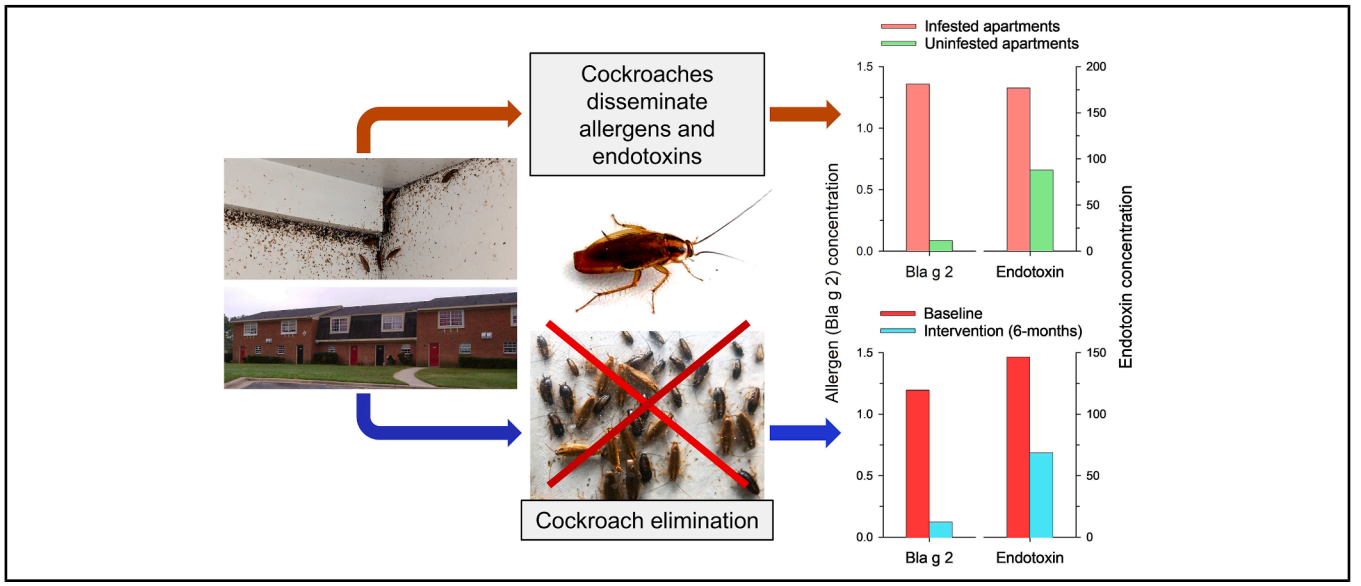
Indoor allergens and endotoxins in relation to cockroach infestations in low-income urban homes

Madhavi L. Kakumanu, MS, PhD,[a]* Zachary C. DeVries, MS, PhD,[a]*‡ Richard G. Santangelo, BS,[a] Jeffrey Siegel, MS, PhD,[b] and Coby Schal, PhD[a] *Raleigh, NC; and Toronto, Ontario, Canada*

GRAPHICAL ABSTRACT



Background: Cockroach allergens are well recognized as important risk factors in the development and prevalence of allergic rhinitis and asthma in children, especially in low-income urban households. The German cockroach gut hosts a diverse community of highly abundant microbes, including gram-negative bacteria that shed large amounts of endotoxins in cockroach feces.

Objective: We sought to delineate the causal relationship between the presence of cockroaches in homes and levels of household endotoxins.

Methods: In laboratory assays, we measured the amount of endotoxin produced by cockroaches. In-home monitoring estimated the size of the cockroach population in each home and quantified cockroach allergen Bla g 2 and endotoxin levels in household dust and on heating, ventilating, and air-conditioning (HVAC) filters. An environmental intervention was implemented in a subset of the infested homes to eliminate cockroaches. Bla g 2 and endotoxin levels were quantified for 6 months after the intervention.

Results: Large amounts of endotoxin are excreted by female (2900 endotoxin units [EU]/mg feces) and male (1400 EU/mg) cockroaches. At baseline, household dust and HVAC filters in infested homes had significantly higher levels of allergen (Bla g 2) and endotoxin than uninfested homes. Environmental intervention resulted in significant declines in cockroaches as well as allergen and endotoxin levels. In contrast, cockroach numbers and allergen and endotoxin concentrations remained high in infested-control homes.

Conclusions: Cockroaches are a significant source of both endotoxins and potent allergens, potentially resulting in coexposure of asthmatic children to both. (J Allergy Clin Immunol Global 2026;5:100571.)

From [a]the Department of Entomology and Plant Pathology, North Carolina State University, Raleigh; and [b]the Department of Civil & Mineral Engineering, University of Toronto, Toronto.

*These authors contributed equally to this work.

‡Present address: Department of Entomology, University of Kentucky, Lexington, Kentucky.

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Corresponding author: Corresponding authors: Madhavi L. Kakumanu, MS, PhD, Department of Entomology and Plant Pathology, Campus Box 7613, North Carolina State University, Raleigh, NC 27695. E-mail: mlkakuma@ncsu.edu. Or: Coby Schal, PhD, Department of Entomology and Plant Pathology, Campus Box 7613, North Carolina State University, Raleigh, NC 27695. E-mail: coby@ncsu.edu.

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Exposure to indoor allergens has been associated with an increased risk of allergic sensitization and asthma.[1,2] The German cockroach, *Blattella germanica*, is the most common and persistent indoor pest in low–socioeconomic status (SES) communities, and exposure to cockroaches has been linked to sensitization and the development of IgE-mediated allergic rhinitis and asthma.[3,4] Because cockroach allergens are perennial, triggering indoor asthma year-round, sensitization to cockroach allergens has been identified as one of the strongest risk factors for the development of asthma in low-SES urban populations.[5,6] Cockroach allergens were detected in 85% of inner-city urban homes, where 60% to 80% of children with asthma are sensitized to cockroaches based on positive skin tests.[7,8] Indeed, a causal relationship between cockroach allergens, allergic responses, and asthma has been well established for nearly 5 decades. The causal relationship between cockroach allergens, allergic responses, and asthma has been confirmed in multiple studies,[9-12] as well as by environmental interventions,[13-16] and even by the translocation of asthmatic children from a high-poverty urban neighborhood with high cockroach allergens to a low-poverty neighborhood with significantly lower cockroach allergen levels.[17]

More than 20 different inhalant allergen groups have been identified from cockroaches, including the most investigated Bla g 1 and Bla g 2 from *B germanica*.[4,18] However, the immune response to cockroach allergens is not dominated by 1 or a few major allergens, as for mite, cat, rodent, and mold allergens, and nearly 20% of cockroach-sensitized subjects do not respond to any of the known cockroach allergens.[4,19] The reasons for these unusual patterns are unknown, but it has been suggested that the abundance, distribution, stability, and possibly molecular properties of cockroach allergens might play a role. Moreover, allergies to cockroaches might be clustered with and exacerbated by other indoor triggers or adjuvants, such as volatile organic compounds and microbial contaminants. Herein, we present evidence that cockroaches excrete not only allergens, but also endotoxins, resulting in coexposure to both in the indoor environment of cockroach-infested homes.

Several observations motivated us to investigate the idea that cockroaches excrete not only the well-investigated allergens, but also endotoxins. First, endotoxins, the lipopolysaccharide (LPS) component of the outer membrane of all gram-negative bacteria, have proinflammatory effects,[20,21] and inhalation of endotoxins is linked to fever, headaches, wheezing, nose and throat irritation and respiratory tract inflammation.[22] Second, Mendy et al[23] examined the clustering patterns of endotoxins with various allergens in house dust and their association with asthma outcomes in the homes of 6963 participants. They found that high endotoxin levels were clustered with cockroach, *Aspergillus*, dust mite, and rodent allergens in low-SES homes. Third, the German cockroach hosts a diverse and highly abundant gut microbiome dominated by gram-negative bacteria.[24] As cockroaches defecate, molt, and die, they spread considerable amounts of live microbes and their cellular components, including endotoxin, into the home environment. Indeed, cockroaches shape the indoor microbiome, as evidenced by observations that the bacterial communities in infested apartments overlap more with those in cockroach gut than with uninfested homes.[24] Fourth, a preliminary study indicated that German cockroaches excrete large amounts of endotoxin.[25] Fifth, recent research has documented that when weakly allergenic proteins are coadministered to mice together with endotoxin, the animals become sensitized to the allergen and develop allergic asthma on subsequent exposure to it.[26] Thus, endotoxin appears to function as an environmental adjuvant, potentiating the effects of allergens. Finally, several studies have shown that the elevated allergen burden in cockroach-infested homes can be mitigated by interventions that eliminate cockroaches.[13-16] However, endotoxin levels in homes have never been analyzed in relation to cockroach infestations, and the outcomes of eliminating cockroaches on endotoxin levels have not been investigated. Therefore, the main goal of this study was to quantify the relationship between cockroach infestation size and cockroach allergen and endotoxin levels before, during, and after implementing environmental interventions that reduced or eliminated the cockroach populations in low-SES homes.

