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Urinary levels of triclosan and parabens are associated with aeroallergen and food sensitization

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Abstract

Background—Endocrine-disrupting compounds (EDCs) have immune-modulating effects. We were interested in determining their association with allergic sensitization.

Objective—To determine the association between EDCs and allergic sensitization and if this relationship depended on the antimicrobial properties of the EDCs and/or gender.

Methods—Data were obtained from the 2005–2006 National Health and Nutrition Examination Survey in which urinary bisphenol A, triclosan, benzophenone-3, and propyl, methyl, butyl and ethyl paraben, and specific IgE were available on 860 children. Aeroallergen and food sensitization were defined as having at least one positive (> 0.35 kU/L) specific IgE to an aeroallergen or a food. Logistic regression was used to determine the association of EDCs and sensitization. Analyses were adjusted for urinary creatinine, age, ethnicity, and poverty index ratio.

Results—The odds of aeroallergen sensitization significantly increased with the level of the antimicrobial EDCs triclosan and propyl and butyl paraben ($p = 0.04$). The odds of food sensitization significantly increased with the level of urinary triclosan among male subjects (odds ratio for 3rd versus 1st tertile 3.9, $p=0.02$ for trend). There was a significant interaction between gender and triclosan, with males being more likely to be food sensitized with exposure ($p=0.03$). Similar associations were not identified for the non-antimicrobial EDCs bisphenol A and benzophenone-3 ($p>0.2$).

Conclusions—As a group, EDCs are not associated with allergen sensitization. However, levels of the antimicrobial EDCs triclosan and parabens were significantly associated with allergic sensitization. The potential role of antimicrobial EDCs in allergic disease warrants further study as they are commonly used in Western society.

Keywords

Triclosan; paraben; benzophenone; bisphenol A; endocrine disrupting compound; aeroallergen; sensitization; food; allergy

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Introduction

Endocrine disrupting compounds (EDCs) are a diverse group of synthetic and naturally occurring chemicals that enhance or inhibit hormone signaling¹. Evidence from animal and human studies suggest that EDCs have effects on reproduction, breast development, cancer, thyroid signaling, metabolism and obesity, and the cardiovascular system². Several of these compounds also modulate immune responses³. Given the dramatic increase in the prevalence of allergic disease in developed countries over the last several decades, some have hypothesized that changes in common lifestyle practices may be a significant contributor to the allergy epidemic^{4–13}. While the overall health effects of EDCs are controversial^{1, 14–15} the potential role of EDCs in the development of allergic disease^{3, 16} has recently gained attention, as use of these compounds has accompanied a transition to a Western lifestyle.

Many EDCs have effects on immune responses in experimental systems, in addition to their effects on hormone signaling, suggesting a biologic plausibility for a role for EDCs in allergic disease. For example, bisphenol A (BPA) can increase IL-4 and IgE in experimental animals¹⁷. Triclosan causes a reduction in proinflammatory cytokines such as prostaglandin E2, leukotrienes and interferon-gamma^{18–20} in response to LPS challenge, and down-regulation of TLR signaling²¹.

In addition to effects on hormonal activity, a subset of EDCs also have antimicrobial properties (Table I). Triclosan is bacteriostatic for gram positive and gram negative bacteria, and some mycobacteria²². As a result, it is a common ingredient in personal care products such as mouthwash and hand sanitizer. Parabens are also antimicrobials which work by destabilizing microbial membranes²³ and are used typically as food, medication, and cosmetic preservatives¹⁵. Several studies have suggested associations between commensal human bacterial flora and allergic outcomes^{24–28}. Therefore, it is possible that EDCs with antimicrobial properties may modify risk for allergic disease by altering the human microbiome.

We hypothesized that environmental exposure to EDCs would be associated with allergic disease. We were further interested in whether the relationship between EDC and allergy was dependant on whether an EDC had antimicrobial properties, or was a result of direct immune modulation by the EDC. To gain insight into these relationships, we used data from the National Health and Examination Survey which collected urinary biomarker data on antimicrobial EDCs (triclosan and propyl, methyl, butyl, and ethyl paraben) and non-antimicrobial EDCs (bisphenol A and benzophenone-3, also known as oxybenzone) to determine if exposure to these compounds was associated with aeroallergen and food sensitization, markers of allergic disease.

