietic malignancies (16).

On average, >100 kg of active ingredient are applied annually on each swine farm to control cockroaches (Schal, pers. obs.). Most commonly, the least expensive, older pyrethroid insecticides are used in the U.S., and organophosphate and carbamate insecticides are used in other countries. Few of the newest insecticides and the modern baits are labeled for use around livestock. Although the older insecticides can effectively reduce cockroach populations if properly applied (17), they also expose people and animals to unnecessary health and environmental risks (review: 18). Moreover, their efficacy becomes limited because insecticide resistance can develop rapidly in cockroach populations.

### **Economic Damage**

Cockroaches tend to aggregate within electrical conduits, relays, and electronic switching equipment. There are no estimates of the cost of mechanical damage caused by cockroaches, but a conservative estimate of \$1,000–\$2,000 of damaged equipment per swine farm per year, not including interruption of production (feed not getting to hogs, warmers not working, sprinklers disrupted), and assuming a 30% infestation rate of large farms (based on an NCSU Extension survey), this impact alone amounts to \$8.14 million in North Carolina

alone. Unfortunately, there are no reliable estimates of the monetary cost of cockroach infestations in loss of contaminated food, restaurant closings, litigation, and loss of return customers (as for example, on cruise ships).

In light of the significant and harmful effects of cockroach infestations in residential settings, hospitals, farm structures, food-processing facilities and food warehouses, as well as in transportation networks and recreational settings, it is astonishing that aesthetic injury level (AIL) has become a widely adopted concept in urban entomology. While the occasional smokybrown or wood cockroach that is trapped in a home may pose aesthetic concerns to residents, German cockroach infestations in hospitals, nursing homes, and inner-city apartments clearly pose public health concerns – AIL applied to German cockroaches trivializes their public health importance.

## **Status of German Cockroach Control**

Various approaches for controlling German cockroach infestations have been reviewed. Of particular interest are the following reviews: 18, 19, and 20.

### **Habitat Modification, Physical Changes, and Mass Removal**

Physical modification of the environment aims to reduce resources that sustain population growth, it stimulates movement to facilitate contact with residual insecticides, and it reduces the areas that require insecticide treatment. Structural modifications include maintenance of proper construction and sanitation, use of repellent sorptive dusts in wall and cabinet voids, sealing and caulking runways such as plumbing and electrical conduits between structures, removing resources such as food, water, and favorable shelters, treatment of structures with heat or freezing temperatures, and use of repellents to create “pest exclusion zones.” Mass removal of cockroaches can be implemented with food- or pheromone-baited traps and vacuum devices. All these approaches, however, appear to be effective only in combination with efficacious formulations of insecticides. Gold (21) reviews alternative, non-pesticide-based approaches.

### **Biological Control Approaches**

Although alternative approaches for cockroach control are sorely needed and it is essential that safe, effective, and environmentally compatible insect control techniques be developed and incorporated into sustainable IPM programs, biological control approaches are poorly developed for cockroaches (22, 23). Parasitoids have been used with some success to reduce outdoor and greenhouse populations of the American, oriental, and brownbanded cockroaches. However, there are no known parasitoids of *B. germanica* and various parasitic nematodes, viruses, fungi, bacteria, and protozoa have been tested against the German cockroach, with generally unimpressive results (23).

Nevertheless, Zurek et al. (17) showed that concurrent dosing of German cockroaches with the fungus *Metarhizium anisopliae* and boric acid (either topically applied as a dust or diluted in drinking water) killed more cockroaches faster than either material alone. The synergistic interaction between these two insecticides needs to be explored in the field.

In the course of molecular ecology studies of cockroach populations, we recently discovered a new entomopathogenic densovirus, *Blattella germanica* DNV (*BgDNV*). Infected cockroaches display several symptoms of pathology, including lethargy, flaccidity, poorly coordinated movements, and partial or complete paralysis of the hind legs (24). Several features make densoviruses potentially effective biological control agents against cockroaches: They tend to be highly host-specific, they infect most tissues of their hosts, they do not appear capable of infecting vertebrates, and they resist extreme environmental conditions. The tendency of cockroaches to aggregate and the ready movement of materials among them should facilitate the use of *BgDNV* in attractive baits to initiate and maintain epizootics.

## Chemical Approaches

Wickham (25; see also other reviews in 19) and Braness (26) reviewed the active ingredients and formulations that are used to control household pests, and Ebeling (27) compiled a thorough review of inorganic insecticides used against the German cockroach.

