Environmental Research Communications

PAPER

Association between triclosan levels and white blood cell counts in US adults from NHANES, 2011–2012

Judy Yan1, Michael A Joseph1, Simone A Reynolds1, Ryne J Veenema and Laura A Geer

1 Department of Environmental and Occupational Health Sciences, SUNY Downstate Health Sciences University, Brooklyn, New York, United States of America
2 Department of Epidemiology and Biostatistics, SUNY Downstate Health Sciences University, Brooklyn, New York, United States of America

E-mail: Laura.Geer@downstate.edu

Keywords: triclosan, human exposure, white blood cells, antimicrobial, antibacterial, NHANES, immunotoxicity

Abstract

Triclosan is a broad-spectrum antimicrobial agent used in a multitude of healthcare and consumer products. Epidemiological studies link triclosan exposure to several adverse health outcomes including alterations in thyroid function and an increased risk for allergies and asthma suggesting an immunomodulatory role for the endocrine disrupting synthetic chemical. The effects of triclosan on the human immune system, particularly on the levels and function of white blood cells, have yet to be fully characterized. Using cross-sectional data from the NHANES 2011–2012 survey, we examined the relationship between triclosan exposure levels and white blood cell counts in adults 18–65 years of age. Results from multivariable linear regression analysis show lack of a statistically significant association between urinary triclosan levels and white blood cell counts ($\beta = -0.0007, p = 0.90, 95\% CI = -0.012, 0.010$). Findings may demonstrate an absence of association or may indicate that triclosan exposure levels were too low to have a significant detectable impact on white blood cell counts. Considering that prior animal and epidemiological studies have established links between triclosan exposure and alterations in immune system parameters and susceptibility to allergic diseases, the effects of triclosan exposure on the immune system should continue to be evaluated.

1. Introduction

Triclosan is an antifungal and antibacterial agent used in a variety of domestic, commercial, and healthcare settings [1, 2]. A number of studies [3–5] have raised questions on whether triclosan is hazardous to human health; however, the impact of the agent on human health has yet to be fully characterized. Epidemiological studies report a link between triclosan exposure and several adverse health outcomes including alterations in thyroid function and an increased risk for hypersensitivity diseases suggesting an immunomodulatory role for the synthetic chemical. Over the last decade, researchers have shown that endocrine disrupting chemicals, such as triclosan, can affect the development, function, and lifespan of immune cells. Triclosan may attenuate immunity against infections or cause a hyperactivity of immune responses such as allergy and autoimmune disease [6–8]. Triclosan has been found to increase the risk of atopic asthma and sensitization to aeroallergens in children 6–18 years of age [9]. The ability of triclosan to increase susceptibility to hypersensitivity disorders suggests potential immunological changes such as increased CD4+ and CD8+ ratios, decreased proliferation of mononuclear cells, and increased frequency of auto-antibodies [5]. In a recent study, Udoji et al found that concentrations of triclosan of up to 10 $\mu$M could almost completely suppress the lytic function of human natural killer cells [10], an essential innate immune system defense response to cancerous and virally infected cells [11]. Clayton et al (2011) [5] found that in addition to altering other human systemic functions, triclosan negatively alters immune function over the life course [5]. From recent NHANES data (1999–2004), urinary triclosan levels in males were positively associated with the presence of antinuclear antibodies, an indicator of autoimmune disease processes [12]. Contrary to the above studies, A 2017 prospective longitudinal study did not find a...
significant association between maternal plasma or childhood urine triclosan levels and childhood asthma, food, or environmental allergies at 3 years of age [13]. Nevertheless, due to the potential threat triclosan poses to human health, in 2016 the Food and Drug administration issued a ban on triclosan usage in liquid, foam, and gel soaps. However, triclosan continues to be incorporated as an active ingredient in a variety of products including household cleaners, plastic kitchen utensils, children’s toys, toothpaste, mouthwash, hand sanitizer, sutures, and medical implant devices [8, 14]. With proper function of the immune system being a major determinant of human health through the life course, the continued widespread use of triclosan may represent a significant public health risk [15]. While previous studies have established the potential for triclosan to alter immune system function in general, gaps exist in our understanding of the effect of triclosan exposure specifically on human white blood cell levels and function. White blood cell (WBC) count is a marker of inflammation and has been found to be associated with the development of numerous diseases [16, 17]. It can be one of the most important markers for health conditions in the general population [18]. Therefore, the aim of our study was to evaluate the association between triclosan exposure levels and WBC counts in adults. With previous findings suggesting that exposure to triclosan can disrupt the immune system and increase susceptibility to allergic diseases, we hypothesized that triclosan exposure is associated with decreased WBC count.