Abbreviations used

EU: Endotoxin units
GM: Geometric mean
HSD: Honestly significant difference
HVAC: Heating, ventilating, and air-conditioning
NHANES: National Health and Nutrition Examination Survey
SES: Socioeconomic status

METHODS

Laboratory studies of endotoxin in cockroach feces

A colony of the German cockroach was reared at 27°C and a photoperiod of L12:D12 hours and provided with water and rodent chow (Purina 5001 Rodent Diet; PMI Nutrition International, St Louis, Mo). Feces were collected from 4-day-old adult male and nongravid female cockroaches. To collect feces, 10 male and 10 female cockroaches were placed in separate 90 mm × 10 mm sterile plastic Petri plates and provided only with water so as not to contaminate the dish with food-based endotoxin; feces were collected for 24 hours. Each of these treatments was replicated 5 times. The fecal material was stored at −20°C until further analysis for endotoxin.

Study design

Recruitment and treatment groups. The North Carolina State University Institutional Review Board approved this study. Before participation, adult participants (>21 years old) provided informed consent.

The study was conducted in 2018-2019 in Raleigh, North Carolina. Cockroach-infested and uninfested homes were recruited in the same low-SES multiunit housing communities within the city limits of Raleigh (Fig 1, *A*). The apartments remained occupied throughout the study period. On the initial visit (baseline), homes were sampled for cockroaches with traps (Victor Roach Pheromone Traps; Woodstream, Lititz, Pa) for 1 to 3 days to estimate the relative size of cockroach infestations.[13,27] Four traps were deployed in the kitchen, 4 in 1 bedroom, and 4 in the living room (Fig 1, *B*). To be eligible to participate in the study, trap catch needed to be ≥10 cockroaches

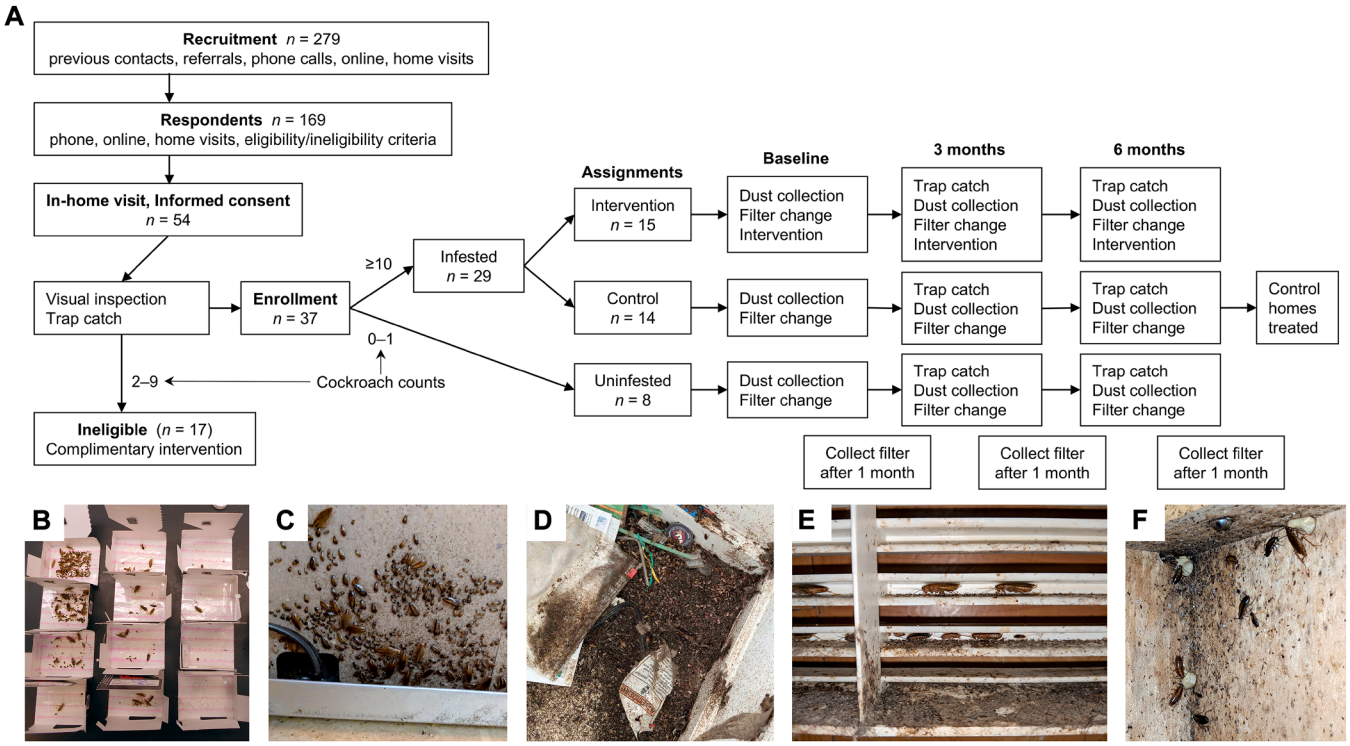

FIG 1. Study design and images of cockroaches in infested homes. **(A)** Study design showing various stages of recruitment, eligibility, enrollment, assignment to the 3 arms of the study, and study progress over 6 months. **(B)** Typical cockroach trap catch showing (from left to right) 4 kitchen traps, 4 bedroom traps, and 4 living room traps. **(C)** Cockroaches and cockroach feces (black specks) on the back of a refrigerator. **(D)** Cockroaches and cockroach feces behind and under a refrigerator. **(E)** Cockroaches and cockroach feces on the air register (return) of the HVAC system. **(F)** Cockroaches and cockroach feces in a kitchen cabinet showing bait placements and cockroaches feeding on the bait.

per home per day (infested group) or zero to 1 cockroach trapped (uninfested group). In each enrolled home, the cockroach counts obtained during the recruitment home visit were used as baseline counts. Based on their infestation status, 37 residences were enrolled, 29 homes into the infested arm and 8 homes into the uninfested arm of the study (Fig 1, *A*). The 29 cockroach-infested homes were further divided into 2 treatment groups: infested-control (no intervention; 14 homes at baseline; 4 homes withdrew from the study, and 10 homes were retained for 6 months) and infested-intervention (cockroach control; 15 homes). Of the 4 homes that withdrew from the study, 3 did so after baseline sampling and 1 after the 3-month sampling. The available data from the homes that withdrew were included in the analyses.

Intervention, follow-up, and sampling. The homes in the intervention group were treated with US Environmental Protection Agency–registered commercial insecticidal gel baits (see Table E1 in this article's Online Repository available at www.jaci-global.org) immediately after the baseline sampling. Because cockroaches are often distributed throughout the home (Fig 1, *B-F*),[13-15] small dabs of bait (approximately 0.1-0.2 g each) were placed throughout the entire home in areas where cockroaches tend to aggregate (Fig 1, *F*). Our goal was to eradicate the cockroaches; therefore, depending on trap counts, a different bait was applied in subsequent visits, as needed. The cockroach traps were set again 3 and 6 months later (Fig 1, *A*). Homes in the infested-control group (no bait intervention) received a thorough courtesy intervention after the final sampling at 6 months.

House dust was sampled in all homes at baseline and 3 and 6 months later. Settled dust was collected for 2 minutes along the perimeter of the kitchen floor of each home with a Eureka Mighty-Mite 9.0-ampere vacuum cleaner (Eureka Company, Bloomington, Ill) fitted with a Dustream collector and filter (40 μm; Indoor Biotechnologies Inc, Charlottesville, Va). Similar sampling was conducted along the perimeter of 1 bedroom. Airborne dust was collected from the heating, ventilating, and air-conditioning (HVAC) filter in each home. At each visit, a new HVAC filter (Filtrete MPR 600, MERV 7; 3M, St Paul, Minn) was installed and recovered after 1 month. In the laboratory, dust was collected from the filters using the same Eureka vacuum cleaner fitted with a Dustream sampler and stored until further analysis.[28,29] Vacuumed floor dust samples were sieved through a 450 mesh nylon sieve to remove large particles and stored at −20°C until further use. The dust samples were weighed before and after sieving.

