

Urinary and air phthalate concentrations and self-reported use of personal care products among minority pregnant women in New York city

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Diethyl phthalate (DEP) and di-*n*-butyl phthalate (DnBP) are used extensively in personal care products, including fragrances (DEP) and nail polish (DnBP). Between May 2003 and July 2006, we gathered questionnaire data on the use of seven product categories (deodorant, perfume, hair spray, hair gel, nail polish/polish remover, liquid soap/body wash, and lotion/mist) over 48 h during the third trimester of pregnancy from 186 inner-city women. A 48-h personal air sample was collected and analyzed for DEP and DnBP; a maternal spot urine sample was collected and analyzed for their monoester metabolites, monoethyl phthalate (MEP) and mono-*n*-butyl phthalate (MnBP), respectively. In all, 97% of air samples and 84% of urine samples were collected within ± 2 days of the questionnaire. During the 48 h, 41% of women reported perfume use and 10% reported nail polish/polish remover use. In adjusted analyses, no association was seen between nail product use and air DnBP or urine MnBP concentrations. Women reporting perfume use had 2.3 times higher (95% CI 1.6, 3.3) urinary MEP concentrations. Personal air DEP increased by 7% for each 25% increase in a composite indicator of the six other product categories ($P < 0.05$), but was not associated with perfume use. Air DEP was correlated with urine MEP concentrations only among non-perfume users ($r = 0.51$, $P < 0.001$). Results suggest that perfume use is a significant source of DEP exposure.

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Introduction

Phthalates are diesters of phthalic acid that are commonly used in a wide variety of consumer products. Human exposures come from their use in toys, household materials, medical devices, in the processing and packaging of foods, and personal care products (Schettler, 2006). Some phthalates are under increasing scrutiny in epidemiological studies examining potential associations with adverse reproductive and developmental outcomes including changes in gestational age, urogenital tract development, sperm quality, and asthma among other end points (Swan, 2008). However, relatively few studies have examined the relation between sources, exposure pathways, and internal dosimeters.

Two phthalates, diethyl phthalate (DEP) and di-*n*-butyl phthalate (DnBP), are added as a solvent for fragrances or to prevent products from becoming brittle, and have been found at higher concentrations than other phthalates in testing of personal care products in the United States, South Korea, and China (Houlihan et al., 2002; Koo and Lee, 2004; Hubinger and Havery, 2006; Shen et al., 2007). Among personal care products, DEP and DnBP have been found at the highest concentrations in fragrance products, including perfume (DEP), and in nail polishes (DnBP). Figure 1 shows an adaptation of results from the analysis of DEP in 48 personal care products in the United States (Hubinger and Havery, 2006). The five fragrance products tested had concentrations of DEP ranging from 5486 to 38,663 p.p.m., and the next highest DEP concentration of any other product tested was in a deodorant with 2933 p.p.m. (Hubinger and Havery, 2006). In these data, fragrances have consistently higher concentrations of DEP compared with all other products tested, supporting the separate analysis of perfume from other personal care product categories as potential sources of DEP. According to a review of patent records, nail polishes might contain

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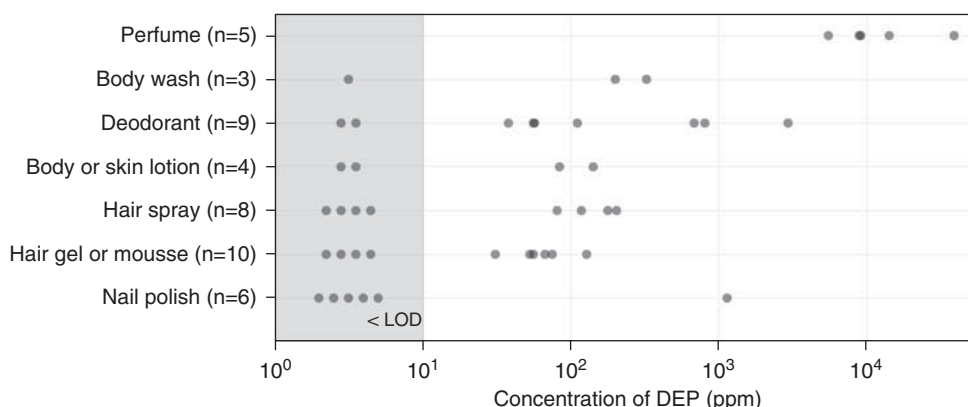


Figure 1. Diethyl phthalate in personal care products, adapted from Table 2 of Hubinger and Havery (2006). A total of 48 products purchased in the Washington, DC area were tested. Non-detectable values are displayed as less than the limit of detection of 10 p.p.m. Hand cream ($n = 2$) and shampoo ($n = 1$) are not shown. No direct product testing took place in this study.

50,000 p.p.m (5%) DnBP (Houlihan et al., 2002), a finding that was supported by a study that tested six nail enamel products and found concentrations that ranged from below the limit of detection to 59,815 p.p.m., or roughly 6% (Hubinger and Havery, 2006). Thus, nail polishes should be analyzed separately from other categories of personal care products as potential sources of exposure to DnBP because nail polishes seem to be more likely to contain DnBP and at higher concentrations than other product categories. Under current regulations in which ingredients used in fragrances are exempted from disclosure, phthalates are not generally listed as ingredients on consumer products in the United States (Steinmann, 2009).