2. Materials and methods

2.1. Sample selection

Using data from the National Health and Nutrition Examination Survey (NHANES) 2011–2012 survey, cross-sectional analyses were conducted to evaluate the potential association between urinary triclosan levels and white blood cell counts of adults 18–65 years of age. The NHANES is an annual nationwide survey that combines interviews and physical examinations to assess the health and nutritional status of adults and children in the United States. Its main objectives are to determine the prevalence of major diseases and risk factors for diseases. For the 2011–2012 design, in addition to the usual oversampling of Hispanics, non-Hispanic Blacks, older adults, and low-income Whites/Others of the NHANES data, there is an oversample of non-Hispanic Asians. Because total sample size of any survey year is fixed, sample sizes for Hispanics and non-low-income White and Other persons were decreased in order to increase the sample size for the Asian population. The 2011–2012 NHANES surveyed 9,756 participants (weighted \( N = 306,590,681 \)) but collected environmental (phenols and parabens) data on a sub sample of 2,594 participants (weighted \( N = 282,460,101 \)). Our data analysis was performed using this subsample. We excluded missing data (including ‘refused’ or ‘don’t know’ responses) \((n = 539)\) for variables used in our multivariable model, leaving a total of 2,055 participants (weighted \( N = 237,792,421 \)). Normal reference ranges for WBC counts in adults may be different for infants, children, and the elderly [19, 20]. One study [20] observed differences in various immune parameters during aging, such as with T-cells, a type of WBC. For example, CD3+ T-cells increased significantly from infancy and childhood to adulthood, and then decreased in the elderly. Similar CD4+ T-cells decreased up until adolescence, and then increased in adults. Neutrophils increased continuously with age, while lymphocytes and basophils decreased with age. To limit the confounding effect of age, we restricted the sample to subjects between 18–65 years. Because the introduction of triclosan into consumer products began in the 1960s [2], this age restriction also allows for a reasonable amount of opportunity for exposure. Thus, the final analytical sample consisted of 1,239 participants (weighted \( N = 170,810,468 \)).

2.2. Primary and confounding measures

To examine the levels of triclosan exposure, we used laboratory data on urinary triclosan levels. Contact with triclosan is limited to the oral mucosa and skin surfaces and the major route of triclosan excretion is in the urine [21]; therefore, urinary triclosan levels serve as an accurate marker of systemic exposure [22]. As part of a standard procedure with NHANES data, for triclosan levels below the level of detection, an imputed fill value of 1.63 was placed in the analytic results to indicate lower limit of detection divided by the square root of 2 (LLOD or 2.3/sqrt(2)). Potential confounding variables for triclosan included sex, age, race, BMI, family income, smoking status [5, 23–25], and creatinine levels [26, 27]. Factors such as food sensitization [7, 9], frequency of use of personal care products [13], and additional sources of exposure to triclosan and other similar chemicals [25] may also be important confounding factors but were not available in the NHANES 2011–2012 survey. Table 1 summarizes the various potential confounders used for this study including references for the categorical variables.

- Sex as a binary variable
- Age as a continuous variable and restricted to adults ages 18–65 years. 
Table 1. Description of Study Variables.

| Variable name                  | Type of variable | Description                                      |
|--------------------------------|------------------|--------------------------------------------------|
| WBC Count (1000 cells/μl)      | Continuous       | Lab Values                                       |
| Urinary Triclosan (ng/ml)      | Continuous       | Lab Values                                       |
| Sex                            | Binary           | M/F                                              |
| Race                           | Categorical      | Black, White (reference), Asian, Mexican-American/Hispanic / Other |
| BMI (kg/m²)                    | Continuous       | Low-income’ (>25th percentile), Mid-income’ (25th–75th percentile), High-income’ (>75th percentile) |
| Annual Income                  | Categorical      | Lab Values                                       |
| Cotinine Levels (ng/ml) (as proxy for smoking status) | Binary | 'Nonsmoker' (lower than 10 ng ml⁻¹) |
| Creatinine Levels (mg dl⁻¹)     | Continuous       | 'Smoker' (10 ng ml⁻¹ or greater) [32]            |