Bla g 2 analysis

Weighed sieved dust samples were added to PBS containing 0.05% Tween-20 and 1.0% BSA at a concentration of 50 mg/mL. Samples were briefly vortexed and mixed end to end on a laboratory rocker (24 rpm, Model 88861041; Fisher Scientific, Waltham, Mass) for 2 hours at room temperature and centrifuged at 2500*g* for 20 minutes at 4°C. Supernatants were decanted into new tubes and stored at −20°C. Bla g 2 concentration in samples

was measured using a monoclonal capture and polyclonal detector (antibodies: mAb 7C11; polyclonal rabbit anti Bla g 2; peroxidase conjugated goat anti-rabbit IgG) ELISA (Indoor Biotechnologies) as described by Pollart et al.[30] The lower limit of detection was 0.78 ng/mL, and the allergen concentration is reported as nanograms of Bla g 2 per gram of dust (ng/g).

Endotoxin analysis

Endotoxin was extracted and analyzed following the National Health and Nutrition Examination Survey (NHANES) protocol.[23] The homogenized individual dust samples were accurately weighed, and pyrogen-free water + 0.05% Tween-20 solution was added at a concentration of 50 mg dust/mL. Dust samples with lower availability (≤ 5 mg) and cockroach fecal samples were extracted at a concentration of 5 mg/mL. The samples were gently shaken for 1 hour at room temperature (22°C) on an orbital shaker (200 rpm, Model 361; Fisher Scientific) and centrifuged at 600*g* for 20 minutes at 4°C. The supernatants were collected and used for endotoxin quantification.

The extracts from individual dust and fecal samples were analyzed at 4 dilutions for endotoxin with Lonza reagents using the Kinetic Chromogenic LAL (kQLAL) assay, as described by Thorne[31] for the NHANES study. The increase in absorbance of samples was measured at 405 nm every 30 seconds over 90 minutes using a SpectroMax microplate reader and Softmax Pro 5.4 analysis software (Molecular Devices, Sunnyvale, Calif). The samples were evaluated against a 12-point standard curve using *Escherichia coli* 055:B5 control standard endotoxin (Lonza). Endotoxin concentrations in fecal samples are reported in endotoxin units (EU) (EU/mg feces or EU/insect/day). Endotoxin concentrations in dust are reported in EU/mg of dust with a lower limit of detection of 0.005 EU/mL.

Statistical analysis

Statistical analysis was performed in JMP Pro 17.0 for Windows (SAS Institute, Cary, NC) and Stata Release 9 (Stata Corp LB, College Station, Tex). Descriptive statistics were summarized as median, range, minimum and maximum, and missing samples for each variable separately by time point. Cockroach counts are represented by the number of cockroaches trapped per day rounded up for kitchen and bedroom separately and the total counts for the whole residence (kitchen, bedroom, and living room combined) for each home. The cockroach data were analyzed using count +1 to enable geometric mean (GM) calculations and log-transformation with 0 counts. All the dust samples from the 3 treatment groups collected at the baseline and 3- and 6-month time points were analyzed for allergens and reported by location, ie, kitchen, bedroom, and HVAC filter. Half of the lower limit of detection for Bla g 2 (8 ng/g dust) was added to samples that had allergen levels below the detection limit. Due to the limited availability of dust, endotoxin concentrations were analyzed only for baseline and 6-month samples. As the cockroach count, Bla g 2, and endotoxin data were not normally distributed (Shapiro-Wilk test), the statistical analysis was done on log10-transformed values. We used full factorial repeated measures ANOVA, with apartment as a random effect for assessing the within-apartment variance of repeated measures over time for each sampling location (kitchen, bedroom and HVAC filter). We used the Satterthwaite approximation to calculate degrees of freedom. Tukey honestly significant difference (HSD) test was used for multiple comparisons between the main effects treatment, time, and treatment × time interaction for cockroach counts and Bla g 2 data, and Student *t* test was used for endotoxin data. Spearman correlation was used to assess correlations between cockroach numbers and allergen and endotoxin levels in household dust. All analyses were 2-tailed, and $P < .05$ was considered statistically significant. Data are presented as GM ± 95% CI of the mean.

RESULTS

Large amounts of endotoxins excreted by German cockroaches

Our laboratory studies showed that adult female cockroaches produced significantly more fecal mass per day than adult male cockroaches (*t* test, $t_8 = 13.11$, $P < .001$) (Fig 2, *A*), consistent with their higher food consumption.[32,33] The mean endotoxin concentration in female cockroach feces was 2900 EU/mg, more than twice the endotoxin concentration in male feces (1400 EU/mg) ($t_8 = 5.62$, $P < .001$) (Fig 2, *B*). On average, each male and female German cockroach disseminates approximately 750 EU/day and approximately 5000 EU/day in its feces, respectively (Fig 2, *C*).

Effective interventions eliminate cockroach infestations

A mixed factorial model indicated significant effects of treatment ($F_{2,30.3} = 59.52$, $P < .0001$), time ($F_{2,60.3} = 45.40$, $P < .0001$), and treatment × time interaction ($F_{4,60.4} = 18.37$, $P < .0001$). At baseline, the GM of total cockroach trap counts was 47.2 (95% CI = 33.9, 65.8) per home per day in the 29 infested homes, and there was no significant difference in the total cockroach count per home between the infested-control (n = 14) and infested-intervention (n = 15) arms of the study (Tukey HSD test, $P = .9945$). More cockroaches were trapped in kitchens (41.8; 95% CI = 30.3, 57.7) than in bedrooms (3.8; 95% CI = 2.4, 6.1), consistent with the ecology of the German cockroach.

In the kitchens, there were significant effects of treatment ($F_{2,31.4} = 61.14$, $P < .0001$), time ($F_{2,61.7} = 40.77$, $P < .0001$), and treatment × time interaction ($F_{4,61.8} = 16.83$, $P < .0001$). In the infested-intervention homes, the GM cockroach counts were significantly reduced from 35.9 (95% CI = 22.5, 57.4) cockroaches at baseline to 1.3 (95% CI = 0.9, 1.8) at both 3 and 6 months (96.4% decline, $P < .0001$) (Fig 3, *A*). The median counts followed a similar pattern, declining from 39.0 at baseline to zero at both 3 and 6 months (Table E2 in the Online Repository at www.jaci-global.org). In the infested-control homes, the GM cockroach counts also decreased, but only moderately, from 49.1 (95% CI = 30.0, 80.3) at baseline to 18.3 (95% CI = 6.5, 51.4) at 3 months ($P = .0885$) and 15.3 (95% CI = 5.2, 45.1) at 6 months ($P = .0212$) (Fig 3, *A*); the respective medians followed a similar pattern (Table E2).

Although the cockroach counts in bedrooms were significantly affected by treatment ($F_{2,15.9} = 8.47$, $P = .0031$), time ($F_{2,40.1} = 6.55$, $P = .0035$), and treatment × time interaction ($F_{4,40.1} = 5.77$, $P = .0009$), they were approximately 10-fold lower than in kitchens. The cockroach counts in infested-intervention bedrooms significantly decreased over the 6-month period

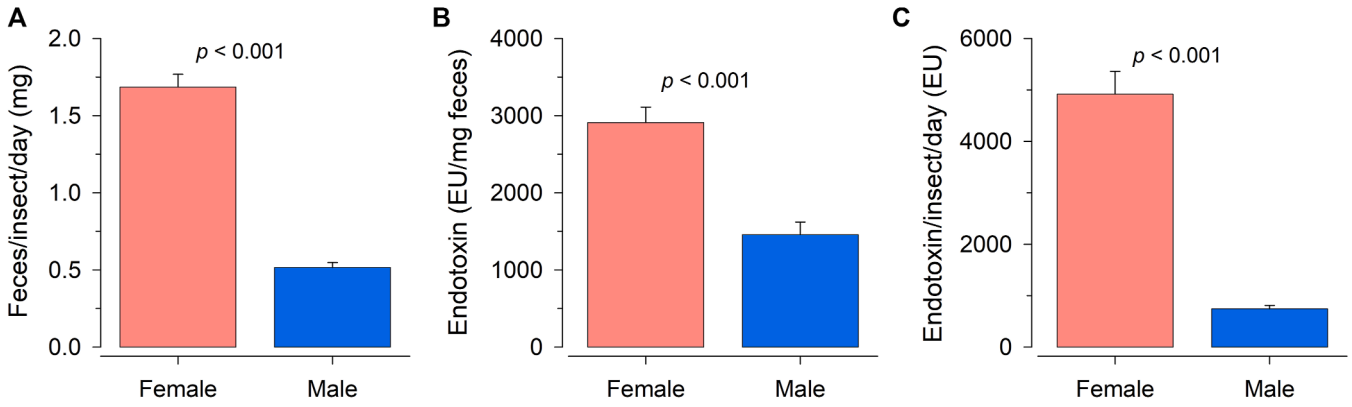

FIG 2. Cockroaches excrete large amounts of endotoxin in their feces. **(A)** Amount of feces (mean + SE) produced by individual cockroaches per day. **(B)** Amount of endotoxin detected per milligram of cockroach feces (mean + SE). **(C)** Amount of endotoxin produced per cockroach per day (mean + SE). n = 5 adult females and 5 adult males (10 insects/replicate, totals of 50 females and 50 males). *P* value for each *t* test is shown.