Phthalates can enter the body through ingestion, dermal absorption, parenteral intake from medical devices, and inhalation. They undergo rapid hydrolysis to monoesters; short-alkyl chain phthalates such as DEP and DnBP are principally excreted in the urine as hydrolytic monoesters or as their corresponding glucuronidated conjugates (Silva et al., 2003). In 16 human volunteers who ingested a labeled dose of DnBP, 69% was excreted as mono-*n*-butyl phthalate (MnBP) in urine with undetectable levels of urinary MnBP after the first 24 h (Anderson et al., 2001). Half-lives of DEP were equally short in animal studies (Api, 2001). Both DEP and DnBP are also taken up dermally with an estimated 6% and 2%, respectively, excreted as their urinary metabolites monoethyl phthalate (MEP) and MnBP by human volunteers after dermal application (Janjua et al., 2008). The majority of dermally absorbed DEP was excreted within 8 h and MnBP excretion lagged slightly compared with MEP but was largely excreted within 24 h. Urinary MEP concentrations from a representative sample of the US population (National Health and Nutrition Examination Survey (NHANES) 1999–2000) were highest at a midday collection, which was hypothesized to be related to the application of personal care products in the morning (Silva et al., 2004).

Some evidence already exists for an association between frequency of personal care product use and urinary concentrations of phthalates. Men reporting the use of cologne or aftershave over 48 h had higher urinary MEP concentrations than other men (Duty et al., 2005). Another study reported an association between the use of baby care products and concentrations of MEP and two other phthalate metabolites but not MnBP in infant urine samples (Sathyanarayana et al., 2008). An increase in the number of personal care products used in the previous 48 h was associated with higher urinary MEP in 19 pregnant women in Israel (Berman et al., 2009). Working as a manicurist in a nail-only salon was associated with urinary concentrations of MnBP in two occupational studies among nail-only salon workers. Post-shift urinary MnBP concentrations were 49% higher than pre-shift in 37 manicurists from Massachusetts in 2004–05 (Kwapniewski et al., 2008). In 26 manicurists in Maryland studied between 2003 and 2005, those using gloves had 50% lower post-shift MnBP concentration compared with non-users (Hines et al., 2009). Collectively, these five studies indicate the potential importance of dermal absorption for exposures to DEP and DnBP and the suitability of urinary metabolites to assess these exposures.

We have reported previously that DEP and DnBP and their metabolites were found in 100% of personal air and urine samples collected from inner-city women during pregnancy (Adibi et al., 2008). The purpose of this study was to determine whether personal care product use was associated with measures of phthalate exposure in air and urine samples among the same urban cohort of pregnant women. To carry out this, we evaluated the relationship between self-reported prenatal personal care product use and concentrations of DEP and DnBP in personal air samples and MEP and MnBP in urine samples. The particular focus was on perfume and nail product use and exposures to DEP and DnBP, respectively.

Methods

Study Subjects

Participants ($n = 186$) were selected from the Mothers and Newborns cohort study of the Columbia Center for Children's Environmental Health (CCCEH) based in Northern Manhattan and the South Bronx, New York (Perera et al., 2003; Whyatt et al., 2003). Selection was based on the availability of a product-use questionnaire and phthalates measured within a week in either a personal air and/or urine sample collected during the third trimester of pregnancy. Overall, 97% of air samples and 84% of urine samples were collected within 2 days of the product-use questionnaire. In most cases there was no difference when the analysis was limited to the subsets within 2 days and results are given for the whole cohort unless otherwise specified. The enrollment criteria for the CCCEH cohort have been described elsewhere (Perera et al., 2003; Whyatt et al., 2003). The study was restricted to women 18–35 years old who self-identified as either African American or Dominican and had resided in Northern Manhattan or the South Bronx for at least 1 year before pregnancy. Women were excluded at enrollment if they reported that they smoked cigarettes or used other tobacco products during pregnancy, used illicit drugs, had diabetes, hypertension or known HIV, or had their first prenatal visit after the 20th week of gestation. Study procedures, including questionnaires, personal air monitoring, and collection of biological samples, were explained to each subject at enrollment and a signed consent, approved by the IRB of Columbia University and the Centers for Disease Control and Prevention (CDC), was obtained.

Product-Use Questionnaire

A brief questionnaire that was administered in the third trimester (mean gestational age 35 weeks) asked participants to recall their use of various types of personal care products over the previous 48 h and throughout the individual trimesters of pregnancy. They were asked about use (yes or no), the number of total uses over 48 h, and the frequency of use during each trimester (>1 per day, 1 per day, 2–3 per week, 1 per week, <1 per week–1 per month, and <1 per month). From the questionnaire, we selected seven product categories for this analysis: deodorant, lotion or mist (spray application), perfume, liquid soap or body wash, hair gel, hair spray, and nail polish or polish remover. As the questionnaire asked about nail polish or polish remover together, we refer to this category as nail products. The product categories selected were those that are likely to contain DEP or DnBP and which were used by $\geq 10\%$ of participants. Information on the frequency of use of product categories in the 48-h period and third trimester was missing for 6 and 20 participants, respectively.

