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Young Children's Exposure to Phenols in the Home: Associations between house dust, hand wipes, silicone wristbands, and urinary biomarkers

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Abstract

Background: Environmental phenols, such as parabens, bisphenol A, and triclosan, are ubiquitous in indoor environments because of their use in packaging, plastics, personal care products, and as anti-microbials. The primary pathways of exposure, as well as habits and behaviors that may lead to greater exposure, are still unclear.

Objectives: Herein, we investigate the relationships between phenols found in residential environments by comparing levels in paired samples of house dust and hand wipes with children's

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Dr. Xiaoyun Ye is included posthumously as an author for her work on the quantification of phenols biomarkers.

Author contributions: HMS, TFW, KH conceptualized study and planned for sample collections; SCH, ALP and KH helped collect the samples; SCM, ALP, and SZ performed all sample extraction and analytical measurements of abiotic samples; XY and AMC performed all sample extraction and analytical measurements of urine samples; JLL, SCH, and KH, performed statistical analyses, JLL, SCH, KH and HMS wrote the manuscript and all authors provided feedback and edits.

The authors declare no competing financial interests.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Associated Content

Supporting Information

Additional information on the study sample, sensitivity analyses and analytic methods is provided in supplemental information.

urine. In addition, phenols were analyzed in a novel exposure tool, the silicone wristband to investigate which external matrix best correlates with individual exposure based on urinary phenol biomarkers.

Methods: Children aged 3–6 years in central North Carolina, United States, provided paired hand wipe (n = 202), wristband (n = 76), and three spot urine samples that were pooled (n=180), while legal guardians completed questionnaires on habits and behaviors. House dust samples (n = 186) were collected from the main living area during home visits completed between 2014–2016.

Results: Environmental phenols were detected frequently in all matrices investigated. Ethyl, methyl, and propylparaben levels observed in hand wipes, dust, and on wristbands were significantly correlated to their associated urinary biomarkers. In addition, intra-paraben correlations were noted, with biomarkers of ethyl, methyl, and propylparabens generally positively and significantly correlated, suggesting co-application of parabens in products. Triclosan levels in dust were positive and significantly correlated with levels in hand wipes and wristbands and with urinary concentrations, suggesting non-personal care product sources may be important in children's overall triclosan exposure. Generally, chemicals on wristbands were more highly correlated with urinary biomarkers than with chemicals in hand wipes or house dust. In addition, more frequent lotion use was positively associated with urinary concentrations of paraben biomarkers.

Conclusions: Our results suggest that the home environment is an important source of exposure which has been under-investigated for some environmental phenols (e.g. triclosan in house dust). Associations between wristbands and biomarkers of exposure, which were stronger than for hand wipes and house dust, suggest that silicone wristbands may provide a suitable exposure assessment tool for some phenols.

Introduction

Environmental phenols, including parabens and triclosan, are regularly used in personal care products (PCPs) and household items. Biomarkers of these semi-volatile organic compounds (SVOCs) are, therefore, commonly detected in the majority of the United States population (CDC, 2019). Phenols are some of the most abundant chemicals found in the indoor environment and can be detected at higher concentrations than many other classes of chemicals measured in U.S. indoor dust (Mitro et al., 2016). Though the ubiquity of exposure to environmental phenols in residential environments is undisputed, some disagreements in the literature exist as to the extent to which environmental phenols are associated with adverse health outcomes, or whether they represent a health risk. However, results from in vitro, animal, and human studies have linked a range of environmental phenols to endocrine system modulations, including thyroid disruption, testosterone and estrogen antagonism, carcinogenicity, and childhood growth, amongst other health effects (Aker et al., 2018; Bledzka, Gromadzińska, & Wasowicz, 2014; Gao & Kannan, 2020; Koeppe, Ferguson, Colacino, & Meeker, 2013). Because of the possible health effects associated with exposure to environmental phenols, an accurate measurement of residential exposure to these compounds is relevant to formulating a risk assessment.

Environmental phenols cover a large range of compounds. Uses of environmental phenols widely vary across PCPs and household products, and are found in objects such as room deodorizers, flame retardants, antimicrobials, plastics, toothpaste, and building materials. The compounds discussed in this manuscript and their uses are detailed in Table S 1. Human exposure to environmental phenolic chemicals or their precursors is thought to occur via several pathways. Because many of these chemicals are applied directly to the skin in adults and children alike, particularly in the case of parabens (i.e., as PCPs and cosmetics), both inhalation and dermal exposure are of particular relevance when estimating overall exposure. For some compounds, such as parabens, 2,4-dichlorophenol, and BPA, stratum corneum to gas partitioning coefficients have been determined and range from $10^{7.4}$ to $10^{11.3}$ (Weschler & Nazaroff, 2012; Weschler & Nazaroff, 2014), highlighting the importance of both the dermal and inhalation exposure routes for all ages. Exposures to environmental phenols may also occur through ingestion due to their presence in food packaging and drinking water (e.g., BPA, BPS, BPF, 2,4-dichlorophenol, and 2,5-dichlorophenol) (Liu et al., 2019; Park & Kim, 2018).

Herein, we sought to investigate the associations between urinary phenol biomarkers with ambient measurements in residential settings among a cohort of children aged 3–6 years in North Carolina, United States to increase our understanding of exposure pathways besides diet. Paired environmental samples (hand wipes, house dust, and silicone wristbands) were compared to urinary biomarkers quantified in pooled samples in order to further understanding of children's environmental phenol exposure pathways. Additionally, children's habits and behaviors were investigated to determine if they contribute to an increase in exposure to phenols or their precursors. Environmental phenols of particular interest, and relevant to PCPs, in this study include: 2,4-dichlorophenol, 2,5-dichlorophenol, 2,4,6-tribromophenol, bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), butylparaben, methylparaben, ethylparaben, propylparaben, and triclosan. Although triclocarban is not a phenol, we have included it within this study because of its similar use as triclosan as an anti-microbial. To our knowledge, this is the first quantitative report of many of these environmental phenols on hand wipes and wristbands, and the first report to compare environmental samples of three matrices to environmental phenol urinary biomarkers for children.