- Race was divided into the following categories: Black, White, Asians, and Mexican- American/Hispanic / Other.
- BMI (kg/m²): Triclosan exposure has been associated with increased BMI [28]. Although the categorization of BMI has been the most common analytical strategy, several studies have shown that grouping BMI into classes can bias the degree of risk for various BMI categories [29–31]. Hence, for this study, we measured BMI as a continuous variable to avoid the consequent loss of power and the bias associated with choice of categorization points.
- Annual household income was divided into three groups: ‘Low-income’ (<25th percentile), ‘Mid- income’ (25th–75th percentile), and ‘High-income’ (>75th percentile).
- Cotinine Levels (ng ml⁻¹): To reduce potential recall bias, smoking status was based on cotinine laboratory values. Survey respondents were classified as non- smokers or smokers if their serum cotinine levels were either lower than 10 ng ml⁻¹ or 10 ng ml⁻¹ or greater, respectively. Thresholds are based on the CDC (2013) biomonitoring summary for cotinine [32].
- Creatinine Levels (mg dl⁻¹): Variations in urinary flow rates lead to varying concentration of triclosan in urine due to differences in the dilution of urine. Additionally, urinary flow rate can vary substantially within and across individuals [27]. Researchers measuring exposure biomarkers in urine typically adjust for creatinine or specific gravity to correct for variations in urine diluteness among spot measure samples. Common methods of creatinine adjustment involve dividing the analyte concentration by the creatinine concentration [12, 33, 34]. Alternatively, for multiple regression analysis of population groups, Barr et al [33] recommend controlling for creatinine by including it as a covariate in the regression model. This would allow regression analysis to be independent of the effects of creatinine concentrations. This study utilizes the covariate approach to correct for differences in urinary concentrations of triclosan. Creatinine concentration was measured as a continuous variable.

2.3. Statistical analysis
Continuous variables were assessed based on visual inspection of a normality plot and an assessment of skewness and kurtosis measurements. Results indicated non-normal distributions. Log-transforming data derived from biological assays can be used to approximate normality [35]. To accommodate for the lack of normality, log transformations of the continuous variables were applied. Continuous variables with skewness or kurtosis values outside of −1 to 1 were transformed to improve normality for regression analyses. The following shows raw and transformed skewness (\(S_{raw}, S_{trans}\)) and kurtosis (\(K_{raw}, K_{trans}\)) of the continuous variables. Indeed, log transformation of all variables reduced both skewness and kurtosis of the distribution.

- BMI: \(S_{raw}, S_{trans} = 1.29, 0.46\) \(K_{raw}, K_{trans} = 2.66, 0.21\)
- Urinary Triclosan: \(S_{raw}, S_{trans} = -6.61, 0.80\) \(K_{raw}, K_{trans} = 58.7, -0.39\)
- WBC: \(S_{raw}, S_{trans} = -0.93, 0.09\) \(K_{raw}, K_{trans} = 1.28, -0.08\)
Creatinine: \( (S_{\text{raw}}, S_{\text{trans}}) = 1.44, -0.53; (K_{\text{raw}}, K_{\text{trans}}) = 4.29, -0.03 \)

Multivariable linear regression models were used to evaluate the association between WBC count and the main independent variable, urinary triclosan levels. Potential confounders were selected for the regression analysis if the original beta-coefficient of the univariate model for triclosan changed more than 10% from its original estimate after adjusting for the potential confounding variables. Statistically significant confounders were found to include income category, BMI, race category, and smoking status. Age was not a significant confounder in bivariate models, and therefore was excluded from the final regression model. Creatinine was included in the model as a covariate to correct for variable urine dilution. While developing the regression model, we assessed the potential collinearity among the predictor variables using multicollinearity diagnostic statistics (tolerance and variance inflation factors [VIF]). Although there is no formal cutoff value for determining presence of multicollinearity, a VIF greater than 10 and tolerance below 0.1 [36] is generally indicative of multicollinearity and were used as the cutoff criteria. Findings from the standard diagnostic assessment of the VIF (between 1.04–1.08) and tolerance (all above 0.1) for the predictor variables were indicative of a lack of multicollinearity. Sample weights were employed to account for sampling parameters and to avoid biased estimates and overstatements of significance levels. SAS Enterprise Guide 6.1 was used in the analyses. The level of statistical significance was set at a two-tailed alpha value of 0.05.