Sample Collection and Analysis

Participants carried backpacks for 48 h containing pumps drawing personal air samples at 41/min from near the

breathing zone onto a quartz filter with a polyurethane foam cartridge backup. Air samples were stored in a freezer and shipped on dry ice to Southwest Research Institute (San Antonio, Texas, USA) for extraction and analysis of phthalates through gas chromatography/mass spectrometry (Adibi et al., 2008). Laboratory matrix blanks were extracted and analyzed with each batch of samples to assess laboratory-introduced phthalate contamination. Although DEP and DnBP were often detected, concentrations in the laboratory blanks ($n = 53$) were substantially lower than personal air extracts (average of 993 ± 2617 versus $24,838 \pm 23,047$ ng per extract for DEP and 288 ± 263 versus 6325 ± 5963 ng per extract for DnBP). Personal air samples were collected for 168 of 186 participants (90%).

A spot urine sample was collected generally at the start or conclusion of the 48-h personal air monitoring. The date, but not exact time of collection, was available. The urinary concentrations of nine phthalate metabolites, including MEP and MnBP, were measured at the National Center for Environmental Health, CDC. Urine samples underwent an enzymatic deconjugation reaction followed by solid-phase extraction; the phthalate metabolites were separated with high-performance liquid chromatography, and detected with isotope-dilution tandem mass spectrometry as previously described (Kato et al., 2005; Adibi et al., 2008). The limits of detection, which varied slightly depending on the method used, were in the low ng/ml range. Specific gravity was measured at room temperature at the CDC with a handheld refractometer. Urinary concentrations were adjusted for dilution in statistical analysis using a formula from Hauser et al. (2004) adapted with a constant that is more appropriate for urinary dilution during pregnancy (Teass et al., 1998). The constant value is derived from the median specific gravity of pregnant women in the CCCEH cohort study. The formula is $P_c = P[(1.016-1)/(SG-1)]$, where P_c is the specific gravity-corrected phthalate concentration, P is the observed phthalate concentration and SG is the specific gravity of the urine sample. Urine samples were collected for 164 of 186 participants (88%).

Air and urine samples were collected between May 2003 and July 2006. Extracts from air samples were analyzed between January 2006 and November 2007. Urine samples were analyzed between 2004 and 2007.

Statistical Methods

For personal air concentrations of DEP and urinary concentrations of MEP, perfume use was examined separately from the other products. We aggregated data on other products used by summing the reported number of product uses over the 48-h period for the other six product categories. For analytical purposes, we then assigned study subjects to quartile categories across the distribution of summed product uses. For example, a participant reporting, of the six categories, one use of hair gel, one use of liquid gel, two

uses of lotion, and two uses of deodorant would have six total uses which would put them in the second quartile for use of other products. For analyses of DnBP and MnBP, nail products were examined separately and the use of other products was similarly summed and classified into quartiles. All statistical tests on urinary and air measures were conducted with natural logarithm-transformed concentrations after adjustment of urinary data for specific gravity. Assumptions of normality were assessed visually with quantile–quantile plots. Correlation tests used Pearson's correlation coefficient. Simulation using informal Bayesian inference with uniform priors was used to graph uncertainty in regression parameters. For visual interpretation, this displays ~95% of simulation draws of regression slopes within two SEs for each parameter estimate (Gelman and Hill, 2007). Differences in group means were assessed with Student's *t*-test or with a multiple partial F-test for indicator variables in multivariable linear regression when controlling for covariates. Model building began with unadjusted models including only exposure variables derived from the product-use questionnaire. The full model included demographic covariates, selected to be consistent with previous research, for race or ethnicity, age, education, and BMI that might contribute to confounding or increase explanatory power (Duty et al., 2005). Unadjusted models had similar results to the multivariable results presented here. The quartiles of product-use variables were first assessed with a series of three indicator variables relative to the lowest quartile to evaluate the assumption of monotonicity and then, if appropriate, used in multivariable regression as a continuous measure. Parameter estimates from regression were exponentiated and presented as fold changes. The coefficient of determination, R^2 , was examined as the proportion of the variance in the outcome explained by the linear model. All statistical analyses were conducted in R version 2.9.1 (R Development Core Team, 2009).

Results

Sample Size, Demographics, and Reported Product Use

Participant characteristics for the 186 women are detailed in Table 1. Those who were missing an air or urine sample did not differ on demographic characteristics from the remainder.

Product Use

Participants reported using an average of three product types of the seven categories in this analysis. The median for the total number of times the women used any product was 7 with a range from 1 to 26 ($n = 180$). Table 1 lists the frequency of reported use of the product categories in the 48-h period. Deodorant was the product category with the most prevalent use (98%). The most frequently used product category was liquid soap (mean of 3.4 uses in 48 h among

Table 1. Characteristics of 186 pregnant study participants.