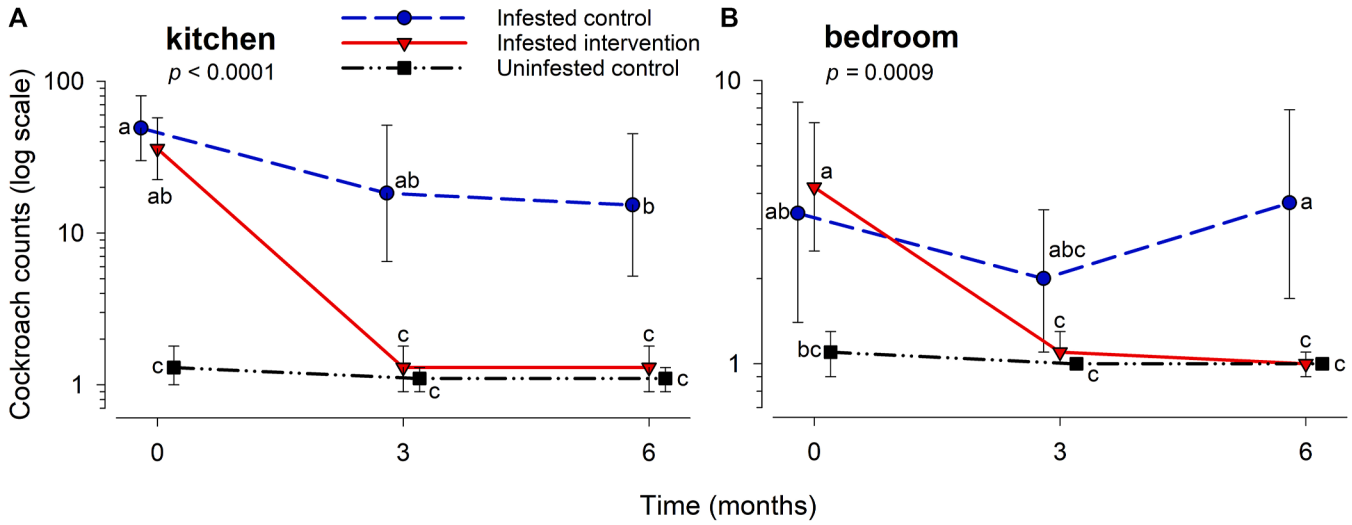

FIG 3. Effects of an environmental intervention on cockroach trap counts over the 6-month study period. **(A)** Kitchen. **(B)** Bedroom. Data are presented as GM ± 95% CI of cockroach trap counts (+1 to account for zeros) per day in the 3 treatment groups. *P* value for the mixed-factorial ANOVA is shown. Treatments were compared with Tukey HSD test, and means that do not share lowercase letters are significantly different.

(*P* < .0001), in contrast to a slight increase in cockroach counts in the infested-control bedrooms (Fig 3, *B*).

Overall, the targeted single intervention was highly effective at reducing cockroach populations in highly infested homes. Based on zero cockroach counts at 6 months, cockroaches were eliminated from 12 of 15 intervention homes. The 8 uninfested-control homes remained uninfested throughout the 6-month study.

Allergen levels decline on cockroach elimination

Fig 4, *A* and *B* (also see Table E3 in the Online Repository at www.jaci-global.org), reports the GM Bla g 2 concentrations (ng/g sieved dust) in settled dust in the kitchen and bedroom by treatment group and sampling time. The respective medians and ranges are reported in Table E4 (in the Online Repository at www.jaci-global.org). The mixed factorial model indicated significant effects of treatment ($F_{2,34.2}$ = 17.61, P < .0001), time ($F_{2,63.6}$ = 3.79, P = .0277), and treatment × time interaction ($F_{4,63.7}$ = 6.48, P = .0002) in the kitchen. At baseline, the GM Bla g 2 concentration was significantly higher in the kitchen dust of cockroach-infested homes (1359 ng/g; 95% CI = 956, 1934; n = 29) than in uninfested homes (89.8 ng/g; 95% CI = 14.6, 551; n = 8) (Tukey HSD test, P < .0129); no significant difference was observed at baseline between infested-control and infested-intervention homes (P = 1.0000). In subsequent sampling, however, Bla g 2 concentrations in kitchen dust gradually increased in the infested-control homes to 2814 ng/g by 6 months (n = 10, P = .8677), but it decreased significantly in the intervention homes at both 3 months

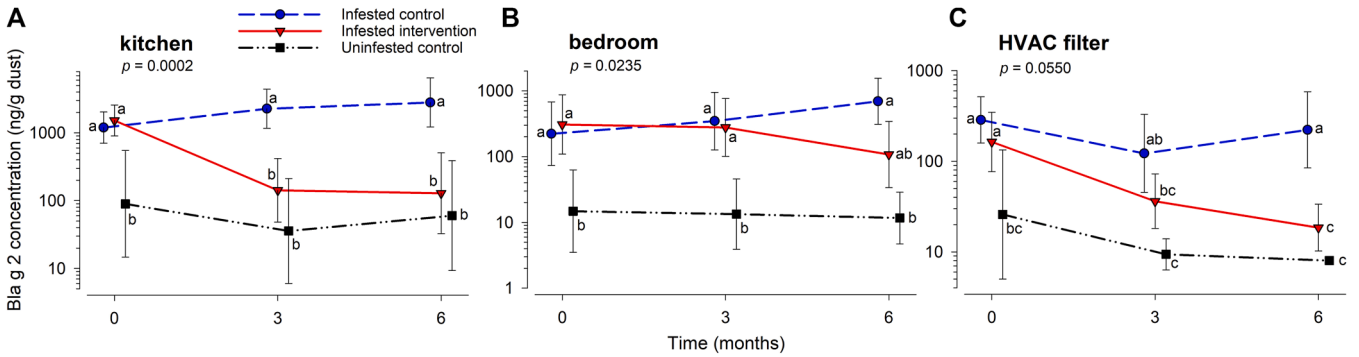

FIG 4. Effects of an environmental intervention on Bla g 2 allergen concentrations in household dust. **(A)** Kitchen. **(B)** Bedroom. **(C)** HVAC filter. Household settled dust was vacuumed from kitchens and bedrooms, and dust was collected from HVAC filters in 3 treatment groups over a 6-month period. Data are presented as GM ± 95% CI. Bla g 2 was quantified (ELISA) from dust samples collected at baseline (0 month), 3 months, and 6 months. *P* value for each mixed-factorial ANOVA is shown. Means that do not share lowercase letters are significantly different.

(142.2 ng/g, n = 15, $P = .0002$) and 6 months (128.7 ng/g, n = 15, $P = .0001$), resulting in a 10-fold decline from baseline to 6 months (Fig 4, *A*; Table E3).

Albeit less pronounced, a similar trend in Bla g 2 concentration was observed in the bedroom dust of infested homes during the 6-month period (treatment [$F_{2,31.2} = 12.69$, $P < .0001$], time [$F_{2,58.6} = 0.15$, $P = .8603$], and treatment × time [$F_{4,58.7} = 3.05$, $P = .0235$]) (Fig 4, *B*). The Bla g 2 level in the uninfested-control homes remained significantly lower ($P < .001$) than in the infested-control homes throughout the study.

We also detected significant effects of treatment ($F_{2,28.7} = 24.70$, $P < .0001$) and time ($F_{2,53.8} = 12.73$, $P < .0001$) and marginal effects of treatment × time interaction ($F_{4,53.7} = 2.48$, $P = .0550$) on Bla g 2 levels in the HVAC filter dust in cockroach-infested homes. Bla g 2 in HVAC filters significantly declined in the intervention homes by 3 months ($P = .0047$) and 6 months ($P < .0001$), respectively (Fig 4, *C*). Bla g 2 concentrations were below the detection limit (< 0.78 ng/mL with < 16 ng/g dust extracted) in 4 of 8 kitchens, 7 of 8 bedrooms and nearly all HVAC filters in uninfested-control homes throughout the 6-month study, as well as in 3 of 15 infested-intervention homes at 3 months and 5 of these 15 homes at 6 months after cockroaches were reduced or eliminated.