### 3. Results

Prior to the age exclusion, which was applied to the entire cohort of 2,594, the 2,055 who did not have any missing covariates did not differ significantly from the 539 who were excluded from the study with respect to age, triclosan, and creatinine levels (all \( p > 0.05 \)). In addition, percentages of participants versus non-participants were similarly distributed between smoking (17.1% versus 12.2%), income (low: 32.8% versus 38.0%; med: 39.0% versus 37.7%; high: 27.2% versus 24.2%), and race categories (MexAmer/Hispanic/Other: 26.9% versus 23.3%; Black: 26.2% versus 28.8%; Asian: 13.0% versus 18.7%; White: 33.7% versus 29.0%), respectively. Means among the 2,055 were statistically significantly higher for BMI (27.4 versus 23.6, \( p < 0.0001 \)), and white blood cell counts (6.96 versus 5.10, \( p < 0.0001 \)).

Weighted mean WBC levels and predictor variables for the final 1,239 study participants can be found in table 2. PROC SURVEYMEANS was used to allow for correct estimation of measures from complex samples for the weighted means. For reference, the unweighted results (also shown) from SAS PROC MEANS produce similar percentages to the weighted procedure. Participants in the analysis had a weighted mean age of 41 years with a BMI of 28.6. Distribution of males (48.6%) and females (49.2%) were relatively similar. Triclosan levels differed among several categories; they were higher among males (Mean = 111.5, SE = 24.2), Mexican American/Hispanics/Others (Mean = 138.3, SE = 16.9), those in the high-income range (Mean = 146.7, SE = 40.1), and those classified as nonsmokers based on standard cotinine cut-off levels (Mean = 116.6, SE = 14.8). Weighted mean WBC counts were similar across sex, race, income, and smoking status. To account for NHANES’ complex sample design, multivariable linear regression was estimated using PROC SURVEYREG (SAS Enterprise Guide, Version 6.1; SAS Institute, Cary, NC). This procedure was used to determine the association between WBC and the main predictor variable, urinary triclosan concentration, while adjusting for the relevant potential confounders. Results showed the overall model was statistically significant with the predictor variables explaining 14.0% of the variance (\( R^2 = 0.140 \) (F(9,17) = 57.40, \( p < 0.0001 \)) in WBCs. Significant individual predictors associated with WBC count were black race \( (t = -3.08, p = 0.007) \), Log(BMI) \( (t = 12.63, p < 0.0001) \), and nonsmokers \( (t = -8.16, p < 0.0001) \). See table 3. The final regression equation was as follows:

\[
\begin{align*}
\text{Log(WBC)} &= 0.999 + (-0.0007(\text{Log Triclosan})) \\
&+ (0.035(\text{Low - Income})) + (-0.009(\text{Mid - Income})) \\
&+ (0.059(\text{Mex/Hisp/Otr})) + (-0.097(\text{Black})) \\
&+ (0.024(\text{Asian})) + (0.323(\text{Log(BMI)})) \\
&+ (-0.163(\text{Nonsmokers})) + (-0.008(\text{Log(Creatinine)}))
\end{align*}
\]