Age (years) ^a	26 ± 5
<i>Ethnicity (%)</i>	
African American	28
Dominican or other Hispanic	72
<i>Education (%)</i>	
High school diploma, GED, or greater	61
Body mass index ^a	27 ± 7
<i>Maternal ETS</i>	
Reporting smoker at home (%)	25
<i>Reported use (yes versus no) of categories of personal care products over a 48-h period (%)</i>	
Deodorant	98
Lotion	82
Perfume	41
Liquid soap	29
Hair gel	25
Hair spray	10
Nail polish or polish remover	10

^aMean ± SD.

participants reporting use of that product), followed by lotion and deodorant. Perfume use in the 48-h period of the questionnaire was reported by 41% of participants and was higher among African Americans (45%) than among Dominicans (40%), although the difference in proportions was not significant. Perfume users had a median of two reported uses over the 48-h period. Overall, 84% reported using perfume at some point throughout their pregnancy and those reporting usage in the 48-h period during the third trimester were more likely to report having used perfume in the first two trimesters ($\chi^2 17.2$ 1 degree of freedom (d.f.), $P < 0.01$). In the 166 participants with information about frequency of use in the third trimester, 61 reported using perfume at least daily (37%). The proportion reporting at least daily use in the third trimester was higher among those reporting perfume use in the 48-h period (63%) compared with those not reporting perfume use in the 48-h period (17%) ($\chi^2 34.4$ 1 d.f., $P < 0.001$). There was no association between perfume use (yes or no) and quartiles of the total uses of the other six product categories ($n = 180$, $\chi^2 1.4$ 3 d.f., $P = 0.7$). Use of nail products over the 48 h was reported by 10% of participants (18 of $n = 186$). Nail product users all reported a single use over the 48-h period. Overall, 69% of participants reported using nail products at some point throughout their pregnancy and those reporting usage in the 48-h period in their third trimester were more likely to report having used nail products in the first two trimesters ($\chi^2 7.2$ 1 d.f., $P < 0.01$). There was no difference in the quartile of the sum of product uses between African-American and Dominican participants ($n = 180$, $\chi^2 0.5$ 3 d.f., $P = 0.92$).

Table 2. Distribution of phthalate diester concentrations in personal air (ng/m³) and metabolite concentrations in urine (ng/ml).

Phthalate diester ^a	Phthalate metabolite ^b	Percentage > LOD	Percentile					GM (95% CI)
			5th	25th	50th	75th	95th	
<i>(ng/m³)</i>								
DEP		100	747	1276	1730	2532	4346	1816 (1668–1977)
DnBP		100	206	310	449	626	1077	459 (421–499)
<i>(ng/ml)</i>								
	MEP	100	37	103	199	489	3184	243 (198–298)
	MnBP	100	6	20	36	84	203	38 (32–45)

Abbreviations: GM, geometric mean; LOD, limit of detection.

^aPersonal air concentrations of phthalates were available for $n = 168$.

^bUrinary metabolite concentrations of phthalates were available for $n = 164$.

Personal Air and Urinary Metabolite Concentrations

DEP and DnBP were detected in 100% of air samples ($n = 168$) and MEP and MnBP were detected in 100% of urine samples ($n = 164$). The distribution of phthalates in personal air and metabolites in urine are summarized in Table 2. We did not see a temporal trend from 2003 to 2006 in concentrations of DEP and DnBP in personal air samples or MEP and MnBP in urine in a visual display using a lowest plot (data not shown).

Air and urine concentrations of phthalates and their metabolites were correlated. The correlation of DEP and MEP ($n = 146$, $r = 0.36$, $P < 0.001$) was similar to the correlation for DnBP and MnBP ($r = 0.32$, $P < 0.001$). Correlations were similar when restricted to urine samples collected within ± 2 days of the conclusion of the 48-h personal air sample ($n = 126$, DEP and MEP, $r = 0.36$, $P < 0.001$; DnBP and MnBP, $r = 0.31$, $P < 0.001$). The concentrations of the two metabolites, MEP and MnBP, were also correlated ($r = 0.40$, $P < 0.001$) as were the concentrations of the two parent compounds, DEP and DnBP, in the personal air samples ($r = 0.33$, $P < 0.001$). There seemed to be no correlation between DEP and MnBP ($r = 0.04$, $P = 0.62$) or between DnBP and MEP ($r = 0.11$, $P = 0.20$).

African Americans had higher concentrations of DEP in their personal air with a geometric mean that was 56% higher than among Dominicans (t -test, $P < 0.001$). The adjustment for individual product categories, including perfume, or for counts of the number of categories of potentially DEP-containing product types or categories of other hair products did not explain this difference (data not shown). Although urinary concentrations of MEP were higher among the African Americans than Dominicans (geometric mean 55% higher, t -test, $P = 0.07$), the difference was of borderline significance.

Results from the adjusted analyses of the relationship between product use and both DEP in personal air and MEP in maternal urine are presented in Table 3. There was no association between perfume use and air DEP concentra-

Table 3. Multivariable regression results for association of product use and covariates with personal air DEP and urine MEP concentrations.

	DEP ($n = 163$; $R^2 = 0.19$)	MEP ($n = 160$; $R^2 = 0.19$)
	Fold change (95% CI)	Fold change (95% CI)
Perfume use ^a	1.09 (0.9–1.3)	2.29 (1.6–3.3)***
Quartile of use of other products ^b	1.07 (1.0–1.2)*	1.26 (1.1–1.5)**
Race or ethnicity ^c	1.53 (1.3–1.8)***	1.22 (0.8–1.8)
Age (years)	0.99 (1.0–1.0)	0.98 (0.9–1.0)
Education ^d	0.96 (0.8–1.1)	1.31 (0.9–1.9)
BMI ^e	1.00 (1.0–1.0)	1.02 (1.0–1.0)

^a0 = no use in previous 48-h period; 1 = yes.

