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Cockroach, Dust Mite, and Shrimp Sensitization Correlations in The National Health and Nutrition Examination Survey

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Shellfish allergy is a common condition, affecting 1–2% of the U.S. population.¹

Tropomyosin, the primary allergen in shrimp, is a muscle protein found in other arthropods, including cockroaches and dust mites (DM), and cross-sensitization to these allergens has been hypothesized to drive shrimp sensitization.^{2,3} In the National Health and Nutrition Examination Survey (NHANES), it was recently demonstrated that there was a marked

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decrease in the prevalence of shrimp sensitization between NHANES III (1988–1994) and NHANES 2005–2006.⁴ The objective of this study was to test the hypothesis that this decrease in shrimp sensitization was associated with concomitant changes in cockroach and DM sensitization.

NHANES consists of a series of cross-sectional studies conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control (CDC). Food-specific IgE (sIgE) to shrimp was measured using ImmunoCAP (Phadia) in participants aged 6–19 in NHANES III and NHANES 2005–2006, as previously described.^{4,5} Two children included in the previous analyses of food sensitization were not included in this study as they did not have shrimp sIgE measured due to sample availability. Shrimp sIgE levels were used to define three *a priori* overlapping categories: overall (sIgE ≥ 0.35 kU/L), moderate (sIgE ≥ 2 kU/L), and high (sIgE ≥ 5 kU/L) level sensitization. Aeroallergen sensitization was defined by skin prick testing (SPT) in NHANES III and by sIgE measurements in NHANES 2005–2006. Further details about these methods can be found in the e-supplement.

In order to assess whether cockroach and DM sensitization explained the differences seen in shrimp sensitization between these surveys, multiple logistic regression models with and without cockroach and DM sensitization were assessed. These models were adjusted for age, sex, race/ethnicity, income, asthma, and allergic rhinitis. Only survey weights were used for these models, as the NHANES sampling units and pseudo-strata could not be combined between these two surveys. Correlation coefficients for shrimp, cockroach, and DM were calculated for each survey independently, due to the differences in aeroallergen sensitization measurements. Finally, lowess curves were generated to visually depict the relationship between cockroach, DM and oak (as a representative allergen not thought to be related to shrimp) sIgEs in NHANES 2005–2006.

Overall, 7,894 children were included in these analyses (NHANES III $n=4,994$; NHANES 2005–2006 $n=2,900$). The prevalence of shrimp sensitization significantly decreased from 11.2% (95%CI 10.0–12.5%) in NHANES III to 6.1% (95%CI 4.5–7.7%, $p<0.001$) in NHANES 2005–2006, as previously reported.⁴ Similarly, there was a significant decrease in the prevalence of sensitization to cockroach (23%; 95%CI 21–24% versus 10%; 95%CI 9–2%; $p<0.001$) and DM (28%; 95%CI 26–31% versus 22%; 95%CI 19–24%; $p<0.001$) over this time. Cockroach and DM sensitization both had moderate positive correlations with shrimp sensitization (NHANES III: cockroach 0.48, DM 0.37; NHANES 2005–2006: cockroach 0.53, DM 0.45).

The probability of shrimp sensitization increased with higher levels of cockroach sIgE, and a weaker relationship was seen between shrimp and DM and oak (Figure e1). In multiple logistic regression models, the odds for overall, moderate, and high-level shrimp sensitization were significantly lower in NHANES 2005–2006 versus NHANES III. When adjusting for cockroach, the decreased odds of overall and moderate-level, but not high-level, shrimp sensitization between years were no longer significant (Table 1), suggesting that changes in shrimp sensitization are not independent of changes in cockroach sensitization. In contrast, adjusting for DM sensitization did not account for the decrease observed in shrimp sensitization between the surveys.

In this study, we found that shrimp sensitization correlated with cockroach, and to a lesser extent, DM sensitization. We further demonstrated that the decrease in overall and moderate-level shrimp sensitization seen over time was attenuated when adjusting for cockroach sensitization. While cross-reactivity between cockroach, DM, and shrimp has been hypothesized to drive shrimp sensitization, to our knowledge, this is the first report of longitudinal trends in sensitization to these allergens in the U.S.