Methods

Study Design

Data were obtained from the 2005–2006 National Health and Nutrition Examination Survey (NHANES)²⁹, a US-based survey designed to be representative of the non-institutionalized US population. Participation in the survey is voluntary. A total of 10,348 subjects participated in NHANES 2005–2006. Children aged 6–18 years were included in the analyses because childhood is when most sensitization develops. Socio-demographic data, urinary EDC levels, total and specific IgE levels, respiratory disease questionnaire data, and medical conditions questionnaire data were included in the dataset. Urinary EDC levels were collected in a randomly selected 1/3 subsample of participants aged 6 and over. A participant was considered to have doctor-diagnosed asthma if he or she responded

affirmatively to the following question: “Has a doctor or other health professional ever told you that you have asthma?” A participant was considered to have had wheeze in the preceding 12 months if he or she responded affirmatively to the following question: “In the past 12 months, have you had wheezing or whistling in your chest?” Atopic asthma was defined as having doctor diagnosed asthma in addition to at least one positive ($> 0.35\text{kU/L}$) aeroallergen specific IgE, while non-atopic asthma was defined as having doctor diagnosed asthma with negative specific IgE testing. Similarly, atopic wheeze was defined as having a history of wheezing in the past 12 months in addition to at least one positive ($> 0.35\text{kU/L}$) aeroallergen specific IgE while non-atopic wheeze was defined as having a history of wheezing in the past 12 months with negative specific IgE testing.

Laboratory evaluations

Measures of urinary EDCs (BPA, triclosan, benzophenone-3, and propyl, methyl, butyl, and ethyl paraben) were measured in a randomly selected one-third subsample of participants in NHANES aged 6 years and over using solid phase extraction coupled on-line to high performance liquid chromatography and tandem mass spectrometry. The detection limits in $100\text{ }\mu\text{L}$ of urine are 0.1–2 nanograms per milliliter. For values below the limit of detection of the assay, a value of $\frac{1}{2}$ the lower limit of detection was used for analysis.

Serum total IgE levels were measured with the ImmunoCAP system (Phadia, Uppsala, Sweden). The following aeroallergen specific IgE levels were measured with the ImmunoCAP system: cat, dog, mouse, rat, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, cockroach, ragweed, thistle, rye, Bermuda, oak, birch, *Alternaria* species, and aspergillus. The following food specific IgE levels were measured with the ImmunoCAP system: milk, egg, peanut, and shrimp. A subject was considered to have aeroallergen or food sensitization if an aeroallergen or food specific IgE was 0.35 kU/L or greater. A subject was considered to lack sensitization if specific IgE to aeroallergens or foods were not detected.

Statistical analyses

Statistical analyses were performed with STATA 12.0 (StataCorp, College Station, Texas). The primary sampling units and strata were taken into account using the variables provided in the NHANES dataset to account for the complex survey design. Sampling weights provided by the NHANES were used to generate estimates that are representative of the US non-institutionalized civilian population.

In most cases urinary EDCs had a non-normal distribution, and exposures were divided into tertiles, or dichotomized when $\geq 50\%$ of subjects had detectable levels (the case for ethyl and butyl paraben). The chi-square test was used to determine if there were any differences between the urinary EDC subsample and NHANES participants who were not in the subsample. Linear regression was used to determine if mean urinary EDC levels varied by race/ethnicity.

Logistic and linear regression were used to determine the association between EDCs and food and aeroallergen sensitization, atopic and non-atopic asthma and wheeze, and total IgE level. A test for trend was performed using the variable for tertile of the EDC, without inclusion of dummy variables. Multivariate models were adjusted for age, sex, race/ethnicity, urinary creatinine³⁰, and poverty income ratio, which is the ratio of family income to the poverty threshold. Because males have a higher prevalence of atopic disease in childhood³¹, we further stratified analyses by gender. Predicted probabilities for aeroallergen and food sensitization were derived from a logistic regression model using log-transformed values of urinary triclosan as a continuous variable.

For food sensitization, an ordinal logistic regression model was constructed to determine if increasing triclosan levels were associated with an increasing likelihood of clinically significant food allergy, after adjusting for age, gender, urinary creatinine, poverty index ratio, and ethnicity. The outcome variable was a categorical variable that indicated the level of food specific IgE in relation to the likelihood of clinical reactivity³² as follows: 0, food specific IgE <0.35 kU/L; 1, food specific IgE 0.35–<2kU/L; 2, food specific IgE between 2 kU/L and the 95th percentile predictive level for clinical reactivity; 3, food specific IgE 95th percentile for clinical reactivity. We used the following 95th percentile predictive values for clinical reactivity: egg, 7 kU/L; milk 15 kU/L; peanut 14 kU/L; shrimp 5 kU/L³³.