^bQuartiled sum of uses in 48-h period of deodorant, lotion, liquid soap, hair gel, hair spray, and nail polish or remover.

^c0 = Dominican; 1 = African American.

^d0 = no high school degree or equivalent; 1 = high school degree or greater.

^ePre-pregnancy body mass index (kg/m²).

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Parameter estimates are exponentiated to aid interpretability as a multiplicative fold change.

tions. However, DEP increased by 7% for each quartile increase in the sum of uses of the other six products ($P < 0.05$). Perfume use was significantly associated with MEP concentration in urine samples. Specifically, women reporting perfume use in the 48-h questionnaire period had 2.3 times higher concentrations of urinary MEP than those not reporting use in the same period (95% CI 1.6–3.3, $P < 0.001$). Further, controlling for perfume use, there was a significant association between quartiles of use of the other six products and urinary MEP concentration (a 26% increase in MEP concentrations for each quartile increase in the sum of product uses, $P < 0.01$). The full model explains 19% of the variance in urinary MEP. To further evaluate the dose–response relationship between perfume use and urinary MEP, analyses were restricted to subjects with urine collected within 2 days of the questionnaire ($n = 137$). Results are presented in Figure 2 and show a dose–response relationship

between urinary MEP and reported number of times perfume was used over the 48-h period after adjustment for race or ethnicity (*t*-test on regression coefficient for continuous measure, $P < 0.001$). We also examined the correlation

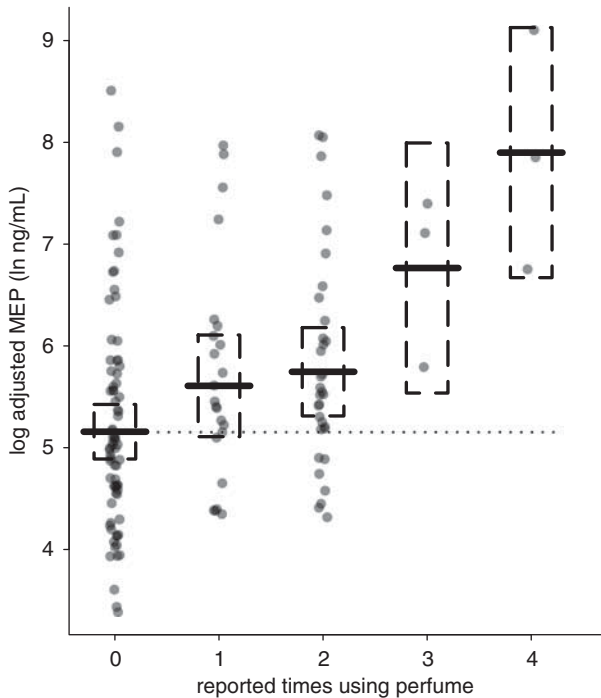


Figure 2. Log urinary MEP concentrations (adjusted for specific gravity) for participants with 0–4 reported uses of perfume over a 48-h period and samples collected within 2 days of the questionnaire controlling for race or ethnicity ($n = 137$). Group means shown with dashed rectangles indicating 95% CI. The dotted line extends the group mean for non-users. The group means for those using perfume two, three, or four times are all higher than non-users with single users of borderline significance ($P = 0.08$).

between DEP in air and MEP in urine in the same subset of study participants. It is interesting that among perfume users, there was no correlation ($n = 57$, $r = 0.12$, $P = 0.36$). However, among non-perfume users, the correlation was highly significant and stronger than seen for the full cohort ($n = 69$, $r = 0.51$, $P < 0.001$). Results are displayed in Figure 3.

Participants reporting use of nail products had no differences in DnBP concentrations in their personal air ($n = 16$) compared with non-users ($n = 152$), (geometric mean and 95% CI, 392 (292–521) versus 466 (427–510) ng/m³ DnBP). Similarly, those reporting use had no differences in MnBP concentrations in their urine ($n = 16$) compared with non-users ($n = 148$) (geometric mean and 95% CI, 42 (27–64) versus 39 (34–45) ng/ml). As shown in Table 4, there was no association between reported use of nail products or the composite indicator of the use of other products and either DnBP in personal air or MnBP in urine. In addition, none of the other covariates were significant predictors of either DnBP or MnBP concentration and the regression models explained $\leq 5\%$ of the variance in DnBP and MnBP (see Table 4).

Discussion

The use of personal care products was common during pregnancy among women in this urban cohort study. Participants used multiple products and many used perfume on a daily basis in the third trimester of pregnancy. Nail product use, though common throughout pregnancy, was less frequent than other categories of personal care product use.