Endotoxins in relation to cockroach infestation

To understand the causal link between cockroaches and endotoxin levels in homes, we analyzed the settled dust collected at baseline and 6 months from the kitchens and bedrooms of infested and uninfested homes. Overall, we observed large variation in the endotoxin levels between homes and between locations within each home. Regardless of treatment, the GM endotoxin levels in kitchen dust were higher than in bedroom dust (Fig 5, *A* and *B*; Table E5 in the Online Repository at www.jaci-global.org). The respective medians and ranges are reported in Table E6 (in the Online Repository www.jaci-global.org). For kitchen dust, the mixed factorial model indicated a significant effect of treatment ($F_{2,27.3} = 4.06$, $P = .0287$) on endotoxin concentration but not of time ($F_{1,22.8} = 3.17$, $P = .0884$) and treatment × time interaction ($F_{2,23.0} = 1.08$, $P = .3571$). At baseline, higher levels of endotoxin were found in both the kitchens and the bedrooms of cockroach-infested homes than in uninfested homes (Fig 5; Table E5). At 6 months, the endotoxin level in kitchen dust remained high in the infested-control homes (185.7 EU/mg), whereas it declined significantly in the infested-intervention homes to 69.0 EU/mg (*t* test, $P = .0459$) (Fig 5, *A*; Table E5), nearly to the level in uninfested-control homes (54.9 EU/mg) and consistent with the elimination of cockroaches. Even though the endotoxin concentration in bedrooms was higher in infested homes, no significant effect was observed for treatment ($F_{2,32.8} = 2.08$, $P = .1417$), time ($F_{1,29.0} = 0.08$, $P = .7773$), and treatment × time interaction ($F_{2,29.0} = 1.36$, $P = .2714$). A slight increase in endotoxin was observed in bedroom dust in infested-intervention homes at 6 months, but it was not significantly different from the baseline level. No significant difference was observed in the endotoxin level in the uninfested homes, which remained lower than in the infested homes at both time points (Fig 5, *B*). Endotoxin levels in HVAC filter dust were low and highly variable, and no discernible pattern was evident for the effects of treatment ($F_{2,29.5} = 0.32$, $P = .7255$), time ($F_{(1,25.7)} = 0.69$, $P = .4127$), and treatment × time interaction ($F_{2,25.6)} = 0.49$, $P = .6178$); nevertheless, a trend toward increasing endotoxin level was detected in the infested-control homes (Fig 5, *C*).

We conducted correlation analyses of cockroach trap counts versus Bla g 2 concentrations and endotoxin concentrations across all apartments at all time points. In kitchen dust, Bla g 2 concentration (Spearman correlation, $\rho_{1,102} = 0.612$, $P < .0001$) and endotoxin concentration ($\rho_{1,58} = 0.515$, $P < .0001$) were significantly correlated with the kitchen cockroach trap counts (Fig 6, *A* and *B*). Because HVAC filters represent whole home air, we correlated total cockroach counts (kitchen, bedroom, and living room) to HVAC filter results. We observed a highly significant correlation between HVAC filter Bla g 2 concentration and whole home cockroach trap counts ($\rho_{1,93} = 0.773$, $P < .0001$) (Fig 6, *C*). However, there was no significant correlation between HVAC filter endotoxin concentration and cockroach counts ($\rho_{1,57} = 0.141$, $P = .2884$) (Fig 6, *D*).

We also conducted correlation analyses of Bla g 2 concentrations versus endotoxin concentrations across all apartments at all

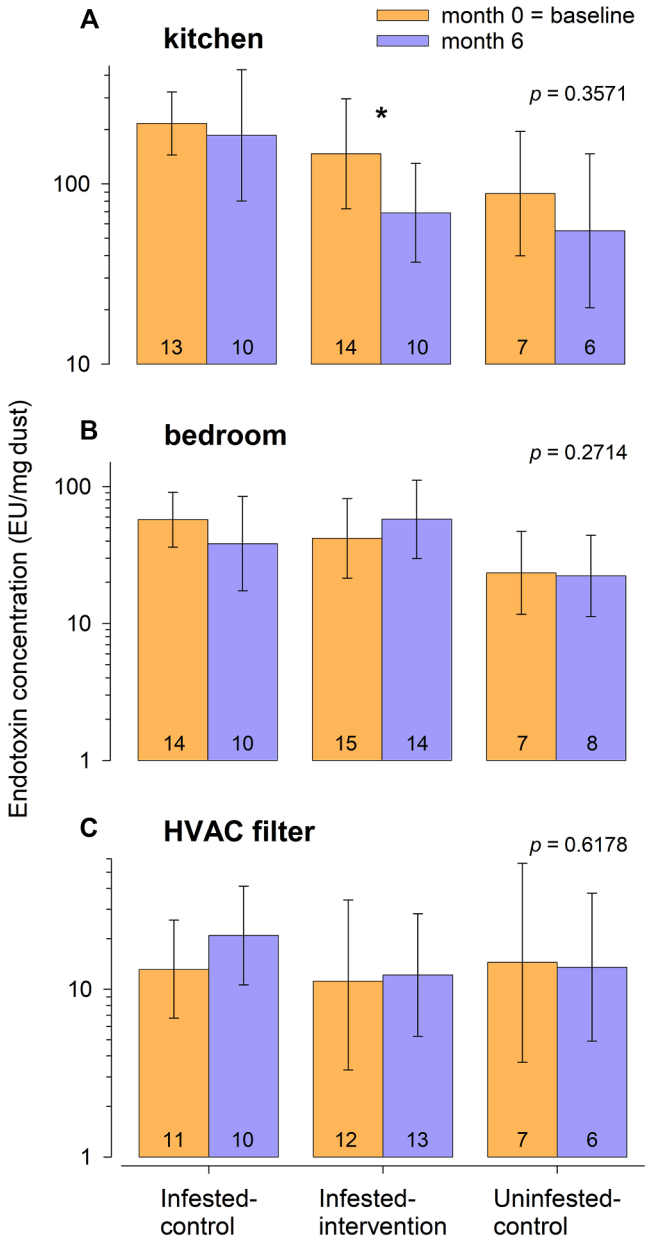

FIG 5. Effects of 6-month environmental intervention on endotoxin concentrations in household dust. **(A)** Kitchen. **(B)** Bedroom. **(C)** HVAC filter. Settled dust was vacuumed from kitchens and bedrooms, and dust was collected from HVAC filters in 3 treatment groups at baseline (0 month) and 6 months later. Data are presented as GM ± 95% CI. *P* value for each mixed-factorial ANOVA is shown. *Significant difference ($P < .05$) between respective baseline and 6-month samples.

time points. In kitchen dust, we observed a highly significant positive correlation between Bla g 2 concentration and endotoxin concentration ($\rho_{1,58} = 0.466$, $P = .0002$) (Fig 5, *E*). However, the correlation in HVAC dust was not significant ($\rho_{1,54} = 0.214$, $P = .1130$) (Fig 5, *F*).

DISCUSSION

Exposure to endotoxins in the home environment has been linked to respiratory health and asthma in both antagonistic and synergistic ways.[34-37] Early life exposure to endotoxins was shown to have a protective effect on children growing up in agricultural settings.[38,39] However, endotoxins along with cockroach allergens are among several important predictors associated with childhood asthma and are often detected at higher concentrations in the house dust of asthmatic children in low-SES households. Previous studies found associations between endotoxin and cockroach allergen levels (eg, Mendy et al[23]), and their causal relationship has been suggested.[25] However, the role of cockroaches as sources of endotoxin has not been investigated directly or experimentally in the home environment. In this study, we strategically analyzed cockroach allergen (Bla g 2) and endotoxin levels in settled and HVAC filter dust of uninfested and cockroach-infested homes before and during an intensive environmental intervention that eliminated cockroaches in most homes. Thus, positive correlations between the severity of cockroach infestations, cockroach allergen concentrations, and endotoxin concentrations strongly implicate the pivotal role of cockroaches as major sources of both allergens and endotoxins. This causal link is further supported by the large amounts of endotoxin that we quantified in cockroach feces, produced by their diverse and highly abundant gram-negative commensal microbial communities.[40]

Our study demonstrated that an effectively deployed single intensive environmental intervention can significantly reduce or eliminate indoor cockroach populations, corroborating previous findings.[13-16,41] The cockroach counts in the intervention group reached near zero by month 3 of the study and remained at zero until the end of the study at month 6. Our intervention targeted the whole home, so the cockroach counts declined in both the kitchen and the bedroom. Although the cockroach counts in the infested-control homes remained significantly higher than in the intervention homes, they trended downward in kitchens throughout the study. This could be due to seasonal effects. However, because we have seen a similar effect in previous interventions.[15] we suspect that it is related to social interaction. Homes in all 3 arms of the study were often next-door neighbors. It is possible that noticeable cockroach declines in nearby homes inspired cleaning and insecticide use in control homes.