### *Insecticide Sprays*

“Space” treatments with various aerosol dispensers usually deploy nonresidual insecticides, such as synergized pyrethrins, allethrin, esfenvalerate, and resmethrin. Nevertheless, residual pyrethroids (e.g., cypermethrin) and insect growth regulators (e.g., hydroprene) are often used in consumer products, such as total-release aerosols (“foggers”). Nonresidual formulations, most containing pyrethrins, are also used by pest control technicians as flushing agents and by consumers in direct application to the pest. The efficacy of such treatments against the German cockroach is poorly documented.

For several decades, both consumers and pest control technicians have favored applications of broad-spectrum insecticides with long residual activity because the insecticides can be applied relatively rapidly and this approach allowed for longer intervals between treatments. Even in the context of better targeted approaches, such as the spot or “crack and crevice” treatments, the usual practice often consists of an initial application at a high rate, followed by regularly scheduled applications at lower rates. Broadcast, or general treatments of surfaces and baseboards with carbamates (bendiocarb, propoxur), organophosphates (acephate, chlorpyrifos, diazinon, propetamphos), abamectin, and pyrethroids were common practices into the early 1990s. Recently, however, such treatments, especially with carbamate and organophosphate insecticides, have declined due to federal regulations (e.g., U.S. Food Quality Protection Act

of 1996), insecticide resistance, and the development of highly effective bait formulations (below). Nevertheless, high-volume perimeter applications of pyrethroids, fipronil, chlorfenapyr, and neonicotinoids are used as residual barriers to control or repel various outdoor pests, including cockroaches, even though little data are available in support of the efficacy such treatments.

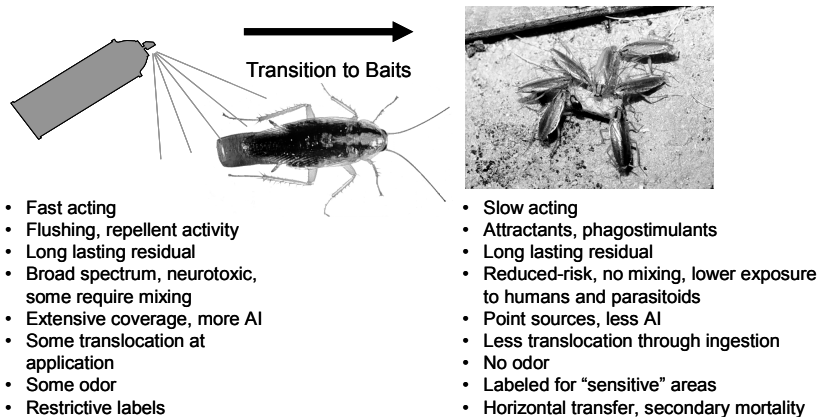
Crack-and-crevice spray applications utilize the same insecticides and formulations as do broadcast sprays. However, these applications use much less insecticide and they rationally target only cockroach aggregations and potential shelters. Also, crack-and-crevice approaches are not limited to spray formulations, as baits and dusts are also most efficacious when applied to cracks and crevices.

Though highly efficacious against *B. germanica*, residual application of powdered boric acid remains an underutilized approach, probably because it can be messy to dispense and its efficacy is slow compared to most other insecticides. Nevertheless, because boric acid has a very good safety record for mammals, we tested its efficacy against German cockroach infestations in farrowing rooms of a swine farm and compared it to the efficacy of cyfluthrin, a residual pyrethroid insecticide commonly used for cockroach control (17). Overall, boric acid dust and cyfluthrin spray treatments had comparable efficacy, but boric acid is less expensive and there are no known cases of pest resistance to it. We further showed, under similar field conditions, that boric acid significantly synergized the pathology of the fungus *Metarhizium anisopliae* against the German cockroach (28). Although boric acid dust can be used as an adequate alternative to conventional insecticides to control German cockroach infestations, its adoption into integrated cockroach management programs has been significantly constrained by technical limitations (e.g., expensive dusters) and potential human exposure and respiratory health risks associated with dust inhalation.