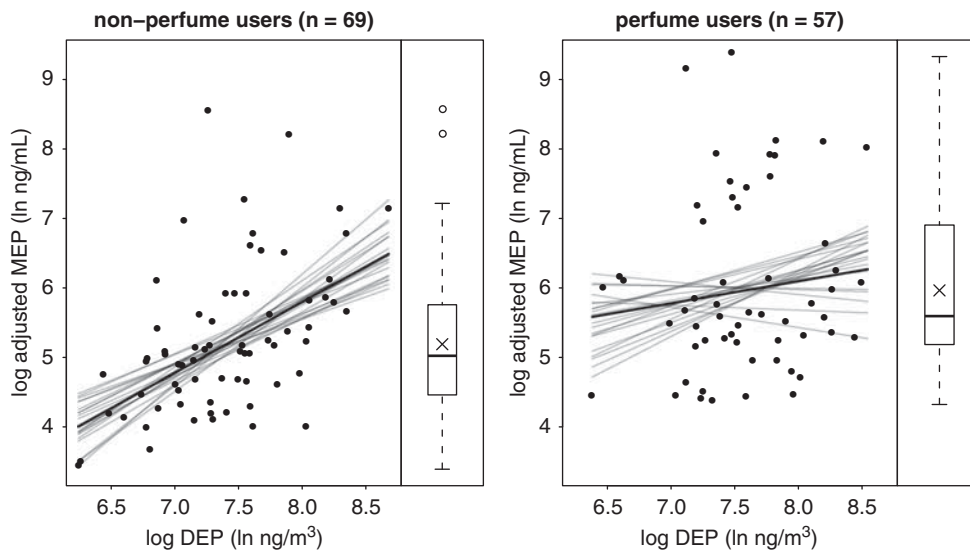


Figure 3. Association between DEP concentrations in personal air and the urinary metabolite MEP concentrations (adjusted for specific gravity) stratified by perfume use using linear regression of log-transformed values. Lighter lines represent predictive uncertainty in regression parameters from informal Bayesian simulations (20 simulation draws with uniform priors). Box plots show the distribution of MEP with means (“X”).

Table 4. Multivariable regression results for association of product use and covariates with personal air DnBP and urine MnBP concentrations.

	DnBP (<i>n</i> = 163; <i>R</i> ² = 0.05) Fold change (95% CI)	MnBP (<i>n</i> = 160; <i>R</i> ² = 0.04) Fold change (95% CI)
Nail polish or remover use ^a	0.84 (0.6–1.1)	1.08 (0.7–1.7)
Quartile of use of other products ^b	1.05 (1.0–1.1)	0.96 (0.9–1.1)
Race or ethnicity ^c	0.95 (0.8–1.2)	0.78 (0.6–1.1)
Age	0.99 (1.0–1.0)	0.98 (1.0–1.0)
Education ^d	0.87 (0.7–1.1)	1.05 (0.8–1.4)
BMI ^e	1.00 (1.0–1.0)	1.02 (1.0–1.0)

^a0 = no use in previous 48-h period; 1 = yes.

^bQuartiled sum of uses in 48-h period of deodorant, lotion, liquid soap, perfume, hair gel, and hair spray.

^c0 = Dominican; 1 = African American.

^d0 = no high school degree or equivalent; 1 = high school degree or greater.

^ePre-pregnancy body mass index (kg/m²).

None of the parameter estimates are significant for *P* < 0.05.

Parameter estimates are exponentiated to aid interpretability as a multiplicative fold change.

Perfume use over a 48-h period was associated with increased concentrations of MEP, the urinary metabolite of DEP. Women who reported using perfume had on average 2.3 times higher concentrations of urinary MEP after adjustment for urinary dilution and covariates in a multiple regression analysis. Our results further show a significant dose–response relationship between the number of perfume uses in a 48-h period and urinary concentration of MEP. Increased use of other product types (deodorant, lotion or mist, liquid soap or bodywash, hair gel, hair spray, and nail products) was associated with higher concentrations of DEP in air and MEP in urine.

Although perfume use was associated with urinary MEP, we found no association between use and DEP in personal air sample. This lack of association was unexpected, as we had hypothesized that DEP would volatilize during perfume use and contribute to inhalation exposures. It is entirely possible that the lack of association is a result of limitations in the available data set. However, another possible explanation is that the contribution of perfume use to total exposure comes more from dermal uptake than inhalation. Further, if perfumes, which have higher concentrations of DEP than other personal care products, contributed substantially to total exposure and did so primarily through dermal uptake, it might explain why there was no correlation between air DEP and urinary MEP among perfume users. In contrast, among non-perfume users there was a relatively strong correlation between air DEP and urinary MEP suggesting that the backpack monitors were useful in measuring exposures through inhalation. This association, although not a pharmacokinetic model to quantify the mass-balance contribution of inhalation,

is consistent with inhalation as a pathway of exposure to some product categories. A shorter time frame of exposure monitoring, coordinated to capture episodic events, might have been a better sampling design for detecting associations with episodic high exposures. However, these data are not generally available in observational studies, including in the current cohort, in which 48-h personal air samples were collected to characterize the exposure profile of the late pregnancy period.