Materials and Methods

Study Population

Mothers who participated in the Newborn Epigenetics STudy (NEST), a prospective pregnancy cohort study Durham, North Carolina, were invited to participate in the Toddler's Exposure to SVOCs in the Indoor Environment (TESIE) study with their children (Hoffman et al., 2018; Hoyo et al., 2011). A detailed description of recruitment and enrollment procedures for the TESIE study was included in Hoffman et al., 2018. In summary, 203 children aged 3–6 from 190 families participated in the TESIE study from September 2014 to April 2016. Study team members completed home visits with each family enrolled in the TESIE study to collect biospecimens and environmental samples. In addition, the study team collected information about the home environment as well as children's health and behavior

through questionnaires. Study protocols and related materials were reviewed and approved by the Duke Medicine Institutional Review Board. The Centers for Disease Control and Prevention (CDC) laboratory's participation did not constitute engagement in human subject research. All legal guardians provided informed consent before participation in the TESIE study, and all mothers previously provided informed consent to participate in NEST.

Home Environment Characteristics

Research personnel administered questionnaires to parents or legal guardians during home visits. This questionnaire focused on housing characteristics, children's health and behavior, and the use of PCPs in the home. Information collected included the frequency of child's product use (such as the use of nail polish, baby wipes, and lotion) and familial habits (such as how often children consumed food microwaved in plastic containers).

Hand Wipe Collection and Extraction

Families were instructed to not wash children's hands for at least 1 hour prior to the study team's visit. During this home visit, research personnel collected a single hand wipe sample from each child using cotton twill wipes (4 × 4 in., MG Chemicals) that were solvent extracted and cleaned, as previously described (Phillips et al., 2018). In summary, gloved research staff soaked the wipe with 3 mL of isopropyl alcohol and wiped the entire surface area of each of the child's hands. Hand wipes were assessed on a per-wipe basis, as previous work has indicated that normalizing to the surface area of hands does not reduce variability in the hand wipe measurements (Stapleton et al., 2008). Hand wipes were then wrapped in aluminum foil and stored at −20°C until analysis. Full details of the hand wipe analysis was described previously (Phillips et al., 2018). In summary, wipes were spiked with the following internal standards: $^{13}C_{12}$-BPA (53.6 ng), $^{13}C_{12}$-triclosan (178.6 ng), and d_5-ethylparaben (40.4 ng). All analytical standards, both labelled and unlabeled, were sourced from either Cambridge Isotope Laboratories, Inc. (Tewskbury, MA) or Wellington Laboratories (Guelph, Ontario). Wipes were extracted in a 1:1 hexane/dichloromethane (v/v) solution using sonication. Extracts were concentrated to approximately 1 mL using a SpeedVac Concentrator then fractionated using Florisil solid-phase extraction (SPE) cartridges (Supel-clean ENVI-Florisil, 6 mL, 500 mg; Supelco). F3 fractions were eluted with 6 mL methanol and concentrated to approximately 1 mL prior to analysis using liquid chromatography-tandem mass spectrometry (LC/MS/MS). LC/MS/MS conditions and ions monitored can be found in the Supporting Information (Item S1, Table S 5). Recovery of internal standards was assessed using $^{13}C_6$-triclocarban (10 ng) for all of the internal standards. Field blanks (n = 13) were analyzed alongside the samples for quality assurance and control (Table S 6).

Wristband Collection and Extraction

As described in detail in Hammel et al., 2020, adjustable silicone wristbands were purchased in an array of colors (diasstro adjustable silicone wristband bracelets, Amazon.com) and prepared for deployment to TESIE children. Briefly, wristbands were cleaned using sequential Soxhlet extractions and dried passively in a fume hood, then individually wrapped in pre-cleaned aluminum foil and stored in an air-tight amber 40 mL glass jar until deployment. TESIE children were asked to wear their wristbands continuously 7 days during

all daily activities, including sleeping and bathing. At the end of the sampling period, wristbands were wrapped in clean foil, returned to the amber jar, and stored at −20°C until extraction.

A detailed description of the wristband extraction procedure can be found in Hammel et al., 2020. To summarize, about one-third of each wristband, lab blank (n = 5), and field blank (n = 8) was removed from the total wristband for analysis, with the remainder re-wrapped and returned to storage for future analyses. This segment (~1.5 g) was accurately weighed and placed in a glass centrifuge tube. After spiking the internal standards $^{13}C_{12}$-BPA (50.0 ng), $^{13}C_{12}$-triclosan (100.0 ng), and d_5-ethylparaben (100.0 ng), the samples were extracted via sonication using 1:1 hexane/dichloromethane (v/v). Like the hand wipe and dust extracts, the wristband extract was then concentrated to approximately 1 mL using a Thermo Scientific SpeedVac Concentrator. Extracts were fractionated using Florisil SPE cartridges and sequential solvent elution to obtain 3 fractions, which were then concentrated again to approximately 1 mL. The F2 fractions, which was eluted using 10 mL ethyl acetate, were solvent exchanged to hexane (for analyses detailed in Hammel et al., 2020) and then to methanol for analysis here. Extracts were filtered then analyzed for phenols and parabens via LC/MS/MS. For quality assurance and quality control (QA/QC), laboratory blanks (n = 5) and field blanks (n=8) were analyzed alongside the samples (Table S 6). Recovery of internal standards was evaluated using $^{13}C_6$-triclocarban (10 ng) (Table S 2).