Our study shows no evidence of a significant association between triclosan and WBC counts \( (\beta = -0.0007, p = 0.90, 95% \text{ CI} = -0.012, 0.010) \). In contrast to previous studies on the association between triclosan and immunity, our findings do not support our hypothesis that triclosan exposure decreases WBC counts.
| Independent variables | Categories | Unweighted N (%) | Weighted N (%) | Weighted Mean (SE) |
|----------------------|------------|------------------|----------------|--------------------|
|                      |            |                  |                | Unweighted N (%)   | Weighted N (%) |
|                      |            |                  |                | Mean               | Unweighted N (%) | Weighted N (%) | WBC, 1000 cells/μ |
| Age, years           | N/A        | 1,239            | 170,810,468    | 41.2 (0.76)        | 28.7 (0.28)      | 108.3 (16.6)   | 7.07 (0.11)    |
| BMI, kg m^{-2}       |            |                  |                |                    |                  |                |                |
|                      | N/A        |                  |                |                    |                  |                |                |
|                      | Female     | 610 (49.2%)      | 87,551,662 (51.3%) | 105.4 (13.7)        | 7.20 (0.16)      |
|                      | Male       | 629 (48.6%)      | 83,258,805 (48.7%) | 111.5 (24.2)        | 6.93 (0.12)      |
| Creatinine, mg dl^{-1}|            |                  |                |                    |                  |                |                |
|                      | N/A        |                  |                |                    |                  |                |                |
|                      | Female     | 610 (49.2%)      | 87,551,662 (51.3%) | 105.4 (13.7)        | 7.20 (0.16)      |
|                      | Male       | 629 (48.6%)      | 83,258,805 (48.7%) | 111.5 (24.2)        | 6.93 (0.12)      |
| Sex                  |            |                  |                |                    |                  |                |                |
|                      | Female     | 610 (49.2%)      | 87,551,662 (51.3%) | 105.4 (13.7)        | 7.20 (0.16)      |
|                      | Male       | 629 (48.6%)      | 83,258,805 (48.7%) | 111.5 (24.2)        | 6.93 (0.12)      |
| Race                 |            |                  |                |                    |                  |                |                |
|                      | MexAmer/Hisp/Otr | 308 (24.9%)    | 31,834,633 (18.6%) | 138.3 (16.9)        | 7.47 (0.20)      |
|                      | Black      | 315 (23.4%)      | 19,098,650 (11.2%) | 84.6 (14.4)         | 6.70 (0.12)      |
|                      | Asian      | 186 (13.0%)      | 8,223,472 (4.81%)  | 90.7 (30.4)         | 6.69 (0.18)      |
|                      | White      | 430 (34.7%)      | 111,653,713 (65.4%) | 105.2 (26.4)        | 7.03 (0.20)      |
| Income               |            |                  |                |                    |                  |                |                |
|                      | Low        | 376 (30.3%)      | 35,811,954 (21.0%) | 70.4 (17.8)         | 7.54 (0.29)      |
|                      | Mid        | 484 (39.1%)      | 68,675,815 (40.2%) | 91.1 (15.0)         | 7.00 (0.11)      |
|                      | High       | 579 (40.6%)      | 66,522,699 (38.8%) | 146.7 (40.1)        | 6.89 (0.14)      |
| Smoking Status       |            |                  |                |                    |                  |                |                |
|                      | Smoker     | 303 (24.5%)      | 41,108,010 (24.0%) | 82.4 (29.4)         | 7.94 (0.21)      |
|                      | Non-Smoker | 936 (75.5%)      | 129,702,457 (76.0%) | 116.6 (14.8)        | 6.80 (0.11)      |
Table 3. Regression analysis for WBC count and urinary triclosan, adjusted for significant covariates.

| Independent Variables       | WBC Count |
|-----------------------------|-----------|
|                             | β-coefficient (SE) | 95% CI     | p-value |
| Log (urinary triclosan)     | < −0.001 (0.005)   | −0.012, 0.010 | 0.90    |
| Log (BMI)                   | 0.323 (0.026)      | 0.269, 0.377  | <0.0001 |
| Log (creatinine)            | −0.008 (0.010)     | −0.031, 0.014  | 0.443   |
| Smoking                     | Ref.               | Ref.         | Ref.    |
| Smoker                      | −0.163 (0.020)     | −0.205, −0.121 | <0.0001 |
| Non-Smoker                  | Ref.               | Ref.         | Ref.    |
| Income Categories           |                       |             |         |
| Low                         | 0.035 (0.034)      | 0.036, 0.106  | 0.316   |
| Mid                         | −0.009 (0.018)     | 0.047, 0.030  | 0.637   |
| High                        | Ref.               | Ref.         | Ref.    |
| Race Categories             |                       |             |         |
| Amer/Hisp/Otr               | 0.059 (0.037)      | −0.019, 0.137 | 0.128   |
| Black                       | −0.097 (0.031)     | −0.163, −0.030 | 0.007   |
| Asian                       | 0.024 (0.031)      | −0.040, 0.089  | 0.436   |
| White                       | Ref.               | Ref.         | Ref.    |