Results

Patient Characteristics

A total of 860 subjects had complete data for the primary analyses of urinary EDC levels on aeroallergen sensitization, and 859 had complete data for analysis of EDC levels on food sensitization. Urinary levels of each EDC by tertile or exposure status are shown in Table SI, and urinary levels according to race/ethnicity are shown in Tables SII–III. Males were more likely to have food or aeroallergen sensitization, although this trend was only statistically significant for aeroallergens (Table II). African Americans were significantly more likely to have food sensitization ($p<0.001$). Hispanics had higher levels of urinary triclosan compared to Whites, and African Americans had higher levels of urinary propyl and methyl paraben compared to Whites.

NHANES participants were selected at random for urinary EDC analysis and in general there were no significant differences between subsample participants and non-subsample participants for the primary outcomes or covariates. However, 19% of subjects in the urinary EDC subsample had food sensitization compared to 24% of subjects that were not in the subsample ($p=0.04$). For asthma, 14% of subjects in the subsample had doctor-diagnosed asthma compared to 20% of subjects that were not in the urinary EDC subsample ($p=0.04$).

EDCs with antimicrobial activity

Aeroallergen sensitization—Levels of urinary triclosan, propyl paraben, and butyl paraben were positively associated with aeroallergen sensitization (Table III, Figure 1A). The adjusted odds of aeroallergen sensitization in the 3rd vs 1st tertile of urinary triclosan was 1.73 (95% CI 1.11–2.69, p -value for trend 0.02). The adjusted odds of aeroallergen sensitization in the 3rd vs 1st tertile of urinary propyl paraben was 2.04 (95% CI 1.12–3.74, p -value for trend 0.02). The adjusted odds of aeroallergen sensitization in subjects with detectable levels of urinary butyl paraben was 1.55 (95% CI 1.02–2.33, $p=0.04$). For methyl paraben, there was a significant increase in odds of aeroallergen sensitization with increasing tertile of methyl paraben ($p=0.046$, test for trend) in crude analyses, but this did not remain significant after adjusting for covariates. No association between ethyl paraben and aeroallergen sensitization was identified.

Gender differences in aeroallergen sensitization: We then examined whether the association between aeroallergen sensitization and EDCs varied by gender. Males had consistently higher odds of aeroallergen sensitization in each stratum of triclosan, propyl paraben, and butyl paraben. For triclosan and propyl paraben, there was a statistically significant increase in odds of aeroallergen sensitization with level of EDC among males and this was not observed in females. For example, the odds of aeroallergen sensitization in the 3rd tertile vs 1st tertile of triclosan for males was 2.37 (95% CI 1.01–5.53, p -value for trend 0.046) and for females it was 1.16 (95% CI 0.62–2.19, p -value for trend 0.57).

However, the interaction between gender and EDC level was not statistically significant ($p = 0.2$, Table V).

Food sensitization—Levels of urinary triclosan were positively associated with food sensitization (Table III). The adjusted odds of food sensitization in the 3rd vs 1st tertile of urinary triclosan was 2.39 (95% CI 1.10–5.18, p -value for trend 0.03). None of the parabens were associated with food sensitization. In the ordinal regression of triclosan tertile on likelihood of true food allergy, for every tertile increase in triclosan level, there was a 55% increase in the odds of having a higher category of food allergy probability (OR 1.55, 95% CI 1.04–2.31, $p=0.03$).

Gender differences in food sensitization: In the analysis of food sensitization stratified by gender, there was a significant interaction between urinary triclosan levels and gender ($p=0.03$ for interaction term, Table V). The odds of food sensitization for males with the highest tertile of urinary triclosan levels was 3.91 (95% CI 1.24–12.31, $p=0.02$ for trend) compared to 1.24 (95% CI 0.48–3.20, $p=0.64$ for trend) for females in adjusted analyses. The predicted probability of food sensitization for males and females by urinary triclosan levels is shown in Figure 1B.