The classification of participants into quartiles of the use of non-perfume product types serves as a crude indicator for some of these sources (particularly personal care products). This approach increased our statistical power to detect associations, however, at the expense of sensitivity to identify specific sources. The combined variable was positively associated with both DEP in personal air and MEP in urine. In comparing personal air and urinary exposure, it is important to note that participants were told to keep the backpack monitor out of the bathroom while they showered to avoid humidity that could damage the pump. We cannot discount that this may have had an impact on the association between product use and the collection of personal air samples. However, the association of the composite indicator for non-perfume product types such as hair spray and lotion, which are also products that are likely to be used in the bathroom, with DEP in personal air suggests that personal air monitoring was sampling exposure events resulting from the use of personal care products. Perfume use may represent a greater contributor to DEP exposure than other personal care products. This is consistent with the substantially higher detection frequencies and concentrations of DEP found in perfumes compared with other product types (Houlihan et al., 2002; Koo and Lee, 2004; Peters, 2005; Hubinger and Havery, 2006; Shen et al., 2007). However, reports of perfume use, even among those with a daily use pattern, may be too imperfect a measure of exposure to detect differences in personal air DEP given the limitations of this data set.

There was no association between reported use of nail products or the quartiles of usage of other products over the previous 48 h with concentration of either DnBP in personal air or MnBP in urine samples. Further, our study did not identify any significant predictors of DnBP or MnBP concentration. However, the proportion of nail product users was small (10%) and our questionnaire was designed to characterize the use patterns and grouped the use of nail polish and polish remover together. In addition, DnBP concentrations in nail polish may vary in concentration more than that of DEP in perfume. In one study that sampled six off-the-shelf nail enamel formulations in the United States, the concentrations of DnBP ranged from <10 to 59,815 p.p.m. (Hubinger and Havery, 2006). In addition, some products are being reformulated to remove phthalates and the prevalence of phthalates in nail polish may be changing (Hubinger and Havery, 2006). Thus, a questionnaire

alone might be insufficient to assess potential exposure to DnBP among personal users of these products. In contrast, two occupational studies of nail-only salon workers found associations between shift work and exposure to DnBP as measured by urinary MnBP (Kwapniewski et al., 2008; Hines et al., 2009).

We have reported previously on the distribution of phthalate concentrations in personal air and metabolites in urine (Adibi et al., 2008). Although the personal air results presented here are on a larger sample (168 versus 96 women), the distributions of DEP, DnBP, MEP, and MnBP are entirely consistent with our previous results, which showed that, on average, concentrations of MEP were similar in this population to those in the NHANES (females 18–40 years of age in the 1999–2000 and 2001–02 NHANES) but that participants in the CCCEH had higher urinary concentrations of MnBP (Adibi et al., 2008). Our understanding of the previously reported correlation between personal air DEP and urinary concentrations of MEP is enhanced through stratifying by the use of perfume. Among non-perfume users there is a higher correlation than we have previously reported and among perfume users there is no apparent association between DEP and MEP.

Our questionnaire covered only a subset of potential products used in the home which might contain phthalates. Use of products in these categories could be indicative of a preference for products containing fragrance and perhaps use of other phthalate-containing products as well, such as air fresheners or cleaning products. In addition, our questionnaire did not include the amount of products used that can vary substantially; one study, for example, found an 18-fold range in the average mass of spray perfume used per day among regular female users over a 2-week period (Loretz et al., 2006). Individuals also vary in their uptake of phthalates after exposure, in metabolism of the parent compound into the urinary metabolites, and in the timing of their urine sample relative to product use. We would expect additional contributors to this type of variability among pregnant women due to differences in gestational age at the time of sampling, blood volume, and renal and placental function (Adibi et al., 2008). All these unmeasured factors contribute to variability and the limited explanatory power of the models presented here. Although the multivariable regression model presented in Table 3 explained 19% of the variability in urinary MEP, the R^2 from a univariate model of perfume use (yes or no) alone, though highly significant, only explained 11% of the variance in the specific gravity adjusted and log-transformed urinary concentrations of MEP. Both our multivariable and univariate regression models explained $\leq 5\%$ of the variance in DnBP or MnBP.

In conclusion, we report that pregnant women in this urban cohort used multiple personal care products and that the use of perfume was positively associated with urinary

concentrations of MEP, a surrogate measure of exposure to DEP. It is important to assess if there are adverse effects of human exposures during critical periods given the heightened exposure to DEP associated with the common use of personal care products.

Conflict of interest

The authors declare no conflict of interest.

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Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the CDC.