4. Discussion

To date, this is the first study to investigate the association between triclosan exposure and WBC count in adults. We found no association between WBC counts and urinary triclosan levels. The observed lack of association may indicate that such a correlation does not exist, or that triclosan exposure levels were too low to have a significant detectable impact on WBC counts. Although our study was not designed to assess allergic disease outcomes, our results suggest that triclosan exposure does not contribute to changes in WBC count expected with allergic conditions, supporting a recent prospective cohort study that did not find an association between prenatal and early-life triclosan exposure and allergic disease [13]. This study failed to confirm previous findings [5–8, 10] which suggest that triclosan attenuates immunity against infection, increases susceptibility to hypersensitivity disorders and ostensibly influences white blood cell counts.

Limitations for any cross-sectional observational study includes the possibility of reverse causation and the inability to establish absolute causation. In theory, WBC levels could influence triclosan exposure through alterations in absorption and metabolism of the chemical. With the lack of a complete understanding of the mechanisms of triclosan absorption and metabolism, the possibility for reverse causality cannot be discounted. An additional study limitation was our reliance on a single urine sample to determine triclosan exposure. As is the case for other non-persistent chemicals [37, 38], temporal variability of urinary triclosan levels exists. Because triclosan has a short half-life and is eliminated in the urine within a few hours after exposure, a single urine sample may have not been sufficient to characterize exposure. A single urine sample also fails to differentiate between chronic and acute exposures. However, despite the potential for temporal variability, several studies on triclosan exposure found that a single urine sample sufficiently characterized exposure [39–42]. Thus, triclosan concentration collected from a single spot urine sample, such as those for the NHANES, may serve as a reliable measure of exposure [12]. Also, a proportion (~21%) of respondents were excluded from the study due to missing covariates, which limited the sample size available for analysis. Methods of imputation were not used to complete missing data as they tend to bias results by failing to account for the variability in the hypothetical data [43].

Despite these limitations, the major strength of this study was the use of data from a large population with respondents representing a broad range of ages between 18–65 years. Study findings may be generalized to the larger US population. Other strengths include a relatively large sample size and reduced measurement bias as data on urinary concentrations of triclosan and white blood cell counts were collected using reliable laboratory methods. Sample weights were also employed during the analysis to account for possibilities of selection and non-response biases due to age, gender, and race or ethnicity.

5. Conclusions

Since its introduction into consumer markets in the 1970s, triclosan has been included in many consumer and healthcare products to prevent microbial contamination. The potential for chronic triclosan exposure across the US population through the usage of everyday consumer products raises concerns about the human health risks.
The Florence Statement on Triclosan and Triclocarban (2017) [44], a consensus of more than 200 scientists and medical researchers, highlights the potential dangers of triclosan to human health and the environment and urges the international community of manufacturers, consumers, retailers, and governments to limit their production and use. After decades of incorporation into consumer products, the US Food and Drug Administration recently banned the usage of triclosan in many consumer antiseptic soaps. Despite the ban, exceptions have allowed triclosan usage to continue. The rule applies only to hand and body soaps and restaurants, hospitals, and food service settings are exempt.

Many of the previous studies on the effects of triclosan exposure on the immune system were completed using animal models with human observational studies being limited. Using a nationally representative sample of US adults ages 18–65 years, we examined the association between triclosan exposure and WBC count. Although results from this study failed to demonstrate a statistically significant relationship between triclosan exposure and WBC count, associations may emerge after more chronic exposures or at higher exposure levels. As such, future research should include prospective studies that assess triclosan exposure levels over multiple time points to differentiate between chronic and acute exposures. Our results may also have been influenced by other confounding variables including the vast array of common environmental toxins that have been linked to health problems associated with immune dysfunction and inflammatory dysregulation [45]. Studies should also take into account additional potential confounders such as dietary habits, alcohol consumption, hormone levels, or history of exposures to heavy metals which may further elucidate any potential associations. Considering that prior animal and epidemiological studies have established links between triclosan exposure and alterations in immune system parameters and susceptibility to allergic diseases, the effect of triclosan exposure on the mature and immature immune system should continue to be evaluated.

Acknowledgments

None.

Supplementary materials

None.

Author contributions

The study authors involved in conceptualization included J Y, M J and L G; methodology, J Y and M J, S R; formal analysis, J Y, M J and S R; data curation, J Y and S R; writing—original draft preparation, J Y, M J and L G; writing—review and editing, L G and R V; project administration, L G.