Asthma, Wheeze, and Total IgE—We did not identify a significant relationship between any of the anti-microbial EDCs and atopic asthma or atopic wheeze or total IgE level in crude or adjusted analyses (Tables VI, SVI). However, for triclosan, there was a non-significant trend for increasing risk of atopic asthma and wheeze with increasing level of triclosan (OR for 3rd vs 1st tertile of triclosan and atopic asthma 2.41, 95% CI 0.87–6.71, p -value for trend 0.07; OR for 3rd vs 1st tertile of triclosan and atopic wheeze 2.56, 95% CI 0.76–8.62, p -value for trend 0.12; Table VI).

For non-atopic asthma and non-atopic wheeze, there was a statistically significant protective effect of methyl paraben on the odds of non-atopic asthma and non-atopic wheeze in adjusted analyses (Table VII). The odds of non-atopic asthma was reduced 75% in the highest tertile of methyl paraben exposure (OR 0.25, 95% CI 0.07–0.90, p -value for trend 0.04). The odds of non-atopic wheeze was reduced 77% in the highest tertile of methyl paraben exposure (OR 0.23, 95% CI 0.05–0.99, p -value for trend 0.047). For the other antimicrobial EDCs and non-atopic asthma and non-atopic wheeze, all ORs were less than 1, however, none reached statistical significance.

EDCs without antimicrobial activity

There was no association between urinary levels of BPA and benzophenone-3 with aeroallergen or food sensitization (Table IV). Similarly, there was no association between levels of BPA and benzophenone-3 with atopic or non-atopic asthma, atopic or non-atopic wheeze, or total IgE (Tables SIV–V, SVII).

Discussion

In this large, nationally representative sample, we investigated the relationship between EDCs and atopy. We hypothesized that environmental exposure to EDCs would be associated with allergic disease. We were further interested in determining if the relationship between EDCs and allergic outcomes was dependent on the antimicrobial properties of EDCs. Of the EDCs examined, only urinary levels of triclosan and propyl and butyl paraben were significantly associated with aeroallergen and/or food sensitization. Interestingly, these compounds all have antimicrobial properties and are commonly used in personal care products and/or foods specifically for their ability to inhibit microbial growth. This raises

the possibility that the mechanism by which triclosan and propyl and butyl paraben are associated with allergic sensitization may be via their antimicrobial effects rather than their EDC activity.

Several epidemiologic studies have demonstrated associations between bacterial flora and allergic disease in cross sectional and prospective studies. The presence of specific organisms^{24–26, 34} as well as diversity of microflora^{27, 35} are thought to be relevant in the relationship between allergic disease and the human microbiome. Our data adds to previous studies in that it links use of antimicrobial products to allergic outcomes.

In our study, the increased risk of sensitization was most pronounced for males for all associations identified and for triclosan, there was a statistically significant interaction between triclosan exposure and gender on the risk of food sensitization. It is well known that allergic disease is more prevalent in males³¹ although the mechanistic basis for this is largely unexplained. Because males are at higher risk for allergic disease in general, one potential explanation is that they may be more susceptible to the effects of a second risk factor such as antimicrobial exposure, and this may lend to the observed interaction.

We did not identify a significant association between the EDCs studied and a history of atopic asthma, wheeze, or total IgE level. For triclosan, increasing urinary concentrations were associated with an increased risk of atopic asthma and atopic wheeze, but this did not meet criteria for statistical significance. Our definition of asthma and wheeze was based on self-report rather than objective evidence, and may have resulted in misclassification of the outcome. Interestingly, we did identify a significant protective effect of methyl paraben on the risk of non-atopic asthma and wheeze. Given that methyl paraben has antimicrobial properties this is consistent with an infectious trigger for these non-atopic respiratory conditions. However the effects of methyl paraben on common viral asthma triggers has not been studied, and therefore this mechanism of protection is speculative. Total IgE and allergen sensitization may have different relationships with clinical outcomes and different determinants. For example, total IgE levels are only associated with asthma among atopic subjects³⁶. Here, although we found a relationship between triclosan and propyl and butyl paraben and specific sensitization, we did not find it with total IgE, indicating that the mechanism of the association between the antimicrobial EDCs and sensitization is not related to regulation of IgE itself