References

- Adibi J.J., Whyatt R.M., Williams P.L., Calafat A.M., Camann D., and Herrick R., et al. characterization of phthalate exposure among pregnant women assessed by repeat air, urine samples. *Environ Health Perspect* 2008; 116(4): 467–473.
- Anderson W.A., Castle L., Scotter M.J., Massey R.C., and Springall C.A. Biomarker approach to measuring human dietary exposure to certain phthalate diesters. *Food Addit Contam* 2001; 18(12): 1068–1074.
- Api A.M. Toxicological profile of diethyl phthalate: a vehicle for fragrance, cosmetic ingredients. *Food Chem Toxicol* 2001; 39(2): 97–108.
- Berman T., Hochner-Celnikier D., Calafat A.M., Needham L.L., Amitai Y., and Wormser U., et al. Phthalate exposure among pregnant women in Jerusalem, Israel: results of a pilot study. *Environ Int* 2009; 35(2): 353–357.
- Duty S.M., Ackerman R.M., Calafat A.M., and Hauser R. Personal care product use predicts urinary concentrations of some phthalate monoesters. *Environ Health Perspect* 2005; 113(11): 1530–1535.
- Gelman A., and Hill J. *Data Analysis Using Regression Multilevel/Hierarchical Models*. Cambridge University Press, Cambridge, New York, 2007.
- Hauser R., Meeker J.D., Park S., Silva M.J., and Calafat A.M. Temporal variability of urinary phthalate metabolite levels in men of reproductive age. *Environ Health Perspect* 2004; 112(17): 1734–1740.
- Hines C.J., Nilsen Hopf N.B., Deddens J.A., Calafat A.M., Silva M.J., and Grote A.A., et al. Urinary phthalate metabolite concentrations among workers in selected industries: a pilot biomonitoring study. *Ann Occup Hyg* 2009; 53(1): 1–17.
- Houlihan J., Brody C., and Schwan B. "Not Too Pretty: Phthalates, Beauty Products & the FDA". Environmental Working Group, Coming Clean, Health Care Without Harm, USA, 2002: http://www.ewg.org/files/nottoopretty_final.pdf.

- Hubinger J.C., and Havery D.C. Analysis of consumer cosmetic products for phthalate esters. *J Cosmet Sci* 2006; 57(2): 127–137.
- Janjua N.R., Frederiksen H., Skakkebaek N.E., Wulf H.C., and Andersson A.M. Urinary excretion of phthalates and paraben after repeated whole-body topical application in humans. *Int J Androl* 2008; 31(2): 118–130.
- Kato K., Silva M.J., Needham L.L., and Calafat A.M. Determination of 16 phthalate metabolites in urine using automated sample preparation and on-line preconcentration/high-performance liquid chromatography/tandem mass spectrometry. *Anal Chem* 2005; 77(9): 2985–2991.
- Koo H.J., and Lee B.M. Estimated exposure to phthalates in cosmetics and risk assessment. *J Toxicol Environ Health A* 2004; 67(23–24): 1901–1914.
- Kwapniewski R., Kozaczka S., Hauser R., Silva M.J., Calafat A.M., and Duty S.M. Occupational exposure to dibutyl phthalate among manicurists. *J Occup Environ Med* 2008; 50(6): 705–711.
- Loretz L., Api A.M., Barraj L., Burdick J., Davis de A., and Dressler W., et al. Exposure data for personal care products: hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. *Food Chem Toxicol* 2006; 44(12): 2008–2018.
- Perera F.P., Rauh V., Tsai W.Y., Kinney P., Camann D., and Barr D., et al. Effects of transplacental exposure to environmental pollutants on birth outcomes in a multiethnic population. *Environ Health Perspect* 2003; 111(2): 201–205.
- Peters R.J.B. *Phthalates and Artificial Musk in Perfumes*. TNO Environment, Apeldoorn, The Netherlands, 2005: <http://www.greenpeace.org/raw/content/international/press/reports/phthalates-and-artificial-musk.pdf>.
- R Development Core Team. *R: A Language and Environment for Statistical Computing*. 2.9.1 edn. R Foundation for Statistical Computing, Vienna, Austria, 2009.
- Sathyanarayana S., Karr C.J., Lozano P., Brown E., Calafat A.M., and Liu F., et al. Baby care products: possible sources of infant phthalate exposure. *Pediatrics* 2008; 121(2): e260–e268.
- Schettler T. Human exposure to phthalates via consumer products. *Int J Androl* 2006; 29(1): 134–139; discussion 181–135.
- Shen H.Y., Jiang H.L., Mao H.L., Pan G., Zhou L., and Cao Y.F. Simultaneous determination of seven phthalates and four parabens in cosmetic products using HPLC-DAD and GC-MS methods. *J Sep Sci* 2007; 30(1): 48–54.
- Silva M.J., Barr D.B., Reidy J.A., Kato K., Malek N.A., and Hodge C.C., et al. Glucuronidation patterns of common urinary and serum monoester phthalate metabolites. *Arch Toxicol* 2003; 77(10): 561–567.
- Silva M.J., Barr D.B., Reidy J.A., Malek N.A., Hodge C.C., and Caudill S.P., et al. Urinary levels of seven phthalate metabolites in the US population from the National Health and Nutrition Examination Survey (NHANES) 1999–2000. *Environ Health Perspect* 2004; 112(3): 331–338.
- Steinemann A.C. Fragranced consumer products and undisclosed ingredients. *Environ Impact Assess Rev* 2009; 29(1): 32–38.
- Swan S.H. Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. *Environ Res* 2008; 108(2): 177–184.
- Teass A., Biagini R., and DeBord D. Application of biological monitoring methods. In: Eller P.M. (Eds). *NIOSH Manual of Analytical Method*. National Institute for Occupational Safety and Health Division of Physical Sciences and Engineering, Cincinnati, OH, 1998. pp. 52–62.
- Whyatt R.M., Barr D.B., Camann D.E., Kinney P.L., Barr J.R., and Andrews H.F., et al. Contemporary-use pesticides in personal air samples during pregnancy and blood samples at delivery among urban minority mothers and newborns. *Environ Health Perspect* 2003; 111(5): 749–756.