Dust Collection and Extraction

Families were instructed to not vacuum their homes for at least two days prior to the scheduled study team visit. To collect the house dust sample, the entire exposed floor area in the room in which the child or children spent the most time active and awake was vacuumed by a study team member using a Eureka Mighty Mite vacuum fitted with a cellulose thimble within the hose attachment (Stapleton et al., 2012). Thimbles were wrapped in aluminum foil and stored at −20°C until analysis.

Before extraction, each dust sample was sieved to < 500 μm. Dust extraction is described in detail in Phillips et al., 2018. Briefly, dust extracts were first split by mass into aliquots for various analyses. Half of the original dust sample was used for the targeted analysis described herein. Internal standards, $^{13}C_{12}$-BPA (51.7 ng), $^{13}C_{12}$-triclosan (172.4 ng), and d_5-ethylparaben (77.9 ng), were spiked before extraction. The F3 fraction, which was eluted in the SPE step using 6 mL methanol and concentrated to approximately 1mL, was analyzed for the phenols and parabens via LC/MS/MS. Recovery of internal standards was assessed using $^{13}C_6$-triclocarban (10 ng) for all of the internal standards. For quality assurance and quality control, analysis of laboratory blanks (n = 6) and house dust standard reference materials (n = 5; SRM 2585 National Institute of Standards and Technology (NIST), Gaithersburg, MD) were included in each batch. Measurements of phenols and parabens in SRM 2585 are included in the supplementary information (as well as our comparisons to the literature).

Urine Collection and Analysis

TESIE families received urine sample collection kits during home visits. Three spot urine samples from each child were collected over a 48 h period. Samples were stored in freezers in the families' home during the sampling period and were transported to the Duke University research laboratory on ice where they were then stored at −20°C. Before analysis, individual samples were thawed and thoroughly mixed. Equal volumes of each of the three urine samples were pooled and composite samples were used for all analyses. The composite urine samples were analyzed for phenolic biomarkers by the CDC laboratory(Ye et al., 2006; Ye, et al., 2005), as described previously in Hoffman et al., 2018. Specific gravity (SG) of pooled samples was measured using a digital handheld refractometer (Atago) and all analyses were conducted with specific gravity corrected urinary biomarker concentrations (Boeniger et al., 1993).

Statistical Analysis

All analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC) for analytes detected in > 60% of the samples. All values in samples were blank corrected by subtracting the average laboratory or field blank. Method detection limits (MDLs) for dust, hand wipes, and wristbands were calculated using three times the standard deviation of lab blank concentrations. Urinary MDLs were calculated as three times the standard deviation as the concentration approaches zero (Taylor, 1987). For chemicals detected in >60% of samples (e.g., urine, hand wipes, dust or wristbands), values that were less than MDL replaced with MDL/2 in statistical analyses (Antweiler & Taylor, 2008).

Spearman correlations were first used to assess relationships within and between matrices. To examine predictors of phenol biomarkers in urine, generalized estimating equations were used to account for residual intra-family correlations that may occur due to the inclusion of a small number of siblings in our study sample. Analyses were conducted for questionnaire data: child's nail polish use, child's hand lotion use, frequency of child's food consumption from microwaved plastic, frequency of eating out, child's handwashing frequency, frequency with which child eats out of a plastic bag, and child's use of scented and unscented wipes. In addition, parent compounds on hand wipes, wristbands and in dust were categorized into quartiles for analyses. Urinary biomarkers were adjusted for specific gravity to account for dilution and $\log_{10}$-transformed before analysis to account for skewed distributions.

Covariates

Covariates included in regression analyses were based on a priori expectations of association with outcomes and predictor variables of interest. Previous work within the TESIE study observed changes in exposure biomarkers based on temperature (Hoffman et al., 2018; Phillips et al., 2018). Average outdoor temperature information from the National Weather Service website was collected based on the week of sample collection. Models that examined predictors of urinary biomarkers included mother's race/ethnicity, mother's education level at the time of child's birth, and average outdoor temperature (modeled as a continuous variable), child's age and sex.

Though participants were asked to provide all dust, hand wipe, and urine samples, particular circumstances arose in which certain samples could either not be collected (e.g. a family unwilling to collect urine samples). In addition, wristband collection began in the second half to the TESIE study (starting April 2016), and as a result, not all children were asked to wear a wristband. Thus, there is not a complete overlap in the number of participants with each sample type. Relationships were evaluated for the maximum number of available paired samples. However, to ensure conclusions were not driven by our use of different sample sizes, all statistical analyses were repeated limiting to children with complete data for all matrices (Figure S 1).

Results and Discussion

Demographic characteristics of the TESIE study population as well as characteristics of children's homes are described in Table 1 and were discussed extensively in Hoffman et al., 2018. In brief, the TESIE study contained 203 children from 190 unique households. Slightly more than half of TESIE children were male (56%). Children's age ranged from 38 to 73 months, with a median age of 54 months (4.5 years). Mothers mostly self-identified as non-Hispanic White (41%) or non-Hispanic Black (37%), while the remaining mothers identified as Hispanic (20%) or other race/ethnicity (2%). Those mothers identifying as other race/ethnicity (n = 3) were excluded from the adjusted analyses. Nearly half of all mothers had at least a four-year college degree (44%) at the time of their child's birth. Data collected from the questionnaire included information on product use and behavioral characteristics of children within the household. Questionnaire responses and frequencies are also included in Table 1.

As previously described in Hammel et al., 2020, children began wearing wristbands during the second half of the recruitment phase. As a consequence, we have a smaller number of participants with paired wristbands (n = 77), and these children tended to be older than those in the larger TESIE cohort, ranging in age from 50 to 67 months (median = 57 months), as shown in Table S 3. Children wearing wristbands were more likely to identify as non-Hispanic Black (31%) or Hispanic (43%) than children in the TESIE study as a whole (37% identified as non-Hispanic Black, 20% identified as Hispanic), due in part to our ability to recruit Spanish speakers in the second half of the study. As a sensitivity analysis, all statistical models were additionally evaluated for the subset of children with data available for all exposure matrices (Table S 4). Results were quite similar, and we focus our presentation of results on analyses using the largest samples size available.