Our study has several limitations. The primary limitation is that our data is drawn from a cross-sectional study. In order to provide evidence that antimicrobials such as triclosan and parabens have a causal role in allergic sensitization, prospective studies documenting that exposure to these antimicrobials precedes allergic sensitization are necessary. However, our data is from a nationally representative population based study, which lends strength to our findings. Our cross sectional design is also limited by the possibility of reverse causation, in that subjects with allergy may use more products containing triclosan and parabens. Further, our use of allergen sensitization as an outcome was limited by lack of clinical correlation of allergic disease. We attempted to overcome this by use of validated specific IgE cutpoints for clinically significant food allergy, and showed that the likelihood of clinical food allergy increased with increasing exposure to triclosan. Finally, we used urinary EDC levels as biomarkers of exposure, which has been validated for milk and serum levels of triclosan³⁷, but validation studies for urinary triclosan as well as the other EDCs have not been reported. While urinary levels are generally assumed to correlate with exposure³⁸, urinary biomarkers of EDCs may not necessarily reflect actual exposure. Nevertheless, misclassification bias arising from use of urinary EDC as a biomarker for exposure would be expected to be non-differential and would not result in marked positive or negative bias.

In summary, we identified a significant concentration- dependent association between exposure to the commonly used antimicrobials triclosan and parabens and aeroallergen and food sensitization in a representative US population. Because these compounds are found in personal care products such as toothpaste and mouthwash and/or are commonly used as preservatives in foods, drugs, and cosmetics, they are frequently encountered in daily life in Western society. While triclosan has previously been associated with a history of allergic rhinitis¹⁶, this is the first report of an association of food sensitization and likely food allergy with triclosan, and of an association with triclosan and parabens and aeroallergen sensitization. Our data suggest that the effects of these compounds on allergic sensitization may be due to their antimicrobial properties, rather than their endocrine disrupting effects. Future studies will need to examine directly the effects of these antimicrobial EDCs on skin, oral, and gut flora and to determine the temporal relationship between exposure to these compounds and the development of allergic sensitization and manifestations of allergic disease including asthma. The potential role of these compounds in the allergy epidemic warrants further study.

Acknowledgments

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Abbreviations

BPA	Bisphenol A
CI	Confidence interval
EDC	Endocrine Disrupting Compound
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio

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Clinical Implications

Urinary levels of the antimicrobial compounds triclosan and propyl and butyl paraben were associated with aeroallergen and/or food sensitization. The potential role of antimicrobials in allergic disease warrants further study.

Figure 1A.

Figure 1B.

Figure 1. Predicted probability of sensitization and 95% confidence interval by urinary triclosan levels. A. Aeroallergen sensitization for all subjects. B. Food sensitization for males and females.

Table I

Characteristics of Endocrine Disrupting Compounds Studied

Compound	Hormonal Systems Affected	Antimicrobial Properties	Method of Exposure
Bisphenol A	R ³⁹ ; T ⁴⁰ ; A ⁴¹	No	Leached from plastics, industrial uses ¹⁴
Triclosan	R ⁴² ; T ⁴³⁻⁴⁴	Yes	Personal care products (toothpaste, hand sanitizers) ⁴⁵
Benzophenone-3	R ⁴⁶ ; A ⁴⁷	No	Sunscreens
Propyl paraben	R ^{48, 49}	Yes	Food and drug preservative, personal care product ingredient (cosmetics) ¹⁵
Methyl paraben	R ^{48, 49}	Yes	Food and drug preservative, personal care product ingredient (cosmetics) ¹⁵
Butyl paraben	R ^{48, 49}	Yes	Food and drug preservative, personal care product ingredient (cosmetics) ¹⁵
Ethyl paraben	R ^{48, 49}	Yes	Food and drug preservative, personal care product ingredient (cosmetics) ¹⁵

R, reproductive; T, thyroid; A, adrenal.

Table II

Aeroallergen and Food Sensitization by Demographic Characteristics.

Characteristic	Aeroallergen Sensitivity		p value	Food sensitivity		p value
	Yes	No		Yes	No	
Gender						
Males	59%	46%	<0.01	57%	50%	0.22
Females	41%	54%		42%	50%	
Age						
6-<12	35%	47%	0.10	40%	42%	0.74
12-18yr	65%	53%		60%	58%	
Ethnicity						
% White	58%	65%	0.06	52%	65%	<0.001
% African American	19%	10%		25%	11%	
% Hispanic	13%	13%		10%	13%	
% Other	10%	12%		14%	10%	
Poverty Index Ratio						
<1	19%	19%	0.97	22%	19%	0.30
1	81%	81%		78%	81%	

Table III
Odds ratios (and 95% CI) for aeroallergen and food sensitization by level of EDCs with antimicrobial activity.