### *Insecticide Baits*

The German cockroach must feed before molting to the next stage, and food intake and reproduction are intimately linked in adult females (29) suggesting that baits should provide efficacious pest management, especially where food resources are limited. Indeed, a major shift has occurred in cockroach control in the last two decades, from residual sprays to gels and containerized baits (bait stations) (Figure 2). Insecticide baits can be placed in delimited zones and they reduce potential environmental contamination. Some baits may be used almost anywhere including sensitive areas such as food processing and preparation areas, hospitals, and biomedical laboratories. Because cockroaches tend to ingest much larger amounts of insecticide than they would otherwise absorb from a residual spray, and efficacious baits tend to kill more slowly, the insecticide, along with potentially toxic metabolites may be defecated or excreted before the cockroach dies, facilitating horizontal transfer of the active ingredient within cockroach aggregations, and potentially secondary mortality. Paradoxically, while the number of active ingredients and the diversity of their modes of action has slowed for residual insecticides, which are mainly an

outcome of discovery programs that target agricultural pests, the assortment of active ingredients and modes of action in cockroach baits continue to increase. Abamectin, acetamiprid, boric acid, fipronil, hydramethylnon, imidacloprid, indoxacarb, and sulfluramid are some actives used in baits, and others, including other neonicotinoids, ryanodine receptor activators, and spinosyns are some new materials being considered against cockroaches. It will be interesting to determine whether the comparative efficacy of these new chemistries is due to low repellency, efficacy at lower dosages, different modes of action, lack of resistance, delayed activity, or the effects of secondary mortality.



**Figure 2.** Comparison of characteristics of spray-based formulations of residual insecticides (left) and reduced-risk bait formulations (right) for German cockroach control. A gravid female is shown (center, with egg case at left) and adults feeding (right).

Moisture is a limiting resource for cockroaches, and it is likely that gel formulations of baits increase the attraction, acceptability, and efficacy of baits. In addition, unlike containerized bait stations that contain pastes or solid bait matrices, gel baits are dispensed in many more locations that are in close proximity to cockroach aggregations, probably further enhancing their efficacy. Given the superior efficacy of gel baits, it is surprising, however, that liquid baits have not been studied for cockroach control. We evaluated the effectiveness of borate-sugar-water liquid baits in choice and no-choice assays against the German cockroach. Boric acid was more effective than sodium tetraborate or disodium octaborate tetrahydrate, and aqueous solutions containing mixtures of up to 2% boric acid and up to 1 M of several inexpensive sugars (fructose, glucose, maltose, and sucrose) provided rapid and mortality of German cockroaches (30). Subsequent trials with liquid baits consisting of 1 or 2% boric acid and 0.5 M sucrose showed that these formulations effectively reduced cockroach infestations in a swine farm nursery (31). This approach, however, has not been used in residential settings.



Despite the dramatic rise in bait use, and the indisputably higher efficacy of baits than residual sprays, the basis for selecting an insecticide or a formulation for use in the indoor environment is often less rooted in efficacy and more related to inventories, costs, ease of application, odor, residual material (e.g., tank mix) from a previous application, or consumer preferences.

### *Horizontal Transfer and Secondary Kill*

Certain features of the ecology and reproductive physiology of the German cockroach may constrain the efficacy of bait formulations. For example, females spend most of their adult life in a gravid state during which they feed little and only intermittently (32); therefore, baits might be less effective against such females. Likewise, early instar *B. germanica* nymphs forage much less than older nymphs and adults (33), and this might reduce the efficacy of insecticidal baits, especially because early instars comprise a large fraction of cockroach populations. Careful placement of baits near cockroach aggregations may alleviate this problem of differential foraging. Another approach is to employ foraging individuals to deliver insecticide or pathogens to non-foraging cockroaches. In principle, this strategy would function best in gregarious or social insects and would require slow-acting insecticides so that foraging insects could return to the aggregation or nest before becoming immobilized by the insecticide.