Bla g 2 is a potent allergen that was shown to have the highest sensitization among cockroach allergens,[42,43] it was associated with cockroach-specific IgE and higher lymphocyte proliferative responses in younger children,[44,45] and it has a sensitization threshold of 40 ng/g dust; 80 ng/g dust has been associated with symptoms and morbidity.[46] The baseline allergen concentrations in all the cockroach-infested homes in our study were well above the Bla g 2 sensitization threshold. Settled dust in infested kitchens had 17-fold more Bla g 2 (1526 ng/g) than uninfested kitchens (89.8 ng/g), and infested bedrooms (308.3 ng/g) had 20.8-fold more Bla g 2 than uninfested bedrooms (14.8 ng/g). Thus, Bla g 2 levels were highly correlated with cockroach counts at baseline, consistent with previous studies.[13-16] Allergen levels were significantly reduced in the intervention homes as cockroaches were eliminated. At 6 months, the allergen levels in many of the intervention homes declined below the lower detection limit. In some homes, however, Bla g 2 remained above the detection limit, likely because Bla g 2 and other cockroach allergens are highly persistent, and in the absence of more extensive abatement (eg, extensive cleaning), reservoirs of cockroach allergens, such as behind large appliances (Fig 1, *C* and *D*), can redistribute to other parts of the home. In contrast, allergen levels in the infested-control homes remained high and even increased during the 6-month study. These patterns were consistent in settled dust in the kitchens and bedrooms of these homes, as

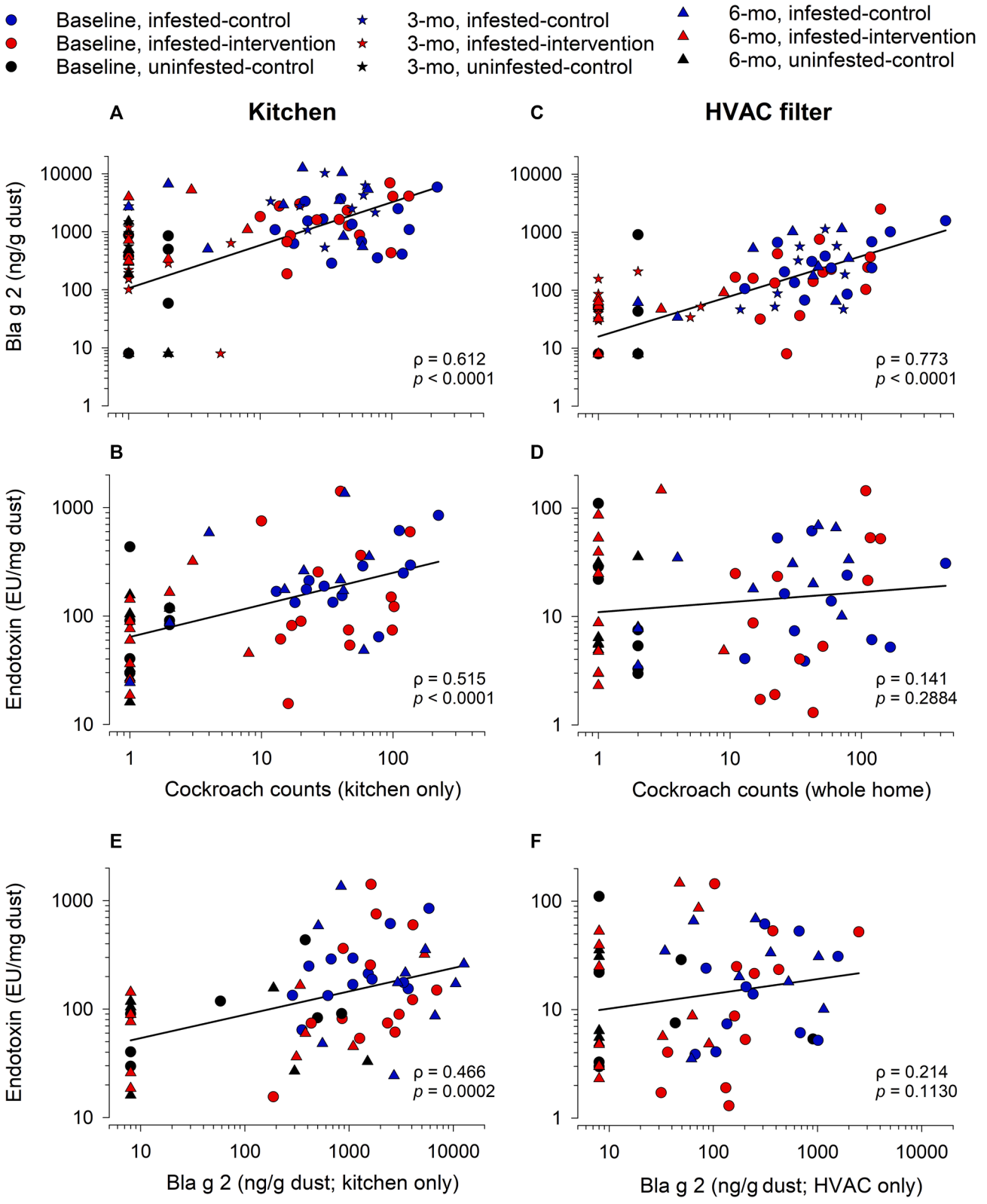

FIG 6. Correlations between the cockroach infestation (trap counts per day) and indoor Bla g 2 allergen and endotoxin concentrations. **(A, B,** and **E)** Kitchen. **(C, D,** and **F)** HVAC filter. Correlations between trap counts (+1) in the kitchen and Bla g 2 concentration (ng/g) in settled kitchen dust *(A)* and endotoxin concentration (EU/mg) in settled kitchen dust *(B)*. Correlations between whole-home cockroach trap counts and Bla g 2 concentration (ng/g) in HVAC filter dust *(C)* and endotoxin concentration (EU/mg) in HVAC filter dust *(D)*. Correlations between Bla g 2 concentration and endotoxin concentration in the kitchen *(E)* and HVAC filter *(F)* of each home. Spearman ρ and *P* value are shown.

well as in HVAC filter dust, highlighting the utility of HVAC filters as a convenient approach for measuring a temporal and spatial average of relative air-borne allergen concentration in homes.[28]

It is noteworthy that the marginal declines in cockroach counts in the infested-control homes had minimal effects on allergen concentrations. In a previous study, 1 intervention arm reduced cockroach counts by approximately 82% at 6 months. However, both Bla g 1 and Bla g 2 concentrations remained high and not significantly different from baseline levels.[13] We suspect that a nominal decrease in cockroaches is not sufficient to reduce allergen levels, as live cockroaches continuously excrete fresh allergens. Rather, cockroaches need to be eliminated to effect substantial declines in cockroach allergens. Regrettably, cockroach counts are rarely reported in asthma intervention studies, so outcomes (ie, allergen decline, health outcomes) cannot be linked to the efficacy of the cockroach intervention.

Thorne et al[47] noted a positive correlation between endotoxin levels and self-reported cockroach problems. Likewise, the NHANES study found a significant positive correlation between high endotoxin concentrations and allergen levels from various sources, including cockroaches in the homes of asthmatic children.[23] Major sources of indoor endotoxins include pets, humans, and environmental bacteria from both outdoor and indoor environments. However, the role of persistent pests as sources of household endotoxins has not been considered. At the baseline sampling, endotoxin concentration in settled floor dust was highly variable across homes, ranging from 15.5 EU/mg to 1410 EU/mg in kitchens and 7.0 EU/mg to 354.1 EU/mg in bedrooms. The respective GM of endotoxin in infested homes were 176.9 EU/mg (kitchen) and 48.8 EU/mg (bedroom), and in uninfested homes 88.2 EU/mg (kitchen) and 23.5 EU/mg (bedroom). These are much higher concentrations than the highest GM of 23.96 EU/mg dust reported by the NHANES study in a cluster of mainly low-income homes,[23] but consistent with findings in New York City low-income homes of 75.9 EU/mg in bedroom dust.[48] Thus, the levels of endotoxin in low-SES homes in Raleigh, North Carolina, and New York City appear to be more similar to each other and much higher than those obtained in national surveys that include a wide range of SES households.

There have been fewer studies of endotoxins in HVAC filters, but 1 study found median concentrations of 29 EU/mg and 33.9 EU/mg (summer and winter, respectively) in low-income homes in Central Texas,[49] lower than the values reported here at baseline. Although we recognize that comparisons of endotoxin concentrations across studies can be misleading due to variations in collection and extraction techniques, large and broadly distributed populations of the German cockroach are more common in low-SES urban homes, and our findings underscore that they contribute significantly to the endotoxin load in these homes.