EDC	Tertile/Level	Aeroallergen Sensitization		Food Sensitization	
		Crude OR	Adjusted OR	Crude OR	Adjusted OR
Triclosan	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.85 (1.15–2.97)	1.85 (1.15–2.98)	1.64 (0.84–3.23)	1.53 (0.78–3.02)
	3	1.79 (1.19–2.68)	1.73 (1.11–2.69)	2.43 (1.14–5.15)	2.39 (1.10–5.18)
	Test for trend (<i>p</i> -value)	0.006	0.02	0.02	0.03
Propyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.35 (1.00–1.82)	1.51 (1.15–1.99)	1.06 (0.58–1.95)	0.96 (0.55–1.69)
	3	1.74 (0.98–3.08)	2.04 (1.12–3.74)	1.49 (0.94–2.38)	1.21 (0.64–2.27)
	Test for trend (<i>p</i> -value)	0.04	0.02	0.12	0.57
Methyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.11 (0.82–1.47)	1.21 (0.87–1.70)	1.00 (0.64–1.57)	0.89 (0.48–1.66)
	3	1.74 (1.02–3.11)	1.86 (0.90–3.88)	1.28 (0.82–2.01)	0.92 (0.43–1.97)
	Test for trend (<i>p</i> -value)	0.046	0.09	0.92	0.79
Butyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.30 (0.95–1.78)	1.55 (1.02–2.33)	1.18 (0.60–2.32)	1.19 (0.60–2.35)
Ethyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.15 (0.80–1.66)	1.12 (0.76–1.73)	1.12 (0.67–1.86)	1.01 (0.56–1.82)

Values in boldface are statistically significant ($p < 0.05$).

OR, Odds ratio; CI, Confidence interval.

Adjusted for urine creatinine, gender, age, race/ethnicity, and poverty index ratio.

Table IV

Odds ratios (and 95% CI) for aeroallergen and food sensitization by level of EDCs without antimicrobial activity.

EDC	Tertile/Level	Aeroallergen Sensitization		Food Sensitization	
		Crude OR	Adjusted OR	Crude OR	Adjusted OR
Bisphenol-A	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.82 (0.46–1.46)	0.77 (0.42–1.43)	0.96 (0.51–1.81)	0.81 (0.42–1.59)
	3	1.18 (0.75–1.86)	1.05 (0.64–1.71)	1.22 (0.72–2.07)	0.94 (0.51–1.74)
	Test for trend (<i>p</i>-value)	0.39	0.70	0.40	0.93
Benzophenone-3	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.99 (0.63–1.55)	1.04 (0.62–1.72)	1.03 (0.50–2.12)	1.07 (0.55–2.08)
	3	1.55 (0.67–2.04)	1.35 (0.71–2.56)	1.28 (0.71–2.28)	1.41 (0.76–2.68)
	Test for trend (<i>p</i>-value)	0.53	0.30	0.34	0.24

Values in boldface are statistically significant ($p < 0.05$).

OR, Odds ratio; CI, Confidence interval.

Adjusted for urine creatinine, gender, age, race/ethnicity, and poverty index ratio.

Table V

Odds of aeroallergen and food sensitization for males and females by level of EDC.

EDC	Sensitization type	Tertile/level	Males	Females
			Adjusted OR (95% CI)	Adjusted OR (95% CI)
Triclosan	Aeroallergen	1	1.0 [REF]	1.0 [REF]
		2	2.15 (0.99–4.69)	1.61 (0.83–3.11)
		3	2.37 (1.01–5.53)	1.16 (0.62–2.19)
		Test for trend (p-value)	0.046	0.57
		p-value for interaction	0.20	
Triclosan	Food	Tertile 1	1.0 [REF]	1.0 [REF]
		Tertile 2	2.01 (0.88–4.62)	1.14 (0.45–2.89)
		Tertile 3	3.91 (1.24–12.31)	1.24 (0.48–3.20)
		Test for trend	0.02	0.64
		p-value for interaction	0.03	
Propyl paraben	Aeroallergen	1	1.0 [REF]	1.0 [REF]
		2	1.70 (0.95–3.06)	1.27 (0.64–2.54)
		3	2.47 (1.42–4.28)	1.69 (0.64–4.46)
		Test for trend (p-value)	<0.001	0.26
		p-value for interaction	0.24	
Butyl paraben	Aeroallergen	Undetectable	1.0 [REF]	1.0 [REF]
		Detectable	1.79 (0.93–3.45)	1.30 (0.75–2.24)
		p-value for interaction	0.27	

Values in boldface are statistically significant ($p < 0.05$).