Silverman et al. (34) proposed that German cockroaches redistribute ingested hydramethylnon from baits within aggregations and concluded from translocation assays of radio-labeled hydramethylnon in small cages that coprophagy played a major role in this process. Using assays that differentially excluded nymphs or adults from feeding on insecticide baits, Kopanic and Schal (35) quantified the relative contributions of direct (ingestion of bait) and indirect (ingestion of insecticide-laden feces) routes of insecticide uptake in large cages in the laboratory and in field populations. Exclusion of adult females from baits was associated with low mortality of 1<sup>st</sup> instars, suggesting that under normal conditions high neonate mortality could be attributed primarily to adult-mediated horizontal toxicant transfer through feces. In contrast, mortality of 2<sup>nd</sup> instars was high and significantly less dependent on adult foraging, suggesting a shift to active foraging (i.e., direct ingestion of bait) during the 2<sup>nd</sup> stadium. These results are consistent with our understanding of the adaptive benefits of coprophagy in the German cockroach. Starved 1<sup>st</sup> instars survive significantly longer with access to conspecific feces than when deprived of feces (36). In contrast, 2<sup>nd</sup> instars provided adult feces survived only marginally longer than starved counterparts, showing that coprophagy is stage-specific, as predicted from the bait transfer experiments of Kopanic and Schal (35). It appears that the benefit accrues from undigested nutrients in conspecific feces, more than from a symbiotic association with microbes, because nymphs given female feces were more likely to molt into the 2<sup>nd</sup> stadium than nymphs given male feces, and 1<sup>st</sup> instars that were fed the feces of adults that had been maintained on a high

protein diet survived longer than other cohorts fed the feces of adults that had been maintained on medium (22.5%) and low (5%) protein diets (36).

Other bait active ingredients are also horizontally transferred among cockroaches, but the mechanisms may differ, depending on their modes of action and speed of kill. When adult cockroaches were fed boric acid, chlorpyrifos, fipronil, or hydramethylnon in either small or large cages, exposure to the corpses and feces killed all 1<sup>st</sup> instars and most 2<sup>nd</sup> instars (37). However, when the dead cockroaches were removed from the large arenas and replaced with new cockroaches (i.e., in the absence of cannibalism and necrophagy), only residues of slow-acting hydramethylnon killed most of the nymphs and adults, whereas residues of fast acting insecticides (chlorpyrifos and fipronil) killed fewer nymphs and adults, even when the concentrations of chlorpyrifos and hydramethylnon were equivalent; abamectin baits failed to cause significant mortality in cockroaches that contacted the residues. It is possible that the relatively high concentration of hydramethylnon in the bait (2.15%) and its apparent stability in the digestive tract and feces contribute to the efficacy of hydramethylnon in secondary kill.

Buczowski and Schal (38) evaluated the effects of three different methods of delivering fipronil to adult male German cockroaches on secondary mortality in nymphs and adults. Topical application with an LD<sub>99</sub> dose (5 ng) was the least effective method for subsequent secondary kill, followed by exposure to residual fipronil deposits on a glass surface, which resulted in some mortality of early instars. Ingested fipronil bait was most effectively translocated, however, and caused high mortality of untreated adults and nymphs, even when compared to an equivalent amount of topically applied fipronil (25 ng). Because fipronil has high contact activity, the mechanisms that cause secondary kill may include contact with fipronil-contaminated substrates as well as ingestion of excreted residues and cannibalism of bait-fed cockroaches. However, unlike hydramethylnon, which is translocated primarily through coprophagy, fipronil is excreted mainly during onset of the paralytic symptoms, and most of the radio-labeled fipronil is excreted orally (39). Time-lapse video analysis further showed that 1<sup>st</sup> instars were attracted to these excretions, imbibed the liquid exudates, and died – a process termed emetophagy, which may constitute an important mechanism by which fast-acting, emetogenic insecticides are disseminated within cockroach populations (39). Buczowski et al. (40) further extended these ideas to indoxacarb and tertiary kill, showing that ingested indoxacarb was most effectively translocated when the recipients interacted with freshly symptomatic donors in the absence of alternative food.

The extensive findings from laboratory assays would suggest that horizontal transfer of bait active ingredients might contribute significantly to bait efficacy in the field. Although Kopanic and Schal (35) concluded, based on limited field results, that “horizontal toxicant transfer is a key factor in suppression of cockroach pest populations,” and horizontal transfer of bait is a heavily marketed phenomenon (e.g., as secondary and tertiary kill, domino effect, exponential control), no follow-up studies have been conducted in the field to critically evaluate the magnitude and significance of bait transfer in cockroach control.

## Integrated Cockroach Management

The indoor environment is highly conducive to implementation of a variety of approaches and tools, including use of photolabile active ingredients and physical and structural modifications to manipulate pest behavior and their spatial distribution. However, despite of the plethora of available options, cockroach suppression still relies heavily upon multiple applications of broad-spectrum insecticides to individual units (apartments, rooms in a nursing home, etc.), with little appreciation of the movement patterns of cockroaches. Often, integration of management options consists of mixing several related insecticides. But recent regulatory emphasis on IPM in school systems has resulted in greater emphasis on education and communication among researchers, extension personnel, consultants, pest control technicians, and the concerned public. Concomitantly, several recent studies have documented the superiority of integrated pest management approaches over calendar-based conventional spraying in both schools and residences.