As with allergen levels, the endotoxin concentration in infested homes dramatically declined to 69.0 EU/mg in the kitchen, as cockroaches were eliminated, whereas no major changes were observed in the endotoxin levels in uninfested and infested-control homes. This 53% decline due to the intervention resulted in a significant positive correlation between the severity of the cockroach infestation (trap counts) and the endotoxin levels in kitchen dust. This correlation highlights a causal link between the presence of cockroaches and high levels of indoor endotoxin and the importance of cockroaches as a major source of endotoxins in the home environment, as documented for allergens.

Although endotoxin levels in the bedrooms of infested homes were in general higher than in uninfested homes, there was no major effect of the intervention on the bedroom endotoxin levels. We suspect that these results were confounded by 2 major factors. First, the cockroach populations in bedrooms were much smaller than in kitchens, so a single intervention targeting only cockroaches might be less impactful in the bedroom. Second, carpeted floors in bedrooms can serve as reservoirs for endotoxins (and allergens),[50] requiring extensive postintervention cleaning to remove dead cockroaches, their feces, and endotoxins. In contrast, hard flooring in the kitchen is much easier to clean and less conducive to retention of dust and associated biocontaminants.

As mentioned earlier, the immunomodulating effect of endotoxin can both increase and decrease allergy and asthma risk, depending on the timing of exposure during childhood, exposure severity, and various other factors including environmental setting (farm vs nonfarm) and genetics. The protective effects of endotoxin appear to be most evident with low-level exposures early in life and mainly in farming communities, where coexposure to other environmental factors (eg, diverse environmental microbiome, contact with farm animals) might play a significant role.[38,39,51] In nonfarming communities, and particularly in low-SES homes, coexposure to high levels of allergens, endotoxins, and other pollutants appears to drive adverse asthma outcomes in both children and adults, with no evidence of a protective role for endotoxins. Indeed, the association of endotoxin and allergens with higher prevalence of asthma is well documented in low-SES homes.[9,23,37,52]

The German cockroach is the most prevalent and important pest species in low-SES homes. Our results confirmed that cockroaches excrete large amounts of endotoxin in their feces, so a typical large infestation of thousands of cockroaches can deposit millions of endotoxin units in an infested home. It is unknown what fraction of the fecal endotoxin becomes inhalable, but it is reminiscent of Bla g 1 and Bla g 2, which are also excreted by cockroaches and become airborne as aeroallergens, as evidenced by the presence of 6.3- to 11.0-fold more Bla g 2 in HVAC filters in infested than uninfested homes.

These findings are important because they link the German cockroach to previously observed statistical associations between cockroach allergens, endotoxins, and respiratory disease in low-SES homes. Since the seminal observation decades ago that cockroaches produce potent aeroallergens, cockroach allergens have been recognized as clinically important triggers of allergic airway diseases.[53] Likewise, exposure to endotoxins has been associated with respiratory inflammation and asthma incidence.[36] Coadministration of endotoxins and cockroach allergens synergistically increased pulmonary inflammatory and systemic immune responses in newborn and juvenile mice,[54] suggesting that endotoxins may exacerbate asthmatic symptoms in sensitized individuals. Thus, concurrent exposure to high concentrations of cockroach allergens along with indoor endotoxins may explain, at least in part, epidemiologic observations that children in low-SES homes have higher asthma incidence.

Therefore, development of effective and sustainable cockroach eradication and biocontaminant abatement tactics is urgently needed. Our study highlights that effective home-based environmental interventions eliminate cockroaches and dramatically reduce exposure to cockroach-disseminated allergens and endotoxins. These improvements in indoor environmental quality have been shown to lessen asthma-associated morbidity.[41,55,56] We conclude that environmental interventions in cockroach-infested homes must expeditiously eliminate the cockroach population as the first step of an integrated pest

management program. Because of widespread insecticide resistance, the effectiveness of the intervention must be objectively assessed with traps or other quantitative protocols. Effective environmental interventions, acting jointly with medical interventions, promise to lower the burden of asthma in low-SES, resource-limited households.

Several related limitations of this study warrant consideration. The first is that our study did not address whether our environmental intervention would improve health outcomes in cockroach-sensitized individuals. Instead, we sought to first identify the sources of asthma triggers, then study their distribution, and finally apply this knowledge to future environmental and clinical interventions to control or mitigate health impacts. Therefore, this proof-of-concept report provides a compelling rationale for follow-up clinical studies on whether targeted interventions in the homes of asthmatic children would improve health outcomes. A second, related limitation is the relatively small sample size. Statistical power would significantly improve with more homes in each of the 3 arms of the study, and by extending the study to 12 months or beyond. Future studies in the homes of asthmatic children will require more intervention and control homes. Finally, personnel were not blinded to the treatment in each home. Instead, we used only objective assessments of the effectiveness of the intervention (trap catch, dust samples, analytic measures).

Despite these limitations, our study revealed 3 novel findings. First, cockroaches are a major source of endotoxins, which they disseminate at levels seen only in certain occupational settings. Second, an environmental intervention consisting exclusively of cockroach elimination (ie, single rather than multifaceted intervention) not only eliminated cockroaches, but also resulted in significant declines in both cockroach allergens and endotoxin levels in the intervention homes. Finally, our recovery of endotoxins and cockroach allergens from HVAC filters indicates that both biologic contaminants not only are in settled household dust, but also become air-borne and thus inhalable.

DISCLOSURE STATEMENT

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Key messages

- **Cockroaches disseminate large amounts of allergens and endotoxins in their feces.**
- **Cockroach-infested homes have significantly higher endotoxin levels than uninfested homes.**
- **Elimination of cockroaches from infested homes results in striking declines not only in cockroach allergens, but also in indoor endotoxin levels.**
- **These findings explain previously noted statistical clustering of elevated endotoxin and cockroach allergen concentrations, which were accompanied by high prevalence of childhood asthma.**
- **Efficient and cost-effective cockroach elimination should be adopted as a pivotal first step for improving indoor environmental health.**

REFERENCES

1. Platts-Mills TA, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: report of the Third International Workshop. J Allergy Clin Immunol 1997;100:S2-24.
2. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. Am J Respir Crit Care Med 2022;205:17-35.
3. Rosenstreich DL, Eggleston P, Kattan M, Baker D, Slavin RG, Gergen P, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N Engl J Med 1997;336:1356-63.
4. Pomes A, Arruda LK. Cockroach allergy: understanding complex immune responses to develop novel therapies. Mol Immunol 2023;156:157-69.
5. Togias A, Fenton MJ, Gergen PJ, Rotrosen D, Fauci AS. Asthma in the inner city: the perspective of the National Institute of Allergy and Infectious Diseases. J Allergy Clin Immunol 2010;125:540-4.
6. Call RS, Smith TF, Morris E, Chapman MD, Platts-Mills TA. Risk factors for asthma in inner city children. J Pediatr 1992;121:862-6.
7. Do DC, Zhao Y, Gao P. Cockroach allergen exposure and risk of asthma. Allergy 2016;71:463-74.
8. Sohn MH, Kim K-E. The cockroach and allergic diseases. Allergy Asthma Immunol Res 2012;4:264-9.
9. Salo PM, Arbes SJ Jr, Crockett PW, Thorne PS, Cohn RD, Zeldin DC. Exposure to multiple indoor allergens in US homes and its relationship to asthma. J Allergy Clin Immunol 2008;121:678-84.
10. Sarinho E, Schor D, Veloso MA, Rizzo JA. There are more asthmatics in homes with high cockroach infestation. Braz J Med Biol Res 2004;37:503-10.
11. Sheehan WJ, Rangsithienchai PA, Wood RA, Rivard D, Chinratanapisit S, Perzanowski MS, et al. Pest and allergen exposure and abatement in inner-city asthma: a work group report of the American Academy of Allergy, Asthma & Immunology Indoor Allergy/Air Pollution Committee. J Allergy Clin Immunol 2010;125:575-81.
12. Gold DR, Adamkiewicz G, Arshad SH, Celedon JC, Chapman MD, Chew GL, et al. NIAID, NIEHS, NHLBI, and MCAN Workshop Report: the indoor environment and childhood asthma-implications for home environmental intervention in asthma prevention and management. J Allergy Clin Immunol 2017;140:933-49.
13. Sever ML, Arbes SJ, Gore JC, Santangelo RG, Vaughn B, Mitchell H, et al. Cockroach allergen reduction by cockroach control alone in low-income urban homes: a randomized control trial. J Allergy Clin Immunol 2007;120:849-55.
14. Arbes SJ, Sever M, Mehta J, Gore JC, Schal C, Vaughn B, et al. Abatement of cockroach allergens (Bla g 1 and Bla g 2) in low-income, urban housing: month 12 continuation results. J Allergy Clin Immunol 2004;113:109-14.
15. Arbes SJ, Sever M, Archer J, Long EH, Gore JC, Schal C, et al. Abatement of cockroach allergen (Bla g 1) in low-income, urban housing: a randomized controlled trial. J Allergy Clin Immunol 2003;112:339-45.
16. Wang CL, Eiden AL, Cooper R, Zha C, Wang DS, Hamilton RG. Abatement of cockroach allergens by effective cockroach management in apartments. J Allergy Clin Immunol Pract 2020;8:3608-9.
17. Pollack CE, Roberts LC, Peng RD, Cimbolic P, Judy D, Balcer-Whaley S, et al. Association of a housing mobility program with childhood asthma symptoms and exacerbations. JAMA 2023;329:1671-81.