Phenol Measurements

Urinary biomarkers were quantified at the CDC's laboratory, and measurements in abiotic samples were conducted at Duke University. As a result, there is not complete overlap in the target analytes measured in urine and the abiotic matrices. For example, chlorophenols and benzophenone-3 were measured in urine, but not in the hand wipes, wristbands or dust. In total, 7 environmental phenols were quantified in all matrices and are therefore the primary focus here.

Hand wipes.—To our knowledge, this is the first report of phenol measurements on hand wipes and our results suggest phenols are commonly detected on children's hands. Methylparaben, ethylparaben, propylparaben, and triclosan, were detected in > 60% of hand wipes (Table 2), while 2,4,6-tribromophenol, BPA, butylparaben, and triclocarban were detected less frequently. Methylparaben had the highest median concentration (84 ng/wipe), while triclosan had the largest 95th percentile (3,149 ng/wipe). Both methylparaben and propylparaben were found in 100% of samples. Due to the high detection frequency of ethylparaben, methylparaben, and propylparaben, as well as triclosan on hand wipes, hand-to-mouth behavior and dermal absorption are likely important pathways of exposure for these compounds in particular.

Wristbands.—Phenol detection frequencies in wristbands were the highest among all abiotic matrices analyzed (Table 2). Triclosan was measured in the greatest abundance with a median of 180 ng/g wristband, followed closely by propylparaben with a median of 157 ng/g wristband. As observed in hand wipes, methylparaben and propylparaben were both detected in 100% of samples. In addition, BPA was found in all wristbands analyzed (detection frequency = 100%), though found in far fewer samples of dust or hand wipes (detection frequency = 84% and 57%, respectively) analyzed in this study. To our knowledge, this is the first investigation to quantify these phenols and parabens in silicone wristbands.

House dust.—Phenols were commonly detected in house dust, with a majority detected in > 70% of all samples (n = 186), as shown in Table 2 (see Table S 6 for phenols measured in dust SRM 2585 used for QA/QC). BPA was the most abundant compound measured in the house dust. In the TESIE study homes, the median BPA level in dust was 3,816 ng/g, which is higher than previously reported worldwide median values (Shin et al., 2019; Wilson et al., 2007) but similar to values reported in Korea and Japan (Liao et al., 2012) and substantially higher than values recently reported in China (Zhu et. al., 2020). Propylparaben was the next most abundant compound in dust samples collected in our study (median = 1,048 ng/g dust). Overall, indoor dust levels of parabens were in line with previously reported dust levels (Bledzka et al., 2014; Chen et al., 2018), though they trend towards the higher end of these worldwide median ranges. Triclosan was found in 100% of all dust samples analyzed, and triclocarban was least commonly detected in house dust, with only a 46% detection frequency. Our median triclosan level of 787 ng/g dust was similar to medians reported in other studies across Asia, Europe, and North America which have been reported to be between 200 – 880 ng/g (Canosa et al., 2007; Chen et al., 2018) but higher than levels in China (Zhu et al., 2020). As described by Chen et al., 2018, phenol abundance in indoor dust may be influenced not only by PCP use, but may also be driven by the different usage of building materials, textiles, and paints that incorporate anti-microbial compounds (Halden et al., 2017).

Urinary Biomarkers.—Twelve phenol biomarkers were quantified in urine samples (Table 2). Similar to wristbands, urinary BPA, methylparaben, and propylparaben were detected in 100% of samples analyzed. Of these, methylparaben was found at the greatest concentrations (median = 57 ng/mL). Associations of urinary biomarkers with demographic

variables relevant to this population have been discussed previously (Hoffman et al., 2018). Briefly, concentrations of many of these urinary biomarkers (benzophenone-3, triclosan, and the four parabens) were similar to that observed in the overall U.S. general population between 2008 and 2012 (Calafat et al., 2008; Ferguson et al., 2017) and were generally similar to the median values reported in the 2013–2016 U.S. National Health and Nutrition Examination Survey for older children aged 6–19 years (Jacobson et al., 2019; Lehmler et al., 2018). Urinary biomarker concentrations in our study were also similar to those reported in a previous study of female children aged 6–8 for 2,4-dichlorophenol, 2,5-dichlorophenol, BPA, benzophenone-3, and triclosan (Wolff et al., 2007). Similarly, in a convenience group of 122 3–5 year old children in the United States, median butylparaben, methylparaben, ethylparaben, propylparaben, benzophenone-3, BPA, triclosan, 2,4-dichlorophenol, and 2,5-dichlorophenol volumetric values were all reported as similar to median volumetric urinary biomarker concentrations reported here, with similar detection frequency per compound (Calafat et al., 2017). Note that these comparisons to this dataset were made based on unadjusted concentrations, as different methods were used by Calafat et al. (2017) to account for urine dilution.

Associations between Environmental Samples and Urine.

Correlation coefficients for phenols in dust, hand wipes, wristbands and their urinary biomarkers are listed in Table 3. Correlations were generally greater for hand wipes as compared to dust. Correlations between parent phenol and associated urinary biomarker were generally larger for wristbands than correlations for dust, and were similar to or greater than hand wipe correlations. Similar to correlation analyses, significant associations were observed between parent compound concentrations on hand wipes and urinary biomarker for all parabens and triclosan in adjusted regression models. This trend held for parent compound concentrations in wristbands and urinary biomarkers as well (Figure 1; Table S 7 – Table S 9).

Ethylparaben, methylparaben, and propylparaben all displayed similar correlations (r_s = 0.48, 0.41, and 0.48, respectively, all $p<0.0001$) between parent compound in hand wipes and associated urinary biomarker. Wristband ethylparaben was positively correlated with its urinary biomarker ($r_s = 0.66$, $p<0.0001$), as were propylparaben, methylparaben, and triclosan (r_s = 0.64, 0.56, and 0.51 respectively, all $p<0.0001$). In adjusted regression models using dust levels as the predictor, only ethylparaben and triclosan were positively associated with their respective urinary biomarker concentrations (Figure 1; Table S 8).