Previous studies have suggested that sensitization to environmental allergens such as DM and cockroach may drive shrimp sensitization, as individuals who have never ingested shellfish have been shown to have detectable sIgE levels to shrimp.³ In this study, we found that while the decrease in shrimp sensitization was attenuated by adjusting for cockroach sensitization, no such decrease was seen when adjusting for DM. This finding extends a previous observation by Wang *et al*, in which exposure to cockroach allergen, but not DM, in the homes of inner city U.S. children was associated with higher shrimp and cockroach sIgE levels.² Furthermore, in rural China, sensitization to shrimp was recently shown to be driven by cockroach but not DM sensitization, and tropomyosin was not found to be the dominant cross-reactive allergen.⁶ Other proteins that cross-react with DM and cockroach include arginine kinase and hemocyanin, whereas myosin light chain and troponin C have been shown to uniquely cross-react with cockroach.⁷ It is possible that cross-sensitization to these other allergens may drive shrimp sensitization, but the extent to which this occurs remains unclear.

In this study, we additionally found that while the decrease in overall and moderate-level shrimp sensitization was attenuated when adjusting for cockroach, there was no change in the association with high-level shrimp sensitization. One possible explanation for this finding is the fact that we were unable to adjust for the magnitude of cockroach sensitization in our model, which may have further attenuated the relationship with high-level shrimp sensitization. Alternatively, it is well known that not all individuals with shrimp sensitization are clinically allergic, and those that are clinically allergic have higher sIgE levels to shrimp extract than those who are asymptotically sensitized.⁸ It is thus possible that individuals with lower sIgE levels to shrimp may represent those who are asymptotically sensitized, likely from cross-reactive allergens, and further studies evaluating the predictive value of SPT size and sIgE levels for diagnosing clinical allergy versus asymptomatic shrimp sensitization are needed. While the factors that may promote or protect against the development of clinical food allergy among those who are sensitized is unknown, one could hypothesize that geographical variation of exposure to allergens, infectious exposures, and consumption of shrimp could also play important roles in this relationship.

This study is limited by the different methodologies used to measure aeroallergen sensitization in NHANES III (SPT) and NHANES 2005–2006 (sIgE). SPT has been shown to be a more sensitive test than sIgE,⁹ so this difference may explain the decrease seen in DM and cockroach sensitization between the two surveys. However, as both allergens were assessed in the same manner, it is unlikely that this explains the differential correlation seen with shrimp sensitization. Our study is further limited by the lack of clinical data regarding shrimp allergy or allergic rhinitis in these surveys, as well as the lack of sIgE to specific components of shrimp, DM, and cockroach. In addition, without other data, we cannot

exclude the possibility that changes in sensitization between these surveys are due to sampling differences between the surveys rather than time. However, these weaknesses are balanced by the fact that NHANES are large cross-sectional surveys designed to be nationally-representative, and our results are thus generalizable to the U.S. population. Furthermore, this is the only study to date, to our knowledge, examining the association between DM, cockroach, and shrimp sensitization over time.

In conclusion, we found that the decrease seen in overall and moderate-level shrimp sensitization between 1988–1994 and 2005–2006 was attenuated when adjusting for cockroach sensitization. These findings provide further support of the hypothesis that sensitization to shrimp is largely driven by sensitization to other arthropods, and it provides further evidence of changing patterns of sensitization over time in the U.S.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations/Acronyms:

NHANES	National Health and Nutrition Examination Survey
IgE	Immunoglobulin E

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Table 1:

Adjustment for cockroach and dust mite sensitization in shrimp sensitization models among children aged 6–19 in NHANES

	Crude Model (n=7797)		Dust Mite Adjustment (n=7435)		Cockroach Adjustment (n=7433)	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
<i>Overall Shrimp Sensitization</i>						
NHANES 2005–2006 v. III	0.52 (0.40–0.66)	<0.001	0.60 (0.46–0.79)	<0.001	0.94(0.69–1.3)	0.70
Dust Mite Sensitization	N/A		12.7 (9.5–17.0)	<0.001	N/A	
Cockroach Sensitization	N/A		N/A		24.6 (17.8–33.8)	<0.001
<i>Moderate Shrimp Sensitization</i>						
NHANES 2005–2006 v. III	0.39 (0.27–0.58)	<0.001	0.45 (0.29–0.69)	<0.001	0.72(0.47–1.12)	0.14
Dust Mite Sensitization	N/A		19.0 (11.8–30.6)	<0.001	N/A	
Cockroach Sensitization	N/A		N/A		38.4 (19.3–76.4)	<0.001
<i>High Shrimp Sensitization</i>						
NHANES 2005–2006 v. III	0.26 (0.17–0.39)	<0.001	0.28 (0.18–0.43)	<0.001	0.44 (0.27–0.70)	0.001
Dust Mite Sensitization	N/A		27.9 (14.9–52.2)	<0.001	N/A	
Cockroach Sensitization	N/A		N/A		36.4 (13.7–96.3)	<0.001

Values reported as odds ratio (OR) and 95% CIs

All models adjusted for age, sex, race/ethnicity, income, asthma, and allergic rhinitis.