18. Pomés A, Schal C. Cockroach and other inhalant insect allergens. In: Lockey RF, Ledford DK, editors. Allergens and allergen immunotherapy. London: Taylor & Francis Group; 2020. pp. 237-55.
19. Glesner J, Filep S, Vailes LD, Wünschmann S, Chapman MD, Birrueta G, et al. Allergen content in German cockroach extracts and sensitization profiles to a new expanded set of cockroach allergens determine extract potency for IgE reactivity. J Allergy Clin Immunol 2019;143:1474-81.e8.
20. Cavaillon J-M. Exotoxins and endotoxins: inducers of inflammatory cytokines. Toxicon 2018;149:45-53.
21. Morrison DC, Ryan JL. Endotoxins and disease mechanisms. Annu Rev Med 1987; 38:417-32.
22. Thorn J. The inflammatory response in humans after inhalation of bacterial endotoxin: a review. Inflamm Res 2001;50:254-61.
23. Mendy A, Wilkerson J, Salo PM, Zeldin DC, Thorne PS. Endotoxin clustering with allergens in house dust and asthma outcomes in a U.S. national study. Environ Health 2020;19:35.
24. Kakumanu ML, Maritz JM, Carlton JM, Schal C. Overlapping community compositions of gut and fecal microbiomes in lab-reared and field-collected German cockroaches. Appl Environ Microbiol 2018;84:e0103718.
25. Lai KM. Are cockroaches an important source of indoor endotoxins? Int J Environ Res Public Health 2017;14:91.
26. Cook DN. Role of environmental adjuvants in asthma development. Curr Allergy Asthma Rep 2020;20:42.
27. Nalyanya G, Gore JC, Linker HM, Schal C. German cockroach allergen levels in North Carolina schools: comparison of integrated pest management and conventional cockroach control. J Med Entomol 2009;46:420-7.
28. Haaland D, Siegel J. Quantitative filter forensics for indoor particle sampling. Indoor Air 2017;27:364-76.
29. Mahdavi A, Dingle J, Chan AWH, Siegel JA. HVAC filtration of particles and trace metals: airborne measurements and the evaluation of quantitative filter forensics. Environ Pollut 2021;271:116388.
30. Pollart S, Mullins D, Vailes L, Hayden M, Platts-Mills T, Sutherland W, et al. Identification, quantitation, and purification of cockroach allergens using monoclonal antibodies. J Allergy Clin Immunol 1991;87:511-21.
31. Thorne PS. Inhalation toxicology models of endotoxin- and bioaerosol-induced inflammation. Toxicology 2000;152:13-23.
32. Belles X, Maestro JL, Piulachs M-D. The German cockroach as a model in insect development and reproduction in an endocrine context. Adv Insect Physiol 2024;66:1-47.
33. Schal C, Holbrook GL, Bachmann JA, Sevala VL. Reproductive biology of the German cockroach, *Blattella germanica*: juvenile hormone as a pleiotropic master regulator. Arch Insect Biochem Physiol 1997;35:405-26.
34. Liebers V, Raulf-Heimsoth M, Brüning T. Health effects due to endotoxin inhalation (review). Arch Toxicol 2008;82:203-10.
35. Brade H. Endotoxin in health and disease. 1st ed. Boca Raton (FL): CRC Press; 1999.
36. Thorne PS, Kulhankova K, Yin M, Cohn R, Arbes SJ Jr, Zeldin DC. Endotoxin exposure is a risk factor for asthma: the national survey of endotoxin in United States housing. Am J Respir Crit Care Med 2005;172:1371-7.
37. Thorne PS, Mendy A, Metwali N, Salo P, Co C, Jaramillo R, et al. Endotoxin exposure: predictors and prevalence of associated asthma outcomes in the United States. Am J Respir Crit Care Med 2015;192:1287-97.
38. Stein MM, Hrusch CL, Gozdz J, Igartua C, Pivniouk V, Murray SE, et al. Innate immunity and asthma risk in Amish and Hutterite farm children. N Engl J Med 2016;375:411-21.
39. Schuijs MJ, Willart MA, Vergote K, Gras D, Deswarte K, Ege MJ, et al. Farm dust and endotoxin protect against allergy through A20 induction in lung epithelial cells. Science 2015;349:1106-10.
40. Gonzalez-Morales MA, DeVries ZC, Santangelo RG, Kakumanu ML, Schal C. Multiple mechanisms confer fipronil resistance in the German cockroach: enhanced detoxification and *Rdl* mutation. J Med Entomol 2022;59: 1721-31.
41. Morgan W, Crain E, Gruchalla R, O'Connor G, Kattan M, Evans R 3rd, et al. Results of a home-based environmental intervention among urban children with asthma. N Engl J Med 2004;351:1068-80.
42. Pomes A, Chapman M, Vailes L, Blundell T, Dhanaraj V. Cockroach allergen Bla g 2: structure, function, and implications for allergic sensitization. Am J Respir Crit Care Med 2002;165:391-7.
43. Satinover S, Reefer A, Pomés A, Chapman M, Platts-Mills T, Woodfolk J. Specific IgE and IgG antibody-binding patterns to recombinant cockroach allergens. J Allergy Clin Immunol 2005;115:803-9.
44. Chew GL, Perzanowski MS, Canfield SM, Goldstein IF, Mellins RB, Hoepner LA, et al. Cockroach allergen levels and associations with cockroach-specific IgE. J Allergy Clin Immunol 2008;121:240-5.
45. Finn P, Boudreau J, He H, Wang Y, Chapman M, Vincent C, et al. Children at risk for asthma: home allergen levels, lymphocyte proliferation, and wheeze. J Allergy Clin Immunol 2000;105:933-42.
46. Portnoy J, Chew GL, Phipatanakul W, Williams PB, Grimes C, Kennedy K, et al. Environmental assessment and exposure reduction of cockroaches: A practice parameter. J Allergy Clin Immunol 2013;132:802-8.e1-25.
47. Thorne PS, Cohn RD, Mav D, Arbes SJ, Zeldin DC. Predictors of endotoxin levels in U.S. housing. Environ Health Perspect 2009;117:763-71.
48. Perzanowski MS, Miller RL, Thorne PS, Barr RG, Divjan A, Sheares BJ, et al. Endotoxin in inner-city homes: associations with wheeze and eczema in early childhood. J Allergy Clin Immunol 2006;117:1082-9.
49. Givehchi R, Maestre JP, Bi C, Wylie D, Xu Y, Kinney KA, et al. Quantitative filter forensics with residential HVAC filters to assess indoor concentrations. Indoor Air 2019;29:390-402.
50. Haines SR, Adams RI, Boor BE, Bruton TA, Downey J, Ferro AR, et al. Ten questions concerning the implications of carpet on indoor chemistry and microbiology. Build Environ 2019;170:1-16.
51. Strieker S, Weinmann T, Gerlich J, von Mutius E, Nowak D, Radon K, et al. Farm living and allergic rhinitis from childhood to young adulthood: prospective results of the GABRIEL study. J Allergy Clin Immunol 2022;150:1209-15.e2.
52. Mendy A, Wilkerson J, Salo PM, Weir CH, Feinstein L, Zeldin DC, et al. Synergistic association of house endotoxin exposure and ambient air pollution with asthma outcomes. Am J Respir Crit Care Med 2019;200:712-20.
53. Kang B. Cockroach allergy. Clin Rev Allergy 1990;8:87-98.
54. Kulhankova K, George CLS, Kline JN, Snyder JM, Darling M, Field EH, et al. Early-life co-administration of cockroach allergen and endotoxin augments pulmonary and systemic responses. Clin Exp Allergy 2009;39:1069-79.
55. Eggleston P, Butz A, Rand C, Curtin-Brosnan J, Kanchanaraksa S, Swartz L, et al. Home environmental intervention in inner-city asthma: a randomized controlled clinical trial. Ann Allergy Asthma Immunol 2005;95:518-24.
56. Rabito FA, Carlson JC, He H, Werthmann D, Schal C. A single intervention for cockroach control reduces cockroach exposure and asthma morbidity in children. J Allergy Clin Immunol 2017;140:565-70.