In dust samples, the largest correlations between parent phenol and associated urinary biomarker were observed for triclosan ($r_s = 0.47$, $p<0.0001$) and ethylparaben ($r_s = 0.34$, $p<0.001$). The largest correlation across all matrices observed for triclosan in hand wipes and its associated urinary biomarker ($r_s = 0.50$, $p<0.0001$). Children with the highest levels of triclosan on their wristbands had urinary triclosan concentrations approximately 4.5 times higher than those with the lowest levels on their wristbands ($10^{\beta} = 5.49$; 95% Confidence Interval (CI): 2.47, 12.21; $p<.0001$) (Table S 9).

Importantly, BPA was not detected frequently in hand wipes and as a result, correlation analyses were not conducted Despite frequent detection of BPA in dust and on wristbands,

BPA levels on wristbands and in dust were not associated with urinary BPA in children after adjusting for demographic factors and outdoor temperature. These findings could be explained by BPA's common presence in foodstuffs and may reflect the importance of the ingestion exposure pathway for BPA.

Environmental phenols, particularly parabens and triclosan, can be found in many PCPs applied to skin and/or that employ anti-microbial properties. Results presented here suggest that the parent concentrations measured in hand wipes and wristbands are most strongly associated with urinary biomarkers measured in the children in this study, as compared to measuring the chemical levels in dust. hand wipes and wristbands may both be better able to integrate exposures across multiple microenvironments where a child spends time, compared to dust which is only representative of potential exposure in one microenvironment. Taken together, correlation analyses suggest that exposure to some phenols, parabens or their precursors can be effectively captured using wristbands or hand wipes. We generally observed slightly higher correlations for wristbands as compared to hand wipes. One possible explanation for this pattern is that hand wipes are more variable due to handwashing behaviors.

Correlations of triclosan on hand wipes, wristbands, and dust were significantly correlated with urinary triclosan concentrations. Though exposure to triclosan is primarily considered to occur through the use of PCPs, this finding suggests that the indoor environment important and plays a role in children's overall exposure. We would not expect to see a significant correlation between external exposures such as house dust (from the main living area) and urinary concentrations of triclosan if PCPs such as hand soap were the primary source. Because of the increased potential for dust exposure in children compared to adults, predominantly due to their high rates of hand-to-mouth behavior, exposure to triclosan via external exposure routes such as dust may be of particular interest for future investigations regarding children's exposure.

Wristbands in particular are thought to integrate both inhalation and dermal exposure of semi-volatile organic compounds or SVOCs (Wang et al., 2019), which may provide a better predictor of the urinary biomarker concentrations observed for children, particularly for parabens given their relatively high octanol-air partitioning coefficients (K_{oa} = 107.6 – 108.9) (Weschler & Nazaroff, 2014). Previous modeling of SVOCs suggests that the dermal exposure route is thought to have been severely underestimated in the past and may contribute to overall environmental exposure burdens at levels equal to that of the inhalation pathways for SVOCs (Weschler & Nazaroff, 2014). For parabens, capturing the dermal pathway of exposure may be of particular interest because they are often used in PCPs frequently applied to the skin, which may result in dermal absorption. Dermal absorption of parabens has been demonstrated in humans and animals, though absorption through human skin is thought to be higher than through animal skin (Darbre et al., 2004; Darbre & Harvey, 2014; Janjua et al., 2008; Janjua et al., 2007). Therefore, using hand wipes and/or wristbands may assist in assessing the dermal pathway of exposure for parabens in children.

Associations between Environmental Samples.

Spearman correlations were also calculated between parent phenol concentrations found in dust and hand wipe samples (Table 4). Triclosan was most strongly correlated between the two exposure matrices (r_s = 0.37, p<0.0001), followed by propylparaben (r_s = 0.34, p<0.0001). When evaluating correlations between wristbands and either dust or hand wipes (Table 5), ethylparaben, methylparaben, and propylparaben were most strongly and significantly correlated between hand wipes and wristband measurements (r_s = 0.55, 0.44, 0.54, respectively; p<0.0001). In addition, positive correlations were observed between dust, hand wipes, and wristband matrices for all parabens. Finally, triclosan in both dust and hand wipes significantly and positively correlated with triclosan on wristbands (r_s = 0.44, p<0.0001; r_s = 0.36, p<0.01, respectively).

As shown in Table 3–5, there are a number of phenols that are correlated within and between matrices, suggesting that exposure sources and pathways may be similar (including physical chemical properties and metabolism). For example, the correlations amongst ethylparaben, methylparaben, and propylparaben were particularly strong across all three exposure matrices (p<0.05), except for ethylparaben on wristbands and urinary propylparaben which were not significantly correlated. Correlation patterns likely relate to the use of parabens together in many products, such as lotions and other cosmetics, as has been described previously (Calafat et al., 2010; Guo & Kannan, 2013; Ma et al., 2016). This strengthens the evidence that co-exposure or co-occurrence of parent parabens in residential products is occurring (Bledzka et al., 2014).

Product Use and Exposure Matrices.