OR, Odds ratio; CI, confidence interval.

Adjusted for urine creatinine age, race/ethnicity, and poverty index ratio.

For aeroallergen sensitization, there were 450 males and 410 females. For food sensitization, there were 450 males and 409 females.

Table VI
Odds ratios (and 95% CI) for atopic asthma and wheeze by level of antimicrobial EDC.

EDC	Tertile/Level	Atopic Asthma		Atopic Wheeze	
		Crude OR	Adjusted OR	Crude OR	Adjusted OR
Triclosan	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.69 (0.69–4.15)	1.88 (0.74–4.76)	2.01 (0.79–5.11)	1.95 (0.78–4.90)
	3	2.22 (0.81–6.07)	2.41 (0.87–6.71)	2.66 (0.88–8.09)	2.56 (0.76–8.62)
	Test for trend (p-value)	0.10	0.07	0.08	0.12
Propyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.90 (0.45–1.77)	0.95 (0.45–1.98)	1.12 (0.54–2.33)	1.12 (0.46–2.68)
	3	0.79 (0.32–1.92)	0.82 (0.31–2.15)	0.47 (0.17–1.31)	0.51 (0.13–1.92)
	Test for trend (p-value)	0.53	0.67	0.13	0.42
Methyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	1.11 (0.44–2.80)	1.32 (0.47–3.73)	1.47 (0.60–3.63)	1.97 (0.65–5.93)
	3	1.71 (0.71–4.15)	2.40 (0.57–10.08)	1.33 (0.33–5.31)	1.85 (0.24–13.78)
	Test for trend (p-value)	0.24	0.23	0.58	0.44
Butyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.65 (0.27–1.54)	0.68 (0.34–1.37)	1.08 (0.48–2.40)	1.36 (0.63–2.92)
Ethyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.93 (0.46–1.88)	1.00 (0.60–1.67)	0.68 (0.30–1.53)	0.70 (0.33–1.49)

OR, Odds ratio; CI, Confidence interval.

For atopic asthma, n=915; for atopic wheeze, n=937.

Table VII

Odds ratios (and 95% CI) for non-atopic asthma and non-atopic wheeze by level of antimicrobial EDC.

EDC	Tertile/Level	Non-Atopic Asthma		Non-Atopic Wheeze	
		Crude OR	Adjusted OR	Crude OR	Adjusted OR
Triclosan	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.62 (0.24–1.61)	0.63 (0.24–1.67)	0.30 (0.10–0.87)	0.27 (0.10–0.75)
	3	0.29 (0.07–1.25)	0.29 (0.7–1.17)	0.34 (0.08–1.34)	0.30 (0.07–1.24)
	Test for trend (p-value)	0.09	0.09	0.09	0.08
Propyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.34 (0.10–1.05)	0.28 (0.08–0.96)	0.51 (0.14–2.52)	0.36 (0.07–1.82)
	3	0.56 (0.25–1.27)	0.40 (0.11–1.45)	0.64 (0.20–2.01)	0.29 (0.07–1.27)
	Test for trend (p-value)	0.08	0.10	0.40	0.11
Methyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.57 (0.27–1.20)	0.43 (0.47–3.73)	0.77 (0.31–1.91)	0.51 (0.18–1.46)
	3	0.36 (0.11–1.18)	0.25 (0.07–0.90)	0.43 (0.11–1.67)	0.23 (0.05–0.99)
	Test for trend (p-value)	0.059	0.04	0.22	0.047
Butyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.46 (0.19–1.11)	0.46 (0.16–1.32)	0.71 (0.23–2.22)	0.43 (0.07–2.54)
Ethyl paraben	1	1.0 [REF]	1.0 [REF]	1.0 [REF]	1.0 [REF]
	2	0.53 (0.18–1.57)	0.52 (0.15–1.89)	0.51 (0.14–1.87)	0.33 (0.08–1.36)

OR, Odds ratio; CI, Confidence interval.

Adjusted for urine creatinine age, race/ethnicity, and poverty index ratio.

Values in boldface are statistically significant (p 0.05).

For non-atopic asthma, n=878; for non-atopic wheeze, n=903.