Funding

This research received no external funding.

Conflicts of interest

The authors declare no conflict of interest.

ORCID iDs

Ryne J Veenema https://orcid.org/0000-0003-0766-5438
Laura A Geer https://orcid.org/0000-0003-4300-9796

References

[1] Calafat A M, Ye X, Wong L Y, Reidy JA and Needham L L 2008 Urinary concentrations of Triclosan in the US population: 2003–2004 Environ Health Persp. 116 303–7
[2] Jones R D, Jampani H B, Newman J L and Lee A S 2000 Triclosan: a review of effectiveness and safety in health care settings Am J Infect Control. 28 184–96.
[3] Barros S P, Wirojchanasak S, Barrow D A, Panagakos F S, DeVizio W and Offenbacher S 2010 Triclosan inhibition of acute and chronic inflammatory gene pathways J Clin Periodontal. 37 412–8
[4] Bertelsen R J et al 2013 Triclosan exposure and allergic sensitization in Norwegian children Allergy. 68:84–91
[5] Clayton E M R, Todd M, Dowd J B and Aiello A E 2011 The impact of bisphenol A and triclosan on immune parameters in the U.S. population, NHANES 2003-2006 Environ Health Persp. 119 390–6
[6] Kuo C H, Yang S N, Kuo P L and Hung C H 2012 Immunomodulatory effects of environmental endocrine disrupting chemicals Kaohsiung J Med Sci. 28 S37–42
[7] Savage J H, Matsui E C, Wood R A and Keet C A 2012 Urinary levels of triclosan and parabens are associated with aeroallergen and food sensitization J Allergy Clin Immunon. 130 453–60
[8] Nowak K, Jablonowska E and Ratazczak-Wrona W 2019 Immunomodulatory effects of synthetic endocrine disrupting chemicals on the development and functions of human immune cells Environ. Int. 125 350–64
[9] Spanier A J, Fausnicht T, Camacho T F and Braun J M 2014 The associations of triclosan and paraben exposure with allergen sensitization and wheeze in children Allergy Asthma Proc. 35 475–81
[10] Udof, Martin T, Etherton R and Whalen M M 2010 Immunosuppressive effects of triclosan, nonylphenol, and DDT on human natural killer cells in vitro J Immunotoxicol. 7 205–12
[11] Orange J S 2008 Formation and function of the lytic NK-cell immunological synapse Nat. Rev. Immunol. 8 713–25
[12] Dins G E et al 2016 Associations between selected xenobiotics and antioxidant antibodies in the National Health and Nutrition Examination Survey, 1999–2004 Environ. Health Perspect. 124 426–36
[13] Lee-Sarwar K et al 2018 Prenatal and early-life triclosan and paraben exposure and allergic outcomes J Allergy Clin Immunol. 142 269–78
[14] Weatherly I M and Gosse J A 2017 Triclosan exposure, transformation, and human health effects J Toxicol Environ Health B Crit Rev. 20 447–69
[15] Bedoux G, Roig B, Thomas O, Dupont V and Le Bot B 2012 Occurrence and toxicity of antimicrobial triclosan and by-products in the environment Environ Sci Pollut R. 19 1044–59
[16] Babio N et al 2013 White blood cell counts as risk markers of developing metabolic syndrome and its components in the predimed Study PLoS One 8 e58354
[17] Koren-Morag N, Tanne D and Goldbourt U 2005 White blood cell count and the incidence of ischemic stroke in coronary heart disease patients Am J Med. 118 1004–9
[18] Hasegawa T, Negishi T and Deguchi M 2002 WBC count, atherosclerosis and coronary risk factors J Atheroscler Thromb. 9 219–23
[19] Pagana K D and Pagana T J 2013 Mosby’s Manual of Diagnostic and Laboratory Tests. 5 ed. (St. Louis, MO: Mosby)
[20] Valiathan R, Ashman M and Ashthana D 2016 Effects of ageing on the immune system: infants to elderly. Human Immunology Scandinavian J Immunology 83 255–66
[21] Fang J L, Stingley R L, Beland F A, Harrouk W, Lumpkins D L and Howard P 2010 Occurrence, ef Sci. Total Environ. 393 162–7
[22] Cherkas L F et al 2006 The effects of social status on biological aging as measured by white-blood-cell telomere length Aging Cell. 5 261–5
[23] Mortensen M E et al 2014 Urinary concentrations of environmental phenols in pregnant women in a pilot study of the National Children’s Study Environ. Res. 128 32–8