Associations of the urinary biomarkers of ethylparaben, methylparaben, and propylparaben, as well as biomarkers of triclocarban and triclosan were compared to hand lotion use frequency, nail polish use, use of baby wipes, hand washing frequency and frequency of eating out. In these analyses, the results were largely null (Table S 10 – Table S 16). However, lotion use frequency was positively associated with paraben urinary biomarkers. As shown in Figure 2, propylparaben urinary concentrations in children who used lotion daily were around 5 times as high as in those who did not use lotion (10^{β} = 4.9, 95% CI = 2.5–9.6, p<0.0001); similarly, concentrations of ethylparaben and methylparaben biomarkers were also significantly higher among this highest lotion use frequency group (10^{β} = 2.4, 95% CI = 1.0–5.6, p<0.05; 10^{β} = 3.2, 95% CI = 1.5–6.8, p<0.01, respectively). Similar to our reported values herein, Braun et al. (2014) found that users of lotion had higher propylparaben concentrations (approximately 2.5 times higher) than non-users. Because there is evidence that both methylparaben and propylparaben are present in lotion (Guo et al., 2014), the higher exposure for methylparaben and propylparaben based on children who use lotion most frequently is understandable. One study also found that an intervention successfully decreased paraben urinary biomarker concentrations by changing personal care products, including lotions, to include fewer or no potential endocrine disrupting compounds in adolescents (Harley et al., 2016).

Limitations and Strengths.

Our study included a large population size used for an exposure study of a diverse group of children, and included paired samples of dust, hand wipes, wristbands and urine. Furthermore, three urine samples were collected over 48 hours and then pooled. Nonetheless, our study does have a few potential limitations that should be considered. Home environments could only be measured at a single point in time, which limited our ability to evaluate long-term exposures. Dust was only sampled from the main living area, which may have left out potential exposures of interest that originated in other areas of the home or outside the home, such as at school or daycare. No assessments of personal diet were conducted during these home visits and we cannot estimate how much of the urinary concentrations were attributable to diet. No analyses were conducted on particular products used to verify the presence or absence of particular environmental phenols, which may result in misclassification bias. Importantly, this type of misclassification may have biased associations to the null, suggesting there may be a stronger association between the use of paraben containing lotion and paraben exposure. Finally, the study population was a convenience sample derived from a previous pregnancy cohort and may not be generalizable to the broader population, though we do not expect this to impact the internal validity of the study.

Conclusions

Overall, we found that a number of phenols and phenols biomarkers measured in paired samples of dust, hand wipes, wristbands and urine were moderately to strongly correlated, suggesting that the ambient indoor environment, and PCPs use are primary sources of exposure. Based on correlations with urinary biomarkers, both wristbands and hand wipes demonstrated better estimates of ambient environmental phenols exposures in the TESIE children than house dust. Our results suggest wristbands and hand wipes appear to capture the primary pathways of exposure for several environmental phenols or their precursors where diet is not the main pathway, and particularly parabens. In contrast, while it appears that BPA exposure was detectable on the wristbands, diet is likely the major exposure pathway and explains the poorer correlation with urinary BPA. However, wristbands may ultimately provide better utility than hand wipes because of the increased ease of deployment and collection of an exposure monitoring matrix and due to their ability to measure an aggregate exposure over a set time period. Particularly for environmental phenols, which tend to have a short metabolic half-life, wristbands may better capture aggregate exposure to these compounds than other environmental matrices.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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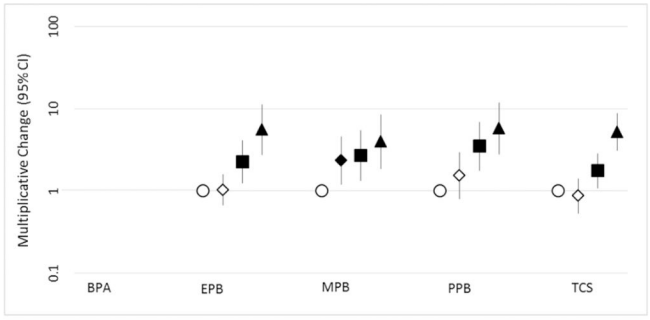
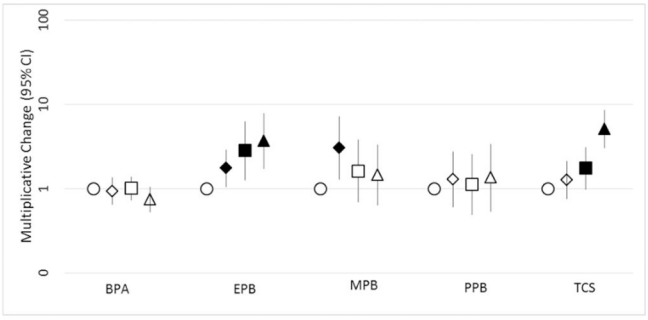
Highlights

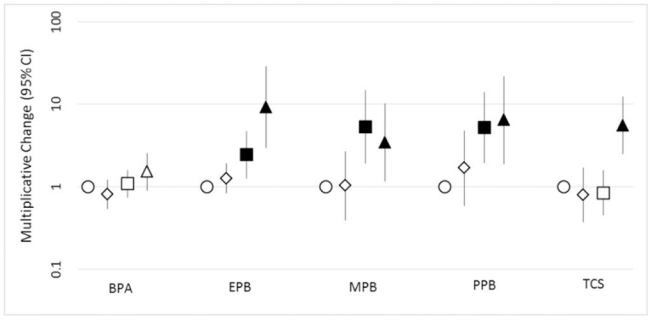
- Paired hand wipe, wristband, house dust and urine samples were analyzed for phenols
- Exposure matrices and urinary biomarkers were positively correlated
- Triclosan in dust, wristbands and hand wipes was correlated with urinary biomarkers
- Lotion use was associated with ethyl, methyl, and propylparaben biomarkers



a. Hand wipes



b. Dust



c. Wristbands

Figure 1.

Multiplicative change in urinary biomarker quartiles versus parent compound in hand wipes, dust, and wristbands and 95% confidence interval (n = 179 for hand wipes, 174 for dust and 74 for wristbands Quartiles defined by ○ (reference/first quartile), ◊ (second quartile), □ (third quartile), and Δ (fourth quartile). Analyses not conducted for BPA on hand wipes due to its low detection frequency.