Miller and Meek (41) compared the long-term costs and efficacy of a monthly baseboard and crack-and-crevice treatment with spray and dust formulations to a monitoring-based IPM treatment that involved vacuuming of apartments followed by monthly or quarterly applications of baits and insect growth regulator in Virginia public housing residences. The expenses associated with the IPM treatment—the costs of technician time and product applied—were higher than for the conventional treatment, but it was also much more effective. Indeed, trap catch data suggested that the conventional treatment had little effect on the cockroach populations over the course of a year.

A similar study, also comparing IPM and conventional approaches, but in North Carolina elementary schools, reached different conclusions. Although the IPM services were significantly more time-consuming, and therefore incurred higher costs associated with labor, the overall costs of the two types of treatments were similar, as was their efficacy of cockroach control (42). However, environmental residues of acephate, chlorpyrifos, and propetamphos were higher in swab samples taken in the conventionally treated schools.

## Allergen Mitigation Strategies

Seven *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. Gore and Schal (43) provide an extensive review of the molecular biology, tissue distribution, and allergenicity of each allergen, as well as sampling methodology, demographics of cockroach allergen exposure and sensitization, and intervention studies aimed at allergen mitigation in infested homes.

## Reduced-Risk Baits: Pivotal Components of Allergen Mitigation

The central tenet of allergic disease and asthma intervention is to minimize exposure through environmental allergen reduction, involving (a) suppression of cockroach populations, and (b) removal of residual cockroach allergens. Indeed, there is a strong correlation between cockroach allergen concentrations in kitchen dust and German cockroach populations based on trap catches, with  $r = 0.73$  for Bla g 1 (*Blattella germanica* allergen 1) and  $r = 0.84$  for Bla g 2 (44). However, most environmental interventions that used a two-pronged approach of pest control and cleaning failed to attain clinically significant reductions of cockroach allergens in infested homes (see supplemental Table in 43). Several reasons likely account for these results, including inadequate or lack of monitoring of the cockroach population, infrequent and outdated pest control treatments that resulted in inferior efficacy, and poor resident buy-in and cooperation with the programs.

More recent studies have followed the recognition that extensive cleaning and resident education could not be fully efficacious without highly effective pest control and impartial assessments of the pest population (hence, efficacy of the intervention). A 6-month intervention study in North Carolina combined extensive monitoring-guided and lay-out maps-guided treatments with reduced-risk hydramethylnon gel bait, resident education, and professional cleaning that was also guided by trap catch (45). For the first time in an allergen mitigation study, large reductions in the cockroach populations were observed in treatment homes: by month 6, the median trap catch was 0 in each monitored room (kitchen, living room, bed room; 113, 76 and 78, respectively at baseline), trap counts were 0 in 9 kitchens, 11 living rooms, and 12 bedrooms of the 16 homes, and 37.5% of the homes had no trapped cockroaches in any room. The high efficacy of cockroach control was accompanied by significant reductions in cockroach allergen levels below the human sensitization threshold: Bla g 1, a major aeroallergen with up to 77% IgE prevalence among cockroach-allergic individuals (46), decreased in concentration (Units per gram dust) from 633 to 24 on kitchen floors (96% reduction), from 25 to 4.3 on living room floors/sofas (83%), from 46 to 7.3 on bedroom floors (84%), and from 6.1 to 1.0 in bedroom beds (84% reduction) (45).

The success of this intervention led us to examine which of the three intervention tactics was key to the observed effects, because the two physical interventions were not equally deployable: whole home cleaning was substantially more expensive and intrusive than pest control. Therefore, a 6-month continuation of the Arbes et al. (45) study, crossed-over the non-intervention control homes to an 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 (47). The results showed that pest control alone resulted in large reductions in the cockroach populations, but surprisingly, it also brought about highly significant reductions in Bla g 1 levels. The mean Bla g 1 concentrations decreased from 287 to 14.4 on kitchen floors (95% reduction), from 28.8 to 5.6 on living room floors/sofas (81%), from 26.7 to 4.7 on bedroom floors (82%), and from 7.2 to

2.4 for beds (67% reduction); similar results were seen for the allergen Bla g 2 (47).