[24] Barr D B, Wilder L C, Caudill S P, Gonzalez A J, Needham L L and Pirkle J L 2005 Urinary creatinine concentrations in the US population: Implications for urinary biologic monitoring measurements Environ Health Persp. 113 192–200
[25] Hays S M, Aylward L L and Blount B C 2015 Variation in urinary flow rates according to demographic characteristics and body mass index in NHANES: potential confounding of associations between health outcomes and urinary biomarker concentrations. Environ Health Persp. 123 293–300
[26] Bank J, Patel C, Cullen M R, Ley C and Parsonnet J 2013 Urinary triclosan is associated with elevated body mass index in NHANES PLoS One 8 e58354
[27] Hegel K M, Kit B K and Graubard B I 2014 Body mass index categories in observational studies of weight and risk of death American Journal of Epidemiology. 180 288–96
[28] Filardo G, Hamilton C, Hamman B, Ng H K T and Grayburn P 2007 Categorizing BMI may lead to biased results in studies investigating in-hospital mortality after isolated CABG J Clin Epidemiology. 60 1132–9
[29] Preston S H, Fishman E and Stokes A 2015 Effects of categorization and self-report bias on estimates of the association between obesity and mortality Annals of Epidemiology. 25 907–11
[30] CDC. Cotinine: Center for Disease Control and Prevention, [updated April 7, 2017]. [Accessed February 5, 2020]https://www.cdc.gov/biomonitoring/Cotinine_BiomonitoringSummary.html
[31] O’Brien K M, Upson K and Buckley J P 2017 Lipid and creatinine adjustment to evaluate health effects of environmental exposuresCurr Environ Health Reports. 4 44–50
[32] Hays S M, Ayward L L and Blount B C 2016 Associations between selected xenobiotics and antinuclear antibodies in the National Health and Nutrition Examination Survey, 1999–2004 Environ. Health Perspect. 124 426–36
[33] Meeker J D et al 2005 Temporal variability of urinary levels of nonpersistent insecticides in adult men J Expo Anal Environ Epidemiol. 15 271–81
[34] Brien K M, Upson K and Buckley J P 2017 Lipid and creatinine adjustment to evaluate health effects of environmental exposuresCurr Environ Health Reports. 4 44–50
[35] Steinberg M R, Schleicher R L and Pfeiffer C M 2013 Regression modeling plan for twenty-nine biochemical indicators of diet and nutrition measured in NHANES 2003–2006 The Journal of Nutrition. 143 9485–9565
[36] Kumsari S S S 2008 Multicollinearity: estimation and elimination J of Contemporary Research in Management. 87–95
[37] Meeker J D et al 2005 Temporal variability of urinary levels of nonpersistent insecticides in adult men J Expo Anal Environ Epidemiol. 15 271–81
[38] Barten R J et al 2014 Reliability of triclosan measures in repeated urine samples from Norwegian pregnant women J Expo Sci Environ Epidemiol. 24 517–21
[39] Teitelbaum S L et al 2008 Temporal variability in urinary concentrations of phthalate metabolites, phytoestrogens and phenols among minority children in the United States Environ. Res. 106 257–69
[40] Koch H M et al 2014 Inter- and intra-individual variation in urinary biomarker concentrations over a 6-day sampling period: ILI Person care product ingredients Toxicology Letter. 231 261–9
[42] Meeker J D et al 2013 Distribution, variability, and predictors of urinary concentrations of phenols and parabens among pregnant women in Puerto Rico Environ. Sci. Technol. 47 3439–47
[43] An B and Enders C K 2010 An introduction to modern missing data analyses J Sch Psychol 48 5–37
[44] Halden R U et al 2017 The florence statement on triclosan and triclocarban Environ. Health Perspect. 125 064501
[45] Dietert R R, DeWitt J C, Germolec D R and Zelikoff J T 2010 Breaking patterns of environmentally influenced disease for health risk reduction: immune perspectives Environ. Health Perspect. 118 1091–9