Note: solid symbols are significant at least at $p<0.05$; BPA: Bisphenol-A, EPB: Ethylparaben, MPB: Methylparaben, PPB: Propylparaben, TCS: Triclosan

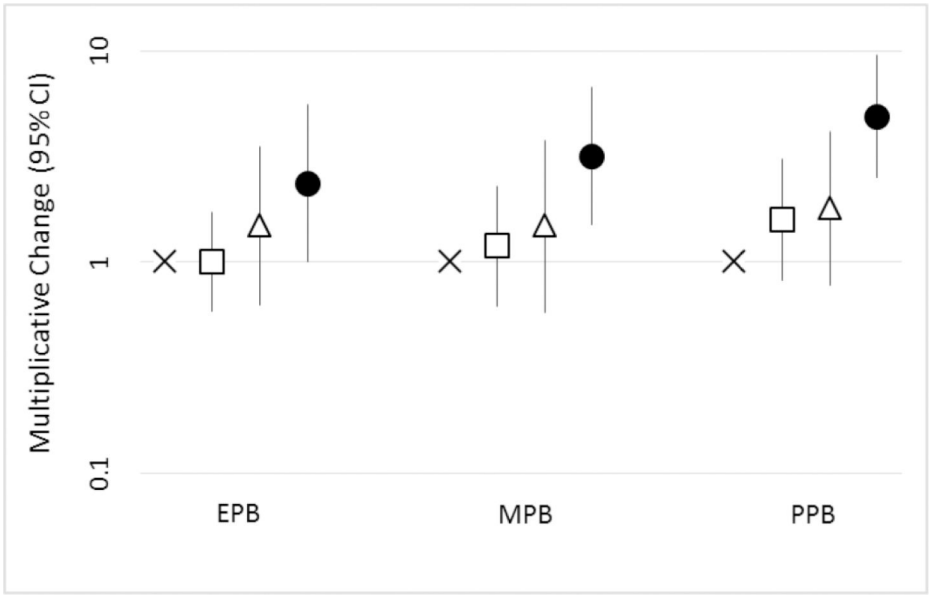


Figure 2.

Multiplicative change in children's paraben urinary biomarker based on child's hand lotion use frequency and 95% confidence interval from adjusted model (n=180). Child's hand lotion frequency defined by x (child never uses hand lotion), ☐ (child uses hand lotion 1–5 times a month), Δ (child uses hand lotion 6–29 times a month), and ○ (child uses hand lotion daily). Analyses were adjusted for child age and sex, maternal race/ethnicity and education, and average outdoor temperature at the time of collection.

Note: solid symbols are significant at least at $p<0.05$; EPB: Ethylparaben, MPB: Methylparaben, PPB: Propylparaben

Table 1.

Select demographic characteristics of children participating in the TESIE study (2014–2016), select product use patterns, and household characteristics of the TESIE study participants.

Characteristic	**N**	**%**
Child Sex		
Male	113	56
Female	90	44
Age		
38–47 months	34	17
48–59 months	130	64
60–73 months	39	19
Ethnicity		
Non-Hispanic white	84	41
Non-Hispanic black	75	37
Hispanic white	41	20
Other	3	1
Maternal education		
Less than college graduate	113	56
College graduate or more	90	44
	Mean	**range**
Child age	53.9	38–73
Average outdoor temp (°C)	15.5	−4.4–29.4
Product Use information	**N**	**%**
Do not use baby wipes	98	48
Use baby wipes (scented)	33	16
Use baby wipes (unscented)	72	36
Do not use nail polish	132	65
Use nail polish	71	35
Microwave plastic	105	52
Do not microwave plastic	97	48
Child never uses lotion	56	28
Child uses lotion 1–5 times/month	40	20
Child uses lotion 6–29 times/month	29	14
Child uses lotion daily	78	38
Child never eats from plastic bag	49	25
Child eats from plastic bag once a month	32	16

Child eats from plastic bag 1–3 times a month	36	18
Child eats from plastic bag >4 times a month	81	41
Child's Behavioral Habits		
Child washes hands 1–4 times per day	66	33
Child washes hands 5–6 times per day	72	36
Child washes hands more than 6 times per day	64	32
Child never eats out	18	9
Child eats out maybe once a week	73	37
Child eats out 1–2 times a week	65	33
Child eats out >3 times a week	42	21

Table 2.

Descriptive statistics for phenols and associated urinary biomarkers as well as triclocarban.

Matrix and Compound	Det. Freq	MDL	Median	95th Percentile
Dust (ng/g) n = 186				
2,4,6-tribromophenol	77	0.3	46	1,967
Bisphenol A	83	27	3,816	27,784
Butylparaben	72	0.3	18	381
Ethylparaben	73	0.9	100	1,095
Methylparaben	91	5.7	1,874	13,788
Propylparaben	98	1.4	1,048	9,750
Triclocarban	46	0.5	ND	431
Triclosan	99	0.2	787	4,175
Hand Wipe (ng/wipe) n = 202				
2,4,6-tribromophenol	38	1.0	ND	129
Bisphenol A	57	7.6	17	193
Butylparaben	44	0.5	ND	10
Ethylparaben	84	0.7	3.7	89
Methylparaben	100	1.9	84	1,358
Propylparaben	100	1.0	40	429
Triclocarban	37	0.2	ND	14
Triclosan	85	1.2	39	3,149
Wristband (ng/g wristband) n = 76				
2,4,6-tribromophenol	70	0.7	2.9	158
Bisphenol A	100	1.1	20	67
Butylparaben	95	0.4	3.9	44
Ethylparaben	72	2.7	7.3	179
Methylparaben	100	0.8	99	816
Propylparaben	100	0.7	157	987
Triclocarban	92	0.9	14.2	1,081
Triclosan	99	1.6	180	3,920
SG-corrected Urine (ng/mL) n = 180				
2,4-dichlorophenol	97	0.10	1.0	32
2,5-dichlorophenol	98	0.10	6.6	1,277
Benzophenone-3	99	0.40	25	1,274
Bisphenol A	100	0.20	2.1	12
Bisphenol F	45	0.20	ND	11
Bisphenol S	99	0.10	0.94	7
Butylparaben	44	0.10	ND	7
Ethylparaben	66	1.0	1.4	123
Methylparaben	100	1.0	57	1,801
Propylparaben	100	0.10	8.5	269

Matrix and Compound	Det. Freq	MDL	Median	95th Percentile
Triclocarban	44	0.10	ND	7
Triclosan	76	1.7	5.7	70

Table 3.