Baits have become a pivotal tool in cockroach control. Wang and Bennett (48) compared a bait-alone intervention with an IPM approach (cockroaches flushed and vacuumed, sticky traps deployed, educational materials delivered, and fipronil- and hydramethylnon-containing baits) on a building-wide basis in public housing in Indiana. No allergen measurements were conducted. Of 5 post-treatment evaluations during a 7 month period, cockroach control was significantly more efficacious in IPM apartments in only 2 evaluations (1 and 4 months after initial treatment), but the 1-month evaluation appeared to be aberrant due to a decline in efficacy from 48% at week 2 to 18% at week 4 and then up to 96% at week 8, and the efficacy at month 4 was 100% (IPM) and 96.4% (bait only). Although Wang and Bennett (48) conclude that “IPM is a more sustainable method of population reduction” the cost of IPM was significantly higher than that of the bait treatment and the benefits appeared to be nominal.

The impressive efficacy of baits alone (47, 48), coupled with the fact that baits constitute a major component of any IPM program of cockroach control, highlight an important public policy implication—under the constraints of tight public housing budgets, most of the intervention effort should be invested in bait-based eradication of cockroach infestations. Extensive cleaning is clearly required to remove residual allergens, but this rather costly effort is best reserved as a follow-up to cockroach eradication.

In a commentary about the Arbes et al. (45) article, Eggleston (49) stated: “[it] is a model of the sort of difficult, well-planned, and well-executed clinical research that will move the field of environmental avoidance forward. It represents what is technically called an efficacy trial in that the investigators chose to apply the treatment with as little reliance on the adherence of the families participating as possible. This is as opposed to an effectiveness trial that would apply the treatment as it might be applied in clinical practice or by a public health department, usually relying on participant adherence.” In light of the general disappointing results of most interventions involving professional pest control (see 43 for a summary), Eggleston’s appeal for an effectiveness trial was well founded.

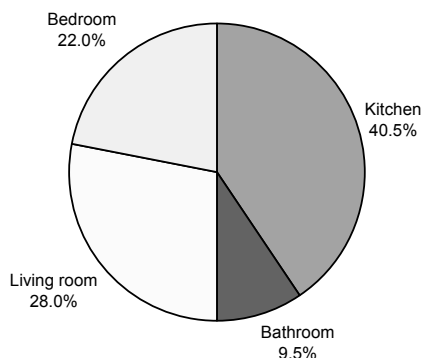
To evaluate the effectiveness of professional pest control in cockroach allergen mitigation, we used untreated control homes and two intervention groups of homes in North Carolina: one treated with insecticide baits applied by research personnel following previously established protocols (lay-out maps, sticky traps, whole-home baiting), and the other provided with professional pest control (50). Once again, the intensive, targeted approach was highly efficacious, reducing the median cockroach trap catch from 426.5 to 0 within 6 months, and cockroaches apparently were eliminated in 62.5% of the homes. From baseline to month 12, mean Bla g 1 concentrations decreased from 64.2 to 5.6 in kitchens (91.3% reduction), 10.6 to 1.1 in living rooms (89.6%), 10.7 to 1.9 on bedroom floors (82.2%), but only 3.6 to 2.3 in the bed (36.1% reduction). In contrast, homes treated by commercial technicians showed a much smaller decline in the cockroach population from 308.5 at baseline to 56.0 at month 6 (81.6% reduction, 1 of 17 homes with 0 trap catch) and Bla g 1 levels decreased from

66.9 to 43.0 in the kitchen (35.7% reduction), 14.3 to 5.7 in the living room (60.1%), 17.3 to 7.2 on the bedroom floor (58.4%), and from 5.5 to 1.9 in the bed (65.4% reduction). However, these changes were not significant compared with the untreated control homes (50). Although the contract-based commercial pest control was substantially less effective at reducing cockroach infestations and allergens, it was comparable to previously reported environmental interventions that employed pest control technicians (see 43 for review).

These results suggest that the relationship between the cockroach population and allergen concentration in a home is not linear—particularly during the decline in the cockroach population that occurs during pest control operations. The actual relationship may be exponential, such that a very large reduction in the cockroach infestation is needed to achieve significant reductions in the allergen level. The real shape of this relationship will have to await experimental evidence with a much higher sample size. But, if correct, the implication of this model is that some pest control practices may be acceptable to the consumer because they reduce the cockroach population, but because allergen levels remain above threshold values these practices may be clinically inferior.

### **Whole-Home vs. Partial Intervention**

Sever et al. (50) consider some of the technical, operational, and economic factors that may underlie the differences between efficacy and effectiveness trials. We speculated that the spatial distribution of the pest control efforts within homes might be important. Most commercial and consumer-based pest control, as well as academic field efficacy trials, treat only the kitchens, pantries and bathrooms, whereas we (45, 47, 50) treated whole homes. The rationale for our approach was that cockroaches in low-income NC homes are distributed throughout the home, including living rooms and bedrooms (Figure 3). Moreover, analysis of allergens in homes has shown that while cockroach allergen concentration is highest on the kitchen floor, the concentration on the living room floor is 67.4% as high, and allergen concentration on the bedroom floor is 55.9% that of kitchen dust (51), and asthmatic children are more likely to be more intimate contact longer with bedroom dust than kitchen dust. It is important to note that these values do not address allergen load in various rooms, that is, the total amount of allergen contained in all dust in the room.



**Figure 3.** Distribution of cockroaches among four rooms of 41 apartments in North Carolina. Four traps were deployed in each room, except the bathroom, which received only two traps. For this analysis, we consider percentage trapped cockroaches per trap per room.

A comparison, in progress, of baiting whole homes with indoxacarb bait versus baiting the kitchen and bathroom only with the same amount of bait suggests that when total trap catch is considered (a) a significantly faster decline in cockroaches is evident in whole home treatments within 7 days after the initial treatment, and (b) differences between the two interventions persist for at least 3 months, to the end of the trial (Santangelo et al., unpublished). As expected, we found no differences in the magnitude of the reductions in cockroach trap catches over time in the two interventions, but much faster and larger reductions were evident in the living rooms and bedrooms of the whole home treatments. Allergen samples from this work are being analyzed.

Interestingly, Wang and Bennett (48) were able to bait apartments over a 29 week period in a cumulative median time of 22 min per apartment, whereas our baiting efforts required at least 45 min per apartment for the initial treatment alone. While these differences might be attributable to different levels of sanitation, clutter, apartment sizes, resident cooperation, and cockroach population sizes, we suspect, again, that they relate to different spatial distributions of the baiting programs. Wang and Bennett (48) treated kitchens, pantries and bathrooms only, whereas we (45, 47, 50) treated the whole home. Using 10 microsatellite loci, we recently genotyped German cockroaches from 18 populations in Raleigh. Our preliminary results indicate that cockroaches collected in various rooms within a single apartment are panmictic, i.e., represent a single population, whereas cockroaches collected from different residences— even adjacent apartments — were genetically differentiated (Crissman et al., unpublished). Because dispersal and gene flow occur more often within apartments than between them, and various rooms in the home can be infested with cockroaches (Figure 3), it seems sensible to treat the whole residence as a target of cockroach control efforts.

## Outcomes of Interventions

A major uncertainty in allergen mitigation studies is the fate of the allergens. Extensive professional cleaning, even with denaturing agents, has generally resulted in only mediocre allergen reductions when pest control is substandard or unreported (see review: 43). In contrast, highly efficacious cockroach control, with or without cleaning, dramatically reduced allergen levels. Obviously, only allergen on accessible (sampled) surfaces was reduced (i.e., vacuumed and sieved for ELISA, see 52) – the allergen load in inaccessible voids and behind and under appliances and kitchen cabinets has not changed. We suggest that as few or no cockroaches remain to forage and defecate, less allergen is detected on exposed surfaces. A major uncertainty is whether the sampled surfaces best represent clinically relevant allergen concentrations, or if the large allergen reservoirs that remain inaccessible (see Figure 1) contribute to the aeroallergen population. Gore and Schal (43) review allergen sampling methodology and the potential health outcomes of successful interventions.

The global success of *B. germanica* has been associated with more constant environmental control and poor maintenance of structures, inferior sanitation, relatively inefficacious and difficult to apply spray insecticides, and a vast array of consumer products of questionable efficacy – especially when improperly deployed. An irony of insecticide discovery is that as biologically and genomically-inspired design, artificial networks, combinatorial chemistry, and high-throughput *in vitro* screening have become more available, market and regulatory forces have acted to slow the pace of introduction of new insecticides with new modes of action against agricultural pests. Hopefully, the recent economic and regulatory successes of bait formulations, as well as their superior efficacy, will continue to fuel a trend counter to that of insecticide discovery in agriculture.

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