Spearman correlation coefficients for phenols and associated urinary biomarkers in paired hand wipes (n = 178 with hand wipes and urine), dust (n = 174 with dust and urine), wristbands (n = 74 children with wristbands and urine) and urinary biomarkers (n=180 with urine samples).

		Urinary Metabolite						
		2,4-dichlorophenol	**2,5-dichlorophenol**	**BPA**	**Ethylparaben**	**Methylparaben**	**Propylparaben**	**Triclosan**
Dust	2,4,6-tribromophenol	−0.10	−0.20#	−0.14	0.004	−0.01	0.05	0.16*
	BPA	0.10	0.19*	−0.07	0.04	0.02	0.01	−0.08
	Ethylparaben	0.15	0.09	0.03	0.34†	0.25#	0.20#	0.12
	Methylparaben	0.15	0.19*	0.10	0.25#	0.25#	0.21#	0.09
	Propylparaben	0.17*	0.23#	0.11	0.29#	0.26#	0.26#	0.03
	Triclosan	0.14	−0.09	−0.15	0.02	−0.07	−0.11	0.47†
Hand Wipes	Ethylparaben	0.02	0.07	0.19*	0.48†	0.22#	0.18*	−0.09
	Methylparaben	−0.04	0.07	0.19*	0.33†	0.41†	0.39†	0.005
	Propylparaben	0.06	0.07	0.19#	0.34†	0.42†	0.48†	0.08
	Triclosan	0.19*	−0.06	0.07	−0.01	−0.02	−0.003	0.50†
Wristbands	2,4,6-tribromophenol	0.12	0.15	−0.01	−0.12	−0.09	−0.11	−0.15
	BPA	−0.17	−0.11	0.23*	0.21	0.15	0.13	−0.15
	Ethylparaben	−0.01	0.10	0.08	0.66†	0.33#	0.21	−0.01
	Methylparaben	−0.08	−0.04	0.04	0.40#	0.56†	0.51†	0.20
	Propylparaben	−0.17	−0.06	0.11	0.33#	0.51†	0.64†	0.02
	Triclosan	0.11	−0.05	−0.06	0.04	0.19	0.02	0.51†
Urinary biomarker	2,4-dichlorophenol	1.00	0.65†	0.23#	0.07	0.11	0.05	0.19*
	2,5-dichlorophenol		1.00	0.28#	0.01	0.15*	0.15*	−0.20#
	BPA			1.00	0.23#	0.29†	0.26	0.01

	Urinary Metabolite						
	2,4-dichlorophenol	**2,5-dichlorophenol**	**BPA**	**Ethylparaben**	**Methylparaben**	**Propylparaben**	**Triclosan**
Ethylparaben				1.00	0.54†	0.42†	0.03
Methylparaben					1.00	0.81†	0.05
Propylparaben						1.00	−0.08
Triclosan							1.00

*p<0.05

#p <0.01

†p<0.0001; dark gray cells represent parent and biomarker pairs.

Table 4.

Spearman correlation coefficients for phenols measured in paired hand wipe and dust (n=197 with both samples).

		Dust					
		BPA	**Butyl Paraben**	**Ethylparaben**	**Methylparaben**	**Propylparaben**	**Triclosan**
Hand Wipes	Ethylparaben	0.01	0.01	0.26#	0.12	0.16*	−0.04
	Methylparaben	0.06	−0.05	0.14*	0.20#	0.24#	−0.05
	Propylparaben	0.08	0.03	0.17*	0.28†	0.34†	0.03
	Triclosan	−0.03	0.11	0.20#	0.23#	0.19#	0.37†

*p<0.05

#p <0.01

†p<0.0001; dark gray cells denote the relationship between the same compound in dust and hand wipes.

Table 5.

Spearman correlation coefficients for phenols in paired hand wipes (n = 76), dust (n = 75).

		Wristbands							
		2,4,6-tribromophenol	**BPA**	**Butylparaben**	**Ethylparaben**	**Methylparaben**	**Propylparaben**	**Triclocarban**	**Triclosan**
Dust	BPA	−0.03	−0.15	−0.14	−0.09	0.09	0.12	−0.05	0.16
	Butylparaben	0.06	−0.01	0.23*	0.17	0.14	0.17	0.05	0.08
	Ethylparaben	0.05	0.06	0.17	0.40#	0.37#	0.28*	0.01	0.10
	Methylparaben	−0.15	0.08	0.02	0.28*	0.36#	0.34#	0.17	0.16
	Propylparaben	−0.15	0.09	0.08	0.23*	0.33#	0.38#	0.17	0.05
	Triclosan	−0.07	−0.02	−0.01	0.17	0.21	0.12	0.04	0.44†
Hand Wipes	Ethylparaben	−0.15	0.21	0.38#	0.55†	0.23*	0.16	0.12	−0.02
	Methylparaben	−0.26*	0.03	0.07	0.29*	0.44†	0.37#	0.12	0.04
	Propylparaben	−0.30#	0.15	0.22	0.27*	0.44†	0.54†	0.05	0.01
	Triclosan	0.01	−0.15	−0.09	−0.02	0.06	−0.02	0.06	0.36#

*p<0.05

#p <0.01

†p<0.0001; dark gray cells denote the relationship between the same compound in wristbands and dust/